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A CROSS-SECTIONAL STUDY TO STUDY THE ASSOCIATION OF VITAMIN D LEVELS WITH GLYCOSYLATED HEMOGLOBIN LEVELS IN ELDERLY OF BANGALORE CITY

Physiology

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ABSTRACT

BACKGROUND: Ageing is a natural process and healthy ageing has become a growing global challenge. The process of ageing affects nutritional needs, they are particularly prone to inadequate intake of VitaminD. Vitamin D is suggested to influence glucose homeostasis. An inverse relationship between serum 25-hydroxyvitamin D (25[OH]D) and glycemic control with type 2 diabetes was reported in previous studies. Hence this study was undertaken to investigate the association between vitamin D and Glycosated Hemoglobin levels in elderly of Bangalore city.

OBJECTIVES: A. To estimate Serum Vitamin D levels in the elderly. B. To estimate Glycated Hemoglobin Levels in the elderly C. To correlate the Vitamin D levels with Glycosylated Hemoglobin Levels in the elderly of Bangalore city.

METHODOLGY: This study involved 80 healthy elderly subjects with consideration of inclusion and exclusion criteria. Written informed consent was taken. For each subject, fasting blood sample of 4ml was collected for Serum 25(OH) Vitamin-D assessment and Glycosylated Hemoglobin levels. Anthropometric measurements were taken. 24-hour dietary recall, General history questionnaire were administered. Results were compiled and statistically analyzed.

RESULTS: Serum 25(OH)D levels were inversely associated with A1C levels. These results are after adjusting for age, sex, A1C, BMI, treatment and duration of diabetes.

CONCLUSION: It can be concluded that Low Serum Vitamin D levels were associated with higher Glycosalated Hemoglobin levels warranting the need for educating the senior citizens the importance of Vitamin D and its supplementation for a Healthy Ageing.

KEYWORDS

Vitamin D, Diabetes Mellitus, Hemoglobin A1c, Glycemic Control

INTRODUCTION

Ageing is defined as gradual, insidious, and progressive decline in structure and function (involving molecules, cells, tissues, organs) that begin to unfold after the achievement of sexual maturity (Caruso LB et al;2008). Old age is regarded as a normal, inevitable physiological phenomenon (Park.k.2008). Government of India defined "Senior Citizen" as persons of age 60 years and above while adopting national policy on older persons in January 19993. Between 2000 and 2030, the number of older adults worldwide is expected to increase from 420 to 974 million (Jeyalakshmi S et al.2012) India has around 100 million elderly at present and expected to increase to 323 million, constituting 20% of the total population by the year 2050.(UNPF.2012)

Adequate nutrition is fundamental to healthy ageing1(Caruso LB et al;2008). Energy requirements decrease with age due to decline in lean body mass and decreased physical activity and slowed rates of protein turnover(Caruso LB et al;2008).. Despite this decrease, older adults are at risk of under nutrition due to medication side effects, functional, visual, or cognitive impairment, oral disease, swallowing disorders, or loss of smell/taste, depression and social isolation, and chronic illnesses (Caruso LB et al;2008).. Although vitamin requirements do not change with age, older adults are particularly prone to inadequate intake of Vitamin D, Vitamin B12 and Calcium and are also associated with reduced Calcium and Vitamin D absorption. (Caruso LB et al;2008).

Vitamin D is a fundamental micronutrient and it's insufficiency has been reported to be a quite common finding in type 2 diabetic patients (Mathieu C et al.2005;ozfirat et al.2010;Maxwell C S et al. 2011). In diabetic and non-diabetic subjects, a significant inverse relationship between glycated hemoglobin (A1C) and serum 25(OH)D levels has been observed

(Tahrani AA et al .2010;Cigolini et al.2006;Kositsawat J et al. 2010). Vitamin D may improve glucose-stimulated insulin secretion in pancreatic b-cells (Kositsawat J et al. 2010), enhance glucose and lipid metabolism in skeletal muscle (Rajakumar K et al.2010;Xuan Y et al.2010), and ameliorate systemic inflammation (Xuan Y et al. 2013). Most, but not all, patients with T2D or glucose intolerance may have lower serum 25(OH)D levels when compared to healthy control subjects (Pittas AG et al. 2010). Therefore, the aim of the present study was to investigate the the correlation between Hb A1C and serum 25(OH)D in the elderly of Bangalore city.

OBJECTIVES

A. To estimate Serum Vitamin D levels in the elderly.
B. To estimate Glycated Hemoglobin Levels in the elderly
C. To correlate the Vitamin D levels with Glycosylated Hemoglobin Levels in the elderly of Bangalore city

METHODOLOGY

In this descriptive correlational study after obtaining the institutional ethical clearance ,80 elderly aged more than 60 years were recruited from an enrichment center in Bangalore. To be included in this study, the subjects were 1) to have no history of Alzheimer's, hepatic disorders, renal disorders, Bone related Disorders, intake of vitamin D or Calcium supplements or drugs known to influence Vitamin D metabolism and sleep, 2) Possessing Verbal communication skills necessary to understand and respond to questions, 3) to be able to care for themselves independently (Informed consent was taken from all subjects or their families if the subject was unable to read or write), 4) to be non-alcoholic and non-smokers, 5) more than High school level education.6) All participants were taking medications for the treatment of DM and its complications. The study was done during the period of June to August 2019 which is neither winter nor summer in Bangalore city. After explaining the entire procedure, Written Informed consent was obtained. General Physical examination and systemic examination was done. Demographic characteristics, past medical history and use of medications were collected via structured questionnaire. Height and weight were measured, and BMI calculated using Quetlet's Index (wt in kg/ Height in m2). For each subject, fasting blood sample of 8 ml was collected by trained registered medical personnel for Serum 25(OH) Vitamin-D assessment and Glycosolated Hemoglobin Levels.

MEASUREMENT OF SERUM VITAMIN D LEVELS:

This study measured serum 25-hydroxyvitamin D, which is the best indicator of vitamin D conditions in the body [Norman AW]. Specimens were kept frozen until they were analyzed by fully automated chemiluminescence immunoassay method. Participants with serum 25 hydroxyvitamin D >30 ng/ml were considered as having sufficient vitamin D levels whereas participants with serum 25-hydroxyvitamin D of 20-30 ng/ml or less than 20 ng/ml were considered as having insufficient or deficient vitamin D levels, respectively (Holick MF et al. 2009).

MEASUREMENT OF GLYCOSOLATED HEMOGLOBIN LEVELS:

The level of HbA1c was determined by turbidimetric inhibition immunoassay (Genc S et al.2012) using a cobas b 101 system (Roche Diagnostics GmbH). According to a recent report from the American College of Physicians that recommended a target HbA1c of 7-8% for adults with DM (Holick MF. 2009), participants with HbA1c <8% were considered as having good glycemic control and participants with

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HbA1c>8% were considered as having uncontrolled Diabetes Mellitus.

STATISTICAL ANALYSIS:

The IBM SPSS statistics 20.0 software (IBM Corp., Armonk, New York, USA) was used to perform statistical analysis. All non-normally distributed continuous variables were log-transformed prior to analysis. Continuous variables were presented as mean ± standard deviation or median (interquartile range). Qualitative variables were presented as number (percentage). Differences in the mean levels of continuous variables between participants with good glycemic control and participants with uncontrolled DM were determined by Student's t-test. Differences in qualitative variables between participants with good glycemic control and participants with uncontrolled DM were determined by $\chi 2$ test. Differences in the mean level of 25-hydroxyvitamin D between participants with deficient, insufficient and sufficient vitamin D levels were determined using one-way analysis of variance with Tukey's post hoc test for multiple comparisons. Correlation analyses between HbA1c, and other continuous variables were performed using the Pearson product-moment correlation test. Multiple linear regression analysis was used to detect independent predictors of HbA1c. All P-values were two sided and considered statistically significant at <0.05.

RESULTS

This study is a prospective Case Control study which intends to estimate Vitamin D and HbA1C and correlate the same in the senior citizens of Bangalore City.

BASELINE CHARACTERISTICS OF THE PARTICIPANTS:

CASES:

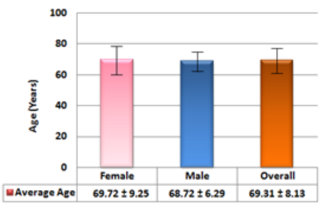
60 Subjects with decreased Vitamin-D levels

CONTROLS:

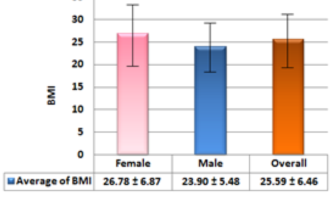
20 Subjects with normal Vitamin-D levels.

The baseline characteristic of the participants is shown in Graphs 1 to 3.

GRAPH – 1 Average Age of Subjects



GRAPH – 2 Average BMI of Subjects



The BMI of subjects ranged from 14.46 to 52.36. Both males and females had BMI within WHO said limits of Normal to Overweight category. None of them were obese.

GRAPH – 3 Dietary Habits of Subjects

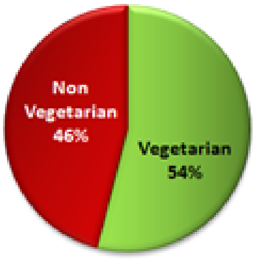


TABLE – 1 25(OH)D levels of the study groups

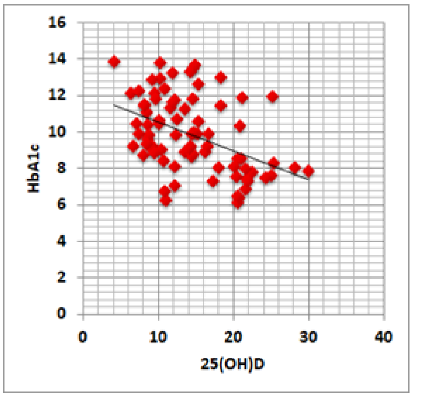
Serum 25(OH)D Concentration	*Cases Vitamin D Deficient (n = 60)*	*Controls Vitamin D Sufficient (n = 20)*
25 (OH) D ng/mL	13.5 ± 3.6	24.7 ± 3.0

TABLE – 2 Comparison of Means of Vitamin D Status, Mean Glycosolated Hemoglobin Levels in Elderly of Bangalore City

Parameters	*Cases Vitamin D Deficient (n = 40)*	*Controls Vitamin D Sufficient (n = 20)*	*P value*
Hb A1C levels	10.82 ± 2.35	7.3 ± 1.26	0.0001*

*P value significant

GRAPH – 4 Correlation between Vitamin D and HbA1c



25 (OH)D vs HbA1c	
R Value	P Value
-0.44008521	0.000044

Graph 4 shows the correlation between serum Glycosolated Hemoglobin levels and serum 25(OH)D levels. The negative correlation between serum Glycosolated Hemoglobin levels and Serum 25(OH)D being mildly significant establishes that as and when Serum 25(OH)D level has decreased, the Serum Glycosolated Hemoglobin Levels has increased.

DISCUSSION

In this Case Control study, 80 elderly citizens of age more than 60 years who met the inclusion and exclusion criteria were recruited for the study after obtaining the ethical committee clearance. Serum 25(OH) D were estimated and all the results were tabulated, statistically treated and expressed in appropriate graphs and tables. Age distribution of participants is shown in Graph 1. The Mean ± SD age of subjects ranged from 65 to 91 years with a mean age (±SD) of 67 (±7.1) years for cases and 67 (±7.1) years for controls. Wortsman et al in their study have proven that vitamin D bioavailability is affected by obesity. Graph 2 shows average BMI of the subjects which was 25.59 (±6.46) kg/m2. The average BMI of female subjects was 26.78 (±6.78) kg/m2 whereas the average BMI of male subjects was 23.90 (±5.48) kg/m2. Both the groups were not obese, thus nullifying one of the confounding factors that would have affected this study. Graph 3 shows the dietary habits of the subjects. There were 46% nonvegetarians and 54% vegetarians in the study. All subjects consumed the same diet every day. Vitamin D intake was almost negligible through vegetarian food. Moreover, the non-vegetarians in the group hardly consumed any nonvegetarian food.

SERUM VITAMIN D LEVELS:

Table 1 shows comparison of serum 25(OH)D levels of Cases and Control study groups. Several previous studies like Fradinger et al and Holick MF et al have reported low serum 25(OH)D levels in the older population. Older adults are at a risk of lower vitamin D due to decreased cutaneous synthesis, decreased dietary intake, and decreased intestinal absorption. In this study the dietary intake of vitamin D was negligible. This was in accordance with study done by Omdahl et al. With advancing age, a gradual vitamin D deficiency becomes evident. This is due to a reduction of the concentration of 7-dehydrocholesterol in the epidermis, typical during aging, and to a consequent decrease of synthesis under UV irradiation. On the other hand, a decreased exposition to UV light is frequent in the elderly people. In addition, a low nutritional intake of vitamin D is present.

SERUM GLYCOSYLATED HEMOGLOBIN LEVELS

The mean HbA1c value was, 10.86% in vitamin D deficiency subjects, 9.93% in vitamin D insufficiency and 7.73% in vitamin D sufficiency subjects which was in unison with the study done by Buhray BM etal. The need of accurate and precise measurement of blood glucose has made HbA1c become the gold standard for monitoring glycemic control in patients with DM from primarily fasting plasma (Higgins T et al.2013). Endorsement of influential diabetes societies and the World Health Organization for using HbA1c as a diagnostic test for diabetes arose due to the clear advantages for HbA1c over glucose monitoring (and in particular oral glucose tolerance test (OGTT)(Florowski C.2013).

ASSOCIATION

In the present descriptive study, the aim was to assess the association between serum 25-hydroxyvitamin D levels and measures of glycemic control in elderly with DM of Bangalore City. Patients with good glycemic control exhibited significantly higher levels of 25 hydroxyvitamin D compared with patients with uncontrolled DM. Additionally, patients with sufficient vitamin D status exhibited significantly lower HbA1c levels compared with patients with deficient vitamin D status. Correlation analysis also revealed significant inverse correlations between 25-hydroxyvitamin D levels and HbA1c levels. These findings are comparable with those reported in previous similar studies. For instance, Zoppini et al and Kostoglou-Athanassiou et al observed a signifcant inverse association between 25-hydroxyvitamin D and HbA1c levels in patients with type 2 DM, though Zoppini et al did not detect a significant correlation between 25-hydroxyvitamin D and FBG levels in their cohort. In addition, Lim et al and Kajbaf et al found a significant inverse association between 25 hydroxyvitamin D and HbA1c levels in type 2 DM patients with chronic kidney disease. In patients with type 1 or 2 DM, Buhary et al also detected a significant inverse association between HbA1c and 25-hydroxyvitamin D levels, and observed that supplementation of vitamin D was able to improve glycemic control by reducing HbA1c levels. This exposes the question of whether the relationship between vitamin D deficiency and glucose homeostasis is causal or confounding (Lips P et al.2017).

However, the possible role of vitamin D in glucose metabolism may be due to its action on VDRs expressed on cells of the pancreatic beta islets (Alvarez JA et al.2010), skeletal muscle and adipose tissue (Alvarez JA et al.2010;Simpson RU et al.1985). Vitamin D binding to these receptors may be involved in enhancing pancreatic insulin secretion and peripheral insulin sensitivity by increasing glucose uptake in skeletal muscle and adipose tissue (Alvarez JA et al.2017). In the current study, 25-hydroxyvitamin D was inversely associated with HbA1c. This suggests that maintaining a sufficient vitamin D level in DM patients may improve HbA1c. The effect of vitamin D on insulin secretion may also be indirect by increasing intracellular calcium (Lips P et.al.2017). One of the principal functions of vitamin D is to increase calcium absorption from the gastrointestinal tract (Christakos S et.al.2017). In the postprandial situation, increased vitamin D-dependent calcium absorption may increase intracellular calcium, which could act as a mediator of postprandial insulin secretion (Lips P et.al.2017) and thus improve HbA1c level. Collectively, the current study confirmed a significant inverse association between serum 25-hydroxyvitamin D and HbA1c levels. In addition, the impact of patients' medications on the association between 25-hydroxyvitamin D and glycemic control was taken in consideration by including these medications in the regression analysis. However, the cross-sectional design prevented investigation into why 25-hydroxyvitamin D level was associated with HbA1c. As such, this association requires further investigation to determine if vitamin D supplementation may improve glycemic control in adults with DM. If vitamin D supplementation was to improve glycemic control, then further research to determine the mechanism by which vitamin D affects glucose homeostasis would be warranted. However, this may encourage future studies into the potential relationship between serum vitamin D and individual DM complications such as eye lesions, vascular lesions and kidney disease.

CONCLUSION

In conclusion, the present study observed a significant inverse association between serum 25-hydroxyvitamin D and HbA1c levels in elderly with DM. Serum 25-hydroxyvitamin D level in patients with good glycemic control was significantly higher than in patients with uncontrolled DM. Advising patients with higher HbA1c to get tested for lower vitamin D values and correct any deficiency if found may result in better blood glucose control and benefit the patient's overall health .These findings may enhance further research to identify if vitamin D supplementation can improve HbA1c level in patients with DM, and if vitamin D can affect glucose homeostasis in DM.

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