


Association Between Decreased Serum Vitamin D Level and Dyslipidemia: A Cross-Sectional Study in Southern Taiwan

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Purpose: Previous studies revealed an inconclusive association between dyslipidemia and decreased vitamin D levels. This study aims to investigate the association between dyslipidemia parameters and decreased serum vitamin D levels among the southern Taiwanese population during a health examination.

Patients and Methods: A retrospective cross-sectional study was conducted from January 2020 to December 2020, enrolling 2430 subjects in a southern Taiwanese medical center. We performed logistic regression to examine the association between lipid profiles and vitamin D insufficiency or deficiency.

Results: The prevalence of vitamin D sufficiency was higher in males (65.9%). Compared to individuals with total cholesterol (TC) <200 mg/dL, those with TC ≥200 mg/dL exhibited vitamin D insufficiency or deficiency (OR, 1.46; 95% confidence intervals (CI), 1.10–1.94) after adjustment for age, gender, waist circumference (WC), fasting blood glucose, and uric acid levels. Compared to triglyceride (TG) levels of <150 mg/dL, TG levels ≥150 mg/dL had a higher association with vitamin D insufficiency or deficiency (OR, 1.48; 95% CI, 1.17–1.86) after adjustment for the same covariates. Post-gender stratification, we found female individuals with TC ≥200 mg/dL had a significantly higher association with vitamin D insufficiency or deficiency (OR, 2.11; 95% CI, 1.36–3.27), whereas TG ≥150 mg/dL in males exhibited a significantly higher association with vitamin D insufficiency or deficiency (OR, 1.70; 95% CI, 1.29–2.24) after adjustment for the same covariates.

Conclusion: The study revealed a negative association between decreased serum vitamin D levels and TC and TG levels. However, no significant association was observed with low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C). Further studies are needed to understand the mechanism.

Keywords: serum 25-hydroxyvitamin D, hypovitaminosis D, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia

Introduction

Vitamin D, a fat-soluble vitamin typically measured by serum 25-hydroxyvitamin D levels, is naturally present in the daily diet and endogenously produced upon skin exposure to ultraviolet sunlight rays.¹ It plays an important role in bone mineralization. Within the body, vitamin D undergoes two hydroxylation steps, primarily in the liver and then in the kidneys, to form its active metabolite, 1,25-Dihydroxyvitamin D (1,25-(OH)₂D).² Various factors can contribute to insufficient vitamin D levels, including dietary deficiencies, inadequate sunlight exposure, or impaired kidney function.² The most significant complications of hypovitaminosis D are osteoporosis and non-specific musculoskeletal aches and pains, including arthralgia and bone pains. Additionally, vitamin D deficiency may reduce intestinal calcium and phosphorus absorption, leading to hypocalcemia and secondary hyperparathyroidism.^{3,4}

Dyslipidemia, characterized by abnormal lipid levels in the blood, is a metabolic condition associated with elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and decreased high-density lipoprotein cholesterol (HDL-C). Being a significant risk factor for atherosclerotic cardiovascular disease (ASCVD), dyslipidemia can stem from dietary habits, obesity, diabetes mellitus type 2, and genetic predispositions.⁵

Various diseases are associated with vitamin D insufficiency. Beyond extraskeletal health, sufficient serum vitamin D levels have been recently found to be beneficial in chronic disease control, including conditions such as sarcopenia, metabolic disorder, inflammatory disease, and cancer.^{6–8} Recent studies showed significant associations between vitamin D insufficiency and obesity, metabolic syndrome, and ASCVD.^{9–11} However, some studies report conflicting results.^{12–14} In addition to the metabolic syndrome and ASCVD, dyslipidemia may be related to vitamin D deficiency. A common explanation is that vitamin D may be stored in adipocytes.¹⁵ A cross-sectional study showed a significant negative correlation between dyslipidemia and vitamin D levels.¹⁶ Conversely, a meta-analysis revealed no statistically significant effect of vitamin D supplementation in patients with diabetes.¹⁷ Given these conflicting results and the increasing prevalence of vitamin D deficiency and dyslipidemia in the Taiwanese aging population, we conducted a cross-sectional study to evaluate the association between vitamin D insufficiency and dyslipidemia parameters among a healthy southern Taiwanese population.

Material and Methods

Subjects

From January 2020 to December 2020, 5481 individuals underwent routine health examinations at a tertiary medical care facility's health management and evaluation center in southern Taiwan. These examinations included physical assessments and blood biochemical analyses. Most subjects were asymptomatic and sought self-paid check-ups. Data on serum 25-hydroxyvitamin D levels, lipid profiles, and other blood biochemical parameters, as well as anthropometric measurements were collected. Subjects with missing data were excluded, yielding a final cohort of 2430 eligible individuals. The study protocol was approved by the Chang Gung Medical Foundation Institutional Review Board (IRB No.: 202400737B0) and conducted following the Declaration of Helsinki. Signed informed consent was waived because of the anonymous retrospective nature of the study.

Measurements of Lipid Profile and Related Covariates

Anthropometric measurements were taken for all subjects, including height, weight, and waist circumference (WC). Height was measured with subjects standing erect, barefoot, with feet close together and looking forward. Weight was measured using an automatic scale without heavy clothing or lifting objects. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2), with a normal BMI defined as 18.5–23.9 kg/m^2 . WC was measured with a tape at the midpoint between the iliac crest and the lower border of the 12th rib while the subjects stood. A normal WC level in men and women was defined as 90 and 80 cm, respectively. Subjects were requested to fast for at least 12 hours before blood sample collection. Blood biochemicals were obtained from peripheral veins and centrifuged at 4 °C for biochemical analysis, including fasting blood glucose, lipid profile (TC, LDL-C, TG, and HDL-C), uric acid, and serum 25-hydroxyvitamin D levels. Electrochemiluminescence immunoassay (ECLIA) was employed to measure the 25-hydroxyvitamin D.

Definition of Dyslipidemia and Vitamin D Levels

In our study, dyslipidemia parameters, including TC, LDL-C, and TG, were categorized into normal (<200 mg/dL, <130 mg/dL, and <150 mg/dL) and dyslipidemia (borderline high plus high level) groups (≥ 200 mg/dL, ≥ 130 mg/dL, and ≥ 150 mg/dL) according to National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII).¹⁸ HDL-C, another dyslipidemia parameter, was also categorized into normal (≥ 40 mg/dL for males and ≥ 50 mg/dL for females) and dyslipidemia group (<40 mg/dL for males and <50 mg/dL for females).

The study subjects were categorized into three groups based on serum 25-hydroxyvitamin D levels: sufficiency (≥ 30 ng/mL), insufficiency (<30 ng/mL and ≥ 20 ng/mL), and deficiency (<20 ng/mL). According to Dietary Reference Intake for Calcium and Vitamin D published by Institute of Medicine, a serum 25-hydroxyvitamin D level of at least 20 ng/mL is recommended, with 30 ng/mL considered a desirable level.¹⁹

Statistical Analyses

Subject characteristics were presented as frequencies for categorical variables and as mean \pm standard deviation (SD) for continuous variables. General characteristics, anthropometric measurements, and laboratory parameters were compared across serum 25-hydroxyvitamin D levels using χ^2 -tests for categorical variables and Student's *t*-tests or analysis of variance for continuous variables. Simple and multiple logistic regressions were employed to examine the association between different lipid profile groups and vitamin D insufficiency or deficiency after adjustment for age, gender, BMI, WC, fasting blood glucose, and uric acid. Results were reported as odds ratios (ORs) with confidence intervals (CIs). Statistical analyses were performed using the Statistical Package for the Social Sciences (version 27.0; SPSS Inc, Chicago, IL, USA), with a two-tailed *p* value of <0.05 considered statistically significant.

Results

The Baseline Characteristics of the Study Subjects (Table 1)

The mean age of 2430 subjects was 52.6 years (SD: 12.8 years; range: 19–89), with 1064 (43.8%) females and 1366 (56.2%) males. Only 315 subjects (12.9%) were included in the vitamin D deficiency group, while 1105 (45.4%) were in the insufficiency group, and 1010 (41.6%) were in the sufficiency group. Individuals in the vitamin D deficiency group were younger with lower WC, fasting glucose, and uric acid levels but higher TC, LDL-C, and TG levels. Furthermore, the prevalence of vitamin D sufficiency was significantly lower in females (34.1%) compared to males (65.9%).

Table 1 Basic Characteristics and Laboratory Parameters in Subjects with Vitamin D Sufficiency, Insufficiency, and Deficiency

| Variables | Vitamin D sufficiency | Vitamin D insufficiency | Vitamin D deficiency | P value |
|------------------------------|-----------------------|-------------------------|----------------------|---------|
| Number | 1010 | 1105 | 315 | |
| Age, years | 57.02 \pm 11.93 | 50.69 \pm 12.44 | 45.43 \pm 11.95 | <0.001 |
| Gender | | | | |
| Female | 344 (34.1%) | 535 (48.4%) | 185 (58.7%) | <0.001 |
| Male | 666 (65.9%) | 570 (51.6%) | 130 (41.3%) | |
| Height, cm | 164.97 \pm 8.59 | 165.14 \pm 8.66 | 164.75 \pm 8.45 | 0.761 |
| Weight, kg | 67.87 \pm 13.13 | 67.79 \pm 13.83 | 66.20 \pm 15.13 | 0.124 |
| BMI, kg/m ² | 24.81 \pm 3.63 | 24.74 \pm 3.99 | 24.22 \pm 4.24 | 0.058 |
| WC, cm | 83.08 \pm 10.52 | 82.02 \pm 10.94 | 80.40 \pm 12.22 | <0.001 |
| Fasting blood glucose, mg/dL | 101.84 \pm 22.85 | 97.79 \pm 17.54 | 96.39 \pm 23.36 | <0.001 |
| Uric acid, mg/dL | 6.16 \pm 1.48 | 5.84 \pm 1.54 | 5.70 \pm 1.61 | <0.001 |
| TC, mg/dL | 201.48 \pm 41.52 | 208.84 \pm 39.43 | 207.49 \pm 39.36 | <0.001 |
| LDL-C, mg/dL | 122.08 \pm 36.00 | 126.99 \pm 34.14 | 125.94 \pm 33.80 | 0.005 |
| TG, mg/dL | 110.62 \pm 66.05 | 121.31 \pm 77.67 | 128.14 \pm 98.51 | <0.001 |
| HDL-C, mg/dL | 49.47 \pm 12.85 | 50.72 \pm 13.89 | 50.87 \pm 13.00 | 0.065 |
| Vitamin D, mg/dL | 37.46 \pm 7.53 | 25.33 \pm 2.72 | 16.80 \pm 2.61 | 0.000 |

Abbreviations: WC, waist circumference; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.

Comparison of Characteristics and Laboratory Parameters Among Females and Males

Table 2 presents the basic characteristics and laboratory parameters among females and males. Males had higher height, weight, BMI, WC, fasting blood glucose, uric acid, TG, and vitamin D levels, while females tended to have higher TC and HDL-C levels. No significant difference in age and LDL-C was found between male and female individuals.

The Subgroup Analysis of Logistic Regression of Dyslipidemia Parameters and Decreased Vitamin D (Table 3)

Compared to TC < 200 mg/dL, TC \geq 200 mg/dL exhibited a higher association with decreased vitamin D (OR, 1.46; 95% CI, 1.10–1.94) after adjustment for age, gender, WC, fasting blood glucose, and uric acid levels. Similarly, compared to TG < 150 mg/dL, TG \geq 150 mg/dL showed a higher association with decreased vitamin D (OR, 1.48; 95% CI, 1.17–1.86) after adjustment for the same covariates. Furthermore, LDL-C < 130 mg/dL or HDL-C \geq 40 mg/dL in males, and \geq 50 mg/dL in females were positively associated with decreased vitamin D. However, this was statistically insignificant after adjustment for the same covariates.

The Association Between Dyslipidemia Parameters and Decreased Vitamin D Stratified by Gender (Table 4)

TC \geq 200 mg/dL in females exhibited a significantly positive association with decreased vitamin D (OR, 2.11; 95% CI, 1.36–3.27) after adjustment for age, WC, fasting blood glucose, and uric acid, while TG \geq 150 mg/dL in males showed a significantly positive association with decreased vitamin D (OR, 1.70; 95% CI, 1.29–2.24) after adjustment for the same covariates. Other dyslipidemia parameters were not significantly associated with decreased vitamin D.

Table 2 Comparison of Clinical Characteristics and Laboratory Parameters Among Females and Males

| Variables | Total | Male | Female | P value |
|------------------------------|--------------------|--------------------|--------------------|---------|
| Number | 2430 | 1366 | 1064 | |
| Age, years | 52.64 \pm 12.82 | 53.02 \pm 13.14 | 52.15 \pm 12.39 | 0.095 |
| Height, cm | 165.12 \pm 8.60 | 170.35 \pm 6.33 | 158.17 \pm 5.86 | <0.001 |
| Weight, kg | 67.62 \pm 13.72 | 74.73 \pm 12.13 | 58.49 \pm 9.64 | <0.001 |
| BMI, kg/m ² | 24.70 \pm 3.88 | 25.71 \pm 3.64 | 23.40 \pm 3.80 | <0.001 |
| WC, cm | 82.25 \pm 10.97 | 87.07 \pm 9.56 | 76.07 \pm 9.46 | <0.001 |
| Fasting blood glucose, mg/dL | 99.29 \pm 20.78 | 101.07 \pm 21.63 | 97.01 \pm 19.41 | <0.001 |
| Uric acid, mg/dL | 5.95 \pm 1.53 | 6.64 \pm 1.37 | 5.07 \pm 1.26 | <0.001 |
| TC, mg/dL | 205.61 \pm 40.44 | 201.63 \pm 40.95 | 210.71 \pm 39.21 | <0.001 |
| LDL-C, mg/dL | 124.82 \pm 34.95 | 124.68 \pm 35.70 | 124.99 \pm 33.97 | 0.829 |
| TG, mg/dL | 117.75 \pm 76.48 | 132.82 \pm 84.43 | 98.41 \pm 59.55 | <0.001 |
| HDL-C, mg/dL | 50.22 \pm 13.36 | 45.22 \pm 10.78 | 56.64 \pm 13.60 | <0.001 |
| Vitamin D, mg/dL | 29.27 \pm 9.10 | 30.96 \pm 9.62 | 27.09 \pm 7.88 | <0.001 |

Abbreviations: WC, waist circumference; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.

Table 3 Relationship Between Different Dyslipidemia Parameters and Vitamin D Insufficiency or Deficiency in Simple and Multiple Logistic Regression

| Variables (mg/dL) | | Normal vitamin D | Deceased vitamin D | OR (95% CI) | ^a OR (95% CI) |
|-------------------|-----------------------------|------------------|--------------------|---------------------|--------------------------|
| TC | <200 | 504 | 600 | Ref | Ref |
| | ≥200 | 506 | 820 | 1.57*** (1.20,2.04) | 1.46** (1.10,1.94) |
| LDL-C | <130 | 595 | 781 | Ref | Ref |
| | ≥130 | 415 | 639 | 0.82 (0.63,1.06) | 0.92 (0.69,1.21) |
| TG | <150 | 806 | 1074 | Ref | Ref |
| | ≥150 | 204 | 346 | 1.21 (0.98,1.49) | 1.48*** (1.17,1.86) |
| HDL-C | ≥40 in men and ≥50 in women | 679 | 943 | Ref | Ref |
| | <40 in men and <50 in women | 331 | 477 | 1.03 (0.85,1.23) | 1.06 (0.87,1.31) |

Notes: ^a Adjusted for age, gender, waist circumference (WC), fasting blood glucose, and uric acid levels. ***P* < 0.01, ****P* < 0.001.

Abbreviations: TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.

Table 4 Relationship Between Different Dyslipidemia Parameters and Vitamin D Insufficiency or Deficiency in Simple and Multiple Logistic Regression Stratified by Gender

| Variables (mg/dL) | | OR (95% CI) | ^a OR (95% CI) |
|-------------------|------|---------------------|--------------------------|
| Female | | | |
| TC | <200 | Ref | Ref |
| | ≥200 | 1.70* (1.12,2.56) | 2.11*** (1.36,3.27) |
| LDL-C | <130 | Ref | Ref |
| | ≥130 | 0.67 (0.45,1.01) | 0.69 (0.45,1.07) |
| TG | <150 | Ref | Ref |
| | ≥150 | 0.86 (0.58,1.26) | 1.05 (0.69,1.62) |
| HDL-C | ≥50 | Ref | Ref |
| | <50 | 0.85 (0.64,1.13) | 0.98 (0.71,1.36) |
| Male | | | |
| TC | <200 | Ref | Ref |
| | ≥200 | 1.14 (0.79,1.65) | 1.10 (0.75,1.61) |
| LDL-C | <130 | Ref | Ref |
| | ≥130 | 1.18 (0.82,1.70) | 1.17 (0.80,1.71) |
| TG | <150 | Ref | Ref |
| | ≥150 | 1.81*** (1.40,2.34) | 1.70*** (1.29,2.24) |
| HDL-C | ≥40 | Ref | Ref |
| | <40 | 1.07 (0.84,1.37) | 1.10 (0.85,1.44) |

Notes: ^a Adjusted for age, gender, waist circumference (WC), fasting blood glucose, and uric acid levels. **P* < 0.05, ****P* < 0.001.

Abbreviations: TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.

Discussion

Our study revealed a significant association between high TC and TG levels and decreased vitamin D levels. Interestingly, we found no significant differences in weight and BMI across different categories of vitamin D levels. This finding aligns with a cross-sectional study by Sharba et al.¹⁶ They reported a negative correlation between dyslipidemia and vitamin D levels, without significant differences in age or BMI among different categories of vitamin D levels. Several studies support the relationship between dyslipidemia and vitamin D deficiency. For example, Karhapää et al.²⁰ reported that vitamin D insufficiency was associated with high levels of TC, LDL-C, and TG. Additionally, Chen et al found that individuals with vitamin D levels below 30 ng/mL had significantly higher ORs for developing atherogenic dyslipidemia compared to those with levels above 30 ng/mL.²¹ Furthermore, a Mendelian randomization study by Yin et al²² revealed a link between vitamin D deficiency and an increased risk of high TG, TC, and LDL-C levels. These findings collectively suggest an existing connection between dyslipidemia and vitamin D deficiency.

However, several studies reported conflicting conclusions. A meta-analysis by Bahadorpour et al revealed that vitamin D levels were inversely related to high TG and low HDL-C levels; nevertheless, no significant association was found with high TC or LDL-C levels.²³ Similarly, Souza et al found no significant relationship between TC, LDL-C, and TG and vitamin D levels in the elderly.²⁴ Regarding the efficacy of vitamin D supplementation to improve dyslipidemia, MacGirley et al reported a significant reduction in TG and an increase in HDL-C in patients with type 2 diabetes mellitus but observed no statistically significant changes in TC or LDL.¹⁷ Another systematic review of randomized controlled trials by Qi et al indicated that vitamin D supplementation did not improve the lipid profile.²⁵ In our study, we found insignificant differences between LDL-C and HDL-C levels and decreased vitamin D levels, suggesting that high TG levels may be the major effect of decreased vitamin D levels on lipid profiles.

Gender differences play a significant role in understanding the correlation between dyslipidemia and vitamin D levels. Studies such as the cross-sectional survey by AlQuaiz et al²⁶ have shown that low levels of HDL-C in males and high levels of TG in females are associated with vitamin D deficiency. Similarly, Jeenduang et al²⁷ reported a significant reduction in the risk of elevated TG and reduced HDL-C only in females. In another cross-sectional study by Wang et al, reduced HDL-C, elevated TG, and an elevated atherogenic index of plasma correlated with lower vitamin D levels in males. Conversely, higher TC and LDL-C correlated with higher vitamin D levels.²⁸ However, these results present many inconsistencies. Our study found that elevated TG levels were significantly associated with decreased vitamin D levels only in males after stratifying by gender. Conversely, the association between elevated TC levels and decreased vitamin D levels was significant only in females. This could be attributed to the gender-specific lipid profile distribution in Taiwan. According to the Nutrition and Health Survey in Taiwan conducted from 2017 to 2020, the mean TC levels were higher in females compared to males, while the mean TG levels were higher in men compared to women among those aged 19 and above.²⁹

Moreover, the report of the Nutrition and Health Survey in Taiwan 2017-2020 showed that vitamin D levels are 28.4–28.7 ng/mL for males aged 13–18 years, 28.5–33.4 ng/mL for those aged 19–64 years, and 37.1–38.0 ng/mL for those aged 65 and older. For females, the levels are 23.6–25.4 ng/mL, 22.1–27.6 ng/mL, and 30.5–33.0 ng/mL, respectively.²⁹ Borderline vitamin D deficiency is defined in this report as a level between 20 ng/mL and less than 30 ng/mL. These findings indicate that the Taiwanese population, particularly females and younger individuals, generally experiences low vitamin D levels, which aligns with our study results. To date, there has been no other study examining the relationship between dyslipidemia and vitamin D insufficiency, particularly in the Taiwanese adult population. Therefore, our study offers a new perspective on the potential causes of widespread vitamin D insufficiency in Taiwan.

The mechanism underlying how lipid profile influences vitamin D levels remains inconclusive. Speeckaert et al found vitamin D binding protein in very low-density lipoprotein, suggesting that vitamin D may be stored in adipocytes, which could also extract it.¹⁵ Another explanation involves the activation of the vitamin D receptor in hepatocytes, which leads to enhanced activity of 7 α -hydroxylase, associated with bile acid synthesis.³⁰ Additionally, vitamin D levels affect calcium and parathyroid hormone (PTH) concentrations, which may indirectly affect lipid profiles.³⁰ Finally, vitamin

D deficiency may increase insulin resistance by reducing adipose PPAR- γ expression and deteriorating β -cell function, potentially leading to a higher risk of type 2 diabetes mellitus, metabolic syndrome, and dyslipidemia.^{31,32} Further research is needed to elucidate the precise mechanisms underlying the relationship between dyslipidemia and vitamin D levels, particularly considering gender differences.

This study has several limitations. First, the subjects were self-referred participants undergoing routine health examinations at our hospital, potentially introducing a selection bias limiting the generalizability of our findings to the broader population. Second, the cross-sectional design of the study precludes establishing causal relationships between dyslipidemia and vitamin D levels. Third, factors such as personal disease history, medication history, and lifestyle characteristics were not considered due to data limitations. This prevented us from assessing whether subjects were undergoing treatment for dyslipidemia or taking vitamin D supplements before their health examinations. Lastly, all subjects in this study were Taiwanese; thus, the results may not apply to other non-Asian ethnic groups.

Conclusion

This retrospective cross-sectional study conducted in southern Taiwan revealed a significant association between elevated TG and TC levels and decreased vitamin D, while no significant associations were observed with LDL-C and HDL-C levels. Upon stratification by gender, elevated TG was significantly associated with decreased vitamin D in males. Conversely, elevated TC was significantly associated with decreased vitamin D in females. Thus, we recommend that patients with dyslipidemia be screened for vitamin D deficiency and advised to ensure adequate vitamin D intake to improve their condition. Additionally, future studies in Taiwan examining the effects of vitamin D deficiency should consider including lipid profiles as a reference. Further research is warranted to elucidate the underlying mechanisms of the association between dyslipidemia and decreased vitamin D levels.

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