Original Article

Relationships between Serum 25-Hydroxy Vitamin D Levels and Plasma Glucose and Lipid Levels in Pediatric Patients in a Rural Hospital

N C Shivaprakash, Ranjit Baby Joseph[1]

Professor and HOD, Department of Pediatrics, Adichunchanagiri Institute of Medical Sciences, Karnataka, India, [1]Final Year Post-Graduate Resident, Department of Pediatrics, Adichunchanagiri Institute of Medical Sciences, Karnataka, India

Corresponding Author: *Dr. Ranjit Baby Joseph, Room no: 61, Kalpatharu Bhavana, Adichunchanagiri Institute of Medical Sciences, BG Nagara, Mandya District. E-mail: ranjitbaby@gmail.com*

Abstract

Objective: To study the relationships between serum vitamin D levels and plasma glucose or lipid levels in children and adolescents.

Material & Methods: We conducted a prospective study on pediatric patients (age 2-18 years) of Adichunchanagiri Institute of Medical Sciences, BG Nagara from December 2011 to November 2012 with simultaneous measurement of 25-hydroxyvitamin D, fasting plasma glucose and a lipid panel (n=53). Pearson correlation coefficient was used to estimate the correlation between 25(OH) D and plasma glucose or lipid levels. Plasma glucose and lipid levels were compared in subjects with 25(OH) D concentrations greater or less than 20 ng/mL.

Results: 25(OH) D levels were inversely correlated with fasting plasma glucose levels (r=-0.611, P <0.001). Lower 25(OH) D levels were also associated with lower serum high-density lipoprotein cholesterol (HDL) concentrations (r=0.446, P=0.001). The value of vitamin D levels did not vary significantly with age, sex or body mass index. Children who were vitamin D insufficient [25(OH) D <20 ng/mL] had higher fasting plasma glucose (P=0.037) and lower HDL levels (P=0.044) than children who were vitamin D sufficient [25(OH) D >20 ng/mL].

Conclusions: Low 25(OH) D levels in children and adolescents are associated with higher plasma glucose and lower HDL concentrations and these children are more prone to develop type 2 diabetes and cardio metabolic diseases in later life.

Keywords: Vitamin D, Fasting blood sugar, Lipid profile, Obesity, Type 2 diabetes, Cardiometabolic diseases

INTRODUCTION

The discovery of the critical roles of Vitamin D for overall health is a fascinating story in the history of medicine. First are its osseous effects and the association to rickets. Then came the discovery of its anti-infectious role, from the breakthrough by Niels Finson, earning him a Nobel prize in 1903 for the use of a form of 'concentrated light radiation' to treat tuberculosis skin lesions, through the sanatoriums built to treat the patients with sunbathing, until the discovery of cathelicidin- an antimicrobial peptide, regulated by vitamin D, that serves a critical role in mammalian innate immune defense against invasive bacterial infection.[1]

Over the last two decades, understanding of vitamin D synthesis and its function has changed remarkably. With its plethora of biological effects on diverse tissues, vitamin D sustains health throughout the body. It is now believed that vitamin D can protect against multiple sclerosis, type 1 diabetes mellitus and cancer. Among adults low levels of vitamin D have been shown to be associated with increased risks of obesity, hypertension, glucose intolerance, type 2 diabetes mellitus and cardiovascular disease.[2]

In the last 3 decades, there has been a dramatic increase in the prevalence of both childhood obesity and metabolic syndrome, which includes high plasma glucose and low high-density lipoprotein cholesterol (HDL) levels. Because

this profile may predispose children to cardiovascular disease later in life, the identification of modifiable risk factors for metabolic syndrome is crucial in the pediatric age group.[3]

Hypovitaminosis D is now being identified as a prevalent health problem in both adults and children not only in countries with low UV exposure but also in countries close to the equator. Accordingly, vitamin D supplementation could potentially be beneficial to billions of people, but still, hard evidence is lacking especially in Indian children.

There is a relation between the serum 25(OH) D levels and diseases like cancer, cardiovascular diseases and skeletal growth. After supplementation of vitamin D recovery of above said diseases are good.

AIMS AND OBJECTIVES OF STUDY

To study the prevalence of vitamin D deficiency in children and to know whether it has any relation with the age, sex and body mass index (BMI) and to study relationships between serum vitamin D levels and plasma glucose and lipid levels.

Establishment of a significant relationship helps in the prediction of metabolic syndrome and other cardiovascular complications in future and gives an idea about various measures we can take to prevent or treat it.

MATERIALS AND METHODS

Source of Data

The study was a prospective study conducted in pediatric patients both out-patients as well as in-patients in Sri Adichunchanagiri Institute of Medical Sciences and Hospital, (AIMS) B.G.Nagara for the period of 1 year starting from December 2011 to November 2012.

Method of Collection of Data

The data was collected from patients and the following investigations were done:

- Serum vitamin D
- Fasting plasma glucose
- Serum lipid profile.

Inclusion Criteria

- Age between 2 years to 18 years.
- Both out-patients as well as in-patients of Sri Adichunchanagiri Institute of Medical Sciences, B.G.Nagara.
- Patients with symptoms like chronic pain, fatigue, poor growth, bone health concerns and obesity.

Exclusion Criteria

- Age <2 years and >18 years
- Those who are seriously ill
- Hepatic or renal disease
- Metabolic rickets
- Type 1 or 2 diabetes mellitus
- Malabsorptive disorders (inflammatory bowel disease, cystic fibrosis and celiac disease)
- Hyperparathyroidism and hypoparathyroidism
- Earlier kidney, liver or renal transplant
- Malignancy
- Ongoing use of anticonvulsant medications or systemic glucocorticoids
- Congenital heart disease
- Genetic disorders.

Data were collected for patients, including age, sex, height, weight, co-morbidities, and the primary indication for ordering 25 (OH) D levels. Age and sex-specific body mass index (BMI) percentiles were determined with the Agarwal growth charts for Indian children as recommended by the IAP.[4] Vitamin D levels are graded as severe deficiency, deficiency, sufficiency and toxicity as per guidelines.[5] Lipid profile values are analyzed by the suggested cut off values as per lipid profile norms in Indian children.[6]

Laboratory Methods

25(OH)D assays were done by the Elecsys 2010 and Cobas e411 immunoassay analyzers by the technique of Electrochemiluminescence Immuno assay. Measuring range was 3.00–70.0 ng/mL or 7.50–175 nmol/L (defined by the limit of detection and the maximum of the master curve). Values below the limit of detection are reported as <3.00 ng/mL (<7.50 nmol/L). Values above the measuring range are reported as >70.0 ng/mL (>175 nmol/L) Each parameter in lipid profile was estimated by the COBAS INTEGRA 2nd generation cassette which contains an in vitro diagnostic reagent system for the quantitative determination of total cholesterol, HDL, LDL, VLDL and triglycerides in serum and plasma by using the principle enzymatic colorimetric method. Quantitative determination of blood glucose was done on COBAS INTEGRA SYSTEMS by using the principle of enzymatic reference method with hexokinase.

Statistical Methods

Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or

more groups. Pearson correlation has been used to find the correlation between Vitamin D with Lipids. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate tables and graphs.

Obsevations and Results

A total of 53 children formed the study subjects who included 30 male children (56.6%) and 23 (43.4%) female children. Majority of the children were between 11-15 years (39.6%). Mean age of the children studied is 9.72±4.56 years.

43 (81.1%) children were included in the study due to evidence of poor growth and 5 (9.4%) due to overweight (BMI 85th to 95th percentile) and 5 (9.4%) due to obesity (BMI >95th percentile).

4 (7.5%) patients had weight <3rd percentile, 16 (30.2%) had weight between 3rd and 25th percentile, 16 (30.2%) had weight between 25th and 50th percentile, 8 (15.1%) had weight between 50th and 75th percentile, 8 (15.1%) had weight between 75th and 97th percentile and 1 (1.9%) had weight >97th percentile for age and sex.

2 (3.8%) patients had height <3rd percentile, 13 (24.5%) patients had height between 3rd and 25th percentile, 21 (39.6%) patients had height between 25th and 50th percentile, 11 (20.8%) had height between 50th and 75th percentile, 5 (9.4%) had height between 75th and 97th percentile and 1 (1.9%) had height >97th percentile for age and sex.

18 patients(34%) had BMI <5th percentile, 9 patients(17%) had between 5th and 25th percentile, 6 patients (11.3%) had between 25th and 50th percentile, 8 patients (15.1%) had between 50th and 75th percentile,2 patients (3.8%) had between 75th and 85th percentile, 2 patients (3.8%) had between 85th and 90th percentile, 3 patients (5.7%) had between 90th and 95th percentile and 5 patients (9.4%) had >95th percentile for age and sex.

The mean level (SD) for 25(OH) D was 17.49 ng/mL (10.13), with a median of 14.7 and a range of <3 to 39.2 ng/mL. 25(OH) D levels were <20 ng/mL in 35 of the 53 subjects (66%).

Vitamin D levels	No. of patients	%
<5	5	9.4
5-15	22	41.5
15-20	8	15.1
20-50	18	34.0
>50	0	0.0
Total	53	100.0

The glucose values ranged from 63 to 124 mg/dL. A total of 19 subjects (35.8%) had a glucose level >100 mg/dL.

FBS (mg/dl)	No. of patients	%
≤99	34	64.2
100-126	19	35.8
>126	0	0.0
Total	53	100.0

Total cholesterol was found to be <190 in (69.8%) and ≥190 in 16 (30.2%) subjects. HDL was <20 in 3 (5.7%) and ≥20 in 50 (94.3%) subjects. LDL was <130 in 44 (83%) subjects and ≥130 in 9 (17%) subjects. VLDL was <30 in 29 (54.7%) and ≥30 in 24 (45.3%) subjects. Triglycerides was <150 in 29(54.7%) and ≥150 in 24(45.3%) subjects. Total cholesterol/HDL was <5.5 in 37 (69.8%) and ≥5.5 in 16 (30.2%) subjects. LDL/HDL ratio was <4.9 in 51(96.2%) and ≥4.9 in 2 (3.8%) subjects.

Lipid parameter	Cut-off	No. of patients	%
Total Cholesterol (mg/dL)	<190	37	69.8
	≥190	16	30.2
HDL (mg/dL)	<20	3	5.7
	≥20	50	94.3
LDL (mg/dL)	<130	44	83.0
	≥130	9	17.0
VLDL (mg/dL)	<30	29	54.7
	≥30	24	45.3
TGL (mg/dL)	<150	29	54.7
	≥150	24	45.3
Total cholesterol/HDL	<5.5	37	69.8
	≥5.5	16	30.2
LDL/HDL	<4.9	51	96.2
	≥4.9	2	3.8

Vitamin D vs Age: When the vitamin D levels were correlated with the age of the patients, it was found to be not significantly associated (P=0.476).

Age in years	Vitamin D Levels				Total
	<5	5-15	15-20	20-50	
2-5	1 (20%)	5 (22.7%)	4 (50%)	3 (16.7%)	13 (24.5%)
6-10	0 (0%)	9 (40.9%)	2 (25%)	4 (22.2%)	15 (28.3%)
11-15	3 (60%)	7 (31.8%)	2 (25%)	9 (50%)	21 (39.6%)
16-18	1 (20%)	1 (4.5%)	0 (0%)	2 (11.1%)	4 (7.5%)
Total	5 (100%)	22 (100%)	8 (100%)	18 (100%)	53 (100%)

Vitamin D vs Sex: Vitamin D levels were not significantly associated with gender of the patients also (P=0.629).

Gender	Vitamin D Levels				Total
	<5	5-15	15-20	20-50	
Male	3 (60%)	14 (63.6%)	5 (62.5%)	8 (44.4%)	30 (56.6%)
Female	2 (40%)	8 (36.4%)	3 (37.5%)	10 (55.6%)	23 (43.4%)
Total	5 (100%)	22 (100%)	8 (100%)	18 (100%)	53 (100%)

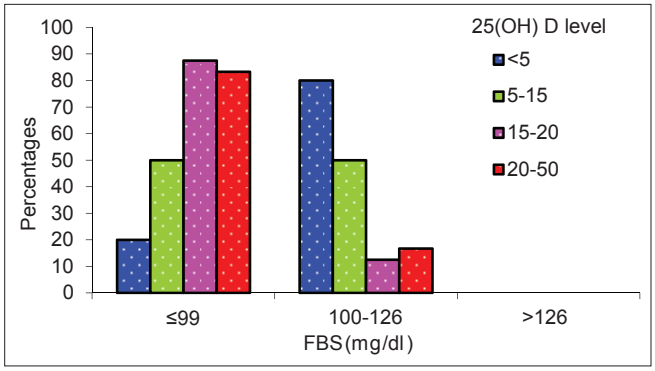
Vitamin D vs BMI: When the vitamin D levels were compared with BMI, it was found not to be significantly correlated (P=0.385)

BMI Percentile	Vitamin D Levels				Total
	<5	5-15	15-20	20-50	
<5th	1 (20%)	8 (36.4%)	4 (50%)	5 (27.8%)	18 (34%)
5th-25th	0 (0%)	6 (27.3%)	1 (12.5%)	2 (11.1%)	9 (17%)
25th-50th	0 (0%)	3 (13.6%)	1 (12.5%)	2 (11.1%)	6 (11.3%)
50th-75th	0 (0%)	3 (13.6%)	1 (12.5%)	4 (22.2%)	8 (15.1%)
75th-85th	0 (0%)	1 (4.5%)	0 (0%)	1 (5.6%)	2 (3.8%)
85th-90th	0 (0%)	0 (0%)	1 (12.5%)	1 (5.6%)	2 (3.8%)
90th-95th	1 (20%)	1 (4.5%)	0 (0%)	1 (5.6%)	3 (5.7%)
>95th	3 (60%)	0 (0%)	0 (0%)	2 (11.1%)	5 (9.4%)
Total	5 (100%)	22 (100%)	8 (100%)	18 (100%)	53 (100%)

Vitamin D vs Lipids: Lipid parameters studied along with the values of vitamin D include total cholesterol, HDL, LDL, VLDL, Triglycerides, total cholesterol/HDL ratio, LDL/HDL ratio. As per the guidelines, cut off values for each parameter were into taken into consideration for comparing with vitamin D. Increasing levels of 25(OH) D were significantly correlated with increasing levels of HDL and TGL. Vitamin D was also found to have some positive correlation with LDL and VLDL.

Vitamin D vs FBS: FBS values were classified as ≤99, 100-126 and >126 for comparing with vitamin D levels. FBS values were found to be significantly associated with vitamin D levels with a P value of 0.012

FBS (mg/dl)	25(OH) D level ng/mL				Total
	<5	5-15	15-20	20-50	
≤99	1 (20%)	11 (50%)	7 (87.5%)	15 (83.3%)	34 (64.2%)
100-126	4 (80%)	11 (50%)	1 (12.5%)	3 (16.7%)	19 (35.8%)
>126	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	5 (100%)	22 (100%)	8 (100%)	18 (100%)	53 (100%)



With the above available values, Pearson correlation coefficient and its P value were calculated. 25(OH)D was found to have significant positive correlation with HDL levels (r=0.446, P value=0.001) and LDL/HDL ratio (r=0.459, P value=0.001). A significant negative correlation was found to be present between 25(OH)D and FBS (r = -0.611, P value=<0.001). 25(OH)D was also found to be positively correlated with LDL (r=0.295, P value=0.032) and TGL (r=0.330, P value=0.016) but with a lesser significance.

DISCUSSION

Studies done from different centers from parts of India have drawn attention towards wide prevalence of vitamin D deficiency (VDD). VDD has been reported in all age groups who are residing in rural and urban India.[7]

Vitamin D Deficiency

Vitamin D deficiency can be easily diagnosed in presence of clinical features of rickets and laboratory support. But rickets is an extreme form of vitamin D deficiency and represents the tip of the iceberg of vitamin D deficiency. Improved understanding of the detrimental effects of insufficient vitamin D before the appearance of rickets led to a growing interest in these lesser degrees of vitamin D deficiency and diagnosing this prerachitic, subclinical vitamin D deficiency is important for nonskeletal health benefits.

Vitamin D deficiency in adults is defined by most experts as a 25(OH) D level <20 ng/mL, on the basis of functional outcomes of vitamin D such as intestinal absorption of calcium and serum parathyroid hormone levels. A level of 25(OH) D of 21 to 29 ng/mL is considered to be indicative of a relative insufficiency of vitamin D, and a level >30 ng/mL is considered to indicate sufficient vitamin D. Because similar studies of functional outcomes have not been evaluated in children, criteria for defining pediatric vitamin D sufficiency and deficiency have not been clearly defined. Therefore, we elected to use a cutoff point of 20 ng/mL for 25(OH) D to divide the study population into vitamin D sufficient and insufficient subgroups as per guidelines given by US Endocrine society.[2,5]

Prevalence of Vitamin D Deficiency

The mean level for 25(OH) D in our study was 17.49 ng/mL, with a median of 14.7 and a range of <3 to 39.2 ng/mL. 25(OH) D levels were <20 ng/mL in 35 of the 53 subjects (66%). In study done by Johnson MD et al in American children, the mean level for 25(OH)D was 28.8 ng/mL, with a median of 27 and a range of 6.5 to 68.0 ng/mL. 25(OH) D levels were <30 ng/mL in 197 of the 302 subjects (65.2%).[2]

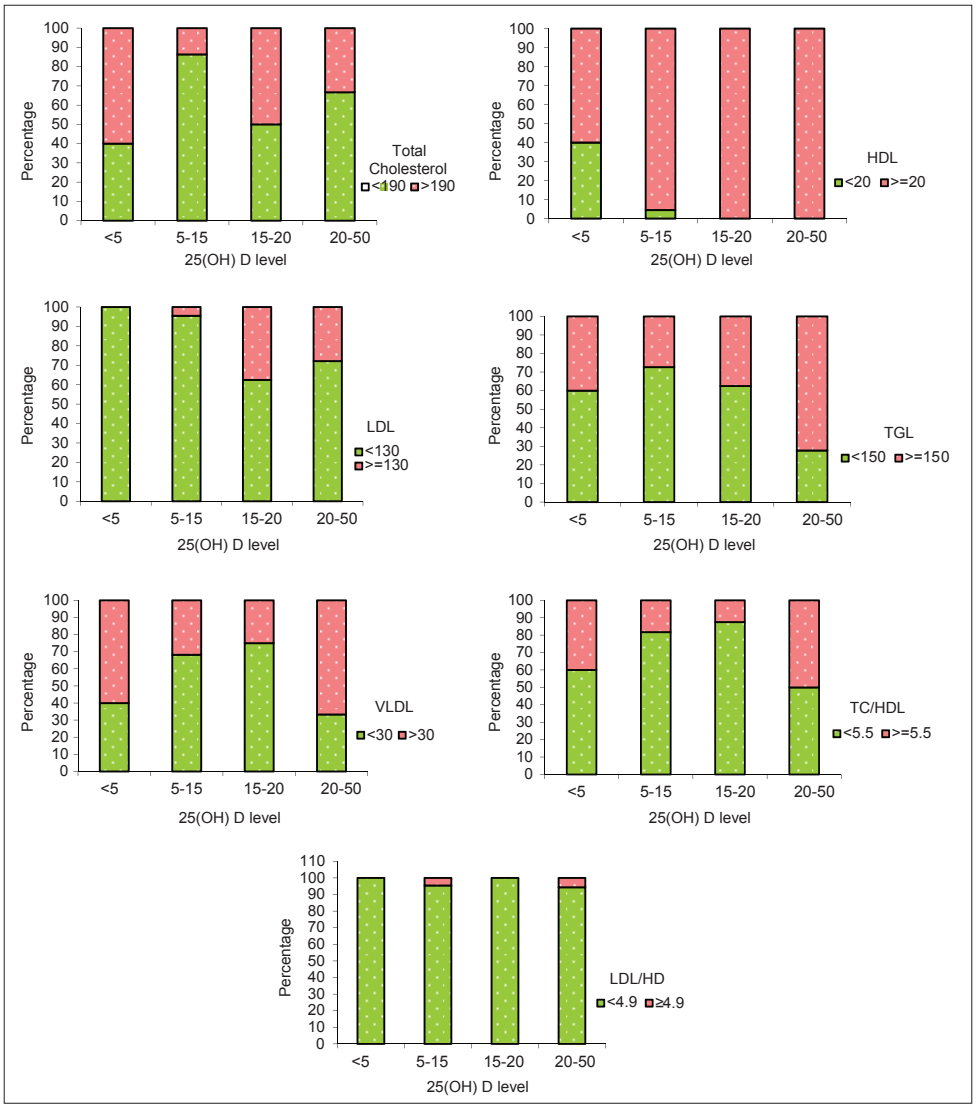
In a study done by Raman MK et al among 290 school girls in Delhi, 93.7% girls were found to be vitamin D deficient.[8]

Study done by Harinarayanan CV et al among 316 children of Andhra Pradesh, 69.3% were found to have vitamin D <20 ng/ml.[9]

Role of Age, Sex and BMI

We could not find any significant relation in vitamin D levels with age, sex and BMI of the patients similar to

Lipids	Cut-offs	25(OH) D level ng/mL				Total (*n*=53)	*P* value
		<5 (*n*=5)	5-15 (*n*=22)	15-20 (*n*=8)	20-50 (*n*=18)		
TC	<190	2 (40%)	19 (86.4%)	4 (50%)	12 (66.7%)	37 (69.8%)	0.088
	>190	3 (60%)	3 (13.6%)	4 (50%)	6 (33.3%)	16 (30.2%)	
HDL	<20	2 (40%)	1 (4.5%)	0 (0%)	0 (0%)	3 (5.7%)	0.005
	≥20	3 (60%)	21 (95.5%)	8 (100%)	18 (100%)	50 (94.3%)	
LDL	<130	5 (100%)	21 (95.5%)	5 (62.5%)	13 (72.2%)	44 (83%)	0.063
	≥130	0 (0%)	1 (4.5%)	3 (37.5%)	5 (27.8%)	9 (17%)	
TGL	<150	3 (60%)	16 (72.7%)	5 (62.5%)	5 (27.8%)	29 (54.7%)	0.038
	≥150	2 (40%)	6 (27.3%)	3 (37.5%)	13 (72.2%)	24 (45.3%)	
TC/HDL	<5.5	3 (60%)	18 (81.8%)	7 (87.5%)	9 (50%)	37 (69.8%)	0.099
	≥5.5	2 (40%)	4 (18.2%)	1 (12.5%)	9 (50%)	16 (30.2%)	
LDL/HDL	<4.9	5 (100%)	21 (95.5%)	8 (100%)	17 (94.4%)	51 (96.2%)	0.872
	≥4.9	0 (0%)	1 (4.5%)	0 (0%)	1 (5.6%)	2 (3.8%)	
VLDL	<30	2 (40.0%)	15 (68.2%)	6 (75.0%)	6 (33.3%)	29 (54.7%)	0.087
	>30	3 (60.0%)	7 (31.8%)	2 (25.0%)	12 (66.7%)	24 (45.3%)	



the study by Johnson MD et al.[2] Abu Shady et al, showed statistically significant inverse association of serum vitamin D with BMI in 215 Egyptian school children but found no significant relation with age and sex.[10]

Vitamin D and FBS

Evidence for low vitamin D status as a risk factor for T2DM has accumulated steadily since calcium was first shown to be necessary for islet insulin secretion and release. Several

lines of evidence support a role for vitamin D in pancreatic beta cell function. Vitamin D receptors are known to be present in pancreatic B-cells. Vitamin D may also have a beneficial effect on insulin action, because vitamin D receptors are present in skeletal muscle. Vitamin D has been demonstrated to increase expression of the insulin receptor in vitro and therefore enhance insulin responsiveness for glucose transport. Vitamin D may also indirectly enhance insulin action by regulating extracellular calcium and thereby affecting calcium influx through cell membranes and maintaining adequate intracellular cytosolic calcium pool.[2]

We found an inverse correlation between 25(OH) D and fasting plasma glucose levels in our population. Although these associations are statistically significant, their clinical significance remains to be determined. Our results are in agreement with observations by several investigators that suggest a link between vitamin D deficiency and alterations in glucose metabolism.

Cross-sectional studies have shown inverse correlations between 25(OH) D levels and fasting plasma glucose values, hemoglobin A1C level and insulin resistance. The association between 25(OH) D levels and plasma glucose levels is likely caused by the effect of vitamin D on both pancreatic beta cell function and insulin sensitivity. Therefore, hypovitaminosis D is a higher risk factor for type 2 diabetes and the metabolic syndrome.[2]

Effects of vitamin D supplementation on glucose homeostasis have been shown in numerous studies. Study done by Talei et al suggested that the insulin resistance appears to be decreased in T2DM patients who had received vitamin D. Inzucchi et al showed a 60% improvement in insulin sensitivity by increased serum 25 (OH)D concentration from 10 to 30 ng/ml, by which metformin or troglitazone were 54% and 13% respectively. Von Hurst (2009) showed that vitamin D supplementation significantly improved insulin sensitivity and insulin resistance. Ken (2004) found an inverse relation between 25(OH)D concentrations and FBS, but a direct relation with insulin sensitivity.[11]

There are some mechanisms for the effects of vitamin D: presence of vitamin D receptors on pancreatic β cells, Vitamin D activating 1α hydroxylase is expressed in pancreatic β cells, presence of vitamin D response element in the insulin gene, presence of vitamin D receptor in skeletal muscle and the fact that 1,25(OH)D increases transcription of insulin receptor genes, and also suppresses the renin gene reducing hyperglycemic-induced increases in renin levels in pancreatic β cells and blockade of renin-angiotensin activity has been proposed as a novel target for diabetes treatment.[11]

Protective effects of vitamin D on diabetes, may be due to well known effects of vitamin D such as its anti-inflammatory properties, its effects on calcium and phosphorus metabolism and regulation of the insulin receptor gene. It seems that vitamin D increases in calcium content of the cells, which in turn leads to increased transport of glucose into the muscle. Vitamin D also regulates nuclear PPAR (Peroxisome proliferative activated receptor) that has an important role in the insulin sensitivity. Vitamin D deficiency is associated with increases in inflammation. It attenuates the expression of proinflammatory cytokines involved in insulin resistance such as interleukins, IL-1, IL-6, TNF-a, also down regulates NF-Kb (Nuclear factor) activity.[11]

Vitamin D and Lipids

In our study, a positive correlation was identified between 25(OH) D levels and HDL level. The relationship between 25(OH) D and the lipid profile has been examined in adults with morbid obesity and in healthy adults. Chiu et al[12] noted a negative correlation between 25(OH) D level and total and low-density lipoprotein cholesterol levels, but did not find relationship between 25(OH) D level and HDL level. The positive association between low 25(OH) D levels and low HDL levels is likely caused by the role of vitamin D in maintaining adequate concentrations of apolipoprotein A-1, the main component in HDL. Decreased concentrations of apolipoprotein A-1 have been reported in adults with hypovitaminosis D[13]. We found that the fasting glucose level was significantly higher and HDL level was significantly lower in the group with vitamin D insufficiency. We have also got a positive association of vitamin D with LDL and TGL which is of lesser significance when compared to that of HDL and FBS and may be due to small sample size.

Study done by Abu Shady et al in 215 Egyptian school children, showed statistically significant inverse association of serum OH vitamin D with BMI, triglyceride, serum cholesterol and LDL-cholesterol and direct association with HDL cholesterol[8]. Xiao Yin et al found among 601 adults of China that 25(OH)D was inversely associated with waist circumference, fasting insulin, triglycerides, fasting glucose, and LDL-cholesterol, positively associated with HDL-cholesterol in a multivariable-adjusted regression model.[14]

Fatih Kardas et al from Turkey conducted a study on 114 obese and healthy children. 25-Hydroxy vitamin D levels were positively correlated with adiponectin and HDL-cholesterol (HDL-C) and inversely correlated with body mass index (BMI), LDL-cholesterol (LDL-C), total cholesterol (T-C), triglyceride (TG), fasting glucose, homeostasis model assessment of insulin resistance (HOMA index), systolic blood pressure (SBP), and diastolic blood pressure (DBP).[15]

John WG et al in their study of British South Asians, showed a positive relation of fasting apo A-I concentrations to serum 25(OH)D concentrations, which is independent of glycemia and other dietary, anthropometric and lifestyle risk factors for type 2 diabetes and ischemic heart disease after multiple regression analyses. Subjects with hypovitaminosis D are likely to have an increased risk of ischemic heart disease independent of their increased risk of type 2 diabetes.[16]

Review of the evidence on hypovitaminosis D as a risk factor for metabolic syndrome and its sequelae, T2DM and CVD, suggests long-term vitamin D repletion could reduce these risks. Much of the studies so far available from randomized controlled trials is weakened by low vitamin D dosages, inadequate power, starting supplementation too late in life or after metabolic syndrome disorders have developed or most importantly by not including of many recognizable confounders. On balance, therefore, maintenance of recommended intakes for bone protection has the potential to prove protective for metabolic syndrome. Supplementation has been shown to increase survival in patients with cardiac disorders, whether higher doses would provide useful protection for apparently healthy people in the general population awaits the outcomes of ongoing randomized-controlled trials that, it is hoped, will prove or disprove causality for hypovitaminosis D in metabolic syndrome and its ill-effects.

RECOMMENDATIONS

There is a need to target high risk groups such as pregnant women and the rapidly growing child. Vitamin D supplementation can be given relatively easily in the form of a 'children's multi-vitamin' supplement. Vitamin D2 (ergocalciferol) or D3 (choleclalciferol) should be provided to pregnant women. We should all be made aware of the need for calcium containing foods and the beneficial role of sunlight. Exposing to sun rays is an effective way of enhancing vitamin D status. Children who are not exposed to sunlight should be supplemented with oral vitamin D and vitamin D rich foods such as oily fish and cod liver oil.

This study has some limitations like lack of information on calcium and vitamin D intake and sunshine exposure of the subjects and the seasonal changes in vitamin D levels. We did not account for parathyroid hormone (PTH) levels. PTH levels may play a role for the effect of VDD. However, effects of PTH levels on metabolic syndrome still remains a controversy as the previous results have been inconsistent. Another limitation is the lack of information on factors influencing glucose and lipid levels such as socioeconomic status, physical activity and family history of diabetes mellitus. The data in this study were derived from a heterogeneous group of children and adolescents coming to pediatric outpatient clinics for various reasons, and therefore the results may not mirror results that might be found in healthy children and adolescents without symptoms.

However, the strengths of the associations found in our study population suggest that prospective interventional trials are needed to determine whether vitamin D replacement impacts glycemic status or lipid levels in healthy children and adolescents or children and adolescents with risk factors for diabetes mellitus and cardiovascular disease.

SUMMARY

It has been suggested that low serum levels of vitamin D may increase insulin resistance and in turn the risk of type 2 diabetes mellitus over time. Our findings relate vitamin D deficiency to dyslipidemia in children and add to the sparse body of literature in this area. We found that children and adolescents with varying levels of vitamin D deficiency had significantly increased risk of dyslipidemia. These findings suggest more aggressive lifestyle and dietary interventions with vitamin D supplementation to reduce the risk of dyslipidemia in high risk children. In this study, high vitamin D levels were positively associated with high HDL levels implicating the role of vitamin D in evolution of metabolic syndrome and cardiovascular diseases as vitamin D deficiency predisposes to low level of protective HDL levels.

CONCLUSION

There is a high prevalence of vitamin D deficiency even in countries receiving abundant sunshine like India. Growing evidence supports a physiologic role for vitamin D in many chronic diseases, in addition to known effects on bone. In children, further studies are needed to determine the optimal circulating concentration of 25(OH)D, and the effects of a given 25(OH)D on various organs. Knowledge gaps also exist regarding the potential physiologic impact of vitamin D deficiency in childhood on health outcomes throughout the lifespan. Vitamin D supplementation is inversely associated with insulin resistance and some cardiometabolic risk factors. Use of Vitamin D supplementation may have beneficial effects in controlling some complications of childhood obesity. Low vitamin D level in children and adolescents are associated with higher plasma glucose and lower HDL concentrations.

The results of this study may not mirror the results that might be found in healthy children and adolescents as the data in this study were derived from a heterogeneous of children and adolescents coming to out-patient clinics for various reasons. However, the strength of the associations

found in our study population suggest that prospective interventional trials are needed to determine whether vitamin D replacement impacts glycemic status or lipid levels in healthy children and adolescents or children with risk factors for diabetes mellitus and cardiovascular diseases. Sensitizing pediatricians to recognize and treat this pandemic would have great impact on child health in the 21st century. Given the high worldwide prevalence of vitamin D deficiency, well-designed outcomes studies in children are urgently needed to address these research priorities.

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How to cite this article: N C Shivaprakash, Ranjit Baby Joseph. "To Study the Relationships between Serum 25-Hydroxy Vitamin D Levels and Plasma Glucose and Lipid Levels in Pediatric Patients in a Rural Hospital". International Journal of Scientific Study. 2014;1(4):24-31.

Source of Support: Nil, **Conflict of Interest:** None declared.