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ASSOCIATION OF HYPOVITAMINOSIS D WITH POOR GLYCEMIC CONTROL AND OBESITY IN TYPE II DIABETES MELLITUS.

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ABSTRACT… Objectives: To determine the association of low serum vitamin D levels with poor glycemic control and obesity in type 2 diabetic patients. **Study Design:** Descriptive Cross Sectional study. **Setting:** Sakina Institute of Diabetes and Endocrine Research Centre (SIDER), Shalamar Hospital Lahore. **Period:** 1st June to 31th august 2017. **Material & Methods:** After applying strict exclusion criteria, about 450 patients with known type II diabetes were enrolled in the present study and their HBA1C and fasting vitamin D levels were measured. Patients were divided into two groups, group 1 with poor glycemic control (HBA1C>8%) and group 2 with good glycemic control (HBA1C <8%). **Results:** After performing extensive matching in both groups, it was found that vitamin D levels in group 1 with poor glycemic control were significantly low as compared to group 2 with good glycemic control (p value <0.001). Furthermore, approximately 87% of patients with BMI >23 were having suboptimal Vitamin D levels (p value <0.005). **Conclusions:** Low serum vitamin D is associated with poor glycemic control in type 2 diabetics and vitamin d supplementation could possibly play a role in improving glycemic control in these patients. Furthermore, hypovitaminosis D is also associated with obesity.

Key words: BMI, Glycemic Control, HBA1C, Hypovitaminosis D, Obesity, Type 2 Diabetes Mellitus.

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INTRODUCTION

Vitamin D is a multifunctional fat soluble Secosteroid playing a vital role in calcium, magnesium and phosphorous metabolism. Although Vitamin D is present in many vegetarian (such as lichen) and animal sources (mushrooms, cod liver oil, cooked egg yolk, beef liver)[1], but its main source in human body is sunlight dependent skin synthesis from its precursor cholesterol. Vitamin D synthesized in the skin is biologically inactive and require further hydroxylation process in the liver and kidneys for conversion into its biologically active form known as calcitriol (1,25 dihydroxycholecalciferol). Because of its diverse biologic functions, Vitamin D should be considered as a hormone rather than a vitamin or an essential micronutrient. Primarily known for its role in bone growth and reduction in fracture risk[2], Vitamin D has been recently under the spotlight for its possible beneficial role in prevention of cancer[3,4], different infectious[5], autoimmune diseases[6] and cardiovascular diseases.[7] Vitamin D deficiency or insufficiency is a worldwide epidemic mainly and it is estimated that about one billion of World population is vitamin D deficient.[8] According to a study, about 86% of Pakistani adult population is having vitamin D less than 20ng/ml, pointing towards an even bigger epidemic in our country than the rest of the World.[9]

Type II diabetes mellitus is a chronic worldwide epidemic with major implications for human health all across the globe. Pakistan has been one of the worst affected countries with diabetes. According to a recent data of World diabetes foundation; approximately 6.7 million Pakistanis are suffering from diabetes. The Current prevalence of type II diabetes in Pakistan is 11.77% and it is more prevalent in urban (14.81%) as compared to rural (10.34%) areas.[10]

Over the last few years, Vitamin D deficiency has

been viewed as a risk factor for development of type II diabetes mellitus and its possible association with poor glycemic control has led to considerable debate in recent times. Several observational studies have focused on potential association between hypovitaminosis D and metabolic syndrome, a significant risk factor for cardiovascular diseases. Therefore, an association between hypovitaminosis D and individual components of metabolic syndrome (glycemic control, obesity) will definitely help in understanding the impact of vitamin D on cardiovascular system. Studies conducted on possible association of hypovitaminosis D with poor glycemic control and obesity in type II Diabetics are inconclusive and more research work is needed.[10] The main aim of this study is to determine the association of hypovitaminosis D with poor glycemic control and obesity in type II diabetes mellitus.

MATERIAL & METHODS

This descriptive cross sectional study was conducted at endocrinology unit Shalamar Hospital Lahore from 1st June to 31st August 2017. A total of 450 patients with type 2 diabetes were enrolled in our study. Confidence interval was taken as 95% with 5% margin of error. Sample size was calculated using WHO formula.

Patients included in our study were of both gender, aged above 40 years, and known type 2 diabetics using oral hypoglycemic agents ±insulin. Patients excluded from our study were those having age less than 30 years, those with documented type I diabetes, those using multivitamins containing vitamin D, those on vitamin D supplements, pregnant ladies, those with chronic kidney or liver disease, those with systemic inflammation or any trauma, those using antihypertensive or lipid lowering agents.

Written informed consent was obtained from all our patients. Fasting (9hr) samples of our patients were drawn under aseptic measures and sent to biochemistry lab for analysis. Vitamin D level was measured using the electrochemiluminescence immunoassay (ECLIA) method. Vitamin D values less than 30ng/ml were considered to be insufficient while values less than 20ng/ml were considered to be deficient. Information regarding Age, sex, HbA1c and body mass index was obtained as per our designed Performa.

Based on HBA1c values, patients were equally distributed in two groups, each group containing 240 patients. Group 1 consisted of patients with poor glycemic control characterized by HBA1c value more than 8% while group II had patients with good glycemic control characterized by HBA1c less than 8%. SPSS version 23 (Chicago, IL) was used to analyze and summarize the data. Qualitative data like gender was expressed as frequency and percentages, while quantitative data like age (years) was expressed as mean ± SD. P value of 0.05 or less was taken as statistically significant.

RESULTS

In our study, a total of 450 type 2 diabetic patients were enrolled and equally divided into two groups, group 1 with poor glycemic control as evident from HBA1C more than 8% and group 2 with good glycemic control as evident from HBA1C less than 8%. Overall, female gender was dominant in both groups (71.5% in group 1 and 69.7 % in group 2). Mean age of our patients was 51.59 ±12.97 in group 1 and 50.89±11.99 in group 2. Mean HBA1C was 9.26 ± 2.76. Mean BMI was 30.35 ± 6.72 in group 1 and 26.08±5.70 in group 2 which suggested that poor glycemic control is also strongly linked with increased BMI. Mean vitamin D level in group 1 was 17.28±0.5 while it was 26.67±0.7 in group 2 (p value <0.001). The baseline characteristics of our study population are summarized in Table-I.

Vitamin D was insufficient in 46.22 % and deficient in 32.00 % in group 1 while it was insufficient in 37.33% and deficient in 23.11 % in group 2 (Table-II).

Furthermore, vitamin D was deficient in 29.2% and insufficient in 58.3% in those with BMI > 23 (Figure-1), but 21.01% were vitamin D deficient and 45.02% were insufficient in those with BMI less than 23 (p value<0.004) (Figure-2).

Characteristic	Group 1 N (%)	Group2 N (%)	P-Value
Age	51.59±12.97	50.89±11.70	0.56
Gender Male Female	 64(28.45%) 161(71.55%)	 68(30.22%) 157(69.78%)	0.53
Mean age of diabetes onset (years)	41.08±7.6	42.01±8.2	0.69
Sunlight Exposure >1hr daily < 1hr daily	 137(60.89%) 88(39.11%)	 134(59.57%) 91(40.44%)	0.79
25 hydroxyvitamin D(ng/ml)	17.28±0.5	26.67±0.7	<0.001
BMI (kg/m2)	30.35±6.72	26.08±5.70	<0.005
Waist circumference (cm)	101.09±9.80	95.01±8.99	<0.005

Table-I. Baseline characteristics and biomarkers in group 1 and group2

25(OH)D ng/ml	Vitamin D Status	Group1 N (%)	Group 2 N (%)	P-Value
<20	Deficient	72(32%)	84(37.33%)	0.002
20_29.9	Insufficient	104 (46.22%)	52(23.11%)	0.004
>30	Normal	49 (21.78%)	89(39.56)	<0.005

Table-II. Vitamin D status and glycemic control

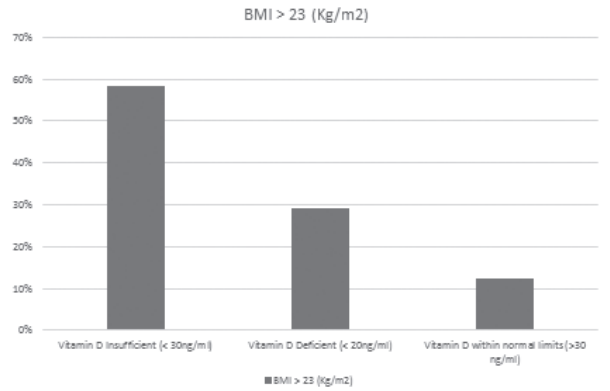

Figure-1. Association of vitamin D with high BMI (>23)

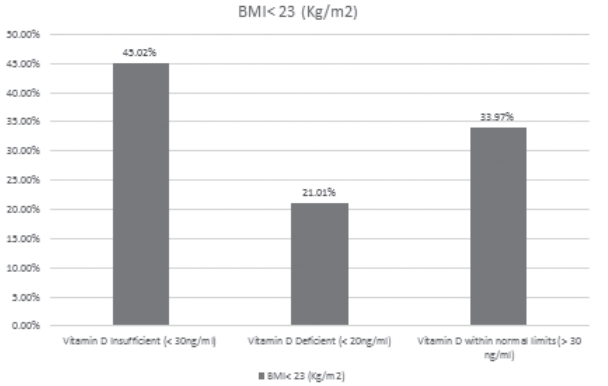

Figure-2. Association of vitamin D with normal BMI (<23)

DISCUSSION

Vitamin D has been recently postulated to have a possible role in glucose tolerance, insulin sensitivity and pancreatic B cell function. Although vitamin D deficiency has been linked with increased morbidity and mortality in type 2 diabetic patients, but no survival benefit of vitamin D supplementation has been noted in these patients.[11-13] To better define the role of vitamin D in the development, pathogenesis, progression, complications and glycemic control in type 2 diabetic population, further high quality observational studies and clinical trials are needed. In our study, we evaluated vitamin D status of about 450 type 2 diabetic patients. Mean vitamin D levels in our study population were 17.28±0.5, about 32 % were vitamin D deficient and 46.22% were vitamin D insufficient. These results were in accordance with already published data in our local population. A study carried out by khalida Iqbal and her colleagues in Agha Khan Hospital Karachi reported that about 25 % of type

2 diabetic patients with poor glycemic control were vitamin D deficient, and another 58.7% were vitamin D insufficient. These results were very close to our study results, but differed from our study in the way that BMI of both the groups (poor glycemic control group and good glycemic control group) was similar.[14] Another study at Agha Khan Hospital Karachi reported that about 52.7% of type 2 diabetic patients with poor glycemic control were Vitamin D deficient and 24.2 % were vitamin D insufficient.[15] Studies carried out in Egypt found a strong association between hypovitaminosis D and poor glycemic control in type 2 diabetic population and strengthened the possibility that vitamin D supplementation may help improve glycemic control in type 2 diabetic patients and prevent microvascular and macrovascular complications. However, in a systemic review, vitamin d supplementation failed to improve diabetic control and prevent its deadly complications.[16] A study conducted in UK on type 2 diabetic patients of south Asian origin showed that oral vitamin D and calcium supplementation led to significant reduction in HBA1C.[17] On the other hand, Sheth et al contradicted the inverse relationship between vitamin d and HBA1C in their study[18], but their study differed from ours in that the mean age of their study population was 57 which could be a significant contributory factor to their overall results. Furthermore, their study population consisted of western India patients paving a way for possible ethnic role too.

The present study also revealed that vitamin D levels were markedly low in those with high BMI (>23). The overall prevalence of hypovitaminosis D was about 87% in those with BMI >23, in comparison to 66% prevalence in those with BMI <23. These results matched a study carried out in Karachi where they found that 40% of obese patients were having hypovitaminosis D, but differed from our study in that they did not take diabetes into account.[19] Similarly, prevalence of hypovitaminosis D was found to be about 81% in Spanish obese children.[20]

In summary, our study provided enough evidence for a possible association of hypovitaminosis D with poor glycemic control and obesity in type II diabetic patients, but large interventional studies implying vitamin d supplementation are needed to confirm our results. The main limitation was the cross sectional nature of our study which failed to establish cause and effect relationship.

CONCLUSIONS

Low serum vitamin D level is associated with poor glycemic control in type 2 diabetic patients and vitamin D supplementation could possibly lead to improved diabetic control in future. Furthermore, there is strong association between hypovitaminosis D and obesity.

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2	Rozina Arshad	Manuscript design / review, statistical analysis.	
3	Zohaib Ahmad Khan	Data collection, Literature review, Proof reading.	