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Evaluating Correlation of Glycosylated Hemoglobin and Vitamin D Levels in Diabetic patients: A cross-sectional study from a tertiary care hospital in Delhi

[1]Dr. Adwaita Gahlot, Department of Pathology, Vardhman Mahavir Medical College and Safdurjung Hospital, Ansari Nagar, New Delhi, Delhi 110029

[1]Dr. Sufian Zaheer, Department of Pathology, Vardhman Mahavir Medical College and Safdurjung Hospital, Ansari Nagar, New Delhi, Delhi 110029

[2]Dr. Mayank Kapur, Department of Respiratory Medicine, Vardhman Mahavir Medical College and Safdurjung Hospital, Ansari Nagar, New Delhi, Delhi 110029

Corresponding Author: Dr. Adwaita Gahlot, Department of Pathology, Vardhman Mahavir Medical College and Safdurjung Hospital, Ansari Nagar, New Delhi, Delhi 110029

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Abstract

Introduction: Previous studies show that vitamin D is implicated in the pathogenesis of diabetic complications. The present study was conducted to assess vitamin D levels among diabetic patients and to correlate these levels with glycosylated haemoglobin (HbA1c).

Methodology: In the present cross-sectional study, diabetic patients who reported poor glycemic control and had HbA1c levels higher than 6% were included. Quantitative analysis of HbA1c and serum 25(OH) D3 levels was done. Clinical records of all patients were thoroughly reviewed for the presence of the microvascular and macrovascular complications.

Results: Of the 105 patients included during the study period, HbA1c levels ranged from 6 to 13.5%, with a mean of 8.54 ± 1.63%. Vitamin D levels ranged from 5.7 to 26.2 ng/dl in our patient population, with a mean of 18.32 ± 4.35 ng/dl. We observed that 56.2% had vitamin D deficiency (< 20 ng/dl), and rest of the 43.8% had vitamin D insufficiency (20 to 30 ng/dl). None of the patients had normal vitamin D levels (>30 ng/dl). Lastly, we assessed correlation of HbA1c with vitamin D levels and found that there was no significant correlation between these two variables (r = 0.17, p value = 0.067). Duration of diabetes mellitus was, however, found to be significantly correlated with the vitamin D levels (r = 0.21, p value < 0.05).

Conclusions: In our population, duration of diabetes correlated significantly with the vitamin D levels, though HbA1c levels were not significantly correlated. Future studies with larger and more diverse populations will help us in bringing more clarity to this contested issue.

Keywords: Diabetic mellitus, Glycosylated hemoglobin, Vitamin D

Introduction

In India, it is estimated that 61.3 million people aged 20-79 years live with diabetes and it is also expected that this number will rise to 101.2 million by 2030. Though the diagnosis of diabetes mellitus is based mainly on glucose tolerance testing, a lot of interest in estimating glycated hemoglobin (HbA1c) levels, a modified hemoglobin molecule with a stable adduct of glucose that is covalently linked to the N-terminal valine of the beta chain. There are various advantages of HbA1c over traditional glucose

testing because it is independent of last meal, has low variability and shows greater consistency in reflecting glucose levels over the last 8-12 weeks. This helps the clinician in understanding how effective their current treatment is in controlling glucose levels in their patient.Vitamin D has important actions on glucose metabolism. These include improved insulin exocytosis, direct stimulation of insulin receptor, improved uptake of glucose by peripheral tissues, improving insulin resistance. Various studies have demonstrated that vitamin D has pleiotropic effects such as suppression of cell mediated immunity, regulation of cell proliferation, stimulation of neurotropic factors like nerve growth factor, Glial cell line-derived neurotrophic factor, neurotropin, reduction of albuminuria, immune-modulatory, anti-inflammatory and anti-angiogenic effects. As a result, via these mechanisms vitamin D is implicated in the pathogenesis of diabetic complications.Some studies have revealed a higher likelihood of progression of prediabetes to diabetes among Vitamin D deficient subjects. A meta-analysis by Song et al reported a beneficial effect of vitamin D on preventing the onset of diabetes. Despite this, the potential benefits of vitamin D supplementation on glycemic control are still debated. The present study was conducted to assess vitamin D levels among diabetic patients and to correlate these levels with HbA1c.

Methodology

Study Design and Sampling: In the present cross-sectional study, patients with an established diagnosis of type 2 diabetes mellitus and visiting the outpatient clinic of a tertiary level care teaching hospital for follow up during the period of January 2020 till March 2020 were included. Only those patients were included who reported poor glycemic control and had HbA1c levels higher than 6%. We excluded patients who had parathyroid disease, were taking vitamin D or calcium supplementation and were pregnant. The study was approved by the Institutional Ethics Committee. All the patients were explained the purpose of the study and an informed written consent was obtained from them.

Data Collection and Data Analysis: Using a pre-designed semi-structured questionnaire patient related data were recorded. Demographic information like age and gender were noted. Smoking history and duration of diabetes mellitus was enquired. After 12 hours fasting, 10 ml of blood was taken from all patients for quantitative analysis of HbA1c and serum 25(OH) D3 levels. HbA1c was measured using high-performance liquid chromatograph and vitamin D levels using competitive protein-binding assay using appropriate kits. HbA1c levels till 6.5% were considered to be within normal limits. Serum vitamin D3 levels were graded as deficiency (<20ng/dl), insufficiency (20 to 30 ng/dl) and normal (> 30 ng/dl). Clinical records of all patients were thoroughly reviewed for the presence of the following complications:

Microvascular complications

1. Neuropathy: Based on clinical diagnosis using modified Neuropathy Disability Score (NDS).
2. Nephropathy: Albuminuria was assessed with immunological visual testing strips for semi quantitative determination of microalbuminuria.
3. Retinopathy: Based on fundus examination. Optic fundi were examined by consultant ophthalmologist, and graded according to International Classification of Diabetic Retinopathy.

Macrovascular Complications

1. Coronary Artery Disease (CAD): Diagnosed by history of myocardial infarction or angina, documented by previous treatment records or by ECG or by 2D Echo.
2. Cerebrovascular Disease (CVD): Diagnosed by history, clinical examination and CT or MRI findings.

3. Peripheral Arterial disease (PAD): Considered to be present if there is definitive history of intermittent claudication and one or more of peripheral pulses is absent in both feet or ankle brachial index < 0.8 by Doppler study.

Continuous variables are represented as mean ± SD and percentages. Pearson correlation coefficients between HbA1c and vitamin D levels were used as a measure of association. The data obtained were statistically analysed using SPSS version 23.0. The significance level for results was set as $p < 0.05$.

Results

In the present study 105 patients were included during the study period. The mean age of the patients was 48.94 ± 12.76 years and majority of them were from 30 to 60 years age group (65.7%). Females comprised 59% of the study population. Approximately half of them had a history of smoking (Table 1). The mean duration of diabetes mellitus in our patient population was 27.22 months. Duration of diabetes mellitus was up to 2 years in 51.5% of the cases, while 23.8% had diabetes mellitus for a duration of between 2 to 5 years and rest of the 24.7% of the patients had diabetes for more than 5 years.

HbA1c levels ranged from 6 to 13.5%, with a mean of 8.54 ± 1.63%. There were only 10 patients (9.5%) who had HbA1c up to the recommended level of 6.5% (Table 2). Vitamin D levels ranged from 5.7 to 26.2 ng/dl in our patient population, with a mean of 18.32 ± 4.35 ng/dl. We observed that 56.2% had vitamin D deficiency (< 20 ng/dl), and rest of the 43.8% had vitamin D insufficiency (20 to 30 ng/dl). None of the patients had normal vitamin D levels (>30 ng/dl). Furthermore, in our patient population, microvascular complications like neuropathy, nephropathy and retinopathy were present in 5.7%, 8.6% and 9.5% of the patients respectively. Macro-vascular complications like CAD and CVD were found in 8.6% and 1% of the patients respectively. Lastly, we assessed correlation of HbA1c with vitamin D levels and found that there was no significant correlation between these two variables ($r = 0.17$, p value = 0.067). Duration of diabetes mellitus was, however, found to be significantly correlated with the vitamin D levels ($r = 0.21$, p value < 0.05) (Table 3 and Figure 1).

Discussion

Diabetes mellitus, especially type 2 diabetes, is a major public health problem1 and is a significant contributor to non-communicable diseases-related morbidity and mortality in India. The present study was conducted to understand the relationship of vitamin D with HbA1c among patients with type 2 diabetes mellitus. Despite being a sub-tropical country with majority of the seasons with full sunlight, vitamin D deficiency was observed in 56.2% and insufficiency in rest of our patients. We observed that microvascular complications like neuropathy, nephropathy and retinopathy were present in 5.7%, 8.6% and 9.5% of the patients respectively and macro-vascular complications like CAD and CVD were found in 8.6% and 1% of the patients respectively. A meta-analysis performed by Iannuzzo et al found that PAD patients have lower vitamin D levels than controls and both vitamin D deficiency and vitamin D insufficiency are significantly associated with PAD. Though not clearly understood, possible mechanisms by which vitamin D could play a role in arterial diseases is by first, vitamin D has been shown to play a vital role in the renin-angiotensin-aldosterone system pathway. Second, vitamin D improves endothelial functioning. The association of serum vitamin D and peripheral neuropathy has also been suggested. A meta-analysis performed by Qu et al. found Asian type 2 diabetic patients with vitamin D deficiency are 1.22 times to suffer from DPN compared with normal vitamin D levels.Using Pearson's correlation,

we observed that HbA1c levels and vitamin D levels were not found to be significantly correlated (r = 0.17, p value = 0.067). Ghavam et al conducted a cross-sectional study to assess HbA1C and vitamin D serum levels and determining the serum level of vitamin D in diabetic patients. The authors reported that Pearson's correlation coefficient test indicated an inverse linear relationship between vitamin D with HbA1C ($p < 0.37$), FBS (0.64), BMI ($p < 0.59$), and disease duration ($p < 0.1$); the relationship was not statistically significant. This is in contrast to the study by Danaei et al, who reported a significant negative relationship has been reported between serum level of vitamin D and HbA1C. Buhary et al conducted a study to examine the association between serum 25-hydroxyvitamin D (25(OH)D) and HbA1c levels, to test the hypothesis that lower 25(OH) D levels are associated with poorer glucose control in diabetes mellitus (DM) patients and to investigate the effect of vitamin D supplementation on HbA1c levels. The authors found that there was an inverse correlation between serum 25(OH) vitamin D and HbA1c ($r = -0.14$, $P < 0.01$) before as well as after vitamin D supplementation. Furthermore, this finding stood true for patients with different levels of severity of vitamin D. Results of our study also show that duration of diabetes mellitus was significantly correlated with vitamin D levels. Ghavam et al, however, reported no significant relationship between diabetes duration and vitamin D ($P < 0.1$ and $r = 0.164$).There are a few limitations of this study. First, we included only those patients who had HbA1c 6% or higher, which can introduce selection bias. Furthermore, the study site is a tertiary care academic referral centre, and this potentially introduces more selection bias. In addition, the diagnosis of various clinical complications were noted from the medical records and not it is possible complications in some of the patients might have been missed. Lastly, no control group or intervention was used in the present study. Future studies are needed which include a control group and assesses the role of vitamin D supplementation in lowering HbA1c levels in diabetic patients.

Conclusion

Given the high prevalence of vitamin D deficiency in diabetic patients, its supplementation can be suggested. However, we need more studies to assess its effectiveness. As for the role of vitamin D in affecting HbA1c levels, the debate continues. Although, in our study, the duration of diabetes significantly correlated with the vitamin D levels, HbA1c levels were not significantly correlated. Future studies with larger and more diverse populations will help us in bringing more clarity to this contested issue.

Table 1: Baseline characteristics of the patients included in the study (n=105)

Variables	**N**	**%**
Age group (in years)		
Up to 30	12	11.4
> 30 to 60	69	65.7
> 60	24	22.9
Gender		
Female	62	59
Male	43	41
Smoking history		
Yes	52	49.5
No	53	50.5
Duration of diabetes mellitus (in years)		
Up to 2 years	54	51.5
2 to 5 years	25	23.8
> 5 years	26	24.7

Table 2: Describing biochemical and complications of diabetes mellitus

Variables	N	%
HbA1c		
Up to 6.5	10	9.5
More than 6.5	95	90.5
Vitamin D levels (ng/dl)		
Up to 20	59	56.2
> 20 to 30	46	43.8
> 30	0	0
Microvascular complications		
Neuropathy	6	5.7
Nephropathy	9	8.6
Retinopathy	10	9.5
Macro vascular complications		
Coronary Artery Disease	9	8.6
Cerebrovascular Disease	1	1
Peripheral Artery Disease	0	0

Table 3: Correlation of vitamin D with HbA1c levels in our study population of diabetes mellitus

Variables	Statistical analysis	Vitamin D level
HbA1c	Pearson Correlation	0.179
	Sig. (2-tailed)	0.067
	N	105
Duration of diabetes mellitus	Pearson Correlation	0.218
	Sig. (2-tailed)	< 0.05
	N	105

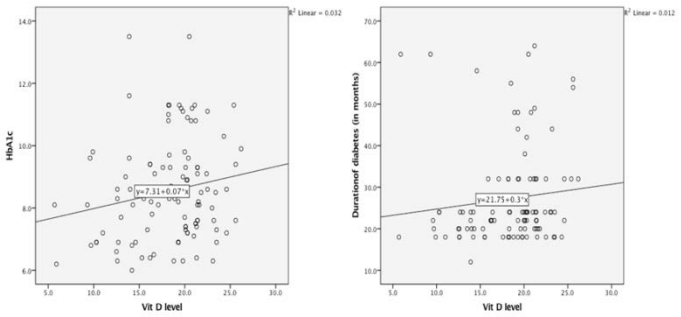

Figure 1: Scatter plots showing correlation of serum vitamin D levels with HbA1c and disease duration

References

1. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 2011;94:311-21.
2. D'Embden M. Glycated haemoglobin for the diagnosis of diabetes. Australian Prescriber.2014;37(3):98-100.
3. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J Clin Endocrinol Metab. 2007;92(6):2017-2029.
4. Mitri J, Dawson-Hughes B, Hu FB, Pittas AG. Effects of vitamin D and calcium supplementation on pancreatic β cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: The Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. Am J Clin Nutr. 2011;94:486–94
5. Zhang Y, Deb DK, Kong J, Ning G, Wang Y, Li G, et al. Long-term therapeutic effect of vitamin D analog doxercalciferol on diabetic nephropathy: Strong synergism with AT1 receptor antagonist. Am J Physiol Renal Physiol. 2009;297:F791–801.
6. Deleskog A, Hilding A, Brismar K, Hamsten A, Efendic S, Östenson CG. Low serum 25-hydroxyvitamin D level predicts progression to type 2 diabetes in individuals with prediabetes but not with

normal glucose tolerance. Diabetologia. 2012 Jun 1;55(6):1668-78.

7. Song Y, Wang L, Pittas AG, Del Gobbo LC, Zhang C, Manson JE, et al. Blood 25-hydroxy vitamin D levels and incident type 2 diabetes: a meta-analysis of prospective studies. Diabetes Care. 2013;36:1422-8.
8. Iannuzzo G, Forte F, Lupoli R, Di Minno MN. Association of Vitamin D deficiency with peripheral arterial disease: a meta-analysis of literature studies. The Journal of Clinical Endocrinology & Metabolism. 2018 Jun;103(6):2107-15.
9. Kaur H, Donaghue KC, Chan AK, Benitez-Aguirre P, Hing S, Lloyd M, et al. Vitamin D deficiency is associated with retinopathy in children and adolescents with type 1 diabetes. Diabetes Care. 2011;34:1400–2
10. Chaychi L, Mackenzie T, Bilotta D, Lynch M, Cohen J, Comi R. Association of serum vitamin D level with diabetic polyneuropathy. Med Practise Rev Feb. 2011;2:11–5.
11. Qu GB, Wang LL, Tang X, et al. The association between vitamin D level and diabetic peripheral neuropathy in patients with type 2 diabetes mellitus: an update systematic review and meta-analysis. J Clin Transl Endocrinol. 2017;9:25–31.
12. Ghavam S, Ahmadi MR, Panah AD, Kazeminezhad B. Evaluation of HbA1C and serum levels of vitamin D in diabetic patients. Journal of family medicine and primary care. 2018 Nov;7(6):1314.
13. Danaei N, Tamadon M, Monsan M. Evaluation of diabetes control and some related factors in patients of diabetes clinic of semnan fatemieh hospital. Komesh 2004;6:31-6.
14. Buhary BM, Almohareb O, Aljohani N, Alrajhi S, Elkaissi S, Sherbeeni S, Almaghamsi A, Khan SA, Almalki MH. Association of glycosylated hemoglobin levels with vitamin D status. Journal of clinical medicine research. 2017 Dec;9(12):1013

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