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Insulin Resistance in Pre-Diabetes and Blood Vitamin D Levels: A Case-Control Investigation

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ABSTRACT

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

Methods: The current observational study was carried out at the General Medicine department for a duration of 9 months. A total of 100 people with diabetes, 96 persons with pre-diabetes, and 70 healthy control individuals were included in the sample. The inclusion criteria used consisted of individuals between the ages of 40 and 75, of either gender, who had persistent impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) throughout two oral glucose tolerance tests (OGTTs).

Results: Maximum pre-diabetes (30) had serum 25 (OH) D >30 ng/ml, diabetes (32) 21-30, and control (26) >30. In diabetes, pre-diabetes, and control subjects, BMI was 25.4 kg/m2, 26.1 kg/m2, and 24.8 kg/m2, waist circumference was 92.6 cm, 89.4 cm, and 87.6 cm, waist-height ratio was 0.86, 0.54, and 0.53, waist-hip ratio was 0.96, 0.91, and 0.87, LDL-C was 98.3 mg/dl, 107.2 mg/dl, and 97.9 mg/dl, HDL-C was 45.1 mg/dl, 47.6 mg/dl, and 48.5 mg HbA1C levels were 7.6%, 6.4%, and 5.4%, with HOMA2-IR values of 2.54, 1.50, and 0.80, HOMA2-β values of 61.5, 82.2, and 84.5, and 25 (OH) D levels of 26.5, 23.1, and 21.7 ng/ml. A substantial difference was found ($P<0.05$). Both 1 hour and 2 hours PG blood glucose showed a strong positive connection with FBS ($P< 0.05$).

Conclusion: Understanding the connection between vitamin D and diabetes is crucial. Insufficient levels of Vitamin-D exacerbated insulin resistance in persons diagnosed with prediabetes.

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

1. INTRODUCTION

Recent study has shown a link between vitamin D and its influence on insulin production and the development of insulin resistance. The activation of Vitamin D in the pancreas occurs via a local process that involves the enzyme 1α-hydroxylase. Vitamin D, when in its active form, promotes insulin release by either directly interacting with its receptors or by modulating levels of calcium inside cells.[1,2] Vitamin D improves insulin sensitivity by either raising the expression of insulin receptors or enhancing the responsiveness of insulin receptors to insulin. Furthermore, it impacts the peroxisome proliferator-activated receptor (PPAR) δ and has a role in controlling extracellular calcium levels.[3-7]

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Vitamin D has the capacity to affect both the production of insulin and the resistance to insulin, which are the fundamental factors contributing to type II diabetes. Individuals diagnosed with diabetes and pre-diabetes often have a notable prevalence of vitamin D inadequacy.[7,8] The treatment for vitamin D deficiency has the potential to be an effective way to preventing diabetes, because to its cost and safety.[9] Various cross-sectional and epidemiological studies have shown an association between a lack of vitamin D and a higher incidence of diabetes.[10-12] However, the results of interventional studies investigating the impact of vitamin D on insulin sensitivity were inconclusive.[13,14] The research have shown that the administration of vitamin D may have either a beneficial, neutral, or detrimental effect on insulin sensitivity. In previous studies done at our center, the provision of vitamin D to pre-diabetic patients who had low levels of vitamin D and were also first-degree relatives of persons with type II diabetes mellitus (T2DM) led to a decrease in insulin sensitivity. Nevertheless, the disparity between the experimental group and the control group did not reach statistical significance.[15]
The aim of this study was to evaluate the association between blood vitamin D levels and insulin resistance in people diagnosed with prediabetes.

2. MATERIALS AND METHODS

The present observational research was conducted in the department of General medicine for the period of 9 months. The approval for the present research was obtained from Ethical review committee.
Inclusion criteria used was subjects in age ranged 40-75 years of either gender with persistent IFG or IGT over 2 OGTTs.
Methodology
A total of 100 people with diabetes, 96 persons with pre-diabetes, and 70 healthy control individuals were included in the sample. A detailed case history file was compiled, with information on gender, waist circumference (WC), hip circumference (HC), waist-hip ratio, HbA1C, and lipid profile parameters including LDL-C, HDL-C, and triglyceride levels. Individuals who had a vitamin-D status of 25(OH)D ≥30 ng/ml were categorized as having sufficient levels of vitamin-D.
Individuals with a vitamin-D level of 25(OH)D: 20-30 ng/ml were categorized as having insufficient levels of vitamin-D. Individuals with a vitamin-D status of 25(OH)D: 10-20 ng/ml were categorized as having mild vitamin-D insufficiency. Finally, those whose vitamin-D level was measured to be 25(OH)D <10 ng/ml were categorized as controls.
The serum insulin measurement was performed using a solid phase, enzyme-labelled chemiluminescent immunometric method. The HOMA2-IR technique was used to estimate insulin resistance in the fasting state, whereas HOMA2-β was used to assess beta cell activity.
Statistical analysis
The data obtained in the present study were subjected to analysis using SPSS version 22. A p-value less than 0.05 indicates a statistically significant level of significance.

3. RESULTS

Table 1: Level of vitamin D in individuals

Category	Serum 25 (OH) D			
	<10	**11-20**	**21-30**	**>30**
Pre-diabetes (96)	14	24	28	30
Diabetes (100)	20	28	32	20

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Control (70)	8	14	22	26

Maximum pre- diabetes subjects (30) had serum 25 (OH) D >30 ng/ml, diabetes (32) between 21-30 ng/ml and control (26) >30 ng/ml.

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, BMI was 25.4 kg/m2, 26.1 kg/m2, and 24.8 kg/m2, waist circumference was 92.6 cm, 89.4 cm, and 87.6 cm, waist-height ratio was 0.86, 0.54, and 0.53, waist-hip ratio was 0.96, 0.91, and 0.87, LDL-C was 98.3 mg/dl, 107.2 mg/dl, and 97.9 mg/dl, HDL-C was 45.1 mg/dl, 47.6 mg/dl, and 48.5 mg 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	-0.34	<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).

4. DISCUSSION

People with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) are often referred to as having prediabetes.[16] The Indian diabetes prevention programme-1 (IDPP-1) discovered that individuals with impaired glucose tolerance (IGT) had a about 18% chance of getting overt diabetes each year. In contrast, the diabetes prevention trial (DPT) conducted in the Chinese diabetes prevention study suggested a risk of only 2.5%. Prediabetes often coexists

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with obesity and other components of metabolic syndrome.[17] Hypovitaminosis-D is often associated with obesity due to the adipose tissue's capacity to store 25-hydroxy vitamin-D [25(OH)D], rendering it physiologically unattainable.[18] A decrease in the concentrations of serum 25-hydroxyvitamin D, calcitriol (1,25-dihydroxyvitamin D), and an elevation in parathyroid hormone (PTH) might result in an elevation in intracellular calcium in adipocytes. This may stimulate adipogenesis, leading to increased adiposity, which in turn elevates the susceptibility of a patient to weight gain and augments the likelihood of developing diabetes.[19,20]

Among the individuals who were pre-diabetic, the majority (30) had serum 25 (OH) D levels over 30 ng/ml. In contrast, those with diabetes (32) had levels ranging from 21 to 30 ng/ml, while the control group (26) had levels above 30 ng/ml. The body mass index (BMI) values for persons with diabetes, pre-diabetes, and control patients were 25.4 kg/m2, 26.1 kg/m2, and 24.8 kg/m2, respectively. The waist circumference measures were 92.6 cm, 89.4 cm, and 87.6 cm, respectively. The waist-height ratios were 0.86, 0.54, and 0.53, respectively. The waist-hip ratios were 0.96, 0.91, and 0.87, in that order. The values of LDL-C (low-density lipoprotein cholesterol) were 98.3 mg/dl, 107.2 mg/dl, and 97.9 mg/dl, respectively. The values of high-density lipoprotein cholesterol (HDL-C) were 45.1 mg/dl, 47.6 mg/dl, and 48.5 mg/dl, respectively. The triglyceride (TG) values were 150.4 mg/dl, 145.2 mg/dl, and 118.4 mg/dl, respectively. The HbA1C readings were determined to be 7.6%, 6.4%, and 5.4%. The HOMA2-IR values were determined to be 2.54, 1.50, and 0.80, whereas the HOMA2-β values were found to be 61.5, 82.2, and 84.5. In addition, the levels of 25-hydroxyvitamin D (25 (OH) D) were tested to be 26.5 ng/ml, 23.1 ng/ml, and 21.7 ng/ml. A significant difference was observed ($P< 0.05$). Gao et al[21] examined the association between blood levels of 25-hydroxy vitamin D (25-OHD) and insulin sensitivity, as well as β-cell activity, in persons who were newly diagnosed with type 2 diabetes. The research comprised a cohort of 395 people who had just received a diagnosis of type 2 diabetes. These people were then divided into three groups depending on their 25-OHD content, with each group representing a distinct tertile (T1, T2, and T3). Significant differences were seen among the three groups in relation to HOMA-IR, Matsuda ISI, and INSR. There was no notable disparity in HOMA-IR, Matsuda ISI, INSR, and DI values among the three groups of male patients. Nevertheless, after the influence of confounding factors was taken into consideration, significant disparities in HOMA-IR, Matsuda ISI, and INSR were seen across the three cohorts of female patients. Dutta et al[22] investigated the association between vitamin-D levels and insulin resistance in a cohort of 157 individuals diagnosed with prediabetes.

The blood glucose levels measured 1 hour after a meal (postprandial) exhibited a statistically significant positive correlation with both the fasting blood sugar levels and the blood glucose levels measured 2 hours after a meal (postprandial) ($P< 0.05$). Shankar et al.[23] examined a cohort of 12,719 people, of whom 52.5% were female, who were free from diabetes. The levels of Serum 25(OH)D were categorized into quartiles, with the threshold values being <17.7, 17.8–24.5, 24.6–32.4, and >32.4 ng/mL. Prediabetes is defined as a 2-hour glucose concentration between 140 and 199 mg/dL, a fasting glucose concentration between 110 and 125 mg/dL, or an A1C test between 5.7 and 6.4%. A significant correlation was found between reduced levels of serum 25(OH)D and prediabetes, even after controlling for various factors including age, gender, race/ethnicity, season, geographic location, smoking, alcohol consumption, BMI, outdoor physical activity, milk consumption, dietary vitamin D, blood pressure, serum cholesterol, C-reactive protein, and glomerular filtration rate. Forouhi et al.[24] performed research with a sample of 524 nondiabetic people, comprising both males and females. The participants' ages ranged from 40 to 69. The research revealed that the mean

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concentration of serum 25(OH)D, adjusted for age, was greater in males (64.5 nmol/l) than in females (57.2 nmol/l). The levels also fluctuated based on the season, with the highest amounts seen during the late summer. There was a negative association between the initial level of 25(OH)D and the 10-year risk of hyperglycemia, insulin resistance, and metabolic syndrome z score. The association remained statistically significant even after controlling for variables such as age, sex, smoking, BMI, season, and the baseline value of each metabolic outcome variable. The relationships between 2-h glucose, insulin, and HOMA-IR remained statistically significant even after including additional covariates such as IGF-1, parathyroid hormone, calcium, physical activity, and socioeconomic status.

5. CONCLUSION

The present study reported 1 hour PG blood glucose had statistically significant positive correlation with FBS and 2 hours PG blood glucose. It is important to understand association of vitamin D and diabetes. Vitamin-D deficiency can lead to worsening of insulin resistance in individuals with prediabetes.

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