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Original Article

Prevalence and Associated Factors of Vitamin D Deficiency in T2DM Patients, pPresenting in Outpatient Department of a private Healthcare Facility of South Punjab, Pakistan

Qazi Masroor Ali,[1] Saba Anjum,[2] Raheel Khan,[3] Ali Imran,[4] Sadaf Shafique,[4] Aleena Masroor[2]

[1]Aleena Hospital, Bahawalpur, [2]Shahida Islam Teaching Hospital and Medical College, Lodhran, [3]Bahawal Victoria Hospital, Bahawalpur, [4]Quaid-e-Azam Medical College, Bahawalpur, Pakistan

Abstract

Objective: To determine the prevalence and associated factors of vitamin D deficiency (VDD) in type-2 diabetes mellitus (T2DM) patients.

Methods: This cross-sectional study was conducted at Outpatient Department of Aleena Hospital, Bahawalpur, Pakistan from 1st January 2023 to 30th June 2023. We analyzed patients of either gender aged above 18 years and diagnosed cases of type 2 diabetes mellitus for minimum duration of 6 months. At the time of enrollment, demographic and clinical characteristics were noted. VDD was described as serum vitamin D levels below 20 ng/ml, insufficiency between 20-29 ng/ml, whereas sufficiency or normal vitamin D levels were declared > 30 ng/ml.

Results: In a total of 90 patients, 62 (68.9%) were females. The mean age and BMI were 51.52±10.64 years and 27.51±5.23 kg/m2 respectively. The mean HbA1c was 9.01±1.87. The mean vitamin D levels were 19.07±8.4 ng/ml. VDD was observed in 55 (61.1%) and insufficiency 26 (28.9%), whereas normal levels were found in 9 (10.0%) patients. Relatively younger age (p=0.029), rising duration of diabetes (p=0.026), higher HbA1c (p=0.034) and hypertension were noted to have statistically significant association with VDD.

Conclusion: Evaluation of vitamin D status in type-2 diabetes mellitus revealed that vast majority of these patients were having inadequate levels of vitamin D. Relatively younger age, duration of diabetes, higher HbA1c and hypertension were having significant association with vitamin D inadequacy.

Keywords: Body mass index, type-2 diabetes mellitus, HbA1c, hypertension, vitamin D.

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Corresponding Author: Prof. Qazi Masroor Ali **Email:** masroorqazi@outlook.com

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Introduction

Among all metabolic noncontagious diseases, the frequency of diabetes mellitus (DM) is considerably higher contributing to morbidity, mortality, and the costs of health provisions.[1] Globally, more than 1.5 million deaths are attributed to DM, making it the 9th largest mortality cause.[2,3] Kidney disease and blindness are major diabetes-related microvascular complications that might end up in an amputation. Macrovascular complications in diabetes are also major contributor to global morbidity and mortality.[4] Financially compromised and middle-class communities are at increased risk of type-2 diabetes mellitus (T2DM). In the recent decades, modernized living styles and dietary habits are thought to be important factors behind high incidence rates of T2DM.[5]

Since, the major functions of vitamin D are to keep blood calcium and phosphorous at supersaturating concentrations, which are necessary for the development and maintenance of the skeletal system, its deficiency can cause skeletal impairments, with osteomalacia and osteoporosis being more common among adults and rickets among children.[6] Depression, cancer, and heart diseases might also occur due to a deficiency of vitamin D.[7,8] Vitamin D adjusts the intracellular levels of calcium, exerting an indirect effect on the secretion of insulin.[9]

Pancreatic tissue and various cell-type immune systems have also been suggested to express vitamin D receptors (VDR).[10] Some of the previous studies describe how the response of the VDR protein is modulated by genetic variants in the VDR gene.[11] Several genetic variants of VDR alter calcium metabolism, adipocyte function, insulin release, and cytokine production, leading to the development of T2DM.[11] Various cross-sectional studies conducted during the last 50 years mention in the "National Health and Nutrition Examination Survey (NHANES)" database that vitamin D3 has a significant association with insulin resistance. However, by analyzing subgroups, this correlation showed variation among different communities around the world.[12]

A regional study indicated that vitamin D deficiency (VDD) was noted among 74.1% of T2DM patients.[13] Researchers from Saudi Arabia revealed that 93.8% of T2DM patients had VDD.[14] Local data reported that 69% T2DM of patients had VDD.[15] Variations exist regarding the burden of VDD among T2DM patients, and not much data from South Punjab, Pakistan, is available exploring the subject; hence, it motivated us to plan this study. The objective of this research was to determine the prevalence and associated factors of VDD in T2DM patients.

Methods

This cross-sectional research was performed at Outpatient Department of Aleena Hospital, Bahawalpur, Pakistan from 1st January 2023 to 30th June 2023. Approval from Hospital Research Committee was acquired (letter number: HRC/05/2022). Informed and written consents were obtained from patients. Sample was calculated to be 90 considering the prevalence of VDD as 93.8%[14] in T2DM having 95% confidence level and margin of error as 5%. Non-probability convenient sampling technique was adopted.

We analyzed patients of either gender aged above 18 years and diagnosed cases of T2DM for minimum duration of 6 months. Patients who were willing to be part of this research and complied to provide blood samples for vitamin D testing were included. Patients of type-1 diabetes mellitus or other known endocrine disorders or conditions that could significantly impact vitamin D metabolism or levels were excluded. Patients who were currently taking vitamin D supplements were not enrolled. Patients having "chronic kidney disease" or "chronic liver disease" were also excluded. Patients using corticosteroids or anticonvulsants were also not included. Pregnant or lactation mothers were excluded.

At the time of enrollment, demographic and clinical characteristics like gender, age, residence, body mass index (BMI), history of smoking and family history of DM were noted. Body mass indexed was classified as "normal (BMI<23 kg/m^2)", "overweight (BMI ≥23 kg/m^2)" and "obesity (BMI ≥25 kg/m2)".[16] Hypertension was labeled if "systolic blood pressure ≥140 mmHg" and/or "diastolic blood pressure ≥ 90 mmHg" or patients on anti-hypertensive drugs or a known case of hypertension as verified by the medical record. Five ml blood was collected from each participant employing aseptic measures, and sent to hospital laboratory for evaluation of vitamin D levels. VDD was described as serum vitamin D levels below 20 ng/ml, insufficiency between 20-29 ng/ml, whereas sufficiency or normal vitamin D levels were declared > 30 ng/ml. Data was analyzed utilizing "Statistical Package for Social Sciences (SPSS)", version 26.0. Categorical data were represented as numbers and percentages. Numeric variables were shown as mean and standard deviation (SD). For comparison of the data, chi-square test or "analysis of variance (ANOVA)" were used considering $p<0.05$ as significant.

Results

In a total of 90 patients, 62 (68.9%) were females representing a female to male ratio of 2.2:1. The mean age was 51.52±10.64 years (ranging between 28-80) years. Residential status of 65 (72.2%) patients was rural. The mean BMI was 27.51±5.23 kg/m^2 (ranging between

Table 1: *Demographic and clinical characteristics (n=90)*

Characteristics		Number (%)
Gender	Male	28 (31.1%)
	Female	62 (68.9%)
Age (years)	<45	18 (20.0%)
	45-60	52 (57.8%)
	>60	20 (22.2%)
Residence	Urban	25 (27.8%)
	Rural	65 (72.2%)
BMI (kg/m^2)	Normal	15 (16.7%)
	Overweight	10 (11.1%)
	Obese	65 (72.2%)
Duration of diabetes (years)	. .	6 (6.7%)
	2-5	48 (53.3%)
	6-10	28 (31.1%)
	>10	8 (8.9%)
HbA1c (%)	<7	19 (21.1%)
	7-9	27 (30.0%)
	>9	44 (48.8%)
Hypertension		14 (15.6%)
History of smoking		5 (5.6%)
Family history of diabetes		10 (11.1%)

17.3 to 38.5 kg/m2). The mean HbA1c was 9.01±1.87 (ranging between 6.2 to 13.8). Table-1 shows details of demographic and clinical characteristics of patients. The mean vitamin D levels were noted to be 19.07±8.4 ng/ml ranging between 7.8 to 43.5 ng/ml. Evaluation of vitamin D status showed that deficiency was observed in 55 (61.1%) and insufficiency in 26 (28.9%) whereas normal levels were found in 9 (10.0%) patients as shown in figure-1.

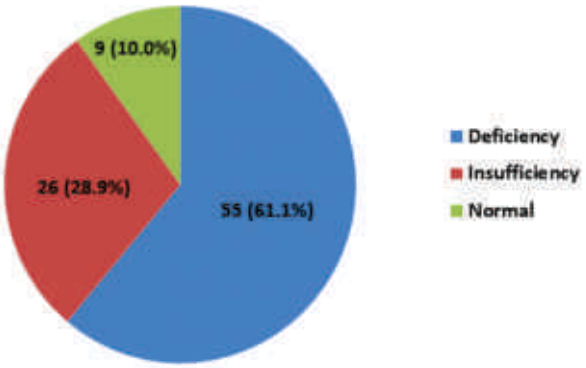

Figure-1: *Status of vitamin D levels (n=90)*

Table 2: *Stratification of demographic and clinical characteristics of patients with respect to vitamin D levels (N=90)*

Characteristics		Vitamin D Levels			P-Value
		Deficient (n=55)	Insufficient (n=26)	Normal (n=9)	
Gender	Male	16(29.1%)	10(38.5%)	2(22.2%)	0.579
	Female	39(70.9%)	16(61.5%)	7(77.8%)	
Age	<45	14(25.5%)	3(11.5%)	1(11.1%)	
	45-60	34(61.8%)	15(57.7%)	3(33.3%)	0.029
	>60	7 (12.7%)	8(30.8%)	5(55.6%)	
Residence	Urban	14(25.5%)	7(26.9%)	4(44.4%)	0.496
	Rural	41(74.5%)	19(73.1%)	5(55.6%)	
BMI (kg/m^2)	Normal	10(18.2%)	4(15.4%)	1(11.1%)	
	Overweight	8 (14.5%)	2(7.7%)	-	0.603
	Obese	37(67.3%)	20(76.9%)	8(88.9%)	
Duration of diabetes (years)	≤1	3 (5.5%)	2(7.1%)	1(11.1%)	
	2-5	36(65.5%)	10(38.5%)	2(22.2%)	
	6-10	13(23.6%)	12(46.2%)	3(33.3%)	0.026
	>10	3 (5.5%)	2(7.7%)	3(33.3%)	
HbA1c (%)		9.24±2.23	8.76±1.08	7.50±0.8	0.034
Hypertension		5 (9.1%)	8 (30.8%)	1(11.1%)	0.039
History of smoking		1 (1.8%)	3 (11.5%)	1(11.1%)	0.152
Family history of diabetes		4 (7.3%)	6 (23.1%)	-	0.057

Relatively younger age (p=0.029), rising duration of diabetes (p=0.026), higher HbA1c (p=0.034) and hypertension were noted to have statistically significant association with VDD (table-2).

Discussion

In this study, 90.0% of T2DM patients were having either deficient (61.1%) or insufficient (28.9%) levels of vitamin vitamin D. Palazhy and colleagues in another regional data revealed that 71.4% of T2Dm cases had VDD, 15%, insufficiency while only 13.6% had adequate vitamin D levels and these findings are very similar to what is reported in this study.[17] Study by Vijay et al in a recently conducted research showed that 25.9% T2DM patients were having normal vitamin D levels.[18] Prasad et al stated that 78.2% of the diabetic patients were found to be deficient in vitamin D.[19] Among newly diagnosed cases of youth-onset T2DM stated that 91.1% patients had VDD.20 Data from Nigeria showed that 63.2% of T2DM patients were having VDD.[21] Another study from Kenya involving T2DM patients who were received in a referral hospital reported VDD and insufficiency rates of 38.4% and 21.9%.[22] In Saudi Arabia, the King Faisal University Health Center observed a comparable trend to the current study, as they found that the people who had T2DM and below-normal vitamin D levels were in the vast majority (97.9%).[23] Local literature is evident of the fact that T2DM has strong correlation with vitamin D deficiency.[24] All of the aforementioned studies, as well as the current exploration, show that T2DM patients worldwide have very high rates of VDD and the difference in the prevalence rates could be attributed to variation in socio-demographic and clinical characteristics, as well as adoption of different laboratory methods for the assessment of vitamin D levels.

The findings of this study could not reflect that gender had any significant relationship with the levels of vitamin D. In a gender comparison through retrospective data of the southern Indian population, similar findings for the contribution of both genders to VDD were described.[17] This study noted significant association between age and existing levels of Vitamin D which is consistent with what has been identified earlier as well.[14,25] In our study, hypertension was found to have significant relationship with vitamin D (p=0.039). A study from South Indian performed at a tertiary care center reported significant association of hypertension with vitamin D levels.[26]

Some researchers in the past have shown that poor vitamin D status is linked with poor glycemic control among T2DM patients and similar findings were reported in this research. The findings of Vijay et al could not establish a significant relationship of glycemic status and vitamin D (p=0.2749).[14] Similar to our findings, it was revealed in a study performed that poorly controlled

diabetes patients were having considerably lower levels of vitamin D.[27] The possible association of VDD and glycemic control needs further research as the currently available literature is unable to establish the role of VDD towards poor glycemic control. A study by Wang et al from China validated the close correlation between diabetic foot ulcer and and vitamin D, establishing vitamin D as an autonomous protective element against diabetic foot ulcer. That study also concluded that vitamin D screening or supplementation could prove advantageous in averting diabetic foot ulcer and enhancing the prognosis for individuals with DM.[28]

This study has enabled us to collect useful information regarding the vitamin D status of the T2DM population of South Punjab, Pakistan. The collection of this data was done by trained staff using uniform and common testing techniques. Vitamin D was not supplemented additionally by any of the participants to assess the actual burden. Being a single center study carried out on a relatively small sample size were some of the limitations of this study. Further prospective trials need to be done to eva-luate the impact of VDD on T2DM progression. Role of vitamin D supplementation and its effect on T2DM also needs further research.

Conclusion

Evaluation of vitamin D status in T2DM revealed that vast majority of these patients were having inadequate levels of vitamin D. Relatively younger age, duration of diabetes, higher HbA1c and hypertension were having significant association with vitamin D inadequacy. T2DM patients should be evaluated for VDD.

Conflict of Interest: *None*

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