

Vitamin D status and its association with diabetes mellitus in population of Udaipur

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Abstract

Studies have shown that Vitamin D is necessary for normal insulin secretion. Vitamin D reduces insulin resistance through regulation of the insulin receptor gene and its effects on calcium and phosphorus metabolism. Therefore, deficiency of vitamin D results in decreased insulin secretion and increased insulin resistance, both of which are characteristics of type 2 Diabetes mellitus. The predisposition of Vitamin D deficiency to Glucose intolerance via altered insulin secretion may be done either through a direct action via Vitamin D receptor (VDR) activation or indirectly via calcemic hormones and also via inflammation. The study is aimed to measure and correlate Vitamin D status with serum level of fasting and postprandial Glucose, Total Cholesterol and Triacylglycerol level in individuals of Udaipur. The study was carried out on total 300 vegetarian subjects, out of which 190 were females and 110 were males with an average age of 54.25 ± 8.94 years. Subjects were divided into two categories depending upon their serum total Vitamin D value. Category A included subjects with total Vitamin D value below 10 ng/ml and category B included subjects with total Vitamin D value between 30-70 ng/ml. The subjects with total Vitamin D value between 10-30 ng/ml were excluded from the study. Results clearly indicated that Category A with Vitamin D value below 10 ng/ml had significantly higher serum fasting, post prandial Glucose, Total Cholesterol and Triacylglycerol level as compared to subjects with Vitamin D value between 30-70 ng/ml (category B) with significance (p value < 0.05). Vitamin D deficiency can lead to dysregulation of Glucose and lipid metabolism. Supplementation of Vitamin D in Vitamin D deficient individuals may reduce the risk of Diabetes mellitus and dyslipidaemia by improving insulin secretion and Glucose tolerance.

Keywords: Vitamin D, Insulin Resistance, Dyslipidaemia, Type 2 Diabetes mellitus

Introduction

Diabetes has been diagnosed in more than 62 million individuals in India. This gives a potential epidemic status to this disease.^(1,2) Prevalence of Diabetes is predicted to double globally with the figures jumping from 171 million in 2000 to 366 million in 2030, with a significant increase in India,^(3,4) estimated to reach approximately 80 million by the year 2030.⁽⁵⁾ In this way India is facing threefold rise in the diabetic prevalence in rural as well as urban areas.^(6,7) Its prevalence is rapidly increasing in both developing and developed countries. After cancer and cardiovascular disease, diabetes is regarded as the 3rd killer of mankind because of its high prevalence, morbidity and mortality.^(8,9) Diabetes mellitus is characterized by hyperglycaemia, metabolic abnormalities and long term complications that affect eyes, kidneys, nerves and blood vessels.⁽¹⁰⁾

Vitamin D is a part of complex steroid hormone system. There are two forms of vitamin D, Vitamin D3 (Cholecalciferol), produced from the conversion of 7-dehydrocholesterol in skin and Vitamin D2 (Ergocalciferol), produced in mushrooms and yeast. The major circulating form of Vitamin D is 25-hydroxycholecalciferol with low biological activity. The biologically active form of Vitamin D is 1, 25 dihydroxycholecalciferol. The nutritional status of Vitamin D is reflected by the concentration of serum 25-hydroxycholecalciferol. Besides its classical actions such as calcium balance and bone metabolism, it plays a key role in non-classical actions like promoting

insulin action and secretion, immune modulation and lung development.⁽¹¹⁻¹⁷⁾ Many studies have shown that Vitamin D is necessary for normal insulin secretion. Vitamin D reduces insulin resistance through regulation of the insulin receptor gene and its effects on calcium and phosphorus metabolism. Therefore, deficiency of vitamin D results in decreased insulin secretion and increased insulin resistance, both of which are characteristics of type 2 Diabetes mellitus. The predisposition of Vitamin D deficiency to Glucose intolerance via altered insulin secretion may be done either through a direct action via Vitamin D receptor (VDR) activation or indirectly via calcemic hormones and also via inflammation.⁽¹⁸⁾ There are studies indicating relationship between type 2 diabetes and subclinical inflammation.⁽¹⁹⁾ The immune-modulating properties of 1, 25-Dihydroxycholecalciferol are responsible for facilitating the correlation between Vitamin D, low-intensity chronic inflammation and insulin resistance in type 2 diabetes by downregulating the production of pro-inflammatory cytokines (20). Considering the above facts, the present study will focus on the effect of total serum Vitamin D status on fasting Glucose, post prandial Glucose, Total Cholesterol and Triacylglycerol in population of Udaipur.

Materials and Methods

The study was conducted on 300 vegetarian subjects, out of which 190 were females and 110 males with an average age of 54.25 ± 8.94 years. The informed

consent was taken before study and statistical significance was calculated by using p value with confidence limit of 95%.

The following criteria were used for exclusion:

1. Muslim women following purdah system
2. Pregnant women
3. Patients suffering from hepatic, renal and cardiac disorders
4. Cancer Patients
5. Diabetic Patients
6. Subjects taking Vitamin D supplements

The study was conducted from April 2016 to August 2016 at Arth Diagnostics Private Limited, Udaipur. The blood of the subjects were collected after an overnight fast of at least ten hours. The blood was collected in plain vial for estimating serum Total Vitamin D, Total Cholesterol and Triacylglycerol. For estimating fasting Glucose blood was collected in fluoride vial. For analysis of post-prandial Glucose blood samples were collected in a fluoride vial exactly after two hours once the subjects were orally administered 75 grams of Glucose, dissolved in water. The serum was obtained by centrifugation, separated into aliquot and analysed. The analysis of total Vitamin D was done by Elecsys, Chemiluminescence method (Competitive protein binding assay) on Cobas e411 (Roche). The estimation of fasting and post prandial Glucose, Total Cholesterol and Triacylglycerol was done on Fully Autoanalyser of Roche, Cobas Integra 400 Plus.

The laboratory reference range for serum total Vitamin D below 10 ng/ml is considered as deficiency, 10-30 ng/ml is insufficiency and levels between 30-70 ng/ml is optimum. The normal range of serum fasting, post prandial Glucose, Total Cholesterol and Triacyl glycerol is respectively 70-110 mg/dl, 70-140 mg/dl, 100-250 mg/dl and 60-150 mg/dl respectively.

Results

Subjects were divided into two categories depending upon their serum total Vitamin D value. Category A included subjects with total Vitamin D value below 10 ng/ml and category B included subjects with total Vitamin D value between 30-70 ng/ml. The values are shown in Table 1 as below:

Table 1: Correlation of Vitamin D with biochemical parameters

Name of Parameter	Category A (Vit D less than 10ng/ml)	Category B (Vit D 30-70ng/ml)	p Value
	Mean±SD	Mean±SD	
Total Vitamin D ng/ml	5.53±3.81	48.74±11.02	< 0.05
Fasting Glucose mg/dl	103.63±9.76	89.63±7.42	< 0.05
Post Prandial Glucose mg/dl	137.33±6.58	108.54±5.49	< 0.05

Total Cholesterol mg/dl	211.95±35.37	148.62±27.3	< 0.05
Triacyl glycerol mg/dl	98.8±26.45	155.36±50.2	< 0.05

Discussion

Deficient levels of Vitamin D may cause predisposition of type 2 Diabetes mellitus. Results clearly indicated that Category A with Vitamin D value below 10 ng/ml had significantly higher serum fasting, post prandial Glucose, Total Cholesterol and Triacylglycerol level as compared to subjects with Vitamin D value between 30-70 ng/ml (category B) with significance (p value <0.05). This study revealed an inverse relationship between total Vitamin D3 and fasting, post prandial Glucose, Total Cholesterol and Triacylglycerol levels. Earlier several studies have also shown similar results with Negative correlation between Vitamin D and Glucose.^(21,22) Inverse relationship was reported in Middle Eastern population.⁽²³⁾ Age dependent inverse relationship between Vitamin D and HbA1C has also been reported in Caucasians.^(24,25) In a study there was association between low level of 25(OH) D3 concentrations and hyper Triacylglycerolemia component of the metabolic syndrome.⁽²⁶⁾ The reciprocal relationship between Vitamin D and serum Total Cholesterol and Triacyl glycerol level is further supported by the study which provides evidence that Vitamin D deficiency was closely associated with increased risk of major adverse cardiovascular disease events.^(27,28) This is further explained that hormonal form of Vitamin D i.e. calcitriol is able to increase the lipoprotein lipase activity in adipocytes resulting in removal of Triacyl glycerol enriched with lipoproteins from the blood.

Adequate levels of Vitamin D is required for optimum functioning of many tissues and organs. The presence of both 1- α -hydroxylase and VDR in pancreatic β cells explains the importance of Vitamin D for insulin synthesis and release.^(29,30) Vitamin D induced impairment of insulin secretion and Glucose tolerance was partially corrected after Vitamin D replenishment in rats.^(31,32) Improvement in insulin secretion and Glucose tolerance as a result of Vitamin D supplementation have been observed by some studies.⁽³³⁻³⁵⁾

Conclusion

This study concludes inverse relationship between Vitamin D and serum Glucose, Total Cholesterol and Triacylglycerol. These effects of Vitamin D are based on its non-classical actions on insulin secretion and sensitivity and also its action in inflammation. Supplementation of Vitamin D in Vitamin D deficient individuals may reduce the risk of Diabetes mellitus and dyslipidaemia by improving insulin secretion and Glucose tolerance.

References

1. Joshi SR, Parikh RM. India- diabetes capital of the world now heading towards hypertension. *J Assoc Physicians India*. 2007;55:323-4.
2. Kumar A, Goel MK, Jain RB, Khanna P, Chaudhary V. India towards diabetes control: Key issues. *Australas Med J*. 2013;6(10):524-31.
3. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes-estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27(3):1047-53.
4. Whiting Guariguata L, Weil C, Shawj. IDF Diabetes atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract*. 2011;94:311-21.
5. Wild S, Roglic G, Green A, Sicree R, King H; Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27(5):1047-1053.
6. Ebrahim S, Kinra S, Bowen L, Andersen E, Ben-Shlomo Y, Lyngdoh T *et al.*; IndianMigration Study Group. The effect of rural-tourban migration on obesity and diabetes inIndia: a cross-sectional study. *PLoS Med.*, 2010;7:e1000268.
7. Agrawal P, Reddy VS, Madaan H, Patra SK, Garg R; Urban-rural differences in atherogenic dyslipidaemia (URDAD Study): A retrospective report on diabetic and non diabetic subjects of northern India. *J Health Popul Nutr.*, 2014;32(3):494-502.
8. Li Y, Xu W, Liao Z; Induction of long term glycemic control in newly diagnosed type 2diabetic patients is associated withimprovement of beta cell function. *Diabetes Care*, 2004;27(11):2597-602.
9. Venkatesh R, Kalaivani K; Lipid profile changes in type 2 diabetes mellitus. *International Journal of Pharmaceutical Research & Development*, 2013;5(7):35-39.
10. American Diabetes Association; Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*, 2009; 32(Suppl 1): S62-S67.
11. Bikle D (2009) Non-classic actions of Vitamin D. *J Clin Endocrinol Metab* 94:26-34.
12. Evans KN, Nguyen L, Chan J, Innes BA, Bulmer JN, *et al.* (2006) Effects of 25-hydroxy vitamin D3 and 1,25-dihydroxy vitamin D3 on cytokines human decidual cells. *Biol Reprod* 75:816-822.
13. Kositsawat JMDM *et al* (2010). Association of A1C levels with Vitamin D status in U.S. adults: data from the National Health and Nutrition Examination Survey, "Diabetes Care,33;1236-1238.
14. Nada AM. (2013) "Correlation between Vitamin D3 and fasting plasma Glucose, A1C and serum lipids in non-diabetic subjects" *Z.U.M.J.* 19(4).
15. Taheri E *et al.* (2012) "The relationship between serum 25-hydroxy Vitamin D concentration and obesity in type 2 diabetic patients and healthy subjects," *Journal of diabetes and metabolic disorders*, 11-16.
16. Maxwell CS and Wood RJ (2011) "Update on vitamin D and type 2 diabetes," *Nutr Rev*, 69(5);291-5.
17. Rodriguez E *et al.* (2009). "Vitamin D in overweight/obese women and its relationship with diabetic and anthropometric variables" *Obesity* 17(4);778-82.
18. Thorand, B.; Zierer, A.; Huth, C.; Linseisen, J.; Roden, M.; Peters, A.; Koenig, W.; Herder, C. Effect of serum 25-hydroxyvitamin D on risk for type 2 diabetes may be partially mediated by subclinical inflammation: Results from the MONICA/RORA Ausburg study. *Diabetes Care* 2011,34,2320-2322.
19. Pradhan, A. Obesity, Metabolic Syndrome, and Type 2 Diabetes: Inflammatory basis of Glucose Metabolic Disorders. *Nutr.Rev.*2007, 65, S152-S156.
20. Flores, M. A role of vitamin D in low-intensity chronic inflammation and insulin resistance in type 2 diabetes mellitus? *Nutr, Res. Rev.* 2005, 18, 175-182.
21. Ken C C *et al.* (2004) "Hypovitaminosis D is associated with insulin resistance and B cell dysfunction." *Am Clin Nutr*, 79:820-825.
22. Jessica A A and Ambika A (2010) "Role of Vitamin D in Insulin Secretion and Insulin Sensitivity for Glucose Homeostasis," *Int J Endocrinol*. 351-385.
23. Marie-H. G *et al* (2009) "Vitamin D in relation to metabolic risk factors, insulin sensitivity and adiponectin in a young Middle-Eastern population". *European Journal of Endocrinology* 160:965-971.
24. Alemzadeh R *et al* (2008) "Hypovitaminosis D in obese children and adolescents: relationship with adiposity, insulin sensitivity, ethnicity and season." *Metabolism* 57:183-191.
25. Hypponen E and Power C (2006). Vitamin D status and Glucose homeostasis in the 1958 British birth cohort: the role of obesity. *Diabetes Care*; 29:2244-2246.
26. Guasch. A *et al* (2012) "Plasma Vitamin D and Parathormone are Associated with Obesity and Atherogenic Dyslipidemia" *Cardiovasc Diabetol*. 11: 149.
27. Wang C (2013) "Role of vitamin D in cardiometabolic diseases," *Journal of diabetes research*, 1-10.
28. Wang TJ *et al* (2008) "Vitamin D deficiency and risk of cardiovascular disease," *Circulation*, 117(4);503-11.
29. Pittas, A.; Dawson-Hughes, B. Vitamin D and diabetes. *J. Sterol. Biochem. Mol. Biol.* 2010, 121, 425-429.
30. Takiishi, T.; Gysemans, C.; Bouillon, R, Mathieu, C. Vitamin D and diabetes. *Endocrinol. Metab. Clin, N. Am.* 2010, 39, 419-446.
31. Norman, A. W.; Frnkel, J. B.; Heldt, A. M.; Grodsky, G. M. Vitamin D deficiency inhibits pancreatic secretion of insulin. *Science* 1980, 209, 823-825.
32. Cade, C.; Norman, A. W. Rapid normalization/stimulation by 1, 25-dihydroxyvitamin D3 of insulin secretion and Glucose tolerance in the vitamin D-deficient rat. *Endocrinology* 1987, 120, 1490-1497.
33. Cade C and Norman AW. (1986) "Vitamin D3 improves impaired Glucose tolerance and insulin secretion in the vitamin D deficient rat in vivo" *Endocrinology* 119(1);84-90.
34. Bourlon PM, Billaudel B and Faure-Dussert A. (1999) "Influence of Vitamin D3 deficiency and 1,25dihydroxyvitamin D3 on de novo insulin biosynthesis in the islets of the rat endocrine pancreas," *J Endocrinol* 160(1);87-95.
35. Maestro B *et al* (2000) "Stimulation by 1,25-dihydroxyvitamin D3 of insulin receptor expression and insulin responsiveness for Glucose transport in U-937 human promocytic cells," *Endocr J*, 47(4);383-91.