Study showing the assessment with correlation of 25-hydroxy Vitamin D and HbA1c in type 2 Diabetes Mellitus

Authors
Dr Garima Sehgal\(^1\), Dr Tejinder Singh\(^2\)
Department of Biochemistry, Government Medical College, Amritsar
Corresponding Author
Dr Tejinder Singh
Department of Biochemistry, Government Medical College, Amritsar

Abstract
Background: Vitamin D deficiency reportedly is associated with type 2 diabetes (T2DM). We aim to examine whether 25-hydroxyvitamin D (25OHD) has clinically significant influence on hemoglobin glycation (HbA1c) in T2DM subjects.

Aim: To assess the serum levels of 25-Hydroxy Vitamin D and HbA1c as well as to study the correlation of these parameters in Known Patients of type 2 Diabetes Mellitus.

Material and Methods: This hospital-based study was conducted on 45 diagnosed type 2 Diabetes mellitus patients and 25 non-diabetic age and gender matched controls. Blood samples were collected in plain vial as well as EDTA vial and serum 25-hydroxy vitamin D levels and HbA1c were evaluated. Results were collected and analyzed statistically.

Results: Vitamin D deficiency was seen in 35.6% and 32.6% of T2DM cases and control subjects respectively. There was no association of serum 25OHD deficiency on HbA1c in Type 2 Diabetes Mellitus patients with r value of -0.171 and -0.237 in study and control group respectively.

Conclusion: Our findings suggest that though vitamin D deficiency is prevalent in T2DM and non-diabetic subjects, its role in hemoglobin glycation could not be established.

Keywords: Diabetes, Vitamin D, HbA1c.

Introduction
Type 2 Diabetes Mellitus (T2DM) is the commonly seen endocrine disorder characterized by hyperglycemia.\(^{[1]}\) The International Diabetes Federation (IDF) estimates around 61.3 million diabetic individuals (2011) in India that is further set to increase to 101.2 million with a global estimate of 552 million by the year 2030.\(^{[2]}\) There are several factors that seem to play a role in its development including genetic, lifestyle, environmental and nutritional conditions. Amongst nutritional factors, vitamin D is likely to have an important role either in glycemic control or in attenuating diabetic complications.\(^{[3,4]}\) The probable mechanisms indicating the role of vitamin D in glucose homeostasis is likely to be through beta cell dysfunction and insulin resistance in cases with vitamin D deficiency.\(^{[5,6]}\) A negative correlation between serum glucose and insulin levels with 25OHD and a positive correlation with insulin sensitivity has been observed in several human and animal model studies.\(^{[6-8]}\) It has also been observed that vitamin D supplementation can improve insulin secretion and reduce insulin resistance in T2DM and non-diabetic subjects.\(^{[7]}\) Thus, accumulating the
evidence from several studies, vitamin D is likely to have a role in T2DM and Hb-glycation.\[9\] Hence, present study was proposed to examine the association of vitamin D (25OHD) levels with HbA1c along with evaluating the serum levels of 25-Hydroxy Vitamin D in Type 2 Diabetes Mellitus patients.

**Material and Methods**

A Hospital based cross-sectional study was carried out in Department of Biochemistry, Rajindra Hospital Patiala on 70 subject including 45 diagnosed cases of type-2 diabetes mellitus and 25 healthy age and gender matched subjects as control. Our study, 25-Hydroxyvitamin D and glycosylated haemoglobin levels were evaluated in 45 cases and 25 controls. Prior Permission from ethical committee was taken.

**Inclusion Criteria** included Patients of type II diabetes mellitus on diet modification /or oral hypoglycemic agents treatment and Patients aged between 35-80 years.

**Exclusion Criteria** included Insulin therapy, Consumption of Vitamin D or Calcium, Renal failure, nephrotic syndrome Liver disorder with Ascites, Hypoalbuminemia, Coagulation disorders and treatment with drugs like Carbamazepine, phenobarbital sodium valproate isoniazid which interfere with Vitamin D metabolism.

Blood sample were collected in plain vial and EDTA vial for estimation of 25-Hydroxy Vitamin D and HbA1c. Serum concentration of 25(OH) D was measured by enzyme linked immunosorbent assay (ELISA) method. Estimation of HbA1c was performed by Ion Exchange method. Vitamin D deficiency was defined as serum 25(OH) D concentration of less than 20ng/ml, insufficiency as 20ng/ml <25(OH) D<30 ng/ml and sufficiency was defined as 25(OH) D higher than 30 ng/ml.\[12\]. HbA1c value interpretation was on the percentage basis with normal or non-diabetic person have Hba1c of 4.2-6.2%, Diabetic person with good control have 5.5-6.8%.Diabetic person but they needed active medication have HbA1c of 6.8-7.6% and person with bad control have > 7.6%. The data were collected and analyzed. To determine correlation between these parameters we used chi square test. A r-value from -1 to 1 was required for two parameters to shows a correlation. A p value of <0.005 was regarded for significance.

**Results**

The general characteristics of the individuals have been described in [Table]. Student t test was used to evaluate the results.

| Parameter                  | Subjects      | Control       | P Value | Significance |
|----------------------------|---------------|---------------|---------|--------------|
| Age                        | 59.60 ± 9.05  | 50.48 ±10.77  | <0.001  | HS           |
| Fasting Blood Sugar        | 145.22±44.37  | 95.72±11.68   | 0.000   | HS           |
| HbA1C                      | 6.86± 0.85    | 5.80 ± 0.66   | 0.000   | HS           |
| 25-hydroxyVitamin D        | 16.31± 14.03  | 26.63 ± 16.54 | <0.007  | S            |

*HS (Highly Significant), S (Significant)
In the study group of diabetes mellitus type 2 patients, 25(OH)D3 levels were lower than in the control group. Mean value of 25(OH)D3 levels being 16.31±14.03 ng/ml and 26.63 ± 16.54 ng/ml in the study and control group, respectively (p <0.007).

In the study group about 16 people with T2DM of 45 (35.6%) were Vitamin D deficient as opposed to 7 of 25 (32.9%) in control non diabetic group.

| Parameter               | STUDY GROUP  | CONTROL GROUP |
|-------------------------|--------------|---------------|
| 25-Hydroxyvitamin D     | 16.31±14.03  | 26.63±16.54   |
| HbA1c                   | 6.86±0.85    | -0.171        |
|                         |              | 5.80±0.66     |
|                         | -0.237       |               |

The r value between 25-hydroxyvitamin D and Hba1c in study group was -0.171 and that of control group was -0.237. So there was no significant association found between these 2 parameters in diabetic patients.

**Discussion**

The increasing incidence of T2DM is taking a great toll of health resources. The diverse effect of vitamin D on glucose and calcium homeostasis has made it an ideal contender to know its role in glycemic control in T2DM. India being a vast tropical country geographically spreading from 8.4° N latitude to 37.6° N latitude, it is expected that sufficient sunlight is received throughout the year. Regardless of this vitamin D deficiency has been observed more commonly in earlier studies from India. The present study has also shown a higher incidence (35.6%) of vitamin D deficiency in overall recruited subjects indicating that both T2DM (91.4%) subjects and non-diabetic control subjects (32.9%) were equally deficient. This is likely to be due to increased skin pigmentation, low exposure to direct sunlight, obesity and malabsorption, as has been observed by several studies from India. Abu et al. have argued by Lo et al. that to meet an adequate requirement of vitamin D, people in India require sun exposure almost double than Caucasians due to increased skin pigmentation. Although in a review by Pittas et al. an association between T2DM and low vitamin-D levels has been demonstrated. Nonetheless, vitamin-D supplementation was not found to be effective in reducing HbA1c as stated by Melville in his news report. Luo et al. also showed that within T2DM subjects, regardless of a common finding of vitamin D deficiency, low vitamin D is associated neither with increased prevalence of the metabolic syndrome, nor is there any association with glycemic control. Several
mechanisms like activation of vitamin D receptor and calcium homeostasis involving impaired pancreatic-β cell function and insulin resistance in T2DM have been suggested.\(^9\) Also a number of studies have shown a consistent inverse association between vitamin D level or vitamin D intake on the incidence of T2DM,\(^3\) but our study could not demonstrate such relationship. Similar observation has been made in studies from New Zealand overweight adult population and British Caucasians demonstrating a weak relationship between HbA1c and vitamin D levels.\(^{17,18}\)

**Limitation**

Firstly we took only one sample in one season for analysis and because of sunshine duration difference in each season level of vitamin D may undulate during the year, so this study cannot predict the condition of hypovitaminosis in this area. In addition, 25(OH)D3 was chosen as a marker of vitamin D deficiency, as currently recommended. However, vitamin D circulates in several forms in the blood and its active form is 1,25(OH)2D3.

**Conclusion**

Though vitamin D deficiency is prevalent in T2DM and non-diabetic control subjects, its relationship in glycation control or insulin resistance in T2DM subjects could not be confirmed in our population. This is potentially an important finding for public health, demonstrating that improvement in vitamin D status is not the only factor responsible for better health of the individuals but lifestyle and dietary changes seem to play a role which will improve the overall health including hemoglobin glycation and insulin resistance along with vitamin D levels.

**Bibliography**

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2009;32:62–7.
2. IDF: One adult in ten will have diabetes by 2030. IDF Press release; 2011.[http://www.idf.org/media_events/press-releases/2011/diabetes-atlas-5th-edition], accessed on 29th August 2014.
3. Pittas AG, Harris SS, Stark PC, Dawson-Hughes B. The effects of calcium and vitamin D supplementation on blood glucose and markers of inflammation in non diabetic adults. Diabetes Care. 2007;30(4):980–6.
4. Pittas AG, Dawson-Hughes B. Vitamin D and Diabetes. J Steroid Biochem Mol Biol. 2010;121(1,2):425–9.
5. Alvarez JA, Ashraf A. Role of vitamin D in insulin secretion and insulin sensitivity for glucose Homeostasis. Int J Endocrinol. 2010;2010:351–85.
6. Heshmat R, Malazy OT, Ahranjani SA, Shahbazi S, Khooshehchin G, Bandarian F, et al. Effect of vitamin D on insulin resistance and anthropometric parameters in Type 2 diabetes; a randomized double-blind clinical trial. DARU J Pharm Sci. 2012;20:10.doi:10.1186/2008-2231-20-10.
7. Talaei A, Mohamadi M, Adgi Z. The effect of vitamin D on insulin resistance in patients with type 2 diabetes. Diabetol Metab Syndr. 2013;5:8. doi:10.1186/1758-5996-5-8.
8. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell function. Am J Clin Nutr. 2004;79:820–5.
9. Pittas A, Lau J, Hu F, Dawson-Hughes B. Review: the role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J Clin Endocrinol Metab. 2007;92:2017–29.
10. Luo C, Wong J, Brown M, Hooper M, Molyneaux L, Yue DK. Hypovitaminosis D in Chinese type 2 diabetes: Lack of impact on clinical metabolic status and biomarkers of cellular inflammation. Diab Vasc Dis Res. 2009;6:194–209.
11. Ritu G, Ajay G. Vitamin D Deficiency in India: Prevalence, Causalities and Interventions. Nutrients. 2014;6:729–75.

12. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28:412–9.

13. Harinarayan CV, Holick MF, Prasad UV. Vitamin D status and sun exposure in India. Dermato-Endocrinol. 2013;5(1):130–41.

14. Harinarayan CV, Joshi SR. Vitamin D status in India-Its implications and Remedial Measures. J Assoc Physicians India. 2009;57:40–8.

15. Lo CW, Paris PW, Holick MF. Indian and Pakistani immigrants have the same capacity as Caucasians to produce vitamin D in response to ultraviolet irradiation. Am J Clin Nutr. 1986;44:683–5.

16. Melville NA. Large Review Casts Cloud Over Vitamin-D Health Benefits. Medscape Medical News. Dec 05, 2013. [http://www.medscape.com/viewarticle/815472], accessed on 27th August 2014.

17. McGill AT, Stewart JM, Lithander FE, Strik CM, Poppitt SD. Relationships of low serum vitamin D3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. Nutr J. 2008;7:4. doi:10.1186/1475-2891-7-4.

18. Hypponen E, Power C. Vitamin D status and glucose homeostasis in the 1958 British birth cohort: the role of obesity. Diabetes Care. 2006;29:2244–6.