

## VITAMIN D LEVELS AND DIABETIC MICROVASCULAR COMPLICATIONS

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### ABSTRACT:

**Background:** Vitamin D deficiency is related to glucose intolerance and type 2 diabetes mellitus. Microvascular complications are common in patients of type 2 diabetes. To see the effect of long term type 2 diabetes microvascular complications on vitamin D levels. **Methods:** This observational study was conducted in patients; coming to department of endocrinology of either sex and age of type 2 diabetes in tertiary care teaching hospital. Finally diagnosed cases with microvascular complications either one or two or all the three in single patient were analyzed. Levels of 25(OH) D<sub>3</sub> and HbA1c were measured by Chemiluminescence method. Chi square test, Student's *t* test and ANOVA were used to analyse the data. **Results:** The mean age of all patients in our study was 55.9.2 ±12.6 years. Mean duration of diabetes in patients was 7.4±4.02. Out of the 250 type 2 diabetics cases 54 (21.6%) had no microvascular complication. Single microvascular complications (retinopathy or neuropathy or nephropathy) was present in 83 (33.20%) of cases, while the combination of two was present in 67 (26.80%) and all three in 46 (18.40%) of cases. Mean Vitamin D level was found 21.03±2.61 in patients of no complication. Mean Vitamin D level further decreased in patients of single complications; nephropathy (19.18±2.13), retinopathy (18.49±2.53) and neuropathy (18.11±1.97). Mean Vitamin D level (16.22±1.02) was found lowest in patients of all three microvascular complications. **Conclusion:** Mean vitamin D levels are decreased in all patients of microvascular complications and as the severity or numbers of microvascular complications increase; mean vitamin D levels further decrease.

**Key words:** Vitamin D, Diabetes, microvascular complications, HbA1c, Chemiluminescence method.

### INTRODUCTION:

Diabetes mellitus is a chronic metabolic disorder characterized by defective insulin secretion, resistance to insulin action, or a combination of

both, leads to altered metabolism of carbohydrates, protein, lipids and an increased risk of vascular complications.<sup>1,2</sup> Diabetes can

affect many different organ systems in the body and, over time, can lead to serious complications which lead to significant cause of increased morbidity and mortality among people with diabetes. Complications from diabetes can be classified as microvascular or macrovascular which are due to hyperglycaemia.<sup>3</sup> Vitamin D deficiency is widely prevalent across all ages, races, geographical regions, and socioeconomic strata. In animals it has been demonstrated that the secretion of pancreatic insulin is inhibited by vitamin D deficiency<sup>4</sup> and that in humans vitamin D deficiency is related to glucose intolerance and type 2 diabetes mellitus.<sup>5,6</sup> Multiple pleiotropic functions have been shown by vitamin D and it has involved in the pathogenesis of various microvascular complications which is found in type 2 diabetes mellitus; like diabetic retinopathy, neuropathy and nephropathy. Neuropathy is the most common microvascular complication in diabetes mellitus, around 50% diabetics suffering with neuropathy in their 20 year of diabetic history<sup>7,8</sup>; while its replacement with vitamin D re-establishes these abnormalities.<sup>9</sup> It has been suggested that vitamin D deficiency be defined as a 25(OH) D<sub>3</sub> below 20 ngm/ mL, insufficiency as a 25 (OH) D<sub>3</sub> of 21-29 ngm/mL, and sufficiency as a 25 (OH) D<sub>3</sub> of 30-100 ngm/mL.<sup>10</sup> So, various studies have been conducted to show the association of low level of Vitamin D and type 2 diabetes. This study was planned to see the effect of long term type 2 diabetes microvascular complications on vitamin D levels.

## MATERIALS & METHODS:

The present observational study was conducted in department of biochemistry at tertiary care

teaching hospital after approval from institutional ethics committee. The study was conducted over a period of one year. In this study all patients coming to department of endocrinology of either sex and age of type 2 diabetes were included. All patients were screened in respective department for associated microvascular complications (neuropathy, nephropathy and retinopathy) by complete physical examination, microfilament test, nerve conduction velocity, detailed fundus examination, ultrasonography of the abdomen and other investigations. Finally diagnosed cases with microvascular complications either one or two or all the three in single patient were analyzed. Informed consent was taken from all the patients. 25(OH) D<sub>3</sub> and HbA1c levels were measured in all patients of type 2 diabetes mellitus. All the patients included in the study were on treatment with diet and oral antidiabetic drugs. Levels of 25(OH) D<sub>3</sub> and HbA1c were measured by Chemiluminescence method which is one of the more advanced, accurate and fully automated method of detection of biochemical parameter in the biological fluids.

Statistical evaluation was performed using suitable tests like Chi square test, Student's *t* test and ANOVA.

## RESULTS:

Total 250 type 2 diabetic patients were randomly selected who came to endocrinology department during the study period and finally 196 patients were analyzed who were having complication either alone or in combination. The patients were from 22 years to 89 years age. The mean age of all patients in our study was  $55.9.2 \pm 12.6$  years. Men and women were almost equal in number (51.4 % male, 48.6% female). Mean duration of

diabetes in patients was 7.4+4.02. Out of the 250 type 2 diabetics cases; 54 (21.6%) had no microvascular complication.

**Table 1: Diabetic microvascular complications and mean vitamin D levels**

Diabetic Complications	No of cases (N=250)	Mean vitamin D levels (ngm/dl )	P value
<b>No complication</b>	54	21.03±2.61	p<0.01*
<b>Nephropathy</b>	29	19.18±2.13	
<b>Retinopathy</b>	26	18.49±2.53	
<b>Neuropathy</b>	28	18.11±1.97	
<b>Nephropathy+ Neuropathy</b>	21	17.10±3.10	
<b>Retinopathy+Neuropathy</b>	24	17.24±2.22	
<b>Nephropathy+ Retinopathy</b>	22	17.90±1.37	
<b>Nephropathy+ Retinopathy+Neuropathy</b>	46	16.22±1.02	

\*Significant difference

Single microvascular complications (retinopathy or neuropathy or nephropathy) was present in 83 (33.20%) of cases, while the combination of two was present in 67 (26.80%) and all three in 46 (18.40%) of cases. (Table 1)

Mean Vitamin D level was found 21.03±2.61 in patients of no complication.

**Table 2: Comparison between mean vitamin D levels among patients of single microvascular complication**

Diabetic Complications	No of cases (N=83)	Mean vitamin D levels (ngm/dl)	P value
<b>Nephropathy</b>	29	19.18±2.13	p>0.05
<b>Retinopathy</b>	26	18.49±2.53	
<b>Neuropathy</b>	28	18.11±1.97	

Mean Vitamin D level further decreased in patients of single complications; nephropathy (19.18±2.13), retinopathy (18.49±2.53) and neuropathy (18.11±1.97).

No significance difference was found in level of Vitamin D among patients of single complications. (Table 2)

Mean Vitamin D level further decreased in patients of double complications as compared to single complications. There was no significance difference found in level of Vitamin D among patients of double complications. (Table 3)

Mean Vitamin D level (16.22±1.02) was found lowest in patients of all complications. There was significance difference in mean Vitamin D value of uncomplicated, single, double and all three complications. (Table 1)

Mean HbA1c of 196 cases of diabetic complication was found to be 8.9%. It was 7.4% in cases who were not having complication.

**Table 3: Comparison between mean vitamin D levels among patients of two microvascular complications**

Diabetic Complications	No of cases (N=67)	Mean vitamin D levels (ngm/dl)	P value
Nephropathy+	21	17.10±3.	
Neuropathy		10	p>0.05
Retinopathy+Neuropathy	24	17.24±2.22	
Nephropathy+Retinopathy	22	17.90±1.37	

## DISCUSSION:

Vitamin D plays various nonskeletal functions in our body systems by regulating different genes.<sup>11,12</sup> There are various evidences that suggest; giving vitamin D to people might help with insulin resistance and so with diabetes. Recent data suggests vitamin D and calcium as modifiers of diabetes risk because they play role in insulin release. So deficiency of Vitamin D and altered calcium homeostasis may also play a role in the development of type 2 diabetes mellitus.<sup>13-15</sup> This could be cheap, safe, effective solution for diabetes patients and also to prevent development of diabetic complications.

In our study mean age of all patients of diabetes was 55.9.2 ±12.6 years. Similar age group was also reported by other studies.<sup>16,17</sup> Men and women were also found equal in number. According to the Centers for Disease Control and Prevention (CDC) in 2012 adults aged 45 to 64 were the most diagnosed age group for diabetes.

In present study prevalence of diabetic microvascular complication in type 2 was found to be 79.4 % in all patients of diabetes who were recruited. Mean duration of diabetes in these patients was 7.4+4.02 years. Study done by Bajaj et al had reported 74.05% prevalence of microvascular complications in their study.<sup>18</sup> This high percentage of complications could be because as the mean duration of diabetes increases; the complications in diabetes patients are also increasing and our hospital is a tertiary care hospital where many referral cases come in specialized endocrinology department.

Mean vitamin D level was found less than 30 ngm/dl which shows that in patients of diabetes mean vitamin D level is decreased. Similar results have been reported by various studies.<sup>19,20</sup> One follow up study done by Gagnon et al had shown lower vitamin D levels in diabetes patients as compared with patients without diabetes.<sup>21</sup> This proves that low level of Vitamin D is common in diabetic patients.

Mean vitamin D level was found significantly less in patients of diabetes with microvascular complications as compared to patients without complications. It was found less than 20 ngm/dl in all patients of complications. This suggests that hypovitaminosis D is more prevalent in diabetics with microvascular complications as compared to patients of diabetics without complications.

In our study mean vitamin D level was significantly less in patients of multiple or all three microvascular complications as compared to single (retinopathy or neuropathy or nephropathy) and two complications (Nephropathy+Neuropathy or Retinopathy+Neuropathy or Nephropathy+Retinopathy). Similar results were also reported

by Bajaj et al study.<sup>18</sup> Patients of two microvascular complications were having significantly lower levels of vitamin D as compared to single complication. There was no significance difference found in levels of vitamin D among patients of single complication or double complications. This shows that as the number of microvascular complications increases; mean vitamin D levels are also inversely decreases. Other studies have also reported that as the severity or numbers of microvascular complications increases in diabetes, mean vitamin D levels are also decreased.<sup>19,20,22</sup>

Mean HbA1c was also found 8.9% in patients of microvascular complications. Various other studies have also reported more than 7% of HbA1c in patients of diabetes complications.<sup>17</sup> This could be because of patients with type 2 diabetes and elevated HbA1c concentrations are at increased risk of complications as compared with patients with lower HbA1c levels.<sup>23</sup>

### **CONCLUSION:**

This study shows that mean vitamin D levels are decreased in all patients of microvascular complications and as the severity or numbers of microvascular complications increase; mean vitamin D levels further decrease.

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