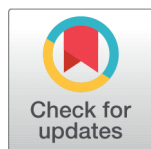


# The impact of vitamin D level on serum lipids in type 2 diabetes mellitus

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## OPEN ACCESS

## ABSTRACT

**Background:** Vitamin D is considered an important regulator of many metabolic processes in the body. Its deficiency was reported to associate with many pathological conditions, with contradicting reports on its role in dyslipidemia.

**Objectives:** to evaluate the role of vitamin D (total and/or free) in improving dyslipidemia of type 2 diabetes mellitus (T2DM).

**Methods:** Sixty-four patients with T2DM, and 73 apparently healthy normal subjects were enrolled in the study from March to October 2020. Their fasting blood glucose, glycated hemoglobin, HbA<sub>1c</sub>, and serum lipids (cholesterol, its fractions and triglycerides) were measured in addition to total and free vitamin D.

**Results:** There was a significant negative correlation between total vitamin D and each of cholesterol and LDL-C in the diabetic group. The correlations between serum vitamin D and all other lipid parameters (HDL-C, VLDL-C and triglycerides) were non-significant in the diabetic group, while in the control groups none of serum lipids showed significant correlations with vitamin D.

**Conclusions:** The significant negative association of vitamin D with total cholesterol and LDL-C in the diabetics reveals the important action of vitamin D in reducing the atherogenic indices, and consequent reduction in the rate of atherosclerosis and cardiovascular disease or stroke.

**Keywords** cholesterol, LDL-cholesterol, serum lipids, T2DM, vitamin D

## INTRODUCTION

Dyslipidemia is characterized by hypertriglyceridemia, hypercholesterolemia, reduced high-density lipoprotein cholesterol (HDL-C), and elevated low-density lipoprotein cholesterol (LDL-C). It is a key factor associated with the increased risk of several cardiovascular diseases,<sup>1-3</sup> and considered as a major causative factor for death.<sup>4,5</sup>

Vitamin D is one of essential fat-soluble vitamins, which supports many functions in the body. The prime source providing vitamin D to humans is exposure to sunlight.<sup>6</sup> The skin contains 7-dehydrocholesterol which after absorption of the ultraviolet B radiation is

converted to provitamin D<sub>3</sub> and after that it is hydroxylated into 25(OH)D and then converted into 1,25-dihydroxyvitamin D<sub>3</sub> with the help of hydroxylases found in the kidneys and liver.<sup>7</sup> Additional sources of vitamin D are oral supplements and diet. Bone metabolism and regulation of calcium are important physiological functions of vitamin D.<sup>8</sup> Other functions of vitamin D, may include reduction of inflammation, modulation of processes like cell growth, neuromuscular and immune function, with evidence of involvement in glucose metabolism.<sup>4,7,9</sup> Many genes encoding proteins that regulate cell proliferation, differentiation, and apoptosis are modulated in part by vitamin D.<sup>9</sup>

Therapeutic interventions for lowering the level of cholesterol can also decrease the mortality and morbidity due to cardiovascular diseases. Some research studies have also demonstrated a link between dyslipidemia and decreased concentration of vitamin D.<sup>9</sup> Contradicting results were reported for the relation between serum vitamin D and serum lipid levels,<sup>10,11</sup> or in vitamin D supplementation<sup>12,13</sup>.

The aim of the present study was to assess the correlation between vitamin D and serum lipids in a group of patients with T2DM.

## MATERIAL AND METHODS

### Study design and subjects

In this case-control study a total of 137 participants were included and divided into two groups. The patients' group consisted of 64 type 2 diabetic patients (38 males and 26 females), with age range of 26 and 75 years. They were all outpatients from the Diabetes Clinic in Al-Immamain Al-Kadhimain Medical City (Baghdad, Iraq) from March to October 2020. Patients with renal, arthritics, cardiovascular diseases or any type of neoplastic diseases were excluded from the study. The control group consisted of 73 healthy individuals (43 males and 30 females) with age range of 24 to 70 years, from the hospital or clinic staff and staff of the Chemistry and Biochemistry Department of Al-Nahrain College of Medicine.

All subjects (patients and controls) were subjected to a questionnaire that included basic background to indicate the patient's gender, age, marital status, education, employment, smoking, and nutrition. It has also indicated the medical condition and the patient's intake of vitamin D supplements. The Institutional Review Board of the Medical College at Al-Nahrain University approved the current study.

### Biochemical parameters

Measurements of total, free and bioavailable vitamin D, were reported in our previous report.<sup>14</sup> While, serum lipids (total cholesterol, LDL-C, HDL-C, VLDL-C and triglycerides) were measured by enzymatic colorimetric methods using Clinical Chemistry Auto-analyzer (Mindary, China).

## Biostatistics

Using package for social sciences (SPSS) version 23 and Microsoft Office Excel 2010 the following processes were done:

- A Chi-square test to evaluate the association between any two variables.
- Independent samples *t*-test to evaluate the difference in the mean of normally distributed numeric variables between any two groups.
- Spearman correlation to evaluate the correlation between any two numeric variables, and the results were expressed as correlation coefficient (*r*) and the level of significance (*p*).

For all the statistical tests, *p*-value of 0.05 was considered statistically significant.

## RESULTS

### Vitamin D

Results of serum total vitamin D, free vitamin D and bioavailable vitamin D for both, patients and controls, were listed in our previous paper; showing significantly lower total vitamin D in diabetic patients than its level in healthy subjects.<sup>14</sup>

### Serum lipid profile

As shown in Table 1, when compared to the control group, serum cholesterol, triglyceride, LDL-C and VLDL-C were significantly higher in the patients' group ( $p < 0.05$ ). While, serum HDL-C was lower in the patients' group in a highly significant manner ( $p < 0.05$ ).

### Correlation analysis

The correlation of serum lipids and total vitamin D in patients with T2DM and control subjects is shown in Table 2. Regarding the control group, serum total vitamin D (log total) was not correlated significantly to any of serum lipids ( $p > 0.05$ ). In patients with T2DM, there was no significant association between triglycerides, nor HDL-C with log total vitamin D ( $p = 0.674$  and  $0.229$ , respectively). However, there was a significant negative correlation between log total vitamin D and each of total cholesterol and LDL-C ( $r = -0.277$ ;  $p = 0.027$  &  $r = -0.305$ ;  $p = 0.014$ , respectively). The same negative correlation was noted between log total vitamin D and VLDL-L ( $r = -0.216$ ), but this correlation was not significant ( $p = 0.086$ ).

## DISCUSSION

**Table 1** Comparison of serum lipid profile between patients and control groups.

Characteristics	Control (n =73)	Patients (n =64)	p
<b>Cholesterol (mg/dl)</b>			
Mean±SD	170.24±24.73	196.79±40.65	<0.001 <sup>I,HS</sup>
Range	115-220	118-290	
<b>Triglyceride (mg/dl)</b>			
Mean±SD	148.16±60.88	213.51±75.71	<0.001 <sup>I,HS</sup>
Range	18-280	50-472	
<b>HDL-C (mg/dl)</b>			
Mean±SD	44.94±7.69	40.24±4.87	<0.001 <sup>I,HS</sup>
Range	30-63.6	32.5-55	
<b>LDL-C (mg/dl)</b>			
Mean±SD	93.97±28.92	108.23±41.99	0.021 <sup>I,S</sup>
Range	28-165	36.3-200	
<b>VLDL-C (mg/dl)</b>			
Mean±SD	33.21±16.20	51.11±27.04	<0.001 <sup>I,HS</sup>
Range	5.5-79.2	7.6-140	

n: number of cases; SD: standard deviation; I: independent samples t-test; HS: highly significant at  $p \leq 0.01$ ; S: significant at  $p \leq 0.05$ , HDL-C, LDL-C, and VLDL-C: high, low and very low-density lipoprotein cholesterol, respectively.

**Table 2** The correlation of serum lipid profile to total vitamin D in patients with type 2 diabetes mellitus and control subjects.

Characteristics	Patients (n =64)		Control (n =73)	
	r	p	r	p
Total cholesterol	-0.277	0.027 <sup>S</sup>	0.004	0.971 <sup>NS</sup>
Triglycerides	-0.054	0.674 <sup>NS</sup>	-0.118	0.319 <sup>NS</sup>
HDL-C	0.153	0.229 <sup>NS</sup>	0.184	0.118 <sup>NS</sup>
LDL-C	-0.305	0.014 <sup>S</sup>	0.022	0.855 <sup>NS</sup>
VLDL-C	-0.216	0.086 <sup>NS</sup>	-0.169	0.154 <sup>NS</sup>

n: number of cases; r: correlation coefficient; NS: not significant (when  $p > 0.05$ ); S: significant at  $p \leq 0.05$ , HDL-C, LDL-C, and VLDL-C: high, low and very low-density lipoprotein cholesterols, respectively.

Our results revealed (in our previous report) that the incidence of vitamin D deficiency in T2DM patients was significantly higher than that of controls (range: 1.70- 48.40 and 3.00-74.00, respectively).<sup>14</sup>

The term “deficiency” for vitamin D may be of the order of  $\geq 20$  ng/ml. Its abundance varies with different factors, age and race are among them.<sup>15,16</sup> Low serum levels were reported to associate with many diseases including cardiovascular diseases, stroke, diabetes and dyslipidemia.<sup>17</sup> The significant negative correlations between total vitamin D and each of cholesterol and LDL-C, in the present study, may coincide, in some aspects, with previous reports<sup>10,11</sup> who found that vitamin D insufficiency or deficiency associates with higher total cholesterol, LDL-C and triglycerides, with a reduction in HDL-C, however; in our study there is no significant correlations between the vitamin and triglycerides or HDL-C.

Moreover, results obtained from giving vitamin D supplement revealed an improvement in the LDL-C only,<sup>13</sup> while in another report, non-significant effects of vitamin D supplementation on total cholesterol, LDL-C, HDL-C, and triglycerides were found by a meta-analysis,<sup>12</sup>. Moreover, a study done in 2018 contradicted all other studies when reported an increase in all serum lipid parameters as effected by vitamin D supplementation.<sup>18</sup>

These contradicting results of different reports about the correlation between vitamin D and serum lipids are similar to those concerned with the effect of vitamin D on cardiovascular disease presented by Zittermann et al 2021,<sup>19</sup> who found a discrepancy between their findings and the real clinical and general population studies. They found an inverse non-linear association between vitamin D status and cardiovascular events, with the highest cardiovascular risk at severe vitamin D deficiency but no strong evidence for beneficial effects of vitamin D on cardiovascular risk, either in the general population or in high-risk groups, and finally suggested that there might be other factors which may cause these results as specific gene variation, certain nutrition or life style factors.

In conclusion, from our present results, we can say that the presence of significant negative correlations between the vitamin and each of total cholesterol and LDL-C, which agrees with most of the previous reports, can confirm the role of vitamin D to improve the atherogenic indices, with a consequent reduction in the rate of atherosclerosis and related risks for cardiovascular disease or stroke.

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## DECLARATION

### Authors' contributions

ZJS, HMH and GAA conducted the practical part. HMH and GAA supervised the project. All the authors reviewed and approved the final form of this paper before publication.

### Conflict of interest

The authors have no conflict of interests to declare.

### Ethical approvals

College of Medicine, Al-Nahrain University and its Institutional Review Board approved the current study.

### Data availability

All the data associated with this paper can be requested from the corresponding author upon reasonable request.

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This work didn't receive any fund.

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