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Original Research Article

A Hospital-Based Study to Evaluate Relationship between Serum 25 (OH) Vitamin D and Insulin Resistance in Prediabetes

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Conflict of interest: Nil

Abstract:

Aim: The aim of the present study was to evaluate relationship between serum 25 (OH) vitamin D and insulin resistance in prediabetes.

Methods: The present study was conducted in the Department of General Medicine and the sample selected was 60 diabetics, 50 pre-diabetes and 40 healthy control individuals. Inclusion criteria used was subjects in age ranged 40-75 years of either gender with persistent IFG or IGT over 2 OGTTs.

Results: Maximum pre-diabetes subjects (16) had serum 25 (OH) D >30 ng/ml, diabetes (20) between 21-30 ng/ml and control (15) >30 ng/ml. In diabetes, pre-diabetes and control subjects had BMI of 24.6 kg/m^2, 25.5 kg/m^2 and 23.7 kg/m^2, waist circumference of 91.7 cm, 88.2 cm and 86.4 cm, waist- height ratio of 0.84, 0.52 and 0.50, waist- hip ratio of 0.94, 0.90 and 0.86, LDL- C of 97.3 mg/dl, 106.4 mg/dl and 98.6 mg/dl, HDL- C of 46.2 mg/dl, 48.4 mg/dl and 49.6 mg/dl, TG of 148.4 mg/dl, 146.4 mg/dl and 117.4 mg/dl respectively. HbA1C found to be 7.3%, 6.5% and 5.6%, HOMA2-IR was 2.52, 1.52 and 0.82, HOMA2-β was 63.7, 82.6 and 86.4 and 25 (OH) D level was 25.5 ng/ml, 24.2 ng/ml and 22.8 ng/ml. A significant difference was observed (P< 0.05). 1 hour PG blood glucose had statistically significant positive correlation with FBS and 2 hours PG blood glucose (P< 0.05).

Conclusion: It is important to understand association of vitamin D and diabetes. Vitamin-D deficiency led to worsening of insulin resistance in individuals with prediabetes.

Keywords: Prediabetes, Insulin Resistance, Hypovitaminosis-D, Hyperglycemia, Serum Vitamin D.

Introduction

Insulin resistance (IR) is a state of metabolic disorder in which the responsiveness of insulin-dependent tissues is reduced, leading to an elevated risk of diabetes mellitus and cardiovascular diseases (CVD). The insulin hormone helps in controlling the amount of glucose in the blood. When there is Insulin Resistance in the body, the target tissues start ignoring Insulin's signal that is to get the glucose out of the bloodstream and put it into our cells. Resultantly, the entry of glucose into the cells becomes difficult, and it starts accumulating in the blood, which ultimately leads to chronic hyperinsulinemia. [1]

Hyperinsulinemia glycemic clamp is the gold standard test for the assessment of IR; nevertheless, because of high associated cost, it is not commonly used. HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) is the most widely used indicator for IR assessment, and it is calculated using plasma glucose and serum insulin levels. However, HOMA-IR is not viable for large-scale studies due to the relatively high cost of serum insulin estimation. Recently, numerous studies have suggested the Triglycerides and Glucose (TyG) index as an efficient marker for the assessment of IR. [2-5] The TyG index is a low-cost marker and easier to calculate as its calculation only requires serum triglycerides (TG) and fasting blood glucose levels. Vitamin D deficiency is a serious public health concern all over the world. It is estimated that approximately more than one billion people worldwide had insufficient levels of vitamin D in 2007. [6]

A decreased amount of serum 25(OH)D, calcitriol [1,25(OH)2D] and raised parathyroid hormone (PTH) can increase intracellular calcium in adipocytes, which can stimulate lipogenesis predisposing a patient to further weight gain and thus increasing the risk of diabetes. [7] Vitamin D deficiency is prevalent in India. Various studies from northern and southern parts of India proved the deficiency of vitamin D in our population. [8-10] Data regarding association of 25(OH) D with insulin resistance in Indians is very limited. Pittas et al. summarized the role of vitamin D on glucose metabolism. [11,12] Many Cross sectional and case control studies suggest an inverse association between vitamin D status, glucose intolerance and type 2 diabetes. [13,14] This could be due the distribution of Vitamin D receptors (VDR) on pancreatic beta cells, adipose tissue and skeletal muscle. Vitamin D status influences insulin secretion or insulin sensitivity. The effect of vitamin D on insulin secretion may be mediated by changes in intracellular calcium concentration in beta cells. [15,16]

The aim of the present study was to evaluate relationship between serum 25 (OH) vitamin D and insulin resistance in prediabetes.

Materials and Methods

The present study was conducted in the Department of General Medicine, Jeevandeep Hospital, Morbi, Gujarat, India for 1 year and the sample selected was 60 diabetics, 50 pre-diabetes and 40 healthy control individuals. Inclusion criteria used was subjects in age ranged 40-75 years of either gender with persistent IFG or IGT over 2 OGTTs.

A case history file containing information regarding gender, waist circumference (WC), hip circumference (HC), waist- hip ratio, HbA1C and lipid profile such as LDL- C, HDL- C and triglyceride was made. Based on the vitamin-D status, individual with vitamin-D sufficiency [25(OH)D ≥30 ng/ml] were prediabetes, vitamin-D insufficiency [25(OH)D: 20-30 ng/ml] were diabetes, mild vitamin-D deficiency [25(OH)D: 10-20 ng/ml] and severe vitamin-D deficiency [25(OH)D <10 ng/ml were controls. Serum insulin was estimated using solid phase, enzyme labelled chemiluminescent immunometric assay. Insulin resistance in basal state was calculated using HOMA2-IR (homeostatic model assessment-insulin resistance) and beta cell function was estimated using HOMA2-β. 1 hour post glucose (1hPG) blood glucose >155 mg/dl was strong predictor for future risk of T2D. Results of the present study after recording all relevant data were subjected for statistical inferences using chi- square test. The level of significance was significant if p value was below 0.05.

Results

Table 1: Level of vitamin D in individuals

Category	Serum 25 (OH) D			
	<10	11-20	21-30	>30
Pre-diabetes (50)	9	11	14	16
Diabetes (60)	12	15	20	13
Control (40)	5	8	12	15

Maximum pre- diabetes subjects (16) had serum 25 (OH) D >30 ng/ml, diabetes (20) between 21-30 ng/ml and control (15) >30 ng/ml.

Table 2: Relationship between anthropometric parameters and diabetes status

Parameters	Diabetes	Pre-diabetes	Normal	P value
BMI	24.6	25.4	23.7	>0.05
Waist circumference	91.7	88.2	86.4	<0.05
Waist- height ratio	0.84	0.52	0.50	<0.05
Waist- hip ratio	0.94	0.90	0.86	<0.05
LDL- C	97.3	106.4	98.6	<0.05
HDL- C	46.2	48.4	49.6	<0.05
TG	148.4	146.4	117.4	<0.05
HbA1C	7.3	6.5	5.6	<0.05
HOMA2-IR	2.52	1.52	0.82	<0.05
HOMA2-β	63.7	82.6	86.4	>0.05
25 (OH) D	25.5	24.2	22.8	>0.05

In diabetes, pre-diabetes and control subjects had BMI of 24.6 kg/m^2, 25.5 kg/m^2 and 23.7 kg/m^2, waist circumference of 91.7 cm, 88.2 cm and 86.4 cm, waist- height ratio of 0.84, 0.52 and 0.50, waist- hip ratio of 0.94, 0.90 and 0.86, LDL- C of 97.3 mg/dl, 106.4 mg/dl and 98.6 mg/dl, HDL- C of 46.2 mg/dl, 48.4 mg/dl and 49.6 mg/dl, TG of 148.4 mg/dl, 146.4 mg/dl and 117.4 mg/dl respectively. HbA1C found to be 7.3%, 6.5% and 5.6%, HOMA2-IR was 2.52, 1.52 and 0.82, HOMA2-β was 63.7, 82.6 and 86.4 and 25 (OH) D level was 25.5 ng/ml, 24.2 ng/ml and 22.8 ng/ml. A significant difference was observed (P< 0.05).

Table 3: Correlation between vitamin-D status and insulin resistance, systemic inflammation and dyslipidaemia in prediabetes

Correlation variables		Variable adjusted	Pearson's correlation	P value
Parameter 1	Parameter 2			
25 (OH) D	HOMA2-IR	BMI, HbA1C	-0.32	<0.05
25 (OH) D	HOMA2-β	BMI, HbA1C	-0.16	>0.05
25 (OH) D	HbA1C	-	-0.07	>0.05
1 hour PG	FBS	-	0.38	<0.05
1 hour PG	2 hours PG	-	0.54	<0.05

1 hour PG blood glucose had statistically significant positive correlation with FBS and 2 hours PG blood glucose (P< 0.05).

Discussion

Subjects with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) are referred to as having prediabetes. [17] Indian diabetes prevention programme-1 (IDPP-1) reported the annual risk of progression to overt diabetes from IGT approximately 18% and 2.5% in the diabetes prevention trial (DPT) in the Chinese diabetes prevention study. Prediabetes is frequently associated with obesity and other components of metabolic syndrome. [18] Obesity in turn is commonly associated with hypovitaminosis-D due to the capacity of adipose tissue to store 25-hydroxy vitamin-D [25(OH)D] making it biologically unavailable. [19] A decreased amount of serum 25(OH)D, calcitriol [1,25(OH)2D] and raised parathyroid hormone (PTH) can increase intracellular calcium in adipocytes, which can stimulate lipogenesis predisposing a patient to further weight gain and thus increasing the risk of diabetes. [20,21] Prediabetes is a stage earlier in the hyperglycemia/diabetes continuum where individuals are at increased risk of developing diabetes and where prevention efforts, including lifestyle modification or pharmacologic intervention, have been shown to be effective in preventing or delaying the onset of diabetes. [22]

Maximum pre- diabetes subjects (16) had serum 25 (OH) D >30 ng/ml, diabetes (20) between 21-30 ng/ml and control (15) >30 ng/ml. Several studies have shown that lower 25- hydroxyvitamin D (25[OH]D) levels are related to an increased risk of cardiovascular disease (CVD). [23-25] In diabetes, pre-diabetes and control subjects had BMI of 24.6 kg/m2, 25.5 kg/m2 and 23.7 kg/m2, waist circumference of 91.7 cm, 88.2 cm and 86.4 cm, waist- height ratio of 0.84, 0.52 and 0.50, waist- hip ratio of 0.94, 0.90 and 0.86, LDL- C of 97.3 mg/dl, 106.4 mg/dl and 98.6 mg/dl, HDL- C of 46.2 mg/dl, 48.4 mg/dl and 49.6 mg/dl, TG of 148.4 mg/dl, 146.4 mg/dl and 117.4 mg/dl respectively. HbA1C found to be 7.3%, 6.5% and 5.6%, HOMA2-IR was 2.52, 1.52 and 0.82, HOMA2-β was 63.7, 82.6 and 86.4 and 25 (OH) D level was 25.5 ng/ml, 24.2 ng/ml and 22.8 ng/ml. Dutta et al [26] evaluated the relationship between vitamin-D status and insulin resistance on one hundred fifty-seven individuals with prediabetes. It was found in this study that vitamin-D deficiency/insufficiency was found in 115 (73.25%) individuals with prediabetes. Shankar et al [27] examined the 12,719 participants (52.5% women) who were free of diabetes. Serum 25(OH)D levels were categorized into quartiles (<17.7, 17.8–24.5, 24.6–32.4, >32.4 ng/mL). Prediabetes was defined as a 2-h glucose concentration of 140–199 mg/dL, or a fasting glucose concentration of 110–125 mg/dL, or an A1C value of 5.7–6.4%. Lower serum 25(OH)D levels were associated with prediabetes after adjusting for age, sex, race/ethnicity, season, geographic region, smoking, alcohol intake, BMI, outdoor physical activity, milk consumption, dietary vitamin D, blood pressure, serum cholesterol, C-reactive protein, and glomerular filtration rate.

A significant difference was observed (P< 0.05). 1 hour PG blood glucose had statistically significant positive correlation with FBS and 2 hours PG blood glucose (P< 0.05). Farouche et al [28] included a total of 524 nondiabetic men and women, aged 40–69 years and found that age-adjusted baseline mean serum 25(OH)D was greater in men (64.5 nmol/l) than women (57.2 nmol/l) and varied with season (highest late summer). Baseline 25(OH)D was associated inversely with 10-year risk of hyperglycemia, insulin resistance and metabolic syndrome z score after adjustment for age, sex, smoking, BMI, season, and baseline value of each metabolic outcome variable. Associations with 2-h glucose, insulin, and HOMA-IR remained significant after further adjustment for IGF-1, parathyroid hormone, calcium, physical activity, and social class.

Conclusion

It is important to understand association of vitamin D and diabetes. Vitamin-D deficiency led to worsening of insulin resistance in individuals with prediabetes. Vit D deficiency is common in prediabetic state and subjects having severe vitamin D deficiency (<10 ng/ml), had the worst insulin resistance. Our study results help in strongly proposing vitamin D levels as an early marker for diabetes and help in recommending vitamin D to be prescribed in the pre diabetic stage itself.

References

1. Gungor N, Hannon T, Libman I, Bacha F, Arslanian S. Type 2 diabetes mellitus in youth: the complete picture to date. Pediatric Clinics. 2005 Dec 1;52(6):1579-609.
2. Mohd Nor NS, Lee S, Bacha F, Tfayli H, Arslanian S. Triglyceride glucose index as a surrogate measure of insulin sensitivity in obese adolescents with normoglycemia, prediabetes, and type 2 diabetes mellitus: comparison with the hyper insulinemic–euglycemic clamp. Pediatric diabetes. 2016 Sep;17(6):458-65.
3. Jhee JH, Nam KH, An SY, Cha MU, Lee M, Park S, Kim H, Yun HR, Kee YK, Park JT, Han SH. Severe vitamin D deficiency is a risk factor for renal hyperfiltration. The American Journal of Clinical Nutrition. 2018 Dec 1;108 (6):1342-51.
4. Irace C, Carallo C, Scavelli FB, De Franceschi MS, Esposito T, Tripolino C, Gnasso A. Markers of insulin resistance and carotid atherosclerosis. A comparison of the homeostasis model assessment and triglyceride glucose index. International journal of clinical practice. 2013 Jul;67(7):665-72.
5. Unger G, Benozzi SF, Perruzza F, Pennacchiotti GL. Triglycerides and glucose index: a useful indicator of insulin resistance. Endocrinología y Nutrición (English Edition). 2014 Dec 1;61(10):533-40.
6. Holick MF, Vitamin D. Deficiency. N Engl J Med. 2007;357(3):266–81.
7. Takiishi T, Gysemans C, Bouillon R, Mathieu C. 6. Vitamin D and diabetes. Endocrinol Metab Clin North Am 2010; 39:419-46.
8. Harinarayan CV, Gupta N, Kochupillai N. Vitamin D status in primary hyperparathyroidism in India. Clinical endocrinology. 1995 Sep;43 (3):351-8.
9. Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. The American journal of clinical nutrition. 2000 Aug 1;72(2):472-5.
10. Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D. Vitamin D status in Andhra Pradesh: A population-based study. 1. Indian Journal of Medical Research. 2008 Mar 1;127 (3):211-8.
11. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and β cell dysfunction. The American journal of clinical nutrition. 2004 May 1;79(5) :820-5.
12. 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. The Journal of Clinical Endocrinology & Metabolism. 2007 Jun 1;92(6):2017-29.
13. Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. Diabetes care. 2004 Dec 1;27 (12):2813-8.
14. Ford ES, Ajani UA, McGuire LC, Liu S. Concentrations of serum vitamin D and the metabolic syndrome among US adults. Diabetes care. 2005 May 1;28(5):1228-30.
15. Bourlon PM, Billaudel B, Faure-Dussert A. Influence of vitamin D3 deficiency and 1, 25 dihydroxy vitamin D3 on de novo insulin biosynthesis in the islets of the rat endocrine pancreas. Journal of Endocrinology. 1999 Jan 1;16 0(1):87-96.
16. Danescu LG, Levy S, Levy J. Vitamin D and diabetes mellitus. Endocrine. 2009 Feb; 35:11-7.
17. Knowler WC. Diabetes Prevention Program Research Group: Reduction in the incidence of type 2 diabetes with life-style intervention or metformin. N. Engl. J. Med. 2002; 346:393-403.
18. Yang W, Lin L, Qi J. The preventive effect of acarbose and metformin on the IGT population from becoming diabetes mellitus: a 3-year multi-centric prospective study. Chin J Endocrinol Metab. 2001; 17:131–6.
19. Nagpal J, Pande JN, Bhartia A. A double-blind, randomized, placebo-controlled trial of the short-term effect of vitamin D3 supplementation on insulin sensitivity in apparently healthy, middle-aged, centrally obese men. Diabet Med. 2009; 26:19–27.
20. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. Indian Diabetes Prevention Programme (IDPP). The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1) Diabetologia. 2006; 49:289–97.
21. Palomer X, Gonzalez-Clemente JM, Blanco-Vaca F, Mauricio D. Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. Diabetes Obes Metab. 2008; 10:185–97.
22. Ford ES, Ajani UA, McGuire LC, Liu S. Concentrations of serum vitamin D and the metabolic syndrome among U.S. adults. Diabetes Care. 2005; 28:1228–30.
23. Kumar S, Mukherjee S, Mukhopadhyay P, Pandit K, Raychaudhuri M, Sengupta N, Ghosh S, Sarkar S, Chowdhury S. Prevalence of diabetes and impaired fasting glucose in a selected population with special reference to

influence of family history and anthropometric measurements–The Kolkata policeman study. JAPI. 2008 Nov; 56:841-4.
24. Holick MF. Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. The American journal of clinical nutrition. 2004 Mar 1;79(3):362-71.
25. Levy JC, Matthews DR, Hermans MP. Correct homeostasis model assessment (HOMA) evaluation uses the computer program. Diabetes care. 1998 Dec 1;21(12):2191.
26. Dutta D, Maisnam I, Shrivastava A, Sinha A, Ghosh S, Mukhopadhyay P, Mukhopadhyay S, Chowdhury S. Serum vitamin-D predicts insulin resistance in individuals with prediabetes. The Indian journal of medical research. 2013 Dec;138(6):853.
27. Shankar A, Sabanayagam C, Kalidindi S. Serum 25-hydroxyvitamin d levels and prediabetes among subjects free of diabetes. Diabetes care. 2011 May 1;34(5):1114-9.
28. Forouhi NG, Cooper A, Boucher BJ, Wareham NJ. Baseline serum 25-hydroxy vitamin D is predictive of future glycemic status and insulin resistance: the Medical Research Council Ely Prospective Study 1990–2000. Diabetes. 2008 Oct 1;57(10):2619-25.