DOI: 10.35845/abms.2024.1.298

ORIGINAL ARTICLE

Advances in Basic Medical Sciences

Lower Calciferol Level in Diabetic People and Their Association with Glycated Haemoglobin

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ABSTRACT

OBJECTIVE: To investigate the relationship between low calciferol levels and glycated hemoglobin in diabetics with normal blood sugar control.

METHODOLOGY: Vitamin D (calciferol) levels and HbA1c levels were examined in 110 individuals with type 2 diabetes and a control group, ensuring both groups were similar in terms of gender and age. Calciferol (25(OH)D3) level was determined using the method of radioimmunoassay (RIA) and High performance liquid chromatography technique (HPLC) was used to determine the glycosylated hemoglobin (HbA1c) level.

RESULTS: Calciferol levels were found low in the test group (type 2 diabetics' patients) 18.16 ± 0.85 ng/ml as compared to the control group 24.38 ±2.01ng/ml with (p≤0.000). The calciferol levels were assessed and it was found that they were inversely related to glycated haemoglobin levels in test group (r (2) = 0.047, linear regression, p ≤ 0.009,). Calciferol levels were also inversely associated with glycated haemoglobin levels in combined analyzed data of test and control groups (p ≤ 0.001, r (2) = 0.079).

CONCLUSION: The study determined that the calciferol levels were found with decreased frequency in diabetic group as compared to the control group and it showed that vitamin D levels have a key role in glycemic control in type 2 diabetics patients. These findings support the idea that type 2 diabetics' patients may improve their glycemic control by using vitamin D supplementation.

KEY WORDS: Calciferol; Adult Onset Diabetes Mellitus; Glycated haemoglobin; Sugar Control, Multivariate analysis

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Submission date: 11th October, 2023
Acceptance date: 21st June, 2024
Publication date: 21st June, 2024

INTRODUCTION

Skeletal cohesion is associated with calciferol level, there is high association of calciferol in extra skeletal effort and integrity and low level of calciferol shown to be associated in occurrence of adult onset diabetes.[1] It has been determined in previous studies that vitamin D level generally increases during pregnancy.[2] There are limited resources available to depict the level of vitamin D in general diabetic population. There have been several mechanisms mentioned in previous studies that highlight calciferol (vitamin D) levels links with HbA1c in diabetics' patients. Insulin secretion was found increase with Vitamin D level in pancreatic β-cells and Vitamin D improves insulin sensitivity in peripheral tissues that facilitate to lower HbA1c levels by consuming glucose level.[4]

Calciferol deficiency is very common among different population, an estimated 40% population of US are facing with Vitamin D deficiency.[5] Vitamin D deficiency are is increasing day by day among Pakistani population and having high incidence of adult Vitamin D deficiency amongst South Asian countries. The deficiency of calciferol levels among Pakistani population is about 73% with average level of 17.93 ng/mL.[6] Vitamin D level has a high impact on the quality of health of pregnant women in Pakistan and it is estimated that in Pakistan approximately 79.7% of population are facing Vitamin D deficiency.[7]

Calciferol (vitamin D) significantly impacts glucose metabolism and its regulation. It interacts with specific receptors and

This Article may be cited as, Kalsoom R, Khan RM, Umer S, Ustrana S, Ahmed I, Kalsoom F. Lower Calciferol Level In Diabetic People And Their Association with Glycated Haemoglobin.. Adv Basic Med Sci.2024;8(1):12-16. DOI: https://doi.org/10.35845/abms.2024.1.298

genetic polymorphisms involved in metabolic syndrome. In gestational diabetes, there is a negative correlation between calciferol levels and glycated hemoglobin (HbA1c). Low levels of calciferol increase the risk of gestational diabetes in the community.[8] Different studies support the idea of association of calciferol level with type 2 diabetes mellitus.[9] Some studies have observed that 41% of women with gestational diabetes mellitus (GDM) have inadequate 25(OH)D levels. These studies suggest that routine testing for 25(OH)D levels should be conducted in all pregnant women during GDM screening and highlight the importance of providing supportive treatment for women with vitamin D deficiency.[2,10,11]

This study was planned to highlight the importance of the association of calciferol level with glycated haemoglobin among diabetic population of Pakistan. There found a very high trend of diabetes among Pakistani population and it needed to explore the importance of Vitamin D and its association with other parameters to further provide a basic guideline for policy makers regarding the impact sufficiency of Vitamin D level among vulnerable Pakistani population and in patients with vitamin D associated disorders.

The aims of our study was to detect the calciferol level and their association allying calciferol and glycated Hb in non-insulin dependent diabetics.

METHODOLOGY

This descriptive cross sectional study was carried out among adult diabetic population at Cardiology Out Patient Department, District Head Quarter Hospital Dera Ismail Khan DIK , and department of Biochemistry Gomal Medical College DIK from January 2019 to June 2019. Ethical approval for the study was taken from ethical review board and formal written consent was taken from each study participants. For sample collection and to detect the HbA1c level 110 study subjects were selected with ages range 26-80 years and mean ages.

Patients who provide written consent, have been diagnosed with diabetes, and are managing it through diet or medication, and who attend the cardiology outpatient department during the study period will be included in the study. Pregnant women, individuals with other chronic diseases such as severe renal or hepatic diseases, and participants with incomplete data or disease profiles will be excluded from the study.

The study subjects were cases (diabetics managing with diet or on antidiabetic medications) and control group (non-diabetics having similar age level) attending cardiology outpatient department. Radioimmunoassay (RIA) technique was used for measuring 25(OH)D3 level. Acetonitrile procedure was used for quick removal of calciferol and other hydroxylated metabolites from blood. After removal of these metabolites, the tempered specimens were probed by competitive RIA procedure by treating with specific 25(OH)D3 antibody. The specimen, antibody and operative elements were incubated for 90 min at 20–25°C then switch to detachment step after 20 mint incubation at 20-25°C by using 2nd antibody impulsive compound. The detected calciferol level was categorized in two cut off levels ≤ 12ng/ml and ≤ 12ng/ml for comparison and interpretation of low and normal level of calciferol level.

After this incubation period and before centrifugation, buffer was added to prevent casual union, the availability of 25(OH)D3 was 100% approximately and sensitivity was ≤ 1.7ng/ml.

Statistical Package for the Social Sciences (SPSS 21) software was used for results examination. Student's *t*-test was applied on case and control groups for comparison. Regression analysis was applied to inspect the association between glycated haemoglobin and cholecalciferol. A pattern used to see the regularity of limiting factors in the regression assay was assessed using histograms and p-p plots. A chi-square test was applied to compare the number of cases having cholecalciferol deficiency within the studied cases and control individuals.

RESULTS

Glycated haemoglobin levels were high in cases as compared to the control group, HbA1c range being 6.1± 0.19 % and 6.3 ± 0.07 % in cases and control groups, respectively (p ≤ 0.05). In the diabetic group calciferol were lower than those in the control group, calciferol levels being 18.24 ± 0.85ng/ml and 24.39 ± 1.07ng/ml in the patient and control group, respectively (p ≤0.009).

Participants	HbA1c Level (%) MEAN ± SD n=110	Calciferol (ng/ml) MEAN±SD n =110	Calciferol	
			≤ 12ng/ml	< 22ng/ml
Patients	7.2±0.18	19.26±0.94	19 (16.6%)	69 (60.5%)
Controls	5.1±0.05	25.48±1.02	8(6.75%)	25 (21.26%)
Multivariate Analysis	p ≤0.005	p ≤ 0.009	p = 0.0067	p ≤ 0.000

Table 1: Multivariate analysis of the glycated Hb and calcerferol level of study participants

In the adult-onset diabetes mellitus (DM) group, 19 out of 110 patients (16.6%) had calciferol deficiency (≤ 12 ng/ml), compared to 8 out of 110 individuals (6.75%) in the non-diabetic control group, with a significant difference (p = 0.0067). Additionally, 69 out of 110 patients with adult-onset DM (60.5%) had calciferol insufficiency (< 22 ng/ml), as opposed to 25 out of 110 individuals (21.26%) in the control group, also showing a significant difference (p ≤ 0.000). (Table 1).

Calciferol levels were seen to be negatively associated with

glycated Hb levels in the community of adult onset DM patients (p = 0.009, r = 0.067, linear multivariate assays) (Figure 1). When the assays was performed in the whole studied community in adult onset DM and control group, it was detected that calciferol levels were negatively correlated with glycated Hb levels (p < 0.005, r2 = 0.075) (Figure 2).

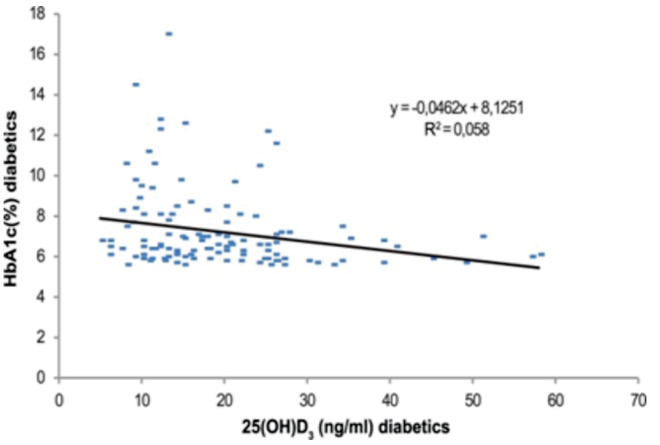

Figure 1: Association of Calceferol level and HbA1c level

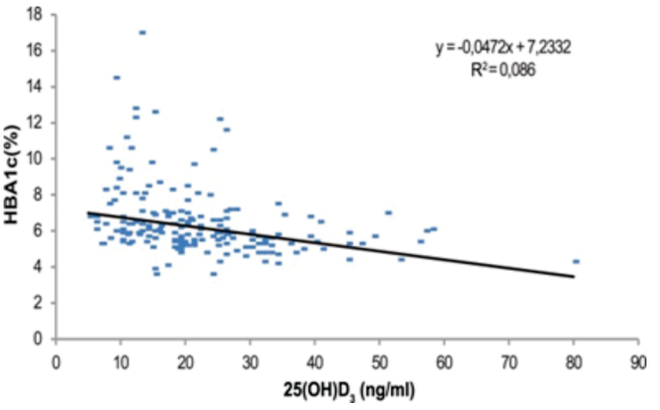

Figure 2: Negative correlation observed in linear multivariate analyses between affected community members in adult-onset diabetics and control subjects

DISCUSSION

This study revealed lower levels of calciferol in adult-onset diabetic patients compared to the control group. Additionally, a contrasting relationship was observed between HbA1c levels and calciferol levels in non-insulin-dependent diabetics, suggesting that calciferol levels may play a role in influencing blood sugar control in adult-onset diabetes. Calciferol play role in immune system increases immune tolerance and bony metabolism because it is synthesis from UV light in the skin.[12] Low calciferol level causes different disorders like multiple sclerosis, Rheumatoid arthritis and DM type-1.[13] In cross-sectional study of eastern population, opposite interaction was noticed between calciferol, fasting insulin, fasting blood sugar and glucose tolerance test, presenting that low level of serum calciferol deranging the blood sugar metabolism.[14] A multimethod research study involving 735 newly diagnosed non-insulin-dependent diabetic women found a higher plasma concentration of calciferol, indicating a reduced risk of adult-onset diabetes.[15] In Asian community, calciferol deficiency was representing a higher chance of spread of adult onset diabetes. A larger sample was taken from middle age people involving 6658 cases initially diabetes-free, serum calciferol levels were negatively correlated with incident diabetes in female than in male.[16] Previous researches have been presenting that low intake of calciferol may be associated with a higher risk of occurrence of adult onset DM and the metabolic syndrome.[17] In our study, calciferol levels were establish to be oppositely associated with glyco hemoglobin and also show negative correlation in gestational diabetes so it is suggested that adequate intake of calciferol may be associated with decreased risk for occurrence of gestational diabetes. Calciferol receptors are situated in pancreatic beta cells, where they also express the alpha 1-hydroxylase enzyme. This enables calciferol to enhance and regulate insulin release from the pancreas' beta cells. Furthermore, calciferol influences the expression of insulin receptors. Therefore, calciferol deficiency can lead to insulin resistance and impair insulin secretion in adult-onset diabetes mellitus (DM).[18]

The injection of 2000 (IU) calciferol daily for 16 weeks was detected to enhance beta cell outcome in those who are endangered for diabetes. Injection of calciferol in diabetic patient with nephropathy was detected to improve albuminuria. Calciferol circulates in blood in different forms but calcitriol is its active form, calciferol also decreases oxidative stress at molecular level.[19]

More studies are required by using highly accurate equipment for diagnosis of calciferol deficiency in humans particularly in diabetic individuals. Further work is required with administration of calciferol supplements and persistent monitoring with sugar control in adult-onset diabetic individuals. Calciferol deficiency also causes metabolic diseases and autoimmunity.[20]

In addition, recent studies have been done which representing the association between DM and adipose tissues because calciferol have adipogenic effect and in this way, it regulates the energy utilization in adipose tissue. The normal range of calciferol in blood of diabetic individuals may regulate sugar control, so in the individuals having tendency to develop adult onset DM, the normal concentration of calciferol in those individual decreases the chance of occurrence of adult onset diabetes mellitus.[21,22]

CONCLUSION

A negative correlation has been found between calciferol levels and glycated haemoglobin among diabetic population with controlled blood sugar. This study supported the idea that a high HbA1c level is always accompanied by a low calciferol level among the diabetic population. Proper treatment and intervention strategy of vitamin D among diabetic population can lower the consequences of diabetes related complications.

CONFLICT OF INTEREST: None

FUNDING: None

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CONFLICT OF INTEREST

Author declared no conflict of interest

GRANT SUPPORT & FINANCIAL DISCLOSURE

Author declared no specific grant for this research from any funding agency in the public, commercial or non-profit sectors

AUTHORS CONTRIBUTIONS

RK: Conception, Design of the work, Data collection, and Drafting, Reviewed, Final approval, Agreement to be accountable.

MRK: Conception, Design of the work, Acquistion, Data Analysis, and Drafting, Reviewed, Final approval, Agreement to be accountable.

SU: Conception, Design of the work, Interpretation of data for the work, and Drafting, Reviewed, Final approval, Agreement to be accountable.

SJU: Conception, Design of the work, Data collection, and Drafting, Reviewed, Final approval, Agreement to be accountable .

IA: Conception, Design of the work, Interpretation of data for the work,Data collection and Drafting, Reviewed, Final approval, Agreement to be accountable.

FK: Conception, Design of the work, Data collection, Data analysis and Drafting, Reviewed, Final approval, Agreement to be accountable.

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