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RELATIONSHIP OF VITAMIN D LEVELS WITH DAIRY INTAKE, AND SUN EXPOSURE IN DIABETIC PATIENTS

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ABSTRACT **Introduction:** Vitamin D deficiency has been shown to alter insulin synthesis and secretion with additional biological roles to the well-known effects, it has on calcium homeostasis. The mechanism of action of Vitamin D in diabetes is thought to be mediated not only through the regulation of plasma calcium levels, which regulate insulin synthesis and secretion but also through a direct action on pancreatic beta-cell function. Therefore, owing to its increasing relevance, this study has focused on the relationship between vitamin D, milk intake, and sun exposure in well-defined diabetes patients along with controls. **Method**: This study was conducted for one year on five hundred adult diabetes and control cases who participated in the interview and medical examination. The relationship between diabetes, milk intake, and sun exposure with serum 25-hydroxyvitamin D levels was evaluated using regression analysis in the presence of demographic and clinical covariates, such as age, education, employment, and persistent hyperglycemia. **Results:** The mean age ranges between 51.52±7.70 and 52.24±7.90 in DM and control groups respectively with male preponderance seen in both groups. The number of patients consuming milk was almost the same (24.11±3.12) and sun exposure for less than 1 hour was 68% which was similar in both DM and controls. It was observed that several males (72%) were more in the control group were consuming milk >250ml/day as compared to DM patients. Sun exposures between 1-3 hours were also similar in both groups. Mean serum 25 (OH) D levels in diabetic cases (24±9.82 nmol/L) are significantly lower than controls (41.14±9.82nmol/L) (p<0.0001). Serum 25(OH)D levels were significantly low in different age groups of DM male and female patients (p<0.001) while no difference was observed in control male and female age groups. **Conclusions:** There is a specific relationship between Vitamin D deficiency and DM. But many other lifestyle factors are well known to cause diabetes which may also cause Vitamin D deficiency.

KEYWORDS : Vitamin D, Dairy Intake, Sun Exposure, Diabetic.

BACKGROUND:

The biologically active form of Vitamin D, 25-hydroxyvitamin D-[25(OH) D], is not a drug but an endogenous, naturally occurring, photo-chemically produced steroidal molecule with essential functions in systemic homeostasis and physiology. It includes modulation of calcium metabolism, cell proliferation, cardiovascular dynamics, immune/inflammatory balance, neurologic function, and genetic expression. Insufficient/deficiency endogenous production due to lack of sufficient sun exposure necessitates, food supplementation like milk intake to meet physiologic needs and may result in slight yet extensive disturbances in cellular function which appear to promote the manifestation of sub-acute long-latency deficiency diseases such as osteoporosis, cardiovascular disease, hypertension, cancer, depression, epilepsy, diabetes, insulin resistance, autoimmune disease, migraine, polycystic ovary syndrome, and musculoskeletal pain. The socioeconomic burdens of these diseases that have been linked to 25(OH)D insufficient/deficiencies, due to milk intake and sun exposure are enormous.

It has recently been emphasized that 25(OH)D insufficient/deficiency might become an unnecessary pandemic affecting developed and developing countries in the public health crisis (1,2). The incidence of Diabetes is increasing worldwide and results from a lack of insulin or inadequate insulin secretion following increases in insulin resistance. Therefore, it has been found that 25(OH) D insufficient /deficiencies play an important role in insulin resistance resulting in diabetes (3). The potential role of 25(OH)D deficiencies in insulin resistance has also been proposed to be associated with inherited gene polymorphisms including Vitamin D-binding protein, Vitamin D receptor, and Vitamin D 1alpha-hydroxylase gene. Other roles have been projected to involve immune-regulatory function by activating innate and adaptive immunity and cytokine release, activating inflammation by upregulation of nuclear factor κB and inducing tumor necrosis factor α, and other molecular actions to maintain glucose homeostasis and mediating insulin sensitivity by a low calcium status, obesity, or by elevating serum levels of parathyroid hormone. These effects of 25(OH)D insufficient /deficiency, either acting in concert or alone, all serve to increase insulin resistance or also affect pancreatic β-cells and insulin sensitivity (4,5).

A meta-analysis of largely observational studies had concluded that there was "a relatively consistent association between low Vitamin D status, calcium or dairy intake, and prevalent Diabetes or metabolic syndrome" (6)

This study aimed to examine the relationships between 25(OH)D levels, milk intake, and sun exposure in well-defined diabetes patients (DM) as assessed by a Fasting blood glucose test (FB)/ Glycosylated Hemoglobin (HbA1c) in a population-based prospective study.

MATERIALS AND METHODS:

Study samples: The study was conducted on indoor and outdoor patients of the Himalayan Institute of Medical Sciences, Dehradun, India for a period of one year (January to December), and an equal number of age and sex-matched controls were taken which included a total of 500 adults. Inclusion criteria were as follows: 30–60 years old, living in Dehradun district (latitude 30° 15' N) for more than 5 years, employed in an office setting, and must be graduate in education. Exclusion criteria included the following: use of Vitamin D and Calcium supplementation within 60 days of screening, current use of cigarettes (self-reported), alcohol abuse (defined as >14 drinks/week for men, >7 drinks/week for women), diagnosis of overt diabetes, cardiovascular disease or other systematic disease, use of medications that influence Vitamin D, glucose, lipid profiles or blood pressure. This study was approved by the Hospital Ethics Committee and all subjects provided written informed consent.

CLINICAL ASSESSMENT: BMI was categorized as normal weight (<24 kg/m2), overweight (24–28 kg/m2) and obese (>28 kg/m2), FB: normal (60 to 100 mg/dl), and HbA1c (controlled<7% and >7% uncontrolled). Vitamin D nutritional status was based on 25(OH) D levels, which were assessed as mild/sufficient (30–50 nmol/L), moderate/insufficient (12.5–29.9 nmol/L), and severe/deficient (<12.5 nmol/L).

STUDY TOOLS: A self-designed structured interview schedule cum questionnaire was used to elicit a detailed history regarding the duration of diabetes, and dietary habits related to milk or its supplements like tea and sun exposure.

STUDY PROTOCOL: Baseline characteristics: (for diabetes and control group): Demographic details were recorded in subject pro forma that included age, sex, address, and occupation.

PATIENTS WERE SUBJECTED TO ROUTINE INVESTIGATIONS.

Serum 25(OH)D levels which were done in all the DM and controls by enzyme immunoassay for the quantitative in vitro diagnostic measurement of a total 25(OH)D (Vitamin D2 and Vitamin D3) (7).

Data Management & Statistical Analysis: Data collected were subjected to statistical analysis, with the help of SPSS version 17, using an unpaired t-test to test the significance.

RESULTS:

The present study was conducted on 500 adults male and female to estimate serum 25(OH)D levels in DM and control groups for over one year. The mean age ranges between 51.52±7.70 and 52.24±7.90 in DM and control groups respectively. Mean BMI was the same but male preponderance was seen in both groups. The number of patients consuming milk was almost the same (24.11±3.12) and sun exposure for less than 1 hour was 68% which was similar in both DM and controls. It was observed that the number of males (72%) was more in the control group who were consuming milk >250ml/day as compared to DM patients. Sun exposures between 1-3 hours were also similar in both groups. Mean serum 25 (OH) D levels in diabetic cases (24±9.82 nmol/L) are significantly lower than controls (41.14±9.82nmol/L) ($p<0.0001$).

Serum 25(OH)D levels were significantly low in different age groups of DM male and female patients ($p<0.001$) while no difference was observed in control male and female age groups. (Table:1)

DISCUSSION:

Recent interest in Vitamin D metabolism has been fueled by worldwide trends in the prevalence of Vitamin D insufficient/deficiency and the potential role of Vitamin D in the development of DM. The action of Vitamin D is probably more complex than initially thought and the association between Vitamin D deficiency and DM deserves a lot of assessment (8).

Vitamin D is a hormone and a fat-soluble vitamin that is synthesized in the body and depends on multiple factors like latitude, atmospheric pollution, clothing, skin pigmentation, calcium or dairy intake, and duration or time of exposure to sunlight. The FAO/WHO expert consultation states that in most locations of the world between 420N and 420S latitude there is abundant sunshine. This is responsible for the physiological production of Vitamin D endogenously in the skin from the 7-dehydrocholesterol present in the subcutaneous fat. Thirty minutes of exposure of the skin over the arms and face to sunlight, without the application of sunscreen. Preferably between 10 am to 2 pm (as maximum ultraviolet B rays are transmitted during this time) daily is adequate to avoid Vitamin D deficiency (9).

Our study was the first population-based prospective study at Dehradun (latitude 30° 15' N) to have investigated the association between Vitamin D status in DM patients by measuring serum 25(OH)D and to see the effects of different parameters like milk intake and sun exposure in the office setting graduate educated persons.

It was suggested from our study that only BMI does not have any relationship between High/ Normal/ Low serum 25 (OH) D in DM or control groups but Wortsman et al in 2000 have reported that some lifestyle factors may be associated with lower Vitamin D concentration, such as reduced physical activity, and increased body mass index due to deposition of Vitamin D in adipose tissue, where it becomes biologically inactive and thus renders the person Vitamin D deficient (10). Vitamin D may affect DM as it is involved in pancreatic cell function including regulating sensitivity to insulin action.

The Women's Health Study has examined an association between Vitamin D intake and the incidence of type 2 DM and reported that a higher intake of Vitamin D was associated with a lower risk of DM (11). A similar effect was also seen in the Nurse's Health study that at higher latitude- countries situated outside of the tropics serum Vitamin D values vary seasonally, with concentrations towards the end of the summer period significantly higher than those found during late winter (12). At latitudes above 400 North or south, photoconversion of 7-dehydrocholesterol to pre–Vitamin D does not occur to any great extent in winter months, and as latitude rises above these levels, even summer synthesis may be blunted (13).

Our study has also suggested that DM patients who were consuming milk more than 250 ml/day had more serum 25(OH) D levels as compared to DM patients who were consuming milk less than 25 ml/day. Milk is very high in calcium, and it helps muscles and nerves to work properly. Calcium plays an important role in maintaining bone while Vitamin D helps to absorb and use calcium. Vitro studies have suggested that calcium may improve insulin sensitivity by increasing the binding affinity of insulin to its receptor and promoting insulin-mediated glucose transport in adiposities. It has been reported a positive association between dietary calcium and 5-year insulin sensitivity, as assessed by the intravenous glucose tolerance test, and an improvement in insulin sensitivity after the daily administration of 1,500 mg of calcium in patients with type 2 diabetes and hypertension (14). It is therefore possible that supplemental calcium may improve insulin sensitivity.

From the above discussion, Vitamin D has a significant role to play in normal glucose metabolism. It acts through several mechanisms on glucose metabolism:

1. Vitamin D directly acts on insulin-producing cells in the pancreas to produce more insulin.
2. Vitamin D directly acts on the muscle and fat cells to improve insulin action by reducing insulin resistance.
3. Vitamin D reduces inflammation which is commonly present in patients with Insulin Resistance Syndrome and DM.
4. Vitamin D indirectly improves insulin production and its action by improving the level of calcium inside the cells.

There is a specific relationship between Vitamin D deficiency and DM. But many other lifestyle factors are well known to cause diabetes which may also cause Vitamin D deficiency and intuitively, vitamin D deficiency can lead to diabetes.

Table 1:

Diabetic Patients (Number=250) (Mean age=51.52±7.70)						
Age in years	Male=160			Female=90		
	30-39	40-49	50-60	30-39	40-49	50-60
Milk Consumers in ml/day	Number (%)					
50-250	26(16)	32(20)	20(12)	18(20)	14(15)	12(13)
250-500	57(35)	15(9)	10(6)	23(25)	15(17)	08(9)
Sun exposure	Number (%)					
< 1 hour	55(34)	45(28)	10(6)	25(28)	13(14)	09(10)
> 1-3 hours	22(13)	13(8)	15(9)	14(15)	06(7)	23(25)
Serum 25 (OH) D Levels in nmol/L	23±8.48	24±9.82	16±15.30	25±6.01	22±7.12	21±6.01
BMI (Mean±SD)	23.07±6.01	25.11±5.61				

Control (Number=250) (Mean age=52.24±7.90)						
Age in years	Male=160			Female=90		
	30-39	40-49	50-60	30-39	40-49	50-60
Milk Consumers in ml/day	Number (%)					
50-250	20(12.5)	22 (14)	15(9)	22(24)	18(20)	10(11)
250-500	63 (39)	25 (16)	15(9)	08(9)	20(22)	12(13)
Sun exposure	Number (%)					
< 1 hour	65 (41)	15 (9)	29 (18)	15(17)	18(20)	20(22)
> 1-3 hours	12 (7)	14 (8)	25 (16)	10(11)	5(6)	22(24)
Serum 25 (OH) D Levels in nmol/L	43±8.11	40±6.62	37±7.30	45±7.23	42±7.22	41±5.01
BMI (Mean±SD)	23.37±2.93	21.11±7.61				

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