ORIGINAL ARTICLE

# ASSOCIATION OF SERUM VITAMIN D WITH GLYCOSYLATED HEMOGLOBIN LEVELS AND DURATION OF DISEASE IN TYPE-II DIABETES MELLITUS PATIENTS

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## ABSTRACT

**Objective:** To find a possible association between levels of vitamin D and glycosylated hemoglobin levels in patients with type II diabetes mellitus.

**Material and Methods:** A cross-sectional study was conducted at a tertiary care hospital in Peshawar over six months. Diagnosed cases of Type-II diabetes mellitus were recruited through non-probability consecutive sampling. The levels of glycosylated hemoglobin and serum vitamin D levels were assessed in 219 selected patients enrolled in the study through Cobas Integra 800 and Enzyme-Linked Immunosorbent Assay respectively. Patients were divided into three categories based on increasing levels of glycosylated hemoglobin. The trend in the levels of vitamin D levels in these categories of increasing HbA1c was identified.

**Results:** Out of 219 Type II diabetic patients, 30.1% (66) were men while 69.9% (153) were women. The mean age was 59.48 ± 9.29 years. Similarly, HbA1c and serum vitamin D, were 9.47 ± 2.88 and 18.63 ± 16.54, respectively. Overall, 59% of the patients were Vitamin D deficient. The decrease in Vitamin D levels was associated with an increase in glycosylated hemoglobin levels (p-value 0.002).

**CONCLUSION:** Vitamin D deficiency in Type-II diabetes mellitus patients increases with increasing levels of glycosylated hemoglobin.

**Keywords:** Diabetes Mellitus, Type II Diabetes, HBA1c, Vitamin D.

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## INTRODUCTION

Type-II Diabetes mellitus (DM) has been reported to be the most widely spread epidemic throughout the world in this century.[1] World Health Organization (WHO) projections reveal that the number of patients suffering from diabetes would escalate to 366 million in 2030. [2]

The economy of a country is highly affected by DM. Dealing with such a chronic condition takes a lot of time and resources from the healthcare system of the country. It is also of a great financial burden to the health system through medical bills. The work hours lost to the morbidity of DM means a decrease in the working force of the country as a whole. By 2045, 7.7% of the world's population would be debilitated by DM and its associated complications.[3] The greatest increase in the prevalence of DM is to be recorded in developing countries where healthcare resources are already scarce.[4]

These strains on the economy and medical resources caused by DM are also reflected in the population of Pakistan. A study conducted in Pakistan concluded that 9.5% rural population and 9.4% urban population in Pakistan is suffering from DM in 2007.[5] A Meta-analysis has revealed that the increased risk of T2M and GDM is associated with worsening deficiency of Vitamin D levels.[6] Vitamin D receptor activation enhances the insulin sensitivity, and secretion of insulin and protects the βcell against cy-

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tokines delaying the βcell maturation.[7]

Over the recent years, many studies have been conducted on the relationship of vitamin D deficiency with the duration and glycemic control of DM, however, most of the data accumulated in this regard have some level of contradiction. This inconsistency in the reported data has led to an emphasis on conducting further studies to assess the association of the levels of vitamin D in patients with DM and the factors affecting it. This study explores the possible association between levels of vitamin D and glycosylated hemoglobin levels in patients with type II diabetes mellitus.

## MATERIAL AND METHODS

This cross-sectional research project was undertaken in the admitted patients and out-patient Departments (OPD) of Endocrinology and Medicine, Hayatabad Medical Complex, Peshawar 6 months after the approval of the synopsis by KMU-ASRB.

We included in the study patients suffering from type-II diabetes mellitus, older than 30 years of age presenting to the department of Endocrinology, Hayatabad Medical Complex, Peshawar.

According to the "International Osteoporosis Foundation current guidelines 2010" vitamin D Insufficiency is defined as "A serum 25-hydroxyvitamin D level from 21-29 ng/ml", vitamin D deficiency defined as "A serum 25-hydroxyvitamin D levels < 20 ng/ml" whereas, vitamin D Optimal / Healthy Level are defined as "Serum 25-hydroxyvitamin D > 30 ng/ml". [8]

The study participants included Patients who were already confirmed as type-II Diabetics or patients having fasting blood glucose levels of ≥126 mg/dl after 8 hours of fasting or patients having plasma glucose levels of ≥ 200mg/dl after 2 hours of a glucose load of 75-g anhydrous glucose load dissolved in water or, Random plasma glucose level of ≥ 200mg/dl in a patient with classic symptoms of hyperglycemia.[9] Sample size was 216 calculated by the WHO formula through Goldberg's Equation.[10] Non-probability convenient sampling technique was employed in this study.

All patients meeting the inclusion criteria and consenting to the study were approached for participation in the study. Those type-II Diabetics who were on vitamin D & calcium supplements, steroids, chemotherapeutic agents, anti-epileptics, Bisphosphonates & Orlistat were excluded. Patients having chronic kidney diseases (eGFR< 60 ml/min), chronic liver diseases, history of Rickets/Osteomalacia or received treatment for it, malabsorption syndrome, thyroid disorders (Hypo & Hyperthyroidism), parathyroid disorders (Hypo & Hyperthyroidism), diabetics who were started on Insulin from the beginning, diabetics who were diagnosed with Ketoacidosis at the time of presentation and diabetics having BMI of < than 18 were not included in the study.

A questionnaire about the patient's demographics, disease duration, and treatment record was recorded. After an informed verbal & written consent, 5ml venous blood was withdrawn with 5ml disposable syringes from the vein of the subjects under aseptic conditions. Three milliliters of the blood was used for 25 Hydroxy-vitamin D levels & 1 ml was used for creatinine estimation.

Data were analyzed using SPSS 20. Categorical variables are expressed as percentages and continuous variables are expressed in means and standard deviations.

The 25-Hydroxyvitamin D was categorized into vitamin D deficient, insufficient, and optimum/ healthy levels. HbA1c was categorized as good control (6-6.67), fair control (6.8-7.65) and poor control (>7.65).[11] The chi-square test was used to evaluate the association between categorical variables HbA1c levels and vitamin D levels. P-value of < 0.05 was considered statistically significant.

## RESULTS

The study included 219 Type II diabetic patients. The mean age of the study participants was 59.48 ± 9.29 years as shown in figure 1. We reported 30.1% (66) of the patients were male while 69.9% (153) were females (table 1).

Overall 59% of the patients were Vitamin D deficient. 31% patients were severe vitamin D deficient while 28% of patients had Vitamin D Insufficiency. 41% of the total patients have optimal vitamin D levels as shown in figure 2.

In order to find out whether the effect of HBA1c on levels of vitamin D, levels of vitamin D were compared with HbA1c, Analysis revealed that vitamin D levels decrease with an increase in HbA1c levels with a p-value of 0.002 (Table 2)

## DISCUSSION

Type-II DM has been reported to be the most widely spread epidemic throughout the world in this century It has grown from 30 million in 1985 to 135 million adults in 1995, soaring up to 173 million in 2002 World Health Organization projections reveal that it would reach 366 million in 2030. [5]

The European Prospective Investigation into Cancer (EPIC)-Norfolk study after conducting a meta-analysis shows that irrespective of gender, duration, sample size, and the diagnostic criterion for T2DM, low levels of vitamin D levels are associated with T2DM while some studies associate different factors like age, gender, socioeconomic status, lifestyle, BMI, dietary intake and duration of T2DM.

**Table 1: Descriptive statistics of the study population**

| Variables | Sub group | Frequency (N) | Percent (%) |
|---|---|---|---|
| Gender | Male | 66 | 30.1 |
| | Female | 153 | 69.9 |
| Vitamin D Status | Vitamin D deficiency | 89 | 40.6 |
| | Vitamin D Insufficiency | 61 | 27.9 |
| | Vitamin D Optimal level | 69 | 31.5 |
| Age group | 40 - 30 years | 5 | 2.3 |
| | 60 - 41 years | 99 | 45.2 |
| | above 60 years | 115 | 52.5 |

**Table 2: Association of vitamin D levels with diabetic control**

| Vitamin D status | HbA1c control | | | p-value |
|---|---|---|---|---|
| | Good control | Fair control | Poor control | 0.002 |
| Vitamin D deficiency | 21 | 21 | 47 | |
| Vitamin D Insufficiency | 8 | 25 | 28 | |
| Vitamin D Optimal level | 23 | 8 | 38 | |
| Total | 52 | 54 | 113 | |

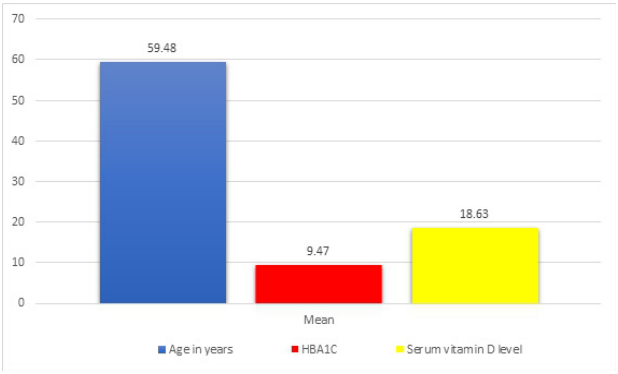


**Fig 1: Demographic data of the Diabetic patients**

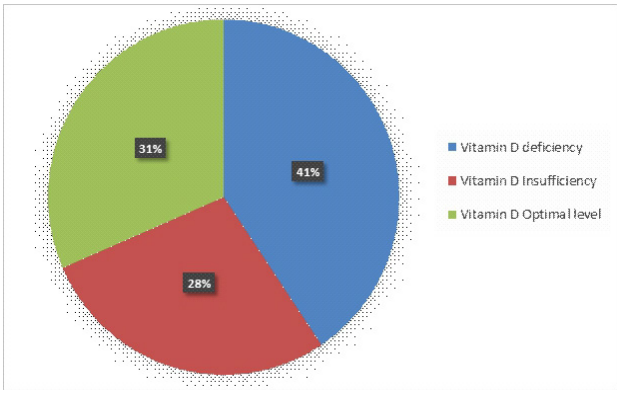


**Fig 2: Vitamin D levels of study population**

In our study, we have covered most of these factors and measured their significance in confounding the effect of diabetes in lowering serum vitamin D levels.[12]

In our study, we found that vitamin D deficiency is associated with T2DM. The association of vitamin D deficiency with T2DM has been found to be impacted upon by several factors. [13] We have found that vitamin D deficiency in T2DM is associated with an increase in age. We reported in our findings that vitamin D deficiency is less common in the age group of 30-40. As the age of the patients in our study increases, there is a progressive decrease in vitamin D levels (p-value 0.03). The decrease in vitamin D levels with increasing age has been depicted by several other studies.[14,15]

Our statistical analysis shows that higher levels of HBA1c have been found to be associated with a decrease in the levels of vitamin D. This association was displayed in the form of an inverse trend, the greater the levels of HBA1c, the lower the values of vitamin D were associated with it with a significant p-value of 0.002. Patients with optimum control of their sugar levels showed a normal range of serum vitamin D levels.[16,17]

## CONCLUSION

Vitamin D deficiency is associated with T2DM. Vitamin D deficiency in T2DM increases with increase in age and increases with poor glycemic control showed by an increase in HBA1c. This needs to be taken into consideration in the management of T2DM patients.

## REFERENCES

1. Moodley N, Ngxamngxa U, Turzyniecka MJ, Pillay TS. Historical perspectives in clinical pathology: a history of glucose measurement. Journal of Clinical Pathology. 2015;68(4):258. https://jcp.bmj.com/content/68/4/258
2. Mukhtar Y, Galalain A, Yunusa U. A modern overview on diabetes mellitus: a chronic endocrine disorder. Europe-

an Journal of Biology. 2020 Nov 23;5(2):1-4.

3. Ogurtsova K, da Rocha Fernandes J, Huang Y, Linnenkamp U, Guariguata L, Cho N, et al. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes research and clinical practice. 2017;128:40-50.
4. Misra A, Gopalan H, Jayawardena R, Hills AP, Soares M, Reza□Albarrán AA, et al. Diabetes in developing countries. Journal of diabetes. 2019 Jul;11(7):522-39.
5. Shera A, Jawad F, Maqsood A. Prevalence of diabetes in Pakistan. Diabetes research and clinical practice. 2007;76(2):219-22.
6. Zhang M-X, Pan G-T, Guo J-F, Li B-Y, Qin L-Q, Zhang Z-L. Vitamin D deficiency increases the risk of gestational diabetes mellitus: a meta-analysis of observational studies. Nutrients. 2015;7(10):8366-75.
7. Dong J-Y, Zhang W, Chen J, Zhang Z-L, Han S-F, Qin L-Q. Vitamin D intake and risk of type 1 diabetes: a meta-analysis of observational studies. Nutrients. 2013;5(9):3551-62.
8. Mithal A, Wahl DA, Bonjour J-P, Burckhardt P, Dawson-Hughes B, Eisman JA, et al. Global vitamin D status and determinants of hypovitaminosis D. Osteoporosis international. 2009;20(11):1807-20.
9. American Diabetes Association Diabetes Care 2018 Jan; 41(Supplement 1); S13-S27
10. Organization WH. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus. Geneva: World health organization, 1999
11. Hamid KM, Bala YG, Mainasara AS, Ahmed A. Serum level of Islet cells autoantibodies (anti-ICA and anti-GAD) and HbA1c among Type 2 diabetic patients. International journal of basic and applied research. 2019;9(3):119-28.
12. Forouhi N, Ye Z, Rickard A, Khaw K, Luben R, Langenberg C, et al. Circulating 25-hydroxyvitamin D concentration and the risk of type 2 diabetes: results from the European Prospective Investigation into Cancer (EPIC)-Norfolk cohort and updated meta-analysis of prospective studies. Diabetologia. 2012;55(8):2173-82.
13. Khan H, Kunutsor S, Franco OH, Chowdhury R. Vitamin D, type 2 diabetes and other metabolic outcomes: a systematic review and meta-analysis of prospective studies. Proceedings of the Nutrition Society. 2013;72(1):89-97.
14. Robinson JG, Manson JE, Larson J, Liu S, Song Y, Howard BV, et al. Lack of association between 25 (OH) D levels and incident type 2 diabetes in older women. Diabetes Care. 2011:DC_101632.
15. Oh J-Y, Barrett-Connor E. Association between vitamin D receptor polymorphism and type 2 diabetes or metabolic syndrome in community-dwelling older adults: the Rancho Bernardo Study. Metabolism-Clinical and Experimental. 2002;51(3):356-59.
16. Abdelsadek SE, El Saghier EO, Abdel Raheem SI. Serum 25 (OH) vitamin D level and its relation to diabetic peripheral neuropathy in Egyptian patients with type 2 diabetes mellitus. The Egyptian journal of neurology, psychiatry and neurosurgery. 2018 Dec;54(1):1-8..
17. Khan H, Kunutsor S, Franco OH, Chowdhury R. Vitamin D, type 2 diabetes and other metabolic outcomes: a systematic review and meta-analysis of prospective studies. Proceedings of the Nutrition Society. 2013;72(1):89-97.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

| | |
|---|---|
| **Mahmood A:** | Conceiving the idea, data collection |
| **Khan NA:** | Literature search writing up the article and Statistical analysis |
| **Ahmad S:** | Data collection |
| **Naz S:** | Literature search |
| **Ahmed F:** | Bibliography |
| **Khan J:** | Data collection |

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.