Original Research Article

Study of relationship between serum 25 (OH) vitamin D and insulin resistance in prediabetic patients

Basavaraj GT[1], Sharanabasappa Nandyal[2*]

[1,2]Assistant Professor Department of General Medicine Basaveshawar Teaching and General Hospital attached to M R Medical College Sedam Road Kalaburgi, Karnataka State India 585105.
Email: Basavgt8@Gmail.Com ,sharannandyal@gmail.com

Abstract

Background: Prediabetes is an intermediate stage between normal glucose levels and the clinical entity of type 2 diabetes. Indian population have one of the highest number of individuals with pre-diabetes and diabetes among all major ethnic groups. Deficiency of Vitamin D may have negative effects on glucose intolerance, insulin secretion. In patients with diabetes, administration of vitamin-D has been shown to decrease insulin resistance.[8] However similar observation among individuals with prediabetes has not been documented. The aim of present study was to find out the relationship between Serum 25 (OH) Vitamin D and insulin resistance among prediabetic individuals. **Material and Methods:** Present study was a cross-sectional, observational study carried out in the Department of Medicine Basaveshawar Teaching & General Hospital attached to Mahadevappa Rampure Medical College, an 50 Prediabetic individuals, 25-50 years with fasting blood glucose between 100 – 125 mg/dl and/or 2-hour post-OGTT blood glucose of 140 - 199 mg/dl were included as cases and other 50 individuals with normal glucose tolerance were included as controls. Vitamin D levels among the two groups were compared by unpaired student t test. Association between vitamin D status and insulin resistance in individuals with prediabetes was studied using Pearson's correlation co-efficient. p-value < 0.05 was considered significant. **Results:** Total 100 patients were studied, 50 prediabetic cases and 50 healthy controls. Age (in years), gender and BMI (kg/m^2) were comparable in both groups. 66% prediabetic individuals had hypovitaminosis D as compare to 16% of healthy controls. A statistically significant difference was noted for Fasting Plasma Glucose, 2-hour Plasma Glucose, Insulin, HOMA-IR and 25 (OH) vitamin D values between prediabetic cases and healthy controls. A statistically significant correlation was noted between 25 (OH) vitamin D values with HOMA-IR and fasting insulin levels. **Conclusion:** The findings of the present study indicate that serum 25 (OH) vitamin D deficiency is common in prediabetic state and serum 25 (OH) vitamin D deficiency is associated with insulin resistance among adults with prediabetes.

Key Words: Vitamin-D deficiency, insulin resistance, prediabetes.

***Address for Correspondence:**
Dr Sharanabasappa Nandyal,Assistant Professor Sri. Nandyal Hospital Beside Santraswadi City Bus Stop Darga Road Kalaburgi , Karnataka State India 585105.
Email:sharannandyal@gmail.com
Received Date: 09/11/2019 Revised Date: 01/12/2019 Accepted Date: 18/01/2020
DOI:https://doi.org/10.26611/10211612

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 13 October 2020

INTRODUCTION

Prediabetes is an intermediate stage between normal glucose levels and the clinical entity of type 2 diabetes (T2D), defined as Impaired Fasting Glucose (IFG) (Fasting plasma glucose 100 - 125 mg/dl) and Impaired Glucose Tolerance (IGT) [2 hr plasma glucose ≥140 and ≤199 mg/dl] after ingesting 75 g of glucose (OGTT); or a combination of both.[1] Indian population have one of the highest number of individuals with pre-diabetes and diabetes among all major ethnic groups[2], and the

How to cite this article:Basavaraj GT, Sharan Nandyal.Study of relationship between serum 25 (OH) vitamin D and insulin resistance in prediabetic patients. *MedPulse International Journal of Medicine.* October 2020; 16(1): 04-08. https://www.medpulse.in/Medicine/

conversion from prediabetes to diabetes occurs more rapidly in this population than other ethnic groups.[3] Pre-diabetic individuals are at increased risk of abdominal obesity, insulin resistance, non-alcoholic fatty liver disease and metabolic syndrome, and future risk for developing T2DM and cardiovascular disease.[2] Prediabetes is considered a harbinger of overt type 2 diabetes mellitus with annual rate of progression to diabetes ranging from 2.5% (Diabetes Prevention Trial) to 18% (Indian Diabetes Prevention Programme-1).[4] According to Indian Council of Medical Research report in 2011, prevalence of diabetes in Indian population was about 62.4 million and of prediabetes was about 77.2 million.[5] Preventive efforts in prediabetic stage have been shown to be effective in delaying or preventing the onset of diabetes. Recent research on prevention of diabetes highlights the importance of modifiable risk factors and nutritional factors. One such factor is vitamin D, which is gaining lot of importance. Vitamin D has positive effects on insulin secretion and sensitivity and on inflammation. While deficiency of Vitamin D may have negative effects on glucose intolerance, insulin secretion, either directly via Vitamin D receptor (VDR) activation or indirectly via calcemic hormones and also via inflammation.[6] A decreased serum 25(OH)D, calcitriol 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] In patients with diabetes, administration of vitamin-D has been shown to decrease insulin resistance.[8] However similar observation among individuals with prediabetes has not been documented. The aim of present study was to find out the relationship between Serum 25 (OH) Vitamin D and insulin resistance among prediabetic individuals.

MATERIAL AND METHODS

Present study was a cross-sectional, observational study carried out in the Department of General Medicine Basaveshawar Teaching and General Hospital attached to M R Medical College. Study period was 6 months (from October 2018 to March 2019). Institutional ethical committee clearance was taken prior to the study. Relatives/attendants of patients coming to our diabetic outpatient department, from age group of 25 - 50 years were screened for present study. Fasting blood glucose estimation (following overnight 8 hours fast) was done, following which patients underwent 75 gm Oral Glucose Tolerance Test. Patients were ask to take 75 gm glucose solution and blood glucose was estimated after 2-hour post-glucose ingestion.

Inclusion criteria

- Prediabetic individuals with fasting blood glucose between 100 – 125 mg/dl (impaired fasting glucose) and/or 2-hour post-OGTT blood glucose of 140 - 199 mg/dl (impaired glucose tolerance) (As per ADA criteria)[10]

Exclusion criteria

- History of any oral antidiabetic medications or insulin
- Associated disorders like primary hyperparathyroidism, chronic kidney disease, liver disease, any chronic illness, malignancy,
- History of chronic drug use like antiepileptic agents, oral contraceptive pills, steroids (can interfere with Vitamin-D metabolism)
- History of calcium or vitamin D supplementation in the last one year

After applying inclusion and exclusion criteria, total 50 prediabetes individuals were included in the study as cases. Other 50 individuals with normal glucose tolerance were included as controls.

Study was explained in local language and a informed written consent from the participants was taken. Demographic data was collected. Body mass index (kg/m^2) was calculated as weight (in kilograms) divided by height (in meter squares). Routine biochemical blood investigations routine investigations (including complete blood count, renal and liver function tests, serum calcium and phosphate levels) and special blood investigations including serum vitamin D levels and insulin levels were done. Fasting serum insulin level was measured by commercially available Insulin IRMA kit (Immune-radiometric assay). Insulin resistance was measured using Homeostasis Model Assessment Insulin Resistance (HOMAIR):

HOMA-IR = Insulin (μIU/L) X Glucose (mmol/l)/22.5.

Serum 25 (OH) vitamin D levels were measured using commercially available DiaSorin 25 (OH) vitamin D 125I RIA (radioimmune assay) Kit (DiaSorin, Stillwater, Minnesota 55082 - 0285, USA). The plasma 25 (OH) vitamin D concentrations were expressed in nano-gram per ml (ng/ml).

Data was analysed by SPSS Software. The vitamin D levels among the two groups were compared by unpaired student t test. Association between vitamin D status and insulin resistance in individuals with prediabetes was studied using Pearson's correlation co-efficient. p-value < 0.05 was considered significant.

RESULTS

Total 100 patients were studied, 50 prediabetic cases and 50 healthy controls. Age (in years), gender and BMI (kg/m^2) were comparable in both groups as shown in table 1. 66% prediabetic individuals had hypovitaminosis D as compare to 16% of healthy controls.

Table 1: Characteristics of prediabetic cases and controls.

Characteristics	Cases (n=50) No. (%)	Controls (n=50) No. (%)	Total (n=100)
Age group in years			
25-40	19 (38%)	21 (42%)	40
41-50	31 (62%)	29 (58%)	60
Gender			
Male	32 (64%)	30 (60%)	62
Female	18 (36%)	20 (40%)	38
Body mass index			
≤ 25 kg/m2	20 (40%)	28 (56%)	48
> 25 kg/m2	30 (60%)	22 (44%)	52
Vitamin D levels (ng/ml)			
Less than 20	33 (66%)	8 (16%)	41
20-29.9	10 (20%)	19 (38%)	29
More than 30	7 (14%)	23 (46%)	30

A statistically significant difference was noted for Fasting Plasma Glucose, 2-hour Plasma Glucose, Insulin, HOMA-IR and 25 (OH) vitamin D values between prediabetic cases and 50 healthy controls.

Table 2: Comparison of Glycaemic parameters, insulin levels, HOMA-IR and vitamin D levels

Variable	Cases (n = 50)	Controls (n = 50)	p-value	Significance
Fasting Plasma Glucose (mg/dl)	100.24 ± 9.18	84.27 ± 7.44	<0.001	Significant
2-hour Plasma Glucose (mg/dl)	153.87 ± 13.56	124.38 ± 11.46	<0.001	Significant
Insulin(uIU/ml)	18.26 ± 12.14	10.81 ± 8.29	<0.001	Significant
HOMA-IR	5.32 ± 2.96	2.31 ± 2.01	<0.001	Significant
25 (OH) vitamin D (ng/ml)	14.88 ± 11.36	22.16 ± 8.47	0.032	Significant

We compared 25 (OH) vitamin D values with Fasting Plasma Glucose, 2-hour Plasma Glucose, Insulin, HOMA-IR with help of Pearson's Correlation co-efficient. A statistically significant correlation was noted between 25 (OH) vitamin D values with HOMA-IR and fasting insulin levels.

Table 3: Correlation between vitamin-D status and other parameters in prediabetes individuals.

Correlation variables		Pearson's Correlation co-efficient	p-value	Significance
Parameter 1	Parameter 2			
25(OH)D	HOMA-IR	-0.275	0.038	Significant
25(OH)D	Fasting insulin	-0.268	0.029	Significant
25(OH)D	Fasting Plasma Glucose (mg/dl)	-0.92	0.071	Non-significant
25(OH)D	2-hour Plasma Glucose (mg/dl)	-0.132	0.075	Non-significant

DISCUSSION

The International Diabetes Federation (IDF) has considered pandemics of vitamin D deficiency and diabetes worldwide.[9] Individuals with IFG and/or IGT have been referred to as having pre-diabetes, indicating the relatively high risk for the future development of diabetes.[10]The risk of progression to diabetes depends mainly on the degree of insulin resistance, deficiency of insulin secretion while other factors are age, family history, overweight or obesity or history of gestational diabetes or PCOS. Prediabetes is associated with increased risk of progressing to overt diabetes and its complications, according to an ADA expert panel, up to 70% of individuals with prediabetes will eventually develop diabetes.[11]Vitamin D deficiency is largely due to inadequate cutaneous production and to a lesser extent from low dietary intake. The production of vitamin D in the body is dependent upon exposure to sunlight which in turn depends on the seasonal changes, latitude, clothing, skin pigmentation and use of sunscreens.In this study, vitamin D deficiency was the predominant vitamin D status among adults with prediabetes. This high prevalence of hypovitaminosis D in our cases group (66%) is in concordance with various other Indian studies who also reported prevalence of hypovitaminosis D in prediabetic individuals.[12,13]Dutta *et al.* in their study among individuals with prediabetes, they noted that those

having severe vitamin D deficiency (< 10 ng/ml), had the worst insulin resistance (HOMA2-IR) as compared to those having higher levels, with an inverse correlation between vitamin-D status and insulin resistance.[14] Manju. M *et al.*.[15] noted a strong negative correlation between Vit D levels and insulin resistance, HOMA 2 IR in prediabetic individuals. Similar results were noted in present study.Studies have demonstrated an inverse relationship between serum 25(OH)D and diabetes, metabolic syndrome, insulin resistance, and beta cell function.[16] The changing lifestyle, urbanization and modernization of Indian population has led to possible reduction of people being exposed to direct sunlight and inadequate intake of dietary vitamin D, thereby leaving the population at increased risk of vitamin D Deficiency and type 2 diabetes. Studies have also explored the possibility of intervention with vitamin D and prevention of progression towards diabetes. Pittas *et al.*. reported a significant reduction in fasting plasma glucose (FPG) and HOMA-IR with supplementation of calcium and Vitamin D over a period of 3 years in people with prediabetes, but not in those with normal glucose tolerance.[17] Indian studies by Harinarayan*et al.*.[18] noted improvement of insulin resistance and metabolism indexes in nondiabetic subjects with vitamin D deficiency after supplementation of Vitamin D. While Dutta *et al.* noted that vitamin D supplementation improved the glycemic control and insulin sensitivity in prediabetic individuals.[19]Limitations of present study were small sample size, cross-sectional study, so our results cannot establish cause and effective relationship between vitamin D and prediabetes. Also a recent meta-analysis failed to show a positive effect of vitamin D supplementation on HOMA-IR and 2-hour plasma glucose after oral glucose tolerance test, but showed significant lowering of FPG and HbA1c in patients with pre-diabetes.[20] So a population based; large sample sized prospective studies are required to assess role of vitamin D in prediabetic, role of supplementation of vitamin D in prevention of diabetes, halting progression from prediabetes to T2DM, and improving glycemic control.

CONCLUSION

The findings of the present study indicate that serum 25 (OH) vitamin D deficiency is common in prediabetic state and serum 25 (OH) vitamin D deficiency is associated with insulin resistance among adults with prediabetes.

REFERENCES

1. Diagnosis and Classification of Diabetes Mellitus, American Diabetes Association, Diabetes Care, Volume 35, Supplement 1, January 2012
2. Shrivastava U, Misra A, Mohan V, *et al.*. Obesity, diabetes and cardiovascular diseases in India: public health challenges. Curr Diabetes Rev 2017;13:65–80.
3. Misra, A. *et al.*. Diabetes, cardiovascular disease, and chronic kidney disease in South Asia: current status and future directions. BMJ. 357, j1420 (2017).
4. Ramachandran A, Snehalatha C, Mary S *et al.*. 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.
5. Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R, *et al.*. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: Phase I results of the Indian Council of Medical Research-India DIABetes (ICMR-INDIAB) study. Diabetologia2011;54:3022-7.
6. Chagas CE, Borges MC, Martini LA, Rogero MM. Focus on Vitamin D, inflammation and Type 2 diabetes. Nutrients 2012;4:52-67.
7. Takiishi T, Gysemans C, Bouillon R, Mathieu C. Vitamin D and diabetes. Endocrinol Metab Clin North Am 2010; 39 : 419-46.
8. Cigolini M, Iagulli MP, Miconi V, Galiotto M, Lombardi S, Targher G. Serum 25-hydroxyvitamin D3 concentrations and prevalence of cardiovascular disease among type 2 diabetic patients. Diabetes Care 2006; 29 : 722-4.
9. International Diabetes Federation: IDF Diabetes Atlas. 2019. Available online: https://www.diabetesatlas.org/upload/resources/2019/IDFAtlas9th_Edition_2019.pdf (accessed on 5 January 2020).
10. Diagnosis and Classification of Diabetes Mellitus, American Diabetes Association, Diabetes Care, Volume 35, Supplement 1, January 2012
11. Gerstein H, Santaguida P, Raina P, Morrison K, Balion C, Hunt D, *et al.*. Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: a systematic overview and meta-analysis of prospective studies. Diabet Res Clin Pract. 2007;78(3):305-12.
12. Modi KD., *et al.*. "Prevalence of vitamin D deficiency across the spectrum of glucose intolerance". Journal of Diabetes and Metabolic Disorders 14.54 (2015): 4.
13. Giri R., *et al.*. "Status of vitamin D3 level and its co-relation with the glycaemic status in Indian population". International Journal of Advances in Medicine 4.4 (2017): 1067-1072.
14. Dutta D, Maisnam I, Shrivastava A *et al.*. Serum vitamin D predicts insulin resistance in individuals with prediabetes. Indian J Med Res 2013; 138 (6): 853-60.
15. Manju. M *et al.*., Serum Vitamin D and insulin resistance in diabetics and prediabetic and diabetic states- A comparative study, International Journal of Clinical Biochemistry and Research, January-March, 2018;5(1):91-96
16. Strange RC, Shipman KE, Ramachandran S. Metabolic syndrome: A review of the role of Vitamin D in mediating susceptibility and outcome. World J Diabetes 2015;6:896-911.
17. 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 nondiabetic adults. Diabetes Care 2007;30:980-6.

18. CV. Harinarayan, S. Arvind, S. Joshi, K. Thennarasu, V. Vedavyas, and A. Baindur, "Improvement in pancreatic β cell function with vitamin D and calcium supplementation in vitamin D deficient non-diabetic subjects," Endocrine Practice, 2013.
19. Dutta D., *et al.*. "Vitamin-D supplementation in prediabetes reduced progression to type 2 diabetes and was associated with decreased insulin resistance and systemic inflammation: an open label randomized prospective study from Eastern India". Diabetes Research and Clinical Practice 103.3 (2014): e18-e23.
20. Poolsup N, *et al.*. Effect of vitamin D supplementation on insulin resistance and glycaemic control in prediabetes: a systematic review and meta-analysis. Diabet Med 2016;33:290–9.

Source of Support: None Declared
Conflict of Interest: None Declared