



## A STUDY OF ASSOCIATION OF VITAMIN D WITH SERUM LIPIDS IN PATIENTS WITH TYPE 2 DIABETES

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**ABSTRACT** Vitamin D deficiency is an emerging health problem that affects approximately one billion people worldwide . Recent evidence suggests that Hypovitaminosis D is common in patients with Type 2 Diabetes mellitus. Vitamin D has direct and indirect effects on insulin secretion, beta cell function and insulin resistance. The most common cause of death in type 2 diabetics is due to deficiency and cardiovascular disease is via it's effect on regulation of lipid profile. Vitamin D deficiency may be a neglected cardiovascular risk factor in patients with Type 2 Diabetes . We are thereby studying the association of vitamin D deficiency with serum lipids in type 2 diabetics.

**KEYWORDS :** Hypovitaminosis D, Diabetes mellitus, lipid profile

### INTRODUCTION

Type 2 diabetes mellitus is a growing global health problem. The highest prevalence rates of type 2 diabetes mellitus are found in developing countries<sup>1</sup>. Diabetes has evolved into the status of potential epidemic in India. WHO states that diabetes will be the seventh leading cause of death in 2030<sup>2</sup>.

Vitamin D is a fat soluble vitamin that functions as a steroid hormone and can be obtained from the diet or from endogenous sources in the skin with exposure to ( UV-B ) ultraviolet B light. Vitamin D nutritional status is best determined through the measurement of Calcidiol or 25-hydroxy vitamin D than Calcitriol , because it is the main circulating form, has a long half life of 2 to 3 weeks and concentrations of calcitriol may be maintained even in instance of vitamin D insufficiency. Serum 25 hydroxy vitamin D is accepted as a functional indicator of an individual's vitamin D status.

Vitamin D deficiency is an emerging health problem that affects approximately one billion people worldwide<sup>3</sup>. Recent evidence suggests that Hypovitaminosis D is common in patients with Type 2 Diabetes mellitus<sup>4</sup>. Vitamin D has direct and indirect effects on insulin secretion, beta cell function and insulin resistance<sup>5,6</sup>. In recent years, many studies have highlighted the association between reduced 25 hydroxy vitamin D levels and type 2 Diabetes as well as Insulin resistance, Obesity and Metabolic syndrome<sup>7,8</sup>. The most common cause of death in type 2 diabetics is due to cardiovascular disease . One of the proposed mechanisms for the relationship between vitamin D deficiency and cardiovascular disease is via it's effect on regulation of lipid profile..

It is known that Insulin resistance is associated with a specific lipid pattern, so called "Lipid triad", characterized by increased levels of triglycerides(TG) ,low levels of high density lipoproteins (HDL) and increased levels of low density lipoproteins (LDL) which is associated with increased atherogenic risk<sup>9</sup>. Vitamin D deficiency is associated with this lipid pattern<sup>10</sup>. Vitamin D deficiency may be a neglected cardiovascular risk factor in patients with Type 2 Diabetes . With this background, we want to study the association of vitamin D deficiency with serum lipids in type 2 diabetics.

### AIM AND OBJECTIVES:

The prime objective of our study is to determine the association between serum levels of Calcidiol or 25- Hydroxy vitamin D and serum lipids in men and women (>30yrs) with type 2 diabetes mellitus of at least one year duration.

### MATERIALS AND METHODS:

50 known Type 2 diabetic op patients under treatment with oral antidiabetic drugs who attended to GIMSR hospital were included for the study.

#### Inclusion criteria:

Patients with confirmed diagnosis of type 2 diabetes with a duration of at least one year , including both men and women aged >30 years were included.

Patients under treatment with oral antidiabetic drugs (OADs) and Patients with no prior use of vitamin D containing preparations.

#### Exclusion criteria:

- Conditions interfering with bioavailability of vitamin D like malabsorption, liver cirrhosis, renal failure , administration of anticonvulsants or corticosteroids ,statins , known case of hypo or hyper thyroidism and known case of hypo or hyper parathyroidism.

Pregnant and lactating women

#### Study design:

A cross – sectional study design on 50 known type 2 diabetics of at least one year duration who attended to GIMSR hospital on outpatient basis was conducted.

The study was conducted from January to august 2017. The study design was approved by Institutional ethics committee.

5 ml of peripheral blood was withdrawn after overnight fasting for 12 hours after taking informed consent from all participants.

Data was collected through detailed history taking of all subjects.

- Blood samples were centrifuged at 3000 rpm for 10 minutes and stored at -20° C.
- Fasting blood sugar (FBS), Glycated hemoglobin (HbA1c) , lipid profile i.e Total cholesterol, HDL-C, LDL-C, Triglycerides and VLDL concentrations were estimated in the serum samples using enzymatic kits ,reagents and standards in ROCHE cobas c311 analyser
- VLDL was calculated as Total cholesterol – ( HDL+LDL).
- Serum levels of 25 – hydroxy vitamin D were measured using chemiluminescence immunoassay on ROCHE cobas e 411

instrument<sup>11</sup>.

- All the subjects were categorized into three groups based on 25 – hydroxy vitamin D levels according to recent Endocrine society clinical practice guideline on evaluation, treatment and prevention of vitamin D deficiency published on July 2011<sup>12</sup>.

First group was vitamin D deficient group whose 25- hydroxy vitamin D level was <=20 ng/ml.

Second group was vitamin D insufficient group whose 25- hydroxy vitamin D level was between 20.1 to 30 ng/ml.

Third group was having normal levels of 25- hydroxy vitamin D i.e > 30 ng/ml.

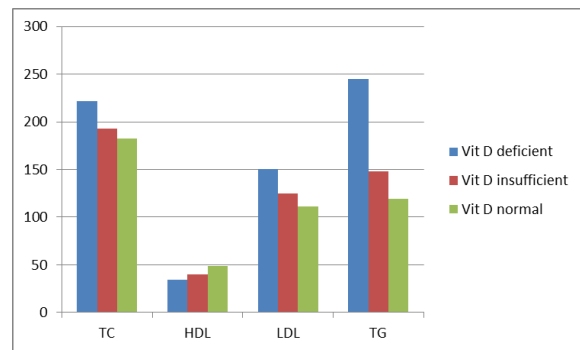
**Results and observations:**

- The statistics of variables will be present in titre of mean +/- SD.
- Vitamin D level was categorised into three categories of Deficient, Insufficient and Normal.
- The means of Fasting blood sugar, Glycated haemoglobin and Lipid profile for the vitamin D groups were compared by one way ANOVA test and P values less than 0.05 were considered to be statistically significant.
- Our study group had 50 participants out of which 20 were men and 30 were female patients. 54% of total were vitamin D deficient , 24% of them were vitamin D insufficient and 22% of participants were having normal levels of vitamin D.

**Table 1 : Statistics of variables when categorized by vitamin D levels**

Variables	Vit D Deficient (n=27)	Vit D Insufficient (n=12)	Vit D Normal (n=11)
	Mean+/-SD	Mean+/-SD	Mean+/-SD
AGE (yrs)	50.08 +/- 3.63	52.62 +/-11.25	53.45 +/- 9.81
FBS mg/dl	213.76+/-43.48	187.92 +/- 37.72	165.55 +/- 22.21
HBA1C %	8.74+/-1.38	6.75 +/- 1.22	5.95 +/- 0.63
Total Cholesterol(TC) mg/dl	221.69 +/- 33.62	192.67 +/- 30.08	182.09 +/- 22.21
HDL mg/dl	33.90 +/-9.70	40.25 +/- 4.77	48.36 +/- 4.01
LDL mg/dl	150.03 +/- 42.02	124.50 +/- 24.12	110.91 +/- 17.04
VLDL mg/dl	38.59 +/-23.96	27.92 +/- 8.95	22.64 +/- 3.75
Triglycerides ( TG) mg/dl	245.00 +/- 66.63	147.92 +/- 20.86	119.00 +/- 19.18

**Figure 1: Comparison of lipid profile among three groups**



**Table 2: ANOVA**

	F-value	P value
FBS	6.670	0.003
HbA <sub>1c</sub> (%)	25.320	0.001
TC mg/dl	8.180	0.001
TGL mg/dl	30.000	0.001
LDL mg/dl	5.930	0.005
VLDL mg/dl	3.430	0.040
HDL mg/dl	13.860	0.001

**Table 3 : Pearson’s correlation of vitamin D with HbA1c and Lipid profile**

		HbA <sub>1c</sub> (%)	TC mg/dl	TGL mg/dl	LDL mg/dl	HDL mg/dl
vitamin D ng/ml	Pearson correlation r	-0.66	-0.45	-0.66	-0.39	0.53
	P value	0.000	0.001	0.000	0.004	0.000

The means of lipid profile among three groups were compared as shown in figure 1. This shows that TC, LDL and TG levels were high in vitamin D deficient group compared to Vitamin D insufficient and normal groups . HDL levels were low in vitamin D deficient group compared to vitamin D insufficient and normal groups.

We compared the means of all dependant variables of three groups by one way ANOVA and there was a statistically significant difference between three groups for HbA1C and all the lipoprotein variables as given by F and P value in table 2.

Table 3 shows the pearson correlation coefficient r value and significance in terms of p value between vitamin D and HbA1C and lipid profile.

HbA1C , TC ,LDL, TGL are negatively correlated with vitamin D .

HDL is positively correlated with vitamin D .

**Discussion:**

The association of vitamin D with other parameters were as follows:

**25 hydroxy vitamin D and HbA<sub>1c</sub> :** The mean of HbA<sub>1c</sub> was significantly high in vitamin D deficient group compared with the vitamin D insufficient and sufficient group as shown in table 1 and table 2 . There is significant negative correlation between vitamin D and HbA1c in our study as shown in table 3. This correlated with the study of P. Josephine latha et al<sup>13</sup> , Kostoglou et al<sup>14</sup> and Zoppini G et al<sup>15</sup> .

**25 hydroxy vitamin D and total cholesterol:**

The mean of TC was significantly high in vitamin D deficient group compared with the vitamin D insufficient and sufficient group as shown in figure 1 and table 1,2 . There is significant negative correlation between vitamin D and total cholesterol in our study as shown in table 3. This correlated with the study of Jaydip Ray chauderi et al<sup>16</sup> , Karhapaa et al<sup>17</sup> , Auwerx et al<sup>18</sup> , martins et al<sup>19</sup> and similar findings were detected in Korean adults<sup>20</sup> .

The mechanism of association of low levels of vitamin D with cholesterol in humans is not clearly known. It is probably due to photometabolism that in the presence of sunlight, the squalene in the exposed skin is converted into 7 –dehydrocholesterol, vitamin D and it's metabolites. In the absence of sunlight, the metabolic pathway is diverted into the formation of cholesterol<sup>21</sup> .

**25 hydroxy vitamin D and LDL:**

The mean of LDL was significantly high in vitamin D deficient group compared with the vitamin D insufficient and sufficient group as shown in figure 1 and table 1,2 . There is significant negative correlation between vitamin D and LDL in our study as shown in table 3 .Low levels of vitamin D are associated with increased levels of LDL which correlated with the study of Auwerx et al<sup>18</sup> , martins et al<sup>19</sup> and similar findings were detected in Korean adults<sup>20</sup> .

**25 hydroxy vitamin D and Triglycerides :**

The mean of TG was significantly high in vitamin D deficient group compared with the vitamin D insufficient and sufficient group as shown in figure 1 and table 1,2 . There is significant negative correlation between vitamin D and triglycerides in our study as shown in table 3. Low levels of vitamin D are associated with increased levels of triglycerides which correlated with the study of Ahmad saedisomeolia et al<sup>22</sup> , Martins et al<sup>19</sup> , Cigolini et al<sup>23</sup> and Hypponen et al<sup>24</sup> .

There are two main mechanisms for vitamin D mediated reduction in serum triglycerides. Firstly, vitamin D increases serum calcium by enhancing intestinal serum calcium absorption. This calcium reduces serum triglycerides by reducing hepatic triglyceride formation and secretion<sup>20</sup>. Second mechanism is that vitamin D has a suppressive effect on serum PTH concentration. Low serum PTH may reduce serum triglycerides via increased peripheral removal<sup>25</sup>.

## 25 hydroxy vitamin D and HDL:

The mean of HDL was significantly low in vitamin D deficient group compared with the vitamin D insufficient and sufficient group as shown in figure 1 and table 1,2. There is significant positive correlation between vitamin D and HDL in our study as shown in table 3. Low levels of vitamin D are associated with low levels of HDL which correlated with the study of Auwerx et al<sup>18</sup>, Choi et al<sup>20</sup>.

## CONCLUSIONS:

- Our study has established an association of 25 hydroxy vitamin D deficiency with serum lipids in type 2 diabetics under treatment with oral hypoglycemic drugs..
- Though this association is emerging clearly whether the supplementation of vitamin D can reduce the risk of cardiovascular disease is unclear.
- More interventional studies have to be done to draw conclusions regarding the effect of supplementation of vitamin D on lipid profile in type 2 diabetics.

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