Original article

Prevalence of vitamin D deficiency in type 2 diabetics and its association with glycemic control

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ABSTRACT

Background: Optimal glycaemic control in type 2 diabetics is of utmost importance in preventing the complications of diabetes which lead to increased morbidity and mortality related to the disease. Some studies have shown that vitamin D deficiency was prevalent in type 2 diabetic patients and was associated with poor glycaemic control. This study aimed to determine the vitamin D3 levels in type 2 diabetic patients and its association with glycaemic control.

Patients and methods: This cross sectional study was carried out in the outdoor department of Medical Unit II of Sir Ganga Ram Hospital/Fatima Jinnah Medical University Lahore from Feb 10, 2019 to May 9, 2019. A total of 45 cases of type 2 diabetes mellitus were enrolled in this study after taking informed consent from them. Demographic details (name, age, gender, including duration of diabetes) were obtained and blood sample were taken for HbA1c and 25-OH vitamin D3 levels. Vitamin D deficiency was diagnosed by taking serum level <20 ng/mL as cut off. The data analysis was carried out in SPSS version 20. Quantitative variables like age and duration of diabetics were taken as mean and standard deviation. Qualitative variables, gender and vitamin D3 levels and HbA1c levels were taken as percentage. Post stratification chi-square test was applied taking p-value <0.05 as significant.

Results: Out of 45 patients, 17 (37.78%) were male and 28 (62.2%) were female. Mean age was 49.56 ± 10.77 years. Mean duration of diabetes was 5.91 ± 3.74 years. Mean vitamin D levels were 36.36±17.9 ng/ml. Out of 45 patients, 7 (15.6%) were found deficient, 10 (22.2%) insufficient, 27 (60%) sufficient and 1 (2.2%) had vitamin D toxicity. Among the patients with sufficient vitamin D levels, 12 (44.4%) were male and 15 (55.5%) were female. Two (16.6%) male patients with sufficient vitamin D levels had good glycemic control as compared to none of the female patients. Two (16.6%) male and 2 (13.3%) female patients with sufficient vitamin D had fair HbA1c. Most of the patients had poor control of HbA1c despite sufficient vitamin D levels including 8 (66.6%) males and 13 (86.6%) females. Mean HbA1c concentration was 9.3±1.66%. Out of 45 patients, 2 (4.4%) had good glycaemic control, 5 (11.11%) had fair and 38 (84.4%) had poor control. It was seen that out of 7 vitamin D deficient, 6 (85.7%) had poor glycemic control, 1 (14.3%) had fair and none had good glycaemic control. The post stratification chi-square test was applied to determine the significant association between vitamin D levels and HbA1c and showed a p-value of 0.196 which is statistically insignificant. The Pearson correlation revealed a value of -0.012 which shows a negative correlation between vitamin D and HbA1c levels.

Conclusions: No statistical significance could be established between vitamin D deficiency and poor glycemic control. There is a weak negative correlation between vitamin D and HbA1c levels showing that low Vitamin D levels are associated with higher HbA1c concentration.

Keywords:

Type 2 Diabetes Mellitus, Vitamin D levels, HbA1c concentration

INTRODUCTION

Diabetes mellitus affects nearly 463 million adults which is expected to increase to around 700 million by 2040.[1] The proportion of type 2 diabetics (T2D) is increasing in most countries. In the UK, the prevalence is around 5.26% whereas in Saudi Arabia it is 33% and is expected to increase.[2] The prevalence of T2D in Pakistan is 16.98%, highest (26.05%) in the age group of 51-60 years according to a population-based survey.[3] Optimal glycaemic control in T2D is of utmost importance in preventing the development of complications of diabetes which lead to increased morbidity and mortality in these patients. There is a significant association between poor glycaemic control and gender; females being more affected. The duration of disease and type of medication used for control are also important along with lifestyle and socioeconomic factors and level of education.[4] In a previous study it was suggested that vitamin D deficiency was prevalent

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in T2D patients and was associated with poor glycaemic control.[5] Similar results have been reported from Pakistan that levels of vitamin D less than 20 ng/ml was significant in patients with poor glycaemic control as compared to people with good control (30.6%).[6] Vitamin D deficiency in adults or osteomalacia is prevalent all over the world with a study in India quoting it as between 40-99%[7] and as 58.17% in Pakistan; 26.65% had insufficient levels of this important vitamin.[8] Another study from Pakistan showed that 63.4% is deficient and only 21.8% had normal levels.[9] Manifestations of vitamin D deficiency can range from bone pains to a poorly responsive immune system. Consequences of long-term deficiency can result in obesity, hypertension, psoriasis and osteoporosis. It predisposes patients to Alzheimer's disease and malignancies and also to develop T2D.[6,10] This study has been conducted at a tertiary care hospital in Central Punjab to establish an association between poor glycaemic control in T2D with deficient levels of vitamin D. Detection of low levels of vitamin D early on in the disease will allow to take appropriate steps to replace the deficient vitamin and hence improve the control of diabetes.

PATIENTS AND METHODS

A cross sectional study was carried out in OPD of Medical Unit II Sir Ganga Ram Hospital/Fatima Jinnah Medical University Lahore for a period of 3 months from 10-2-2019 to 9-5-2019 after approval by the Institutional Ethical Review Committee. A sample size of 45 patients with type 2 diabetes mellitus was calculated with a 95% Confidence Interval and 5% margin of error taking expected percentage of T2D as 10% presenting in OPD of a tertiary care hospital of Lahore using non-probability, consecutive sampling technique. The study included all the diabetic patients presenting to the diabetic clinic in a tertiary care hospital except those who had type 1 diabetes, gestational diabetes, HONK/DKA, rickets, osteomalacia, chronic liver disease, chronic kidney disease, hyperparathyroidism and those on vitamin D supplements. Demographic details were documented, blood sample was taken and stored in vials and was sent for HbA1c analysis and 25-OH vitamin D3 levels. Vitamin D deficiency was diagnosed when its serum level was <20 ng/mL. It was considered insufficient for levels of 21-30 ng/mL with sufficiency being 31-100 ng/mL, whereas values >100 ng/ml represented toxicity. Glycemic control status was considered Good when HbA1c level was 5.5–6.8%, fair control being 6.9-7.6% while poor control as >7.6%. The data analysis was carried out in SPSS version 20. Quantitative variables like age and duration of diabetes were taken as mean and standard deviation. Qualitative variables, gender and vitamin D3 levels and HbA1c levels were taken as percentage. Data stratified with respect to gender and duration of diabetes. Post stratification Chi Square test was applied to determine association between vitamin D levels and HbA1c taking p value <0.05 as significant. Pearson correlation was applied to determine correlation between vitamin D and HbA1c levels.

RESULTS

Out of 45 patients, 17(37.78%) were male and 28 (62.2%) were female. Mean age was 49.56 ± 10.77 years (range 24 to 75 years). Mean duration of diabetes was 5.91 ± 3.74 years (range 2 months to 15 years). Mean vitamin D levels was 36.36 ± 17.9 ng/ml (range 10.42–116.64 ng/ml); 36.72 ± 12.42ng/ml in males and 36.15±36 ng/ml in females. Out of 45 patients, 7 (15.6%) were found deficient, 10 (22.2%) insufficient, 27 (60%) sufficient and 1 (2.2%) had vitamin D toxicity. Among 27 patients with sufficient Vitamin D level, 12 (44.4%) were male and 15 (55.5%) were female. Two (16.6%) male patients with sufficient vitamin D levels had good glycemic control as compared to none of the female patients. Out of 45 patients 2 patients were in good control group with mean HbA1c level 31.25 ± 1.77% and mean vitamin D level 6.45 ± 0.77 ng/dl, 5 patients were in fair control group with mean HbA1c level 37.52 ± 13.39% and mean vitamin D level 6.96 ± 0.35ng/dl, 38 patients were in poor control group with mean HbA1c level 36.48 ± 18.98% and mean vitamin D level 9.56 ± 1.44ng/dl. Two (16.6%) male and 2 (13.3%) female patients with sufficient vitamin D had fair HbA1c. 21 patients (45.67%) despite having vitamin D levels in sufficient category had HbA1c level in poor control category that includes 8 (47.06%) males and 13 (46.43%) females. The mean HbA1c concentration in study group was 9.3 ± 1.66% (n=45), minimum HbA1c noted was 5.9 % and maximum was 12.9 %. Mean HbA1c was 8.9% in males (n=17) and 9.2% in females (n=28). The males had a mean HbA1c of 8.9% while females had 9.2%. Out of 45 patients 2 (4.4%) had good glycemic control, 5 (11.11%) had fair and 38 (84.4%) had poor control. It was seen that out of vitamin D deficient, 4 (80%) had poor glycemic control, 1 (20%) had fair and none had good glycemic control. The post stratification chi-square test showed a p-value of 0.196 which is statistically insignificant. Table 1 shows HbA1c control in relation to vitamin D

Table 1. HbA1c control in relation to vitamin D deficiency

Vitamin D3 levels	HBA1c grade			
	Good control	Fair control	Poor control	Total
	n	*n*	*n*	*n*
Deficient	0	1	6	7
Insufficient	0	0	10	10
Sufficient	2	4	21	27
Toxic	0	0	1	1
Total	2	5	38	45

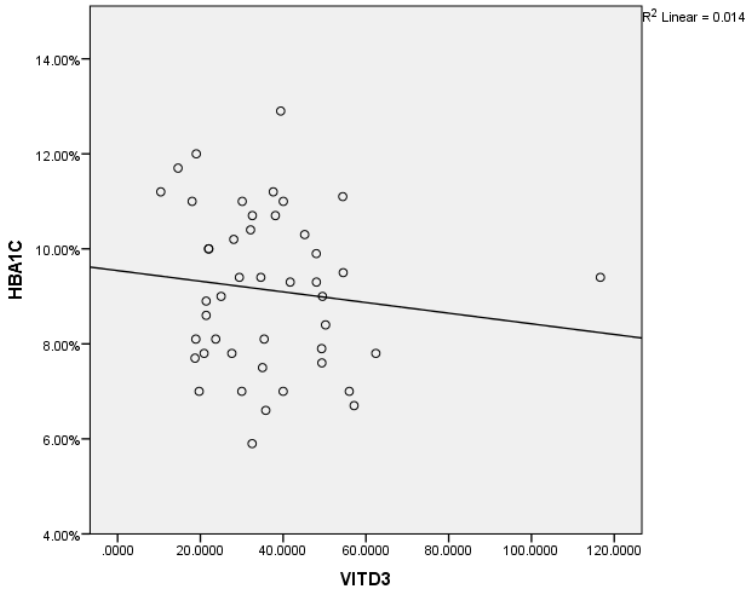

Figure 1. Correlation between Vitamin D3 and HbA1c

levels in male and female patients.

Pearson correlation showed a value of -0.012 which depicts a negative correlation between Vitamin D and HbA1c levels. Figure1 shows a negative correlation between vitamin D levels and HbA1c concentration in patients with type 2 diabetes mellitus, showing that the lower the Vitamin D levels, the higher HbA1c and poor diabetes control.

DISCUSSION

Previous systemic review and meta-analysis of cross sectional and longitudinal studies found significant inverse relationship of vitamin D status with glycemic level in both diabetic (p-value = 0.000) and non-diabetic (p-value = 0.000) subjects.[10] It concluded that hypovitaminosis D is associated with increased risk of hyperglycemia both in diabetic and non-diabetic subjects however we did not find statistically significant relationship in our population may be due to small study population. A general population cross sectional study from Eastern Finland demonstrated an inverse association between vitamin D levels and fasting insulin, fasting glucose and 2 hours glucose tolerance test glucose results implying that low vitamin D may be associated with impaired glucose metabolism.[11] Heaney and colleagues demonstrated an inverse association of insulin resistance with vitamin D levels which was principally found at vitamin levels between 16 and 36 ng/ml.[12] It has been demonstrated that low vitamin D ingestion can be related with a higher risk for the development of T2D and metabolic syndrome.[13,14] Pittas and coworkers conducted a nested case-control study among 608 women with newly diagnosed T2D, higher vitamin D levels were associated with lower risk of T2D in women.[15] While in present study it was poorly correlated with control of diabetes as only 13.3% of female patients had fair HbA1c control, while most of them i.e. 86% had poor glycemic control and none of the study patients had good control at all. This may be due to small sample size in this study. In another prospective study conducted by Pittas and coauthors with 2.7 years mean follow up, higher vitamin D was repeatedly assessed and was associated with lower risk of incident diabetes in high-risk patients.[16] As present study was a snapshot study and only one vitamin D levels was assessed so this comparison cannot be

Table 2. Gender wise statistical correlation (p-value) of glycaemic control with vitamin D levels

Vitamin D levels	HbA1c grades				p-value
	Good control *n*	Fair control *n*	Poor control *n*	Total *n*	
Males					
Deficient	0	0	1	1	0.703
Insufficient	0	0	4	4	
Sufficient	2	2	8	12	
Toxic	0	0	0	0	
Females					
Deficient	0	1	5	6	0.76
Insufficient	0	0	6	6	
Sufficient	0	2	13	15	
Toxic	0	0	1	1	

established. In a prospective study in high risk Asian subjects, vitamin deficiency was associated with a higher risk for the development of T2D mellitus.[17] Kayaniyil and colleagues in a longitudinal study of the determinants of insulin resistance and metabolic syndrome observed a significant inverse association of baseline vitamin D with fasting glucose at follow up.[18] Schöttker and coworkers conducted a large cohort study of older adults involving 7791 subjects who were initially diabetes-free, serum vitamin D levels were inversely associated with incident diabetes in females but not in males.[18,19] Karau and associates conducted a study on long-term follow-up for 151 patients of T2D in Kenya and found a high prevalence of vitamin D deficiency i.e. 38.4% and 21.9 % had insufficient vitamin D levels as compared to our study where 22.2% were deficient which is quite lower than the Kenya population but 15.6% had insufficient levels which is comparable with above study population.[20] Study conducted by Iqbal and colleagues in Pakistan also shows very high levels of vitamin D deficiency among their study group was i.e. 58.7% which is almost three times than in our study.[21] This also demonstrates the variability of data among our Pakistani population where in our study 60% of patient had sufficient vitamin D levels as compare to Iqbal et al study showing almost equal but deficient vitamin D population i.e. 58.7% in same country but in different cities. Furthermore, one of our patients had Vitamin D toxicity. The high prevalence of sufficient vitamin D levels with a single toxic level in local study population may indirectly reflect possible adequate or increased intake of vitamin D supplements. There was significant inverse correlation between vitamin D and glycaemic control (p-value = 0.044) in a Kenyan study.[20] Pakistani population study by Iqbal and coauthors demonstrated vitamin D deficiency was significantly higher in patients with poor glycaemic control compared to patients with good glycaemic control (58.7% vs. 30.6%; p-value=0.006) while we did not find statistical significance (p=0.196).[21] In present study population, 37.8% patients had low vitamin D levels in the form of either insufficient (22.2%) or deficient (15.7%) levels. Interestingly 60% of study population had a sufficient level of vitamin D. Out of total study population, 38 (84.4%) had poor control of diabetes. It was seen that out of vitamin D deficient population, 4 (80%) had poor glycemic control, 1 (20%) had fair and none had good glycemic control which was in conjunction with our study hypothesis though the p-value for this relationship was not significant. While no statistical significance could be established between vitamin D deficiency and poor glycemic control in current study, the study was limited by small sample size and there was no control group for comparison with demographically matched non-diabetic healthy individuals. Some of the patients had diabetes for a short duration. Further studies with a larger population group can help in defining this relationship better. In addition, the impact of vitamin D replacement on improving glycemic control should also be studied to establish the potential relationship.

CONCLUSION

In this study most patient were found to have sufficient vitamin D levels. No statistical significance could be established between vitamin D deficiency and poor glycemic control; however our study was limited by small sample size.

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