

Correlation of Vitamin D Status with Lipid Profile of Outpatient Department Attendees - A Cross Sectional Study in a Rural Tertiary Care Hospital of North Bengal, India

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ABSTRACT

BACKGROUND

Deficient or insufficient vitamin D status is found as a major chunk amongst all age groups all over the Indian subcontinent. Low levels of serum 25 (OH) D are associated with atherogenic lipid profile, and the resultant dyslipidemia is an important risk factor for cardiovascular disease and other atherosclerotic disorders in adults. As, not much literature was available on the deficiency of vitamin D and its effects, in the North Bengal region of West Bengal, India, this study was done to find out the association between vitamin D status and lipid profile of the participants and predict the risk of dyslipidaemia with changes in vitamin D status.

METHODS

430 medicine OPD attendees were selected for the study, interviewed after taking consent, blood parameters were examined and collected data were analysed for correlation and multinomial regression using SPSS v.25.

RESULTS

The mean value and standard deviation of serum 25 (OH) D level was found to be 21.53 ± 7.06 ng / ml. 35 % of vitamin D deficient subjects were found to be dyslipidemic. A negative correlation was observed between vitamin D status and total cholesterol & LDL status. While vitamin D status changed from "Sufficient" to "Deficient", the chance of dyslipidemia increased by approximately 4.6 times.

CONCLUSIONS

Serum vitamin D influences largely the lipid profile of the study population.

KEY WORDS

Vitamin D, Serum 25 (OH) D, Dyslipidaemia, Cholesterol

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DOI: 10.14260/jemds/2021/615

How to Cite This Article:

Banerjee R, Datta S, Rout AJ. Correlation of vitamin D status with lipid profile of outpatient department attendees: a cross sectional study in a rural tertiary care hospital of North Bengal, India. J Evolution Med Dent Sci 2021;10(35):3012-3016, DOI: 10.14260/jemds/2021/615

*Submission 11-01-2021,
Peer Review 21-07-2021,
Acceptance 27-07-2021,
Published 30-08-2021.*

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BACKGROUND

Vitamin D is essential for life in all higher organisms and is found as cholecalciferol (Vitamin D₃) in vertebrates.¹ In humans, most of the vitamin D is synthesized cutaneously through sun-light exposure (by ultraviolet B radiation) while the remaining vitamin D is obtained from the diet.^{2,3,4} The total vitamin D is immediately hydroxylated by the liver to form 25-hydroxyvitamin D [25(OH)D] which is the predominant form of the circulating vitamin D.⁵ In this article Vitamin D and 25 (OH)D have been used interchangeably.

The binding of vitamin D with high-affinity vitamin D receptor (VDR) which acts as a ligand-activated transcription factor, is responsible for its metabolic activities.⁶ Vitamin D reduces the production of IL-2, interferons and stimulates the T-helper type 2 lymphocytes, resulting in a reduction of matrix metalloproteinases and restricting atherosclerotic plaque progression.⁷ It also plays an important role in endothelial function, blood pressure control, calcification of the coronary vasculature, increased vascular resistance and prevention of CVD.⁸

Recent reports have found that hypo 25 (OH) D is associated with atherosclerosis, hypertension, myocardial infarction and stroke.^{9,10,11,12} Observational studies have demonstrated that while sufficient serum 25 (OH)D is associated with a favourable lipid profile, low levels of it, is associated with an atherogenic lipid profile and the resultant dyslipidaemia is an important risk factor for atherosclerosis and cardiovascular disease in adulthood.^{13,14}

Vitamin D deficiency or insufficiency prevails all over the Indian subcontinent, among all age groups.^{5,15,16} As per available literature, not too many articles have been found on the deficiency of vitamin D and its effects, especially for the North Bengal region of West Bengal, India. To enlighten on different aspects of vitamin D deficiency, a larger study was undertaken at North Bengal Medical College and Hospital. An article from the data so collected has already been published with the title "Correlation of vitamin D status with glycaemic status of individuals: a cross-sectional study in a rural tertiary care hospital of North Bengal, India".¹⁷ The present study was done, as a part of the larger study, with the following objectives.

Objectives

1. To find out the association between vitamin D status and lipid profile of study participants
2. To find out the correlation between vitamin D level and different serum lipids
3. To predict the risk of dyslipidaemia with the change of vitamin D status.

METHODS

Post ethical clearance of Institutional Ethics Committee, a cross-sectional study was planned and undertaken for 1 year from July 2016 to June 2017 among the medicine OPD patients with a sample size of 430.¹⁷

In medicine OPD, every alternate attendee, of either sex, were approached for being a study subject. Attendees having frank diabetes, autoimmune diseases, chronic kidney & liver disorders, morbidly obese, immunocompromised, on hormone replacement therapy, taking serum lipid profile, blood glucose and serum 25 (OH) D level altering drugs, or substance abusers, were excluded from the study. Using the same collected data of the larger study, though, on different blood parameters, the present study analysis was made.

Data Collection Procedure

Written informed consents were obtained from the eligible & willing subjects followed by their interview, using a pre-structured, pretested questionnaire. Body mass index (BMI) was calculated using the formula [Weight in Kg/ Height in mt²]. For lab investigations, blood samples were collected from the antecubital vein after 8 hours of overnight fasting, in fluoride & clotted vials. Within 30 - 45 minutes of collection of samples, serum was separated by centrifuge machine.

Estimation of Blood Parameters

An automated analyzer (Erba Mannheim XL-600 & EM-360) was used for the estimation of blood parameters. Serum calcium was estimated using OCPC (O-Cresolphthalein Complex one) method. Cholesterol oxidase-peroxidase (CHOD / PAP) method for total cholesterol and GPO (glycerol phosphate oxidase) method for triglycerides were used. Estimation of HDL was done by modified polyvinyl sulfonic acid (PVS) and polyethylene glycol methyl ether (PEGME) coupled classic precipitation method with the improvement in using optimized quantities of PVS/PEGME and selected detergents. Estimation of VLDL & LDL was done using the Friedewald formula.¹⁸ Serum 25 (OH) D levels were estimated by the ELISA method.

Statistical Analysis

Collected data were checked for completeness & consistency and entered in Microsoft Excel version 2007 and were cleaned. Codification of data and Pearson's correlation, multinomial logistic regression analysis was done in SPSS version 22. Results are presented through tables in the form of percentages and proportions. P-value < 0.05 was considered statistically significant.

Operational Definitions

*Dyslipidaemia Was Defined (ATP III) as One or More of the Following:*¹⁹

- Hypercholesterolemia: Total cholesterol more than 200 mg / dL
- Hypertriglyceridemia: Triglycerides more than 150 mg / dL
- High LDL-C: low density lipoprotein-cholesterol (LDL-C) more than 130 mg / dL
- High VLDL-C: very low density lipoprotein-cholesterol (VLDL-C) more than 30 mg / DL
- Low HDL-C: high-density lipoprotein-cholesterol (HDL-C) levels < 40 mg / dL for men and < 50 mg / dL for women

Vitamin D Status^{20,21}

Status of Vitamin D	Level of Serum [25(OH)D] in ng/ml
Deficient	< 20
Insufficient	20-29
Sufficient	30-70
Potential Toxicity	> 70

RESULTS

Blood Parameters	Mean	Std. Deviation
Vitamin D Level	21.5322	7.05670
Cholesterol	170.50	33.345
Triglyceride	146.45	66.123
HDL	51.13	6.826
VLDL	28.53	13.062
LDL	90.56	27.957
Calcium	8.7224	0.78312

Table 1. Different Blood Parameters of the Study Population (N = 430)

Vitamin D Status	Lipid Status			Chi Square	P Value
	Dyslipidaemi a	Normal Lipid Profile	Total		
Deficient	70 (35)	130 (65)	200 (100)	13.73; df = 2	<0.05
Insufficient	45 (25)	135 (75)	180 (100)		
Sufficient	5 (10)	45 (90)	50 (100)		
Total	120 (7.90)	310 (2.10)	430 (100)		

Table 2. Distribution of Study Population According to Their Vitamin D Status and Lipid Profile

*Figures in parenthesis indicates percentage

Blood Parameters	Pearson's Correlation	Significance Level
Cholesterol	-0.35	< 0.05
Triglyceride	-0.203	< 0.05
HDL	0.026	0.585
VLDL	-0.16	< 0.05
LDL	-0.358	< 0.05
Calcium	0.53	< 0.05

Table 3. Correlation between Serum 25(OH)D with Different Blood Parameters

Lipid State ^a	Predictor Variables	Multinomial Regression Analysis			Sig.
		Adjusted Odds Ratio (AOR)	95% Confidence Interval for AOR		
			Lower Bound	Upper Bound	
Dyslipidaemia	Age	1.011	0.992	1.030	0.262
	Female	1.512	0.977	2.340	0.063
	Male	0			
	Vitamin D Deficient	4.597	1.637	12.911	0.004
	Vitamin D Insufficient	3.176	1.173	8.597	0.023
	Vitamin D Sufficient	0			

Table 4. Multinomial Logistic Regression Showing Risk of Dyslipidaemia

a. The reference category is: Normal Lipid profile.
b. Redundant parameter so is set to zero

It was found that the Mean ± SD of the age of study participants was 37.47 ± 12.63 years. Most of the participants were males (54.7 %). Sufficient vitamin D status was the lowest found (11.63 %) while Deficient status was the most (46.51 %) among the subjects. 41.86 % of participants were found to be with insufficient vitamin D status.¹⁷ Mean ± SD of serum 25 (OH) D level was found to be 21.53 ± 7.06 ng / ml while that of cholesterol and triglycerides were 170.50 ± 33.35 mg/dl and 146.45 ± 66.12 mg/dl respectively (table 1). Among the total 200 vitamin D deficient study subjects, 70 (35 %) were found to be a dyslipidemic while, 45 (90 %) of the total 50 study subjects with sufficient vitamin D status were found to be with normal lipid profile. The difference in lipid profile among different vitamin D status was statistically significant (Table 2). Statistically significant, medium negative correlation was observed between vitamin D status and total

cholesterol (-0.35) & LDL status (-0.358). Though a weak positive correlation was found between vitamin D and HDL it was not statistically significant (Table 3). Taking 'normal lipid profile' as the reference category for the dependent variable and adjusting other independent variables, in multinomial regression analysis showed that, with change in vitamin D status from "Sufficient" to "Insufficient" and "Deficient", risk of dyslipidaemia increased by approximately 3.2 times and 4.6 times respectively and both of the findings were statistically significant (Table 4).

DISCUSSION

Vitamin D Deficiency

In Asian sun-rich countries, vitamin D deficiency is multifactorial. Phosphate and phytate prevalent high fibre diet leads to reduced absorption of vitamin D after oral intake. The increased melanin of the dark complexion population may reduce vitamin D production by absorbing UVB rays.²² Moreover, increased indoor occupational activities, increased pollution, and genetic predisposition contributes to vitamin D deficiency.²³ In the present study, vitamin D deficient subjects were 46.51 % while 41.86 % were vitamin D insufficient. A study on Asian subjects done by Soo Lim et al. showed that 51.6 % had vitamin D insufficiency.²⁴ Another study in the North Indian community had shown a much higher i.e. 75.8 % of participants were vitamin D deficient.¹⁹ Ethnic differences, varying degrees of exposure to sunlight might have played a role behind such diverse findings.

Vitamin D Deficiency Affecting Lipid Profile

Vitamin D has been suggested to affect the regulation of lipid metabolism directly, due to its involvement in the synthesis of bile acid in the liver.²⁵ Chaudhuri et al. had reported that 25(OH)D deficiency was independently associated with dyslipidaemia in Indian subjects.²⁶

The present study results showed an inverse correlation of serum vitamin D3 with serum cholesterol, triglyceride, LDL and VLDL while, a positive correlation of serum 25 (OH) D and serum HDL. Also, the risk of dyslipidaemia increases with low vitamin D levels. The results are in conjunction with some of the recent association with studies done on the Indian population, where vitamin D concentration was inversely correlated with atherogenic lipids (TC, TG, and LDL) and showed a strong positive correlation with athero-protective lipids (HDL).^{5,25,27,28,29,30} Even studies from abroad, like Gaddipati et al. a study done on Americans and Jungert A et al. study in Germany, also showed that serum vitamin D levels were negatively correlated with total cholesterol, triglycerides and LDL and positively correlated with HDL.^{31,32} In contrast, Chiu showed no relationship between serum levels of 25 (OH)D and TG or HDL cholesterol in healthy subjects.³³ Similarly, a study done by Garry John and colleagues among 170 UK Bangladeshi healthy adults showed no relationship between 25 (OH)D and TG or HDL cholesterol.³⁴

The coexistence of hypovitaminosis D and hypercholesterolemia may be explained via photo metabolism. Sunlight converts squalene, in exposed skin, into 7-dehydrocholesterol, vitamin D and photo metabolites of

vitamin D.³⁵ The 7-dehydrocholesterol pathway in the liver is common for cholesterol and 25 (OH)D synthesis.³⁶ In the absence of effective sunlight, its metabolic pathway is diverted into the formation of cholesterol.³⁴ LDL cholesterol has been postulated as a precursor of previtamin D. So, a defect in LDL receptors will increase serum cholesterol due to lower cholesterol uptake with a resultant decrease in serum 25 (OH)D as both share the common synthetic pathway.³⁷

Vitamin D may regulate triglyceride metabolism by causing the expression of VLDL cholesterol receptors in some types of cells.³⁸ Apart from this, few more important mechanisms have been postulated. Vitamin D enhances intestinal calcium absorption. This increased serum calcium could then reduce serum triglycerides by reducing its hepatic formation and secretion.³⁹ Vitamin D has a suppressive effect also on serum PTH concentration. As plasma post heparin lipolytic activity is reduced by elevated PTH concentration, low serum PTH may reduce serum triglycerides via increased peripheral removal.^{40,41} Again, when vitamin D is deficient, the risk of insulin resistance increases and this is associated with defective lipoprotein metabolism resulting in an elevation of VLDL cholesterol and triglycerides and a decrease in HDL-C.^{38,42,43} Even, Garry John study depicting no relationship between 25 (OH)D and TG or HDL cholesterol, admitted that the serum level of 25 (OH)D is an independent predictor of fasting apolipoprotein A₁.³³ This apolipoprotein A₁ is an essential part of HDL cholesterol that acts as a scavenger of cholesterol from tissues and transports it to the liver.⁴⁴

CONCLUSIONS

It can be concluded that serum vitamin D influences largely the lipid profile of individuals. As serum vitamin D shows an inverse correlation with atherogenic lipids, dyslipidemic cardiovascular risks may be an indirect result of vitamin D deficiency. However, to establish a causal relationship between vitamin D status and lipid status of individuals, multi-centric, large scale, longitudinal studies are recommended.

Limitations

As the present study is cross-sectional, the causality effect can't be determined. Variation in the polymorphisms of vitamin D binding protein (DBP) and vitamin D receptor (VDR), sunlight exposure, and the effect of vitamin D supplementation on weight gain also needs to be considered.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jemds.com.

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