Original article

The Association between Vitamin D and Lipid Profile among Healthy Malay Adults in K ota Bharu, Malaysia

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Abstract:

Background:The effect of vitamin D in regulating lipid profiles is one of the proposed mechanisms for the association between vitamin D deficiency and cardiovascular heart disease (CHD). However, the relationship between vitamin D status and lipid profiles remained unclear. ***Objective:*** The objective of this study is to evaluate the association of vitamin D status on serum lipids among healthy adults. ***Material and Methods:*** This is cross-sectional study, involving 120 healthy adults with age of 18-50 years from the Malay adult in Kota Bharu, Malaysia which were selected via random sampling. To decrease the seasonal variability, the study was conducted within 2 months, between July and August 2015. Serum 25(OH)D, serum parathyroid hormone (PTH), serum triglycerides (TG), serum total cholesterol (TC), serum low density lipoprotein cholesterol (LDL-C) and serum high density lipoprotein cholesterol (HDL-C), fasting blood sugar (FBS) and serum insulin were measured. ***Results:*** The mean serum 25(OH) D was 23.50 ± 8.74 nmol/L. Based on the definition of vitamin D deficiency as serum 25(OH)D less than 30mmol/L, the proportion of vitamin D deficiency among our study subjects was 76.7%. Our data revealed that serum 25(OH) D had significant inverse association with HDL-C and significant positive association with TC, TG and LDL-C. ***Conclusions:*** Our study shows highly prevalence of vitamin D deficient among healthy Malay adult population in Kota Bharu, Malaysia. Serum 25(OH) D was positively associated with TC, TG and LDL-C and negatively associated with HDL-C. Perhaps optimizing the level of vitamin D might improve the lipid profiles among healthy Malay adults.

Keywords: Vitamin D; Lipid profiles; Healthy adult

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Introduction:

A fat-soluble vitamin called vitamin D is known for being crucial for maintaining calcium homeostasis and promoting bone formation. It's interesting to note that vitamin D has uses beyond skeletal health. Vitamin D's extra skeletal effects, such as the regulation of immunological function and inflammation, insulin secretion, and cardiovascular protection, are demonstrated by the presence of

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vitamin D receptors in extra skeletal tissues and organs [1].

Around the world, 50% of older people have vitamin D deficiency [2]. Most Omani women of reproductive age [3], 30 to 50% of American adults [4], more than half of Kuala Lumpur, Malaysia's urban primary school students [5], and 96% of North India's newborns [6] are also affected. Vitamin D deficiency was defined by the World Health Organization (WHO) as serum 25(OH)D levels below 50 nmol/L (20 ng/mL)[7]. However, different study populations with varied methodologies for determining vitamin D levels also used various definitions of vitamin D sufficiency or deficiency, which led to variations in vitamin D prevalence. The level of vitamin D is also closely tied to the amount of sunlight exposure because the body generates the majority of its vitamin D through cutaneous synthesis while exposed to sunlight. It's interesting to note that countries like Saudi Arabia, Hawaii, Iran, and India, which have year-round sunshine, have high rates of vitamin D insufficiency [8–10]. Dyslipidemia has been linked to higher rates of CHD [11, 12], as well as high mortality and morbidity [13]. In wealthy nations, there have been declining trends in CHD-related mortality. Yet, both low- and middle-income nations14) and low-income individuals[15] have seen a sharp increase. Vitamin D deficiency is associated with an unfavorable metabolic profile. One of the hypothesized explanations for the connection between vitamin D deficiency and CHD is the impact of vitamin D on the regulation of the lipid profile. It is yet unknown how the lipid profile and vitamin D level are related. Based on 17 randomized control trial studies comparing the intervention group (vitamin D) with the control group (placebo) among type 2 diabetic patients[16], vitamin D significantly reduced total cholesterol (TC), triglycerides (TG), as well as low density lipoprotein (LDL), but had negligible effects on high density lipoprotein (HDL). Another meta-analysis of randomized controlled trials that assessed the effects of vitamin D supplementation on lipid profiles, however, found no significant changes in TC, HDL-C, and TG following vitamin D administration[17]. The objective of this study is to evaluate the association of vitamin D status on serum lipids in healthy Malay adults.

Methods and Materials:

In this cross-sectional study, 120 healthy adult with age of 18-50 years from the Malay adult in Kota Bharu, Malaysia were selected via random sampling. Sample size calculation done using single mean formula. Exclusion criteria included pregnancy, lactation, diabetes mellitus, chronic kidney disease, liver failure, thyroid disorders, hyper or hypoparathyroidism, smoking, established osteoporosis, on any form of drug treatment with possible effect on bone metabolism such as oral contraceptive, hormone replacement therapy, glucocorticoids, anticonvulsive drugs, vitamin D and calcium supplements. Apart from that, subjects who took alcohol was also excluded in this study. To decrease the seasonal variability, the study was conducted within 2 months, between July and August 2015. A written consent form approved by Human Ethics Research Committee (USM) No. 15030091) was signed by all participants.

After overnight fasting, 10 ml of peripheral blood was withdrawn. Blood samples were centrifuged at 2500 rpm for 10 min and the serum was stored at -20°C. Serum levels of 25(OH) D were measured using competitive protein binding assay using Elecsys Cobas e 411 by Roche Diagnostics with CVs for repeatability were between 1.7% to7.8% and the CVs for intermediate precision were between 2.2% to 10.7%. The method used is traceable to a Joint Committee for Traceability in Laboratory Medicine (JCTLM)-approved isotope dilution liquid chromatography mass spectrometry (ID-LC-MS/MS).). A 25(OH) D level of less than 30 nmol/L was considered as vitamin D deficiency and levels of equal and more than 30 nmol/L as sufficient [18]. Serum levels of PTH were measured by second generation assay by Elecsys Cobas e601 with sandwich principle. The CVs for repeatability were 1.5% to 2.7% and the intermediate precisions were between 3.0% to 6.5%.

FBS was measured using hexokinase principle and serum insulin was measured using Elecsys sandwich method on Cobas e601. The insulin resistance was quantified using homeostasis model assessment-insulin resistance (HOMA-IR)[19]. Serum total cholesterol and serum triglyceride level was measured by enzymatic method using commercial kit (RANDOX Laboratories, UK) on Architect analyser. Serum HDL-C was measured by a direct method using prepared reagent on the same analyser. LDL-C concentration was derived from the Friedewald equation[20]. Weight and height were measured using a Seca scale with subject wearing light clothes and no shoes. Body mass index (BMI) was defined as weight (kg) divided by height squared (m^2). Waist

circumference (WC) was measured by placing the tape (in centimeters) wrap around the waist. The waist was defined as midway between top of the hip bone and bottom of the ribs [21].

All continuous values are expressed as mean ± SD and categorical variables are presented as percentage. The Student's *t*-test was employed to compare differences between the means of continuous variables. Simple linear regression analysis was applied to assess the association of 25(OH)D with each component of lipid profiles. The results of linear regression are presented as B (Confidence interval). *P*-value less than 0.05 were considered statistically significant. Data were analyzed by SPSS statistical software (version 20.0).

Ethical clearance:

This study was approved by Human Ethics Research Committee (USM) No. 15030091.

Results:

In this study, 120 individuals were (53.3% men and 46.7% women) recruited. The range of 25(OH) D measured in this study was 8.59 nmol/L to 47.56 nmol/L. The mean serum level of 25(OH) D was 23.50 ± 8.74 nmol/L. The proportion of vitamin D deficiency among study subjects was 76.7%, predominantly among female with mean age of 31.58 ± 7.53 years. Table 1 presents the characteristic of the study subjects according to vitamin D status. In general, waist circumference, BMI and total cholesterol were significantly lower among healthy adult with vitamin D deficiency compared to subjects with serum 25(OH)D more than or equal to 30 nmol/L.

Our data revealed that serum 25(OH)D had significant inverse positive association with HDL, TC and LDL and significant positive negative association with total cholesterol, triglycerides and LDL (Table 2). There were no association between serum 25(OH) D with fasting plasma glucose and HOMA-IR. Significant positive but weak association observed between serum 25(OH)D with BMI and WC.

Table 1: Characteristic of study subjects according to vitamin D status.

Parameter (unit)	Total subjects	Serum 25(OH)D		*P*-value
	n=120	< 30 nmol/L n=92	≥ 30 nmol/L n=28	
Age	32.72±8.42	31.58 ± 7.53	36.46±10.12	0.024
Gender				
Male	53.3 %	44.6 %	82.1 %	*<0.001
Female	46.7 %	55.4 %	17.9 %	
BMI	24.53±4.79	24.05±4.48	25.32±4.48	0.217
WC	82.36±11.69	81.01 ±11.04	86.68±12.86	0.025
TC	5.77±0.96	5.66 ±9.95	6.14±0.91	0.021
TG	1.38±1.42	1.17±0.65	2.06±2.61	0.080
HDL-C	1.17±0.37	1.18±0.39	1.14±0.27	0.626
LDL-C	3.96±0.93	3.94±0.88	4.05±1.10	0.595
PTH	1.86±1.00	1.96±1.06	1.52±0.70	0.410
Insulin	14.89±20.01	13.98±20.53	17.88±18.20	0.369
FBS	4.95±1.86	4.83±1.34	5.36±3.00	0.188
HOMA-IR	3.78±7.13	3.26±5.7	5.49±10.53	0.148

All results analysed by independent t-test except gender

All results are expressed as mean ± SD; Gender are expressed as number of subject(%)

*Pearson Chi-Square test, $p<0.05$ value is taken as significant at 95% confidence interval

Table 2: Regression analysis of serum 25(OH) D and parameters of lipid profile among healthy adult.

Parameter	Crude B (95 % CI)	*p*-value
Total Cholesterol	2.338 (0.739 – 3.937)	0.005
Triglycerides	-5.557 (-9.712 – 1.402)	0.005
HDL	1.679 (0.008 – 3.351)	0.009
LDL	0.829 (-0.013 – 1.671)	0.049

B: Unstandardized Coefficients, CI: Confidence Interval.

Discussion:

The majority of vitamin D deficient research have focused on at-risk populations, such as pregnant women, elderly people, obese children, and menopausal women [22–27]. While fewer research has focused on healthy adults, the prevalence of vitamin D insufficiency in the population is less clearly understood. Wide variations in prevalence between groups may result from non-standard definitions of vitamin D deficiency, various study methodology, and various approaches to estimating the level of vitamin D in blood. Serum levels of 25(OH)D below 30 nmol/L [18], serum levels of 25(OH)D below 50 nmol/L [28–31], and serum levels of 25(OH)D below 75 nmol/L [32, 33] are the cut-offs used to establish vitamin D deficiency. Throughout, there is a high prevalence of vitamin D deficiency, which is indicated by serum 25(OH)D levels below 75, 50, or 30 nmol/L. In this investigation, vitamin D deficiency was determined using a cut-off of 30 nmol/L. We discovered that 92 out of 120 participants had serum 25(OH)D levels < 30 nmol/L, mostly in female participants.

Interventional investigations using vitamin D supplements were unable to reach a consensus on the impact of lipid profiles. While some research found an inverse link between serum 25(OH)D and total cholesterol, TG, and LDL, others found a positive association. From the 8018 patients in Norway, Jorde et al. (2010) discovered negative relationships between serum 25(OH)D levels and TG and positive connections between serum 25(OH)D levels and TC, HDL-C, and LDL-C[34]. We discovered a substantial positive correlation between serum 25(OH)D and TC, TG, and LDL in this investigation, but a significant negative association with HDL-C. Patients with ischemic stroke had previously been shown to have a positive correlation between blood 25(OH)D and TC, TG, and LDL, and their investigation revealed that 70.04% of cases had vitamin D deficiency[35]. Our results might have corroborated the findings of interventional studies on vitamin D supplementation, which found no effect on CVD mortality[36] or the frequency of stroke or myocardial infarction[37]. No significant differences were found between the supplementation of moderate to high doses of vitamin D in adults and the placebo, according to systematic reviews by Wang et al.[38]. Similarly, Raisa et al. found no improvement of lipid parameters among outpatient clinic after 4 years of daily oral administration of 2000 IU/day vitamin D3. [39]

The results of a study including 1475 patients from the Centre for Physical Examination, 306 Hospital of the PLA in Beijing, China, which found inverse correlations between serum 25(OH)D and TC, TG, and LDL, contradicted the findings in this study.[40] When compared to our communities, which have substantially lower vitamin D levels, they chose a higher cut-off to determine vitamin D (50 nmol/L) and only 58.5% were vitamin D deficient. In a similar vein, diabetic patients in Iran had mean serum 25(OH)D levels that were higher than those in the general population (53.41 33.25 nmol/L), and patients with vitamin D deficiency had lower HDL levels than those who had adequate levels [41]. Lower TC, LDL-C, and higher HDL-C levels were observed in patients with higher vitamin D cut-off levels (> 75 nmol/L or > 30 ng/mL) compared to those who were vitamin-D deficient [42]. These findings imply that increasing vitamin D levels could help achieve the desired levels of TC, TG, LDL, and HDL.

Many research revealed that taking vitamin D supplements improved serum 25(OH)D. According to a study, children who received 100,000 U of vitamin D in comparison to those who received 50,000 U dramatically increased their levels of vitamin D and improved their lipid levels. Their research indicates that better lipid profiles are linked to greater vitamin D levels[43]. However, in diabetic patients, increasing blood 25(OH)D above 20 ng/mL or 50 nmol/L with vitamin D treatment only significantly improved TC but not LDL-C and HDL[44].

In conclusion, Kota Bharu, Malaysia has a significant

percentage of vitamin D deficient residents. Healthy adults in the research population had a mean serum 25(OH)D level that is much lower than that of other study populations. Serum 25(OH)D was inversely correlated with HDL-C and favourably correlated with TC, TG, and LDL-C. The lipid profiles of healthy adults may be improved by adjusting vitamin D levels. Additional variables that affect the levels of TC, TG, LDL-C, and HDL-C may be crucial in regulating the lipid profiles of healthy adults in Kota Bharu, Malaysia. Future research should seek to increase the sample size, take additional confounders into account when determining vitamin D levels, and examine giving vitamin D supplements to patients who have hyperlipidemia while also examining the effects of these patients' targeted lipid profiles.

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Conflict of interest

The authors declared no conflicts of interest**.**

Authors's contribution

Noorazliyana Syafii, Tuan Salwani Tuan Ismail, Roznie Aida Mohd Rosdi, Bayani Che Muda, Wan Norlina Wan Azman, Hanim Afzan Ibrahim, Ahmad Badruridzwanullah contributed equally to this work. Noorazliyana Syafii and Tuan Salwani Tuan Ismail supervised and design the study objective and methodology, Roznie Aida Mohd Rosdi and Bayani Che Muda recruited the subjects of the study, Wan Norlina Wan Azman and Hanim Afzan Ibrahim analysed the sample and Ahmad Badruridwanullah lead the data analysis. Noorazliyana Syafii and Hanim Afzan Ibrahim performed the literature review and Tuan Salwani Tuan Ismail and Bayani Che Muda wrote the manuscript. Wan Norlina Wan Azman performed the major work in structuring and harmonizing the overall content. All authors have read and approved the final version of the manuscript.

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