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Assessment of Relationship between Serum 25 (OH) Vitamin D and Insulin Resistance in Prediabetes

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Abstract

Background: To evaluate relationship between serum 25 (OH) vitamin D and insulin resistance in prediabetes. **Subjects and Methods:** We enrolled fifty diabetics, forty pre-diabetes and thirty- five healthy control individuals. In all, waist circumference (WC), hip circumference (HC), waist- hip ratio, HbA1C and lipid profile such as LDL- C, HDL- C and triglyceride was recorded. Serum insulin, HOMA2-IR and HOMA2-β was estimated. Statistical inferences using chi- square test was used. **Results:** Maximum pre- diabetes subjects (15) had serum 25 (OH) D >30 ng/ml, diabetes (16) between 21-30 ng/ml and control (13) >30 ng/ml. 1 hour PG blood glucose had statistically significant positive correlation with FBS and 2 hours PG blood glucose (P< 0.05). **Conclusion:** Vitamin-D deficiency led to worsening of insulin resistance in individuals with prediabetes.

Keywords: prediabetes, insulin resistance, hypovitaminosis-D, hyperglycemia.

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Introduction

Subjects with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) are referred to as having prediabetes.[1] 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.[2] 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.[3] 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.[4,5]

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.[6] The specific mechanisms by which vitamin D effects the risk of type 2 diabetes is not very clear.[7] Insulin resistance and deteriorated β-cell function are the two major pathophysiologic aspects of type 2 diabetes. Studies reported significant association of vitamin D with insulin resistance and β-cell dysfunction.[8,9]

The effect of vitamin D on various tissues is not well clear, but the expression of vitamin D receptors (VDRs) in >30 tissues, including pancreatic islet cells is considered one factor.[10] There is some evidence that polymorphisms in the VDR gene may be associated with insulin resistance, insulin secretion, and fasting glucose concentrations suggesting that vitamin D is likely to contribute to glucose metabolism.[11] Considering this, we attempted this study with the aim to evaluate relationship between serum 25 (OH) vitamin D and insulin resistance in prediabetes.

Subjects and Methods

The approval for the present trial was obtained from Ethical review committee. The sample selected was fifty diabetics, forty pre-diabetes and thirty- five 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

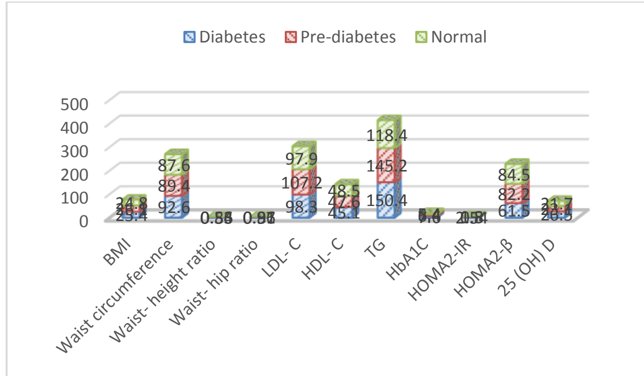
Category	Serum 25 (OH) D			
	<10	11-20	21-30	>30
Pre-diabetes (40)	7	12	14	15
Diabetes (50)	10	14	16	10
Control (35)	4	7	11	13

Maximum pre- diabetes subjects (15) had serum 25 (OH) D >30 ng/ml, diabetes (16) between 21-30 ng/ml and control (13) >30 ng/ml (Table 1).

Table 2 Relationship between anthropometric parameters and diabetes status

Parameters	Diabetes	Pre-diabetes	Normal	P value
BMI	25.4	26.1	24.8	>0.05
Waist circumference	92.6	89.4	87.6	<0.05
Waist- height ratio	0.86	0.54	0.53	<0.05
Waist- hip ratio	0.96	0.91	0.87	<0.05
LDL- C	98.3	107.2	97.9	<0.05
HDL- C	45.1	47.6	48.5	<0.05
TG	150.4	145.2	118.4	<0.05
HbA1C	7.6	6.4	5.4	<0.05
HOMA2-IR	2.54	1.50	0.80	<0.05
HOMA2-β	61.5	82.2	84.5	>0.05
25 (OH) D	26.5	23.1	21.7	>0.05

In diabetes, pre-diabetes and control subjects had BMI of 25.4 kg/m2, 26.1 kg/m2and 24.8 kg/m2, waist circumference of 92.6 cm, 89.4 cm and 87.6 cm, waist- height ratio of 0.86, 0.54 and 0.53, waist- hip ratio of 0.96, 0.91 and 0.87, LDL- C of 98.3 mg/dl, 107.2 mg/dl and 97.9 mg/dl, HDL- C of 45.1 mg/dl, 47.6 mg/dl and 48.5 mg/dl, TG of 150.4 mg/dl, 145.2 mg/dl and 118.4 mg/dl respectively. HbA1C found to be 7.6%, 6.4% and 5.4%, HOMA2-IR was 2.54, 1.50 and 0.80, HOMA2-β was 61.5, 82.2 and 84.5 and 25 (OH) D level was 26.5 ng/ml, 23.1 ng/ml and 21.7 ng/ml. A significant difference was observed (P< 0.05) (Table 2, Graph 1).



Graph 1

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	-0.34	<0.05
25 (OH) D	HOMA2-β	BMI, HbA1C	-0.18	>0.05
25 (OH) D	HbA1C	-	-0.07	>0.05
1 hour PG	FBS	-	0.36	<0.05
1 hour PG	2 hours PG	-	0.58	<0.05

1 hour PG blood glucose had statistically significant positive correlation with FBS and 2 hours PG blood glucose (P< 0.05) (Table 3).

Discussion

This study was conducted with the aim to evaluate relationship between serum 25 (OH) vitamin D and insulin resistance in prediabetes among fifty diabetics, forty pre-diabetes and thirty- five healthy control individuals. Several studies have shown that lower 25-hydroxyvitamin D (25[OH]D) levels are related to an increased risk of cardiovascular disease (CVD).[12,13,14] Some evidence also suggests that 25(OH) D insufficiency may be involved in the development of diabetes. Accumulated evidences indicated that abnormal vitamin D status is associated with the etiology of type 2 diabetes.[15] Compared with subjects with normal glucose tolerance, patients with type 2 diabetes and impaired glucose tolerance (IGT) have lower vitamin D levels. Some prospective studies suggested vitamin D deficiency increases the risk of type 2 diabetes.[16]

Our study revealed that 15 pre- diabetes subjects had serum 25 (OH) D >30 ng/ml, 16 diabetics had between 21-30 ng/ml and 13 control had >30 ng/ml. Gao et al[17] determined the relationship between serum 25-hydroxy vitamin D (25-OHD) and insulin sensitivity and β-cell function in newly diagnosed type 2 diabetes. 395 newly diagnosed type 2 diabetes patients were enrolled and patients were divided into three groups according to tertiles (T1, T2, and T3) of 25-OHD concentration. There was significant difference among three groups for HOMA-IR, Matsuda ISI, and INSR. HOMA-IR, Matsuda ISI, INSR, and DI were undifferentiated among three groups in male patients. But HOMA-IR, Matsuda ISI, and INSR were significantly different among three groups in female patients after being adjusted by confounding factors.

Our study showed that in diabetes, BMI was 25.4 kg/m2, in pre-diabetes was 26.1 kg/m2and in and control was24.8 kg/m2, waist circumference was 92.6 cm, 89.4 cm and 87.6 cm respectively. Dutta et al[18] 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. Severe vitamin-D deficiency (<10 ng/ml) was seen in 14.65 per cent individuals. Individuals with the lowest vitamin-D levels (<10 ng/ml) had the highest insulin resistance (HOMA2-IR: 2.04 ± 0.67). Serum 25(OH)D had a statistically significant inverse correlation with insulin resistance (HOMA2-IR; r=-0.33; P=0.008), and positive correlation with insulin sensitivity (QUICKI; r=0.39; P=0.002), after adjusting for BMI and HbA1c. There was no correlation between vitamin-D status and estimated beta cell mass (HOMA-β). The mean waist-height ratio among individuals with prediabetes was 0.57 (normal<0.5) indicating a high risk of cardiovascular morbidity. Individuals with elevated 1hPG>155 mg/dl had significantly higher BMI and worse insulin resistance, and 1hPG correlated well with 2 hours post glucose blood glucose (r=0.57; P<0.001).

Our study demonstrated that maximum waist- height ratio (0.86), waist- hip ratio (0.96), HbA1C (7.6%), TG (150.4 mg/dl), HOMA2-IR (2.54) and 25 (OH) D level (26.5 ng/ml) was seen in diabetics. Shankar et al[19] 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. Compared with quartile 4 of 25(OH)D (referent), the odds ratio of prediabetes associated with quartile 1 was 1.47 (95% CI 1.16–1.85; P = 0.001 for trend). Subgroup analyses examining the relation between 25(OH)D and prediabetes by sex, BMI, and hypertension categories also showed a consistent positive association.

Results of our study found that 1 hour PG blood glucose had statistically significant positive correlation with FBS and 2 hours PG blood glucose. Forouhi et al[20] 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.

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