



STUDY OF CORRELATION OF GLYCAEMIC CONTROL WITH VITAMIN D3 LEVELS AND LIPID PROFILE AMONG TYPE 2 DIABETES MELLITUS PATIENTS IN DISTRICT AMBEDKARNAGAR, UTTAR PRADESH

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ABSTRACT

Introduction:The prevalence of Diabetes is increasing at an alarming rate all over the world.Among the non communicable diseases diabetes is second highest burden secondary to cardiovascular disease in India. In diabetes mellitus total Cholesterol, Triglycerides, Low Density Lipoprotein are elevated & High Density Lipoprotein is decreased. Hbaic is widely used as a measure of mean Glycemia, a measure of risk factor for development of diabetic complications. Objective of present study aimed to assess the Vitamin D3 Levels and lipid profile among patients with type 2 Diabetes Mellitus depending upon glycemic status **Material and methods:**A cross sectional study was undertaken at MRA medical college and hospital Ambedkarnagar in the medicine OPD. A total of 109 patients diagnosed to have diabetes mellitus were subjected to detailed history followed by clinical examination, measured by standard protocol, laboratory workup including glycemic status and lipid profile after getting informed consent.The distribution of patient characteristics was expressed as frequencies and percentage. All statistical analysis was done using Microsoft excel. **Results:**Out of total subjects, pre-diabetics 37.6%,diabetics 28.5%. Among all diabetics, 12 had good glycemic control while 19 subjects had poor glycemic control.Majority of diabetics patients belongs to the age group 51-60 years and 61-70 years. Among 53 females, 41.5% were controls, 35.8% were pre diabetics, 22.7% were diabetics. Mean value of total cholesterol values were 172.29, 188.63,193.04 and 221 in control group, Pre diabetic, Diabetics with Good glycemic control and Diabetics with poor glycemic control respectively. **Conclusion:** In conclusion, the findings of our study had although causality remains to be proven, our results provide the rationale to further explore vitamin D as a promising marker for dyslipidemia in pre-diabetics and diabetics.

KEYWORDS : Vitamin D3, glycemic, type 2 Diabetes Mellitus

Introduction:

Diabetes mellitus is a frequent and a serious disease with chronic complications and constitutes a substantial load for both patient and health care system. According to the International Diabetes Federation (IDF) Diabetes Atlas 2011, the number of inhabitants living with diabetes is expected to rise from 366 million in 2011 to 552 million by 2030 if preventive programs are not put in place. (1)The major complication of type 2 DM when left untreated are chronic microvascular and macrovascular conditions such as retinopathy, nephropathy, neuropathy and cardiovascular disease (CVD). The well-known factors contributing to the development of T2DM are physical inactivity, poor nutritional practices and obesity. Recently, vitamin D3 was a given some importance worldwide in the pathogenesis of diabetes.(2) One of the most important hallmarks of T2DM is the occurrence of low-grade inflammation as a result of an increase in circulating cytokine such as TNF and IL-6 which contributes in the development of insulin resistance particularly in the muscles and adipose tissues.(3) Vitamin D3 being a potent immunosuppressant, tends to down-regulate the transcription of various proinflammatory cytokine genes like Interleukin-2, Interlukin-12,and TumorNecrosis Factor- α .(4,5) It also has a protective role on β cell mass and prevents it from apoptosis as the beta cell apoptosis would lead on to various pathological manifestations like excessive ROS production and cytokines (TNF- α , IL-6) production, glucotoxicityandlipotoxic city, which are the major features among the patients with T2DM.(6) Few of the recent studies had shown the beneficiary role of vitamin D3 in cardiovascular disease prevention, cancer prevention, inhibiting parathyroid hormone secretion, promoting insulin secretion, inhibiting adaptive immunity while promoting innate immunity as well as inhibiting proliferation and stimulating differentiation of cells (7) and along with it Pittas et al in his study had documented that insulin sensitivity is improved by as much as 60% when levels of 25-hydroxy vitamin D3 are increased from 25 to 75 nmol/L,and this was also quoted by few of the studies done in India.(8,9) Recent studies have shown association of 25-hydroxy vitamin D3 deficiency with an increased risk of stroke death and diabetes itself being one of the major risk factor for cerebro-vascular accidents, so with vitamin D3 deficiency it would further worsen the condition. Researchers had also shown the protective role of vitamin D3 on certain cancers like breast cancer and also on non-Alzheimers dementia.(10,11) Concerned to diabetes vitamin D3 have a direct (via its role on the activation of pancreatic beta-cell and sensitive organs) as well as indirect (by regulation of calcium hemostasis) positive effect on insulin secretion and sensitivity.(12,13) Since as such very few studies had been

conducted in India is assessing the association between vitamin D3 deficiency and diabetes mellitus this study was undertaken to assess the association between them which would help in preventing the further complications due to diabetes. Study aimed to assess the Vitamin D3 Levels and lipid profile among patients with type 2 Diabetes Mellitus depending upon glycemic status.

Materials and Methods:

A cross sectional study was undertaken at MRA medical college and hospital Ambedkarnagar in the medicine OPD. Around 109 diabetic mellitus patients were included from doing January 2018 to January 2020 in present study. The study was carried out after obtaining the clearance from the institutional ethical committee and getting the informed consent from all the patients.

Inclusion criteria:

1. Males and females between 20 – 85 years of age
2. In pre-diabetic patients
3. Patients with at least one-year history of uncomplicated type 2diabetic mellitus (confirmed by symptoms and signs, fundoscopy, albumin/ creatinine ratio).

Exclusion criteria:

1. Patients with acute illnesses
2. Pregnant females
3. Those who were taking medication that altered vitamin D metabolism and status
4. Familial hyperlipidaemia

Study design:

The sample was assorted into 3 groups in whom the vitamin D3 levels were assessed:

Group 1: Control group – healthy individuals of 20- 85 years age male and female.

Group 2: Pre-diabetic patients
Group 3: Diabetic patients

Classification of patients on Glycemic control (HBA1c range)

Control: < 5.6%
Pre-diabetic patients: 5.7% - 6.4%
Diabetic patients: \geq 6.5 %
Good Glycemic control (HBA1c range) \leq 7.0%

Good Glycemic control (HBA1c range) \geq 7.0%

Data Collection:

A questionnaire based direct interview was used to collect information on disease profile, demographic variables, risk factors and medication used. It included information about age, sex, chief complaints along with onset, duration and progress of symptoms, past history, treatment history, personal and family history. A thorough general and systemic examination including fundoscopy was performed with special consideration to note any sign specific for diabetes mellitus and rule out complicated diabetes. Brachial venous blood samples were collected for the required investigations from all subjects in the morning after 12 hours fast at the time of entry of the subjects in the study.

Statistical analysis:

The statistical analysis has been done using the Microsoft excel. Data were presented in number and percentages. Descriptive analysis was used to analyzed data.

Results:

In present study subjects were divided into three groups, in which controls were 37 (33.9%), pre-diabetics 41 (37.6%),diabetics 31 (28.5%). Out of the 31 diabetics, 12 had good glycemic control while 19 subjects had poor glycemic control.

Table 1: Distribution of subjects according to sex

| | Male | Female |
|-------------------------|------------|------------|
| Control | 15(26.8%) | 22(41.5%) |
| Pre-diabetics | 22(39.3%) | 19(35.8%) |
| Diabetics | | |
| a) Good glycemiccontrol | 7(12.5%) | 5(9.4%) |
| b) Poorglycemiccontrol | 12(21.4%) | 7(13.3%) |
| Total | 56(100.0%) | 53(100.0%) |

Table 1 illustrates that the gender wise distribution of study subjects, out of 109 study subjects, 51.4% male and 48.6% were female study subjects. Out of total male subjects 26.8% were controls, 39.3% were pre diabetics, 33.9% were diabetics. Among 53 females, 41.5% were controls, 35.8% were pre diabetics, 22.7% were diabetics.

Table 2: Distribution of subjects according to age group

| Age group (years) | Control | Pre diabetic | Diabetics | | Total |
|-------------------|-----------|--------------|----------------------|----------------------|-------|
| | | | Good glycemiccontrol | Poor glycemiccontrol | |
| 21-30 | 2(5.4%) | - | - | - | 2 |
| 31-40 | 6(16.2%) | 3(7.3%) | - | - | 9 |
| 41-50 | 8(21.6%) | 17(41.5%) | 2(16.7%) | 4(21.1%) | 31 |
| 51-60 | 11(29.7%) | 12(29.3%) | 6(50.0%) | 6(31.6%) | 35 |
| 61-70 | 7(18.9%) | 5(12.2%) | 4(33.3%) | 6(31.6%) | 22 |
| 71-80 | 2(5.4%) | 4(9.7%) | - | 2(10.5%) | 8 |
| 81 and above | 1(2.8%) | - | - | 1(5.2%) | 2 |
| Total | 37(100%) | 41(100%) | 12(100%) | 19(100%) | 109 |

Table 2 shows that the age group wise distribution of study subjects. In age group 21-30 years all subjects were belongs control. Total 9 subjects, in the age group 31- 40 years. Majority of diabetics patients belongs to the age group 51-60 years and 61-70 years. Most of the pre diabetic was in the age group 41-50 years ie, 41.5%. Only two patients belongs to above 81 years, in which 1 patient having poor glycemic control.

Table 3: Mean vitamin D3 level in control, pre diabetic and diabetic patients

| | Control | Pre diabetics | Diabetics | |
|-----------------------|---------|---------------|----------------------|----------------------|
| | | | Good glycemiccontrol | Poorglycem iccontrol |
| Deficiency (ng/ml) | 12.01 | 13.22 | 13.40 | 10.37 |
| Insufficiency (ng/ml) | 25.94 | 25.45 | 25.17 | 24.3 |
| Sufficiency (ng/ml) | 40.79 | 35.71 | 37.65 | - |

Table 3 depicts that the mean vitamin D3 level in control, pre diabetic and diabetic patients in deficiency, insufficiency and sufficiency. In control group, 12.01, 25.94 and 40.79 respectively. In pre diabetics

group 13.22, 25.45 and 35.71 respectively. The mean value of vitamin D in diabetic group with good glycemic control and poor glycemic control were 13.40, 25.17, 37.65 and 10.37, 24.3 respectively.

Table 4: Mean values of lipid profile among subjects depending upon glycemic status (HBA1c Levels)

| | Total Cholesterol | Triglyceride | HDL- C | LDL-C | VLDL |
|-------------------------------------|-------------------|--------------|--------|--------|-------|
| Control | 172.29 | 125.41 | 49.4 | 95.34 | 27.73 |
| Pre diabetic | 188.63 | 153.39 | 48.92 | 101.59 | 38.18 |
| Diabetics with Good glycemiccontrol | 193.04 | 172.2 | 49.02 | 101.9 | 42.08 |
| Diabetics with poor glycemiccontrol | 221 | 183.5 | 44.25 | 135.67 | 41.07 |

Table 4 shows that the mean values of lipid profile among subjects depending upon glycemic status (HBA1c Levels). Mean value of total cholesterol values were 172.29, 188.63,193.04 and 221 in control group, Pre diabetic, Diabetics with Good glycemic control and Diabetics with poor glycemic control respectively. Highest mean value of triglyceride and LDL-C in patients belongs to poor glycemic control. Almostsimilar mean value of VLDL and HDL-C in patients belongs to every group.

DISCUSSION:

International diabetes federation (2013) in its report stated that the countries with the greatest number of individuals with diabetes in 2013 are china (98.4 million), India (65.1 million) , United States (24.4 million) , Brazil (11.9 million) , and the Russian federation (10.9 million). Up to 80% of individuals with diabetes live in low income or medium income countries. Present study reported pre diabetics 37.6% , diabetics 28.5%. (14)According to GR andGupta (2014) vitamin D deficiency prevails in epidemic proportion all over the Indian subcontinent, with a prevalence of 70- 100% in the general population.(15)Present study reported that the mean vitamin D3 level in pre diabetics group were 13.22, 25.45 and 35.71 respectively. The mean value of vitamin D in diabetic group with good glycemic control and poor glycemic control were 13.40, 25.17, 37.65 and 10.37, 24.3 respectively. In addition, a study had shown that the overall prevalence of vitamin D3 deficiency was found to be 95% with 58% having insufficient levels of vitamin D3 and 37% of them had severe vitamin D3 deficiency.(16)Furthermore, study done by Daga et al (17) in the North of India in which he had quoted that 91.1% of diabetic patients had vit D insufficiency and in another study done by Mohammed Ali Bayani etal (18) among the diabetic patients in Iran had shown that the overall prevalence of vitamin D3 deficiency was 90%. In a multi-centric study in Iran, Heshmat et al. reported that the prevalence of moderate to severe vit D deficiency was 47.2, 45.7 and 44.2% in age group of <50, 50-60 and >60 years old, respectively.(19) India is a tropical country and is sunny all around the year. Vitamin D3 deficiency is found to be an epidemic inspite of plenty of sunlight.(20-22) This is mainly due to darker skin pigmentation, reduced physical activity, pollution, inadequate sun exposure (purdah system), low consumption of vitamin D3 rich foods, absence of fortification, old age, female sex, higher latitudes and winter season. The third NHANES reported an inverse association between vitamin D3 and metabolic risk factors.(23,24) Vitamin D3 deficiency per se producing many of the systemic complications and when this is combined along with type 2 diabetes mellitus it further leads on to various systemic manifestations like coronary artery diseases and cerebrovascular diseases.(16)In present study reported that the mean values of lipid profile depending upon glycemic status. Mean value of total cholesterol values was highest in poor glycemic control. Highest mean value of triglyceride and LDL-C in patients belongs to poor glycemic control. In addition, Kansal (2016) did a study cross sectional, included 124 pre-diabetic and 101 controls. Mean value of total cholesterol, triglyceride and LDL for prediabetic cases was more than mean value of controls.(25)Jain et al (2013) observed 150 diabetic and compared the lipid profile between those with good and poor glycemic control. For diabetics with good and poor glycemic control, mean value of triglyceride was 138.61 and 165.39 respectively. (26)Bhatnagar et al (2016) in an observational study on 30 pre-diabetics and 30 diabetics found that the fasting value of triglyceride in pre diabetics was 131.1 and in diabetics 164.9. (27)Present study substantiates vitamin D deficiency as risk factor for worsening glycemic control and dyslipidemia. Our study also provides the

rationale for supplementation of vitamin D for prevention of progression of pre diabetes to diabetes, worsening of metabolic control, and development of metabolic syndrome.

CONCLUSION:

Although causality remains to be proven, our results provide the rationale to further explore vitamin D as a promising marker for dyslipidemia in pre-diabetics and diabetics. Future studies may be necessary to evaluate the relationship of vitamin D deficiency to cardiovascular complications and the mechanisms thereof. Our study also provides the rationale for supplementation of vitamin D for prevention of ischemic stroke.

REFERENCES:

- Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract* 2011;94:311-21.
- Moreira TS, Hamadeh MJ; The role of vitamin D3 deficiency in the pathogenesis of type 2 diabetes mellitus. *Eur J Clin Nutr*. 2010;5:155-165.
- Hotamisligil GS, Arner P, Caro JF, Atkinson RL, Spiegelman BM; Increased adipose tissue expression of tumour necrosis factor-alpha in human obesity and insulin resistance. *J Clin Invest*. 1995;95:2409-2415.
- Schleithoff SS, Zittermann A, Tenderich G, Berthold HK, Stehle P, Koerfer R; Vitamin D3 supplementation improves cytokine profiles in patients with congestive heart failure: a double-blind, randomized, placebo-controlled trial. *Am J Clin Nutr*. 2006;83:754-749.
- Pittas AG, Bess DH; Vitamin D3 and Diabetes. *J Steroid Biochem Mol Biol*. 2010;121:425-429.
- West IC; Radicals and oxidative stress in diabetes. *Diabetic Med*. 2000;17:171-180.
- McGreevy C, Williams D. New insights about vitamin D3 and cardiovascular disease: a narrative review. *Ann Intern Med*. 2011;155:820-6.
- Pittas AG, Harris SS, Stark PC, et al. The effects of calcium and vitamin D3 supplementation on blood glucose and markers of inflammation in nondiabetic adults. *Diabetes Care*. 2007;30:980-6.
- Aljabri KS, Bokhari SA, Khan MJ. Glycemic changes after vitamin D3 supplementation in patients with type 1 diabetes mellitus and vitamin D3 deficiency. *Ann Saudi Med*. 2010;30:454-8.
- Shao T, Klein P, Grossbard ML. Vitamin D3 and Breast Cancer. *Oncologist*. 2012;17:36-45.
- Michos ED, Reis JP, Post WS, et al. 25-Hydroxyvitamin D3 deficiency is associated with fatal stroke among whites but not blacks: The NHANES-III linked mortality files. *Nutrition*. 2012;28:367-71.
- Forouhi NG, Luan J, Cooper A, Boucher BJ, Wareham NJ. Baseline serum 25-hydroxy vitamin D3 is predictive of future glycemic status and insulin resistance: The Medical Research Council Ely Prospective Study 1990-2000. *Diabetes*. 2008;57:2619-25.
- Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. *Am J Clin Nutr*. 2004;79:820-5.
- International diabetes federation (2013) , <http://www.idf.org> accessed at 25 march 2016
- G R, Gupta A. Vitamin D deficiency in India: prevalence, causalities and interventions. *Nutrients*. 2014 Feb 21;6(2):729-75.
- Kirubhakaran Kanakaraju, Rangabashyam Seetharaman Ranganathan, Shankar R. Correlation of vitamin D3 levels and the blood sugar parameters among the patients with type 2 diabetes mellitus. *International Journal of Contemporary Medical Research* 2017;4(4):844-847
- Daga RA, Laway BA, Shah ZA, et al. High prevalence of vitamin D3 deficiency among newly diagnosed youth-onset diabetes mellitus in north India. *Arq Bras Endocrinol Metabol*. 2012;56:423-8.
- Mohammad Ali Bayani, Rogheych Akbari, Bahar Banasaz, and Fayyaz Saeedi. Status of Vitamin-D in diabetic patients. *Caspian J Intern Med*. 2014;5:40-42.
- Heshmat R., Tabatabaei-Malazy O., Abbaszadeh Ahranjani S., Shahbazi S., Khooshehchin G., Bandarian F., et al. Effect of vitamin D3 on insulin resistance and anthropometric parameters in Type 2 diabetes: a randomized double-blind clinical trial. *Daru*. 2012;20(1):10.
- Penckofer S, Kouba J, Wallis DE, Emanuele MA. Vitamin D3 and diabetes: let the sunshine in. *Diabetes Educ*. 2008;34:39-40.
- Matsumoto K, Miyake S, Yano M, Ueki Y, Akazawa S, Tomijnaga Y. Glucose tolerance, insulin secretion, and insulin sensitivity in nonobese Japanese subjects. *Diabetes Care*. 1997;20:1562-68.
- Baynes KC, Boucher BJ, Feskens EJ, Kroumhout D. Vitamin D3, glucose tolerance and insulinemia in elderly men. *Diabetologia*. 1997;40:344-7.
- Grimnes G, Figenschau Y, Almas B and Jorde R. Vitamin D3, Insulin Secretion, Sensitivity, and Lipids Results From a Case-Control Study and a Randomized Controlled Trial Using Hyperglycemic Clamp Technique. *Diabetes*. 2011;60:2748-57.
- Scrugg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D3, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. *Diabetes Care*. 2004;27:2813-8.
- Kansal S Kamble TK. Lipid profile in pre diabetes. *J Assoc Physicians India*. 2016 Mar;64(3):18-21.
- Jain M, Jadeja JM, Mehta N. Correlation between HBA1c values and lipid profile and in type 2 diabetes mellitus. *International journal of basic and applied physiology* . 2013; 2(1): 47-50.
- Bhatnager MK, Goel K, Kumar R, Sud R. Pattern of dyslipidemia in prediabetic and diabetic: A pilot study *Asia Pacific journal of research* 2016; 22(1): 76-81