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The association between vitamin D level, lipid profile, and selected pro-inflammatory markers

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ABSTRACT

Background: Vitamin D has a well-known role in the regulation of calcium hemostasias and controlling bone metabolism. However, little is known about vitamin D status and its relation to inflammation. Recent studies suggest that vitamin D has an anti-inflammatory effect and causes down regulation of inflammation markers production, which favours less inflammation.

Objective: This study investigates the relationship between low vitamin D status, lipid profile parameters, and inflammation markers.

Methods: In this case-control observational study, 52 participants from two cities (Baghdad and Sulaymaniyah) in Iraq were enrolled. Individuals with normal and abnormal inflammatory process were included in the study. The study population was divided into two groups based on their highly sensitive C -reactive protein (Hs-CRP) level, the control group and the study group. Serum Hs-CRP and 25-hydroxy cholecalciferol [25(OH)D] levels were measured for all participants. The data were evaluated to compare differences in vitamin D status between the two groups.

Results: The overall study population showed Hypovitaminosis D, with a mean 25(OH)D level of 22.6 ±15.7 ng/mL. Significantly higher Hs-CRP, ESR, WBC and lower 25(OH)D levels were observed in the study group compared to those in the control group. A higher mean 25(OH)D level was found in the control group compared to the study group (25.1 ng/mL vs. 17.9 ng/mL, p=0.033). The mean values of serum cholesterol, triglycerides, high density lipoprotein– cholesterol (HDL-C), and low-density lipoprotein– cholesterol (LDL-C) were not significantly different across groups.

Conclusions: This study demonstrates that there is an association between low vitamin D status and inflammation markers.

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INTRODUCTION

Vitamin D is a lipid soluble ketosteroid pro-hormone that is crucial for human health. Vitamin D is mainly synthesized in the skin via UVB exposure from sunlight [1]. Pro-vitamin D3 (7-dehydrocholesterol) in the epidermis is converted to pre-vitamin D3, which is then thermally converted to vitamin D3 (cholecalciferol) [2]. Vitamin D can also be obtained from dietary sources in two main forms, D_2 (ergocalciferol) and D_3 (cholecalciferol) [3]. Vitamin D3 migrates from the blood stream to the liver, where it is hydroxylated to 25-hydroxycholecalciferol (calcidiol) [4]. This form of vitamin D is biologically inactive and requires a second hydroxylation in the kidneys to the biologically active form, 1,25-hydroxycholecalciferol (calcitriol) [5].

Vitamin D has a well-known role in promoting and regulating calcium and phosphate metabolism [6]. It is especially important for bone formation and skeletal development. Vitamin D has been significant for human health ever since it was discovered that its deficiency is the root cause of rickets in children and osteomalacia in adults [7]. Vitamin D benefits are not limited to skeletal health, it has numerous non-musculoskeletal effects [8]. It is involved in the regulation of cellular proliferation, differentiation, and the control of innate and adaptive immunity [9]. Additionally, vitamin D deficiency is associated with an increased susceptibility to inflammatory disorders and chronic inflammation, its active form has been shown to inhibit the production of pro-inflammatory markers [10]. Furthermore, chronic inflammation is a contributor to the development of cardiovascular disorders [11], as a modulator of inflammatory pathways, vitamin D can mitigate the inflammatory process involved in CVD [10].

Thus, vitamin D may be important in reducing inflammation, and vitamin D treatment in vitamin D deficient patients can lead to a significant decrease in inflammation markers.

The aim of this study is to gain insight into the association between vitamin D levels, selected inflammatory markers, and lipid profile parameters in Iraqi population.

MATERIALS AND METHODS

Study design: This observational case-control study included participants with normal and abnormal inflammatory process. During a period of one month, a total of 52 participants who were living in two different cities in Iraq were selected. Of these, 25 visited the general laboratory of HQH hospital in the city of Sulaymaniyah and 27 visited the Biomolecules medical laboratory in the city of Baghdad.

The study population was divided into two groups based on their Hs-CRP level. The control group, which consisted of 34 apparently healthy subjects (14 males and 20 females) with no history of chronic inflammatory disease and Hs-CRP<6 mg/L. The study group which consisted of 18 subjects (7 males and 11 females), that had been confirmed to have inflammation and Hs-CRP>6 mg/L. The participants where further divided within their respective groups based on their vitamin D level. These three subgroups were deficient (<20 ng/mL), insufficient (20-30 ng/mL) and sufficient (>30 ng/mL).

The research design and ethics was approved by the research committee at the

American University of Iraq Suleimani/Medical & Health Sciences department under project code (MEDS/CSP/202400158). All sample collections and data analysis were performed based on the established rules and regulation of involved institutions.

Outcome measures: Serum levels of Hs-CRP and 25(OH) D and hematological parameters including WBC count and ESR were measured for all participants. Serum levels of Hs-CRP and 25(OH)D were measured using the COBAS 6000 analyzer (Roche Company) which utilizes a chemiluminescent immunoassay technique. The white blood cell count was determined by using the Beckman Coulter analyzer. The ESR was calculated using the Westergren method.

Additional data containing the values of the participant's cholesterol, triglycerides, HDL-C, and LDL-C were collected and combined with the recorded vitamin D levels. The lipid profile data was obtained for the majority of the study population (43 participants), 28 participants in the control group and 15 in the study group.

Statistical analysis: All data were analyzed using the Statistical Package for Social Science SPSS computer software version 30. Descriptive statistics were adapted to present data in mean $\pm$ standard deviation. Differences between groups were evaluated with Student's-t-test. The Chi-square test of independence was used to analyze categorial data. The level of statistical significance (p-value) was set at <0.05.

RESULTS

The study population had a mean age of 43 years, with a higher percentage of females (60%). No significant difference was found with respect to age between the control and the study group. Significantly higher mean Hs-CRP levels were observed in the study group compared to the control (29.1 mg/L vs. 2.4 mg/L, $p<0.001$). The study group and the control group had significantly different mean ESR levels (37.8 mm/hr vs. 13.9 mm/hr, $p<0.001$). Significantly higher mean WBC levels were observed in the study group compared to those in the control group (8.1x10^3/uL vs 6.7 x10^3/uL, $p=0.006$). The study population had a mean 25(OH) D concentration of 22.6 $\pm$15.7ng/mL, which falls under the insufficient range (20-30 ng/mL). A higher mean vitamin D level was found in the control group compared with the study group (25.1 ng/mL vs. 17.9 ng/mL, $p=0.033$). Table 1 Shows the baseline characteristics of studied subjects divided according to the selected inflammatory markers.

Vitamin D levels were categorized into three groups, deficient (<20 ng/mL), insufficient (20-30 ng/mL) and sufficient (>30 ng/mL). The proportion of participants in the study and control groups with deficient, insufficient and sufficient vitamin D levels is presented in Table 2. In the study group, 50% had vitamin D deficiency, 50% were insufficient and 0% had sufficient vitamin D levels. In the control group, 44% had vitamin D deficiency, 29% were insufficient and 27% had sufficient levels. The percentage of low vitamin D (<30 ng/mL, deficiency and/or insufficiency) was higher in the study group (100%) compared to the control group (73%).

To further investigate the relation between Vit D and the lipid profile of our patients.

We measure the lipid parameters in the patents and compared to our control group. Levels of cholesterol, triglycerides, HDL-C and LDL-C were carefully measured and calculated. Although the levels of Cholesterol, Triglycerides, and LDL were higher in the patients with low vit D level, there was no statistical significance between the study and the control group (Table 3).

DISCUSSION

Several studies have been conducted to examine the effects of vitamin D on inflammatory profile and endothelial function. It has been reported that treatment with vitamin D supplements reduced Hs-CRP levels in chronic kidney disease patients who had vitamin D deficiency [12,13]. Zhou et al [14] conducted study using non-linear Mandelian randomization (MR) analyses and reported that the effect of 25(OH)D on CRP was restricted to the vitamin D deficiency range, whereas higher 25(OH)D levels were associated with lower CRP concentrations.

The present study provides evidence that high levels of selected pro-inflammatory markers (Hs-CRP, ESR, WBC) in the study group is associated with lower vitamin D levels compared to data from the control group. The results confirm a correlation between vitamin D and inflammation, as the mean 25(OH)D level observed in the study group was lower than that observed in the control group. These findings were in agreement with previous studies [12,13,14].

However not all published studies reported an association between vitamin D and inflammation markers. An intervention study conducted on type-2 diabetic patients demonstrated that treatment with vitamin D supplements failed to improve Hs-CRP levels [12,15]. Evidence from clinical studies suggests that vitamin D supplementation may reduce pro-inflammatory cytokines, however it appears to have no association with anti-inflammatory cytokines and CRP levels [16].

Despite differences in mean 25(OH)D between the two groups, this study found no significant difference between the study and control group with regards to lipid parameters (cholesterol, triglycerides, HDL-C, LDL-C). The results indicate that vitamin D status is not associated with lipid profile. In contrast, Hariri et al [17], reported that higher vitamin D intake is associated with lower total cholesterol, LDL-C, and Hs-CRP levels. Their study found no relationship between vitamin D intake and triglycerides or HDL-C levels. Another study [18], demonstrated an association between increased serum 25(OH)D and decreased serum cholesterol and triglycerides levels in vitamin D deficient hyperlipidemic patients. Recent studies suggest that correction of vitamin D deficiency as a treatment for hyperlipidemia is important as it can protect at risk individuals from cardiovascular diseases [19].

Study limitations:

First, the sampling in this study was performed at health facilities which might contribute to biased results in contrast to population based randomized studies. Second, the small sample size of this study may prevent the findings from being extrapolated. A longitudinal study with a larger sample size may be necessary to clarify the relationship between vitamin D

status, lipid profile, and inflammation markers among the general population.

CONCLUSION

The results of this study indicate that there is a correlation between low vitamin D status and the production of widely used inflammation markers such as Hs-CRP, ESR, and WBC. Improving vitamin D status could reduce low-grade inflammation. The association between vitamin D intake and regulation of lipid profile and inflammation levels should be further studied through large scale randomized trials.

CONFLICT OF INTEREST

There is no conflict of interest

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TABLES

Table 1: Baseline characteristics of the study population

Characteristics	Overall (n=52)	Control (n=34)	Study (n=18)	*p*-value
Age (years)	43±16.0	40.1±14.4	49.2±16.0	0.064
Gender				
Male	21 (40%)	14 (41%)	7 (39%)	
Female	31 (60%)	20 (59%)	11(61%)	
Hs-CRP (mg/L)	11.6±17.8	2.4±1.5	29.1±21.7	<0.001
ESR (mm/hr)	22.2±20.8	13.9±10.5	37.8±26.8	<0.001
WBC (x10^3/uL)	7.1±1.8	6.7±1.7	8.1±1.6	0.006
Vitamin D (25-OH) (ng/mL)	22.6 ±15.7	25.1±12.4	17.9±8.1	0.033

Table 2: Proportion of participants in different Vitamin D level subgroups

Vitamin D level (ng/mL)	Control Number (%)	Study Number (%)	*p*-value
<20 (Deficient)	15 (44%)	9 (50%)	0.045
20-30 (Insufficient)	10 (29%)	9 (50%)	
>30 (Sufficient)	9 (27%)	0	

Table 3: Lipid profile variables of the study population

Variable	Overall (n=43)	Control (n=28)	Study (n=15)	*p*-value
Cholesterol (mg/dl)	190.0 ± 38.9	186.3 ± 40.2	196.9 ± 38.2	0.408
Triglycerides (mg/dl)	138.5 ± 72.4	131.9 ± 78.8	150.25 ± 62.9	0.446
HDL-C (mg/dl)	47.5 ± 11.6	47.8 ± 13.3	47.0 ± 8.7	0.828
LDL-C (mg/dl)	124.3 ± 35.4	123.5 ± 35.5	125.5 ± 37.6	0.860