



INSULIN RESISTANCE AND DEFICIENCY OF SUNSHINE VITAMIN: A CROSS-SECTIONAL STUDY

Physiology

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ABSTRACT

Insulin resistance is associated with disturbances of various metabolic, endocrine, inflammatory and neural pathways. Timely correction of these disturbances can improve diabetes and simultaneously prevent or delay onset of various complications. Vitamin D through various mechanisms influences insulin secretion and insulin action. Therefore, we proposed this study to determine the association of vitamin D level in blood with insulin resistance in diabetes mellitus type II. Total 44 diabetics and 47 controls participated in this cross-sectional study. Estimation of vitamin D, fasting glucose and fasting insulin level were done. HOMA-IR index was determined using mathematical formula. Vitamin D deficiency was reported in both diabetics and controls. There was slight negative association between vitamin D deficiency and insulin resistance in our study population. Significant insulin resistance was noted in diabetic population.

KEYWORDS

Diabetes, vitamin D, insulin resistance

Background:-

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects of insulin action, insulin secretion or both. Diabetes has now reached epidemic proportions.(1) As per the reports of International Diabetes Federation about 415 million people in the world are diabetic by 1915. Of these 69.1 million cases were reported from India. This number is expected to rise to 79 million by the year 1928.(2) Long standing diabetes leads to complications affecting cardiovascular, central nervous system, kidney, retina, musculoskeletal system, etc. Treatment of diabetes mellitus and associated complications poses tremendous emotional and financial burden on the family and society.(3)

Genetic predisposition, lifestyle changes inherent with rapid urbanization, increasing occurrence of obesity, higher insulin resistance are some of the major factors predisposing to type II diabetes in Indian population. Poor education, low income, lack of awareness, inadequate health services, disparities in rural and urban treatment facilities are additional contributory factors.(4)

Insulin resistance is associated disturbances of various metabolic, endocrine, inflammatory and neural pathways. Timely correction of these disturbances can improve diabetes and simultaneously prevent or delay onset of these complications. This goal led to discoveries of several modifiable risk factors associated with diabetes.(5) One such factor is vitamin D. Vitamin d has attracted considerable attention in recent past. Vitamin D through various mechanisms influences insulin secretion and insulin action.(6)

Several researchers have studied the association of vitamin D status with insulin resistance and complications of diabetes. However, the results of these studies are conflicting and inconsistent. So we proposed this study to determine the association of vitamin D level in blood with insulin resistance in diabetes mellitus type II.

Aim:-

To study the association of vitamin D deficiency with Insulin resistance in type two diabetes mellitus.

Objectives:-

1. To find out vitamin D, F- BSL & F- Insulin levels in diabetics & controls

2. To find out Insulin Resistance by HOMA index

3. To study the association of vitamin D levels with Insulin resistance (HOMA Index) in type II diabetes mellitus & controls.

Material and Methods:-

Ethical approval for this study was obtained from the Ethical Committee of KIMSUDU. The present study was carried out in Dept. of Physiology, KIMSUDU, Karad.

This is a type of cross-sectional comparative study.

Selection Criteria:-

Cases:-

Inclusion Criteria:- Diagnosed cases of Type 2 DM attending the Medicine OPD, Krishna Hospital, Karad on diet, exercise or oral hypoglycemic agents willing to participate in the study. Age: 28-60 yrs, Both sexes Exclusion Criteria:- cases of Type 1 Diabetes, Type 2 DM with cardiovascular, neural, thyroid, renal or liver complications, Type 2 DM patients on insulin treatment, Pregnant or lactating type 2 DM; patients taking mineral oil products, using antacids regularly, taking cortisone or other steroids, under diuretics, taking weight-loss drugs, under phenobarbital and phenytoin medications, having liver problems, gallbladder disease or gastrointestinal disorders and taking daily multivitamins including calcium; Calcium metabolism abnormalities such as evidence of metabolic disease (Paget's disease or osteomalacia), hyperparathyroidism, renal stone disease, and abnormal levels of calcium, phosphorous and alkaline phosphatase were also excluded.

Controls:- Age & sex matched healthy controls

Informed consent was taken. Preliminary Information regarding age, diet, duration & treatment of diabetes, F/H of diabetes, was collected by questionnaire. Anthropometric measurements were taken. Overnight fasting blood sample was collected for estimation of F-BSL, F- insulin, Vitamin D. Following biochemical tests were performed on both study group and controls:

1. Estimation of vitamin D by enzyme immunoassay (7)
2. Estimation of Fasting Glucose by GOD-POD method (8)
3. Estimation of Fasting Insulin by kit method on TOSOH autoanalyzer (9)

4. Estimation of HOMA index by mathematical calculation.

Calculation of HOMA-IR was done using following formula:
 $HOMA-IR = [Glucose] * [Insulin] / 405$ (Glucose in gm/l) (10)

Statistical Analysis:- Statistical analysis was done by unpaired t test & coefficient of correlation using InStat 3 software.

Results:-

Total 44 cases (age 50.93 ± 8.2 years) and 47 controls (age 49.91 ± 5.77 years) took part in the study. The biochemical profiles of the participants are shown in table 1.

Table 1: Biochemical profiles of the participants:

Parameters	Study Group (n = 44)	Control Group (n = 47)	p-value
Vitamin D (ng/ml)	6.04 ± 5.68	6.51 ± 6.23	0.7126
% Vitamin D deficiency	75	59.57	
HOMA-IR	9.26 ± 5.61	2.30 ± 3	$< 0.001^*$

*significant

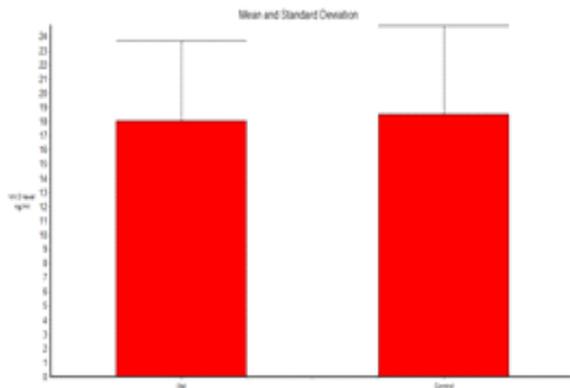


Fig 1: Vitamin D in Diabetics and Control

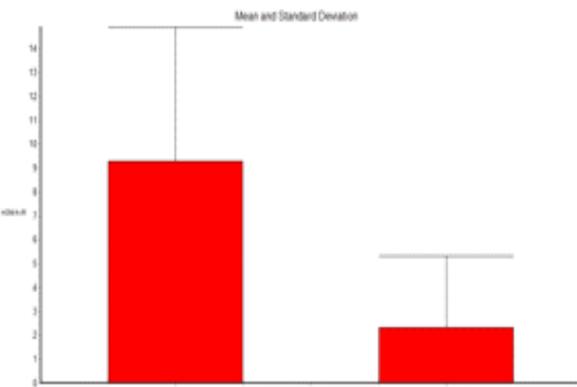


Fig 2: HOMA IR in Diabetics and Control

Both study group and control groups show higher occurrence of vitamin D deficiency. The difference in vitamin D levels in study group and control group is statistically non-significant. The difference in HOMA-IR levels in study group and control group is statistically significant.

Table 2: Correlation between Vitamin D and HOMA:

Parameters	Study Group (n = 44)	Control Group (n = 47)
Correlation Coefficient (r)	- 0.1648	- 0.1937
Coefficient of determination (r ²)	0.02617	0.4151
Two-tailed P value	0.2750	0.1696
Significance	Not significant	Not significant

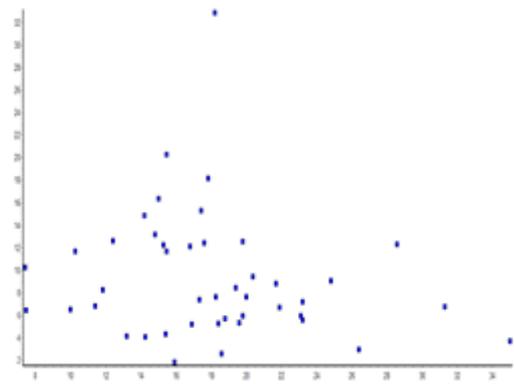


Fig 3: Correlation between Vitamin D and HOMA-IR in Diabetics

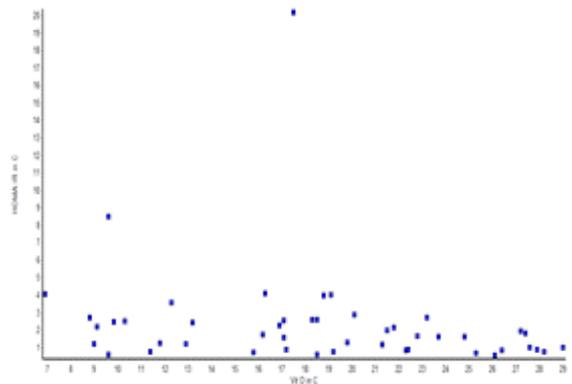


Fig 4: Correlation between Vitamin D and HOMA-IR in Control

Vitamin D levels and HOMA levels show slight inverse association in both study group as well as control group.

Discussion:-

The present study evaluates the association of vitamin D level in blood with insulin resistance in diabetes mellitus type II.

Participants with vitamin D values of < 20 ng/ml were considered as vitamin D deficient and those with vitamin D values of > 20 ng/ml as non-deficient. (6,11) Both study group and control groups show higher occurrence of vitamin D deficiency in this study. Similarly greater proportions of vitamin D deficiency between study and control groups have been reported by Sheth JJ, et al (12), Yang Y, et al (13), Ritu G, et al (14), Harinarayan CV, et al(15, 16), Gandhe MB, et al(17) Sunlight is an excellent source of vitamin D. But excessive skin pigmentation, use of sunscreens, clothing patterns, winter season, preferred indoor work pattern lead to low exposure to sunlight and reduced formation of vitamin D. Malabsorption is another factor that contributes to vitamin D deficiency. (17)

The difference in vitamin D levels in study group and control group is statistically significant. Along with lifestyle changes, diabetic state may be additional factor involved in this. However, the cause and effect relationship cannot be proved with this study.

The homeostasis model assessment of insulin resistance (HOMA-IR) from basal plasma glucose and insulin concentrations gives fair indication of glucose homeostasis in fasting state. (13) The cut-off value of normal HOMA-IR is 2.7. Those with HOMA-IR > 2.7 are considered insulin resistant. (18) The difference in HOMA-IR levels in study group and control group is statistically significant. Similar findings have been reported by Fondjo LA, et al(6), Abbasi F, et al(19), Esteghamati A, et al(20), Vujosevic S, et al(21) and Cai X, et al(22).

This study also reports slight inverse association between vitamin D levels and HOMA-IR in both study group as well as control group. Similar findings have been reported by Al-Shahwan MA, et al(23), Bilge U, et al(24), Kim HJ, et al(25), Gonzalez-Molero I, et al(26), von

Hurst PR, (27), Vujosevic S, et al(20), Boucher BJ (28, 29), Wright ORL, et al(30), Forouhi NG, et al(31)

Vitamin D mediates its antidiabetic effects via following mechanisms:

1. Improves insulin synthesis and signalling
2. Acts via vitamin D receptors on pancreatic islets to promote insulin release
3. Regulate insulin receptors in target cells
4. Increases insulin sensitivity in peripheral tissues and body fat through its anti-inflammatory effect
5. Has indirect role in insulin secretion through calcium homeostasis
6. Suppresses induction of pancreatic islet rennin-angiotensin system to increase insulin secretion.(18, 20, 17, 32,)

Vitamin D deficiency can result in beta cell dysfunction and insulin resistance. This can aggravate pre-existing glucose intolerance. (21, 33, 34, 35, 36)

Limitations:-

1. Estimation of vitamin D levels by immunoassays overestimates 24(OH)D3 levels because the 3- ϵ -24(OH)D3 is also included
2. Euglycemic insulin clamp is the gold standard for determination of insulin resistance. But it was not used because of limited resources and cost constraint. Instead HOMA that gives fairly accurate results was used to determine of insulin resistance.
3. This being a cross-sectional study cause and effect relationship cannot be established
4. HOMA result can be affected by obesity
5. Relatively small sample size
6. PTH and Calcium levels that can affect vitamin D levels were not determined

Suggestions:-

There is urgent need to develop awareness in the general population about the effects vitamin D and vitamin D deficiency disorder. Optimal sun exposure, fortification of milk & other food stuffs with vitamin D can be proposed to prevent vit D deficiency.

Conclusion:-

Higher occurrence of vitamin D deficiency is observed in diabetics and control. The difference in HOMA-IR levels in diabetics and control is statistically significant. This study also reports slight inverse association between vitamin D levels and HOMA-IR in both diabetics and controls. Vitamin D supplementation might prove beneficial to improve insulin resistance. We suggest a large scale study with vitamin D supplementation in diabetics.

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