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ORIGINAL RESEARCH article

Correlation of vitamin D with glycemic control and body mass index in patients with type II diabetes mellitus

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Abstract: Vitamin D deficiency and its effect have attracted considerable research interest due to its relation to glucose homeostasis, insulin secretion, sensitivity and synthesis. This study aimed to evaluate vitamin D levels in patients with type II diabetes mellitus aged between 35-65 years and investigate their relations with glycemic control and obesity. The study included 74 Libyan patients with a known history of type II diabetes mellitus (33 males and 41 females). Serum glucose, glycosylated hemoglobin (HbA1c) and vitamin D levels were biochemically estimated in these patients. Further, body mass index (BMI) was calculated for all diabetic patients (weight in kilogram per height in meter square). The mean level of plasma glucose level was 150.58±63.82 mg/dl (mean±SD). The mean of HbA1c level was 7.90±8.48% (mean±SD). The mean level of vitamin D was 22.75±14.97 ng/ml. The mean of BMI was 26.55±4.10 Kg per m^2. The findings showed that 58.10% of the cases had vitamin D deficiency (Out of which 24.24% were males and 85.36% were females). This study showed significant differences in glucose, HbA1c, vitamin D and BMI between male and female patients. Moreover, elderly ages for both sexes had adverse effects on vitamin D status. Vitamin D levels have negatively been correlated with levels of glucose, HbA1c and BMI. It is concluded that vitamin D deficiency has an adverse effect on glucose homeostasis in patients with type II diabetes mellitus and this can be a contributing risk factor in complications of type II diabetes mellitus development in Libyan patients.

Introduction

Diabetes mellitus (DM) is a chronic metabolic multi-systemic disorder of the pancreatic gland that increases glucose levels in the blood due to low levels of insulin secretion or insufficiency of insulin activity in the body [1]. Type II diabetes mellitus (DM II) leads to decreased insulin sensitivity and poor performance of pancreatic beta cells [2]. The consequence of disruption of insulin activity is disorders of the fats, proteins and carbohydrates metabolism [3, 4]. Vitamin D is a fat-soluble vitamin that is synthesized from 7-dehydro-cholesterol in the skin upon exposure to ultraviolet B (UVB) rays of sunlight. 1, 25-dihydroxy cholecalciferol, is the active form of vitamin D, which plays an important role in the maintenance of calcium homeostasis by binding to its receptors on its target tissues which include bone, kidney and intestine. In addition to its role in maintaining bone health, vitamin D has several important extra skeletal biochemical functions in the body including its role in type I and II diabetes mellitus [5]. Vitamin D has an important role in the metabolism of

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glucose. It directly stimulates insulin secretion from beta cells of pancreas. It increases intracellular calcium levels, which attenuates insulin synthesis. In addition, it improves insulin sensitivity in peripheral muscle and fat cells. DM II is a state of chronic low-grade chronic inflammation. Because of its anti-inflammatory nature, vitamin D exerts beneficial effects on glycemic control and helps in the prevention of complications of DM II [6].

Hypovitaminosis D has commonly been found in obesity which is the most important cause of prediabetes. In obesity, adipose tissues store 25-hydroxy vitamin D making it biologically unavailable resulting in the depletion of calcitriol and a rise in parathyroid hormone (PTH). This in turn increases intracellular calcium in adipocytes stimulating lipogenesis with subsequent weight gain and impaired glucose intolerance [7, 8]. Vitamin D has sparked widespread interest in the pathogenesis and presentation of diabetes [7]. There is considerable interest in vitamin D's role in DM II and insulin resistance beyond its role in bone/calcium metabolism. A published review summarized reports showing a significant positive correlation between serum 1, 25-OH-vitamin D (the active form) and insulin sensitivity and secretion, a negative association between vitamin D deficiency and glycemic control [9]. Previous published studies have shown higher rates of hypovitaminosis in the sunniest areas of the world, including the Middle East and Asian countries such as Qatar, Saudi Arabia, United Arab Emirates, Iran Turkey and India [10, 11]. In 2016, the Food and Agriculture Organization (FAO) reported that 62.0% of Qatari teenagers had vitamin D deficiency and 81.0% of Saudi girls had a deficiency of vitamin D. A highest vitamin D deficiency was reported in Saudi women, up to 85.0% [12]. According to a published systematic review and meta-analysis study, in which 129 studies were reviewed with 21 474 participants from 23 African countries, vitamin D deficiency was prevalent in African countries and most common in Northern African countries [13]. Few studies have been conducted regarding vitamin D status which all was in East and West of Libya. In a cross-sectional Libyan study in Benghazi city, vitamin D deficiency (≤20 ng/ml) was 76.1%, insufficiency (21-29 ng/ml) was 15.2% and sufficient vitamin D concentration (≥30 ng/ml) was 08.7%. Vitamin D deficiency was more prevalent in women. 58.4% of the women had vitamin D deficiency and 25.0% had vitamin D insufficiency, while 26.1% of men were deficient and 21.0% were insufficient in vitamin D [14]. Another Libyan study in Tripoli City, identified 69.0% of nursing mothers had vitamin D deficiency (≤ 20 ng/ml) and 30.0% of nursing mothers had vitamin D sufficiency (≥ 30 ng/ml) [15].

A Libyan study conducted in Misurata city revealed that about 80.0% of the participants had inadequate vitamin D levels and out of which women were more susceptible to vitamin D deficiency which counted for 61.6% < 25 nmol/L and 20.2% between 25-50 nmol per L [16]. Indeed, the majority of Libyan women wear traditional attire and have more indoor lifestyles or avoid sun exposure due to cultural customs as it has been confirmed. Thus, their vitamin D intake relies greatly on the food they eat, which might not be enough to meet the body's requirements [17]. Several previous studies demonstrated the relation of vitamin D deficiency with the development of DM II [6-9], therefore, the primary objective was to estimate vitamin D status among Libyan patients with DM II in the Southwest region of Libya. The second objective was to investigate the relation of vitamin D deficiency with glycemic control and body mass index of the patients.

Materials and methods

Study population: Cross-sectional study was conducted from January to May 2021 at Albalsam Clinic, Garma, Southwest region of Libya. The study group involved 74 patients DM II aged between 35 and 65 years old of both sexes. All the participants were informed about the purpose of the study, and were free to ask questions throughout the study and signed an informed consent form as an ethical approval.

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Collection of samples and site of experiments: Five ml of blood samples collected from each patient after an overnight fasting of eight hours for measurement of blood glucose, HbA1c and vitamin D levels. BMI was calculated for all the patients (weight in kilogram per height in meter square. The blood sample was collected in sodium fluoride to detect glucose and ethylene diamine tetra acetic acid (EDTA) to detect glycosylated hemoglobin (HbA1c). A serum sample was made to detect vitamin D. Demographic characteristics of the patients (name, age and gender), history of risk factors (duration of diabetes illness, family history). Sun exposure was estimated by asking the patients about the time spent outdoors during the week. All blood samples were analyzed in a certified laboratory at Albalsam Clinic, Garma, Wadi Alhayah.

Exclusion criteria: Patients with type I diabetes, patients with diabetes of acute complications, patients with gestational diabetes and pregnancy, patients on insulin anti-diabetic, supplemented patients with vitamin D and calcium, patients suffering from diarrhea, and diseases of kidneys, thyroid, digestive tract, osteoporosis, bone, skin and other diseases that affect the absorption and synthesis of vitamin D.

Biochemical analysis: Serum glucose: The method used was GOD-PAP method by photometer 4040 Fulfils. Plasma glycosylated hemoglobin (HbA1c): The method used was the sandwich immunodetection method by Ichroma made in Korea. Serum vitamin D: The method used was the competitive immunodetection method by Ichroma made in Korea.

Statistical analysis: Data are expressed as mean±standard deviation. All data were analyzed by Statistical Package for Social Sciences (SPSS-version 14). An analysis of variance (one-way ANOVA) test was used to compare the means of the variables among the groups. A Pearson correlation coefficient was applied to investigate the extent relationship between the levels of vitamin D and serum glucose, HbA1c and BMI.

Results

In this study, 74 Libyan patients with known diagnoses of DM II were included for both sexes (33 males and 41 females). **Table 1** shows the mean and standard deviation of biochemical parameters of vitamin D, serum glucose, HbA1c and BMI levels and ages for both sexes of the participants. Mean age was 51.84 ± 9.43 years (52.15±9.73 and 51.59±9.31 years for male and female, respectively). There was no significant difference between the mean ages of male and female groups. The total mean and standard deviation of blood glucose levels was 150.58±63.82 mg/dl (130.06±60.04 mg/dl and 164.66±60.66 mg/dl for males and females, separately). The total mean and standard deviation of HbA1c level was 7.90±8.48% (6.15±1.85 and 7.54±1.89% in males and females, respectively). The total mean and standard deviation of vitamin D level was 22.75±14.97 ng/ml (31.53± 14.95 and 15.69±10.73 ng/ml in male and female patients, respectively). Total mean and standard deviation of BMI was 26.55±4.10 Kg/m^2 (23.66±3.14 and 28.90±3.22 Kg/m^2 for male and female groups, respectively). An analysis of the data by using one-way ANOVA revealed a statistically significant difference in biochemical variables between male and female participants. The study showed a statistical significance in glucose, HbA1c, vitamin D and BMI between males and females at a $p<0.01$.

Table 2 illustrates the age-distribution of the cases about the vitamin D levels for male and female patients. Ages were divided into three groups, the first age group was between 35-44 years (n=8 and n=11 for male and female groups, respectively), the second group was between 45-54 years (n=8 and n=20 for male and female, respectively) and the third group was between 55-65 years (n=17 and n=10 for male and female groups, respectively). In the first group, the mean vitamin D level was 44.77±4.23 and 31.60±6.25 in males and females, respectively. The mean of vitamin D levels in the second group were 39.72±3.98 and 10.87±3.89 in males and females, respectively. In the third group, the mean vitamin D level was 21.39±13.9 and 7.24±1.30 in males and female, respectively. Vitamin D levels in males and female patients were found to be statistically

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significantly different at a $p<0.01$ in the different three groups. Moreover, vitamin D levels in male and female patients were significantly different at a $p<0.01$ in each group. **Table 3** shows the distribution of vitamin D levels with relation to serum glucose levels. The results were revealed by applying a Pearson correlation coefficient to investigate the relationship between vitamin D and serum glucose levels. The findings showed a strong negative correlation between vitamin D and serum glucose levels (r=-0.8). **Table 4** illustrates the distribution of vitamin D levels about HbA1c levels. The findings were tested by the Pearson correlation coefficient for the relationship between vitamin D and HbA1c levels. The results showed a strong negative correlation between vitamin D and HbA1c levels (r=-0.8). **Table 5** reveals the distribution of vitamin D levels in relation to BMI data. By applying the Pearson correlation coefficient to investigate the relationship between vitamin D levels and BMI, a negative correlation between vitamin D levels and BMI was found (r=-0.5). The negative correlation of vitamin D levels with serum glucose, HbA1c and BMI levels are analyzed, thus, in **Figure 1**, the correlation between vitamin D levels and serum glucose levels is presented. It revealed a strong significant negative correlation between vitamin D and serum glucose levels (r=-0.8, $p<0.001$). **Figure 2** illustrates the relation between vitamin D and HbA1c levels. It showed a strong significant reverse relation between vitamin D levels and HbA1c concentration (r=-0.8, $p<0.001$). Finally, **Figure 3** shows the relation between vitamin D and BMI levels, a negative correlation between vitamin D levels and BMI levels was found (r=-0.5, $p<0.01$).

Table 1: Biochemical parameters of Libyan patients with diabetes mellitus (type II)

Parameters	Total	Male	Female	P
Age in years	51.84 ± 9.43	52.15 ± 9.70	51.58 ± 9.31	0.7
Vitamin D (ng/dl)	22.75 ± 14.97	31.53 ± 14.95	15.69 ±10.73	$p < 0.01^{**}$
Blood glucose (mg/dl)	150.58 ± 63.82	130.06 ± 60.04	164.66 ± 60.66	$p < 0.01^{**}$
HbA1c (%)	07.90 ± 8.48%	06.15 ± 1.85%	07.54 ± 1.89%	$p < 0.01^{**}$
BMI (Kg/m^2)	26.55 ± 4.10	23.66 ± 3.14	28.90 ± 3.22	$p < 0.01^{**}$

Table 2: Distribution of the cases according to age and vitamin D level

	Vitamin D in ng/dl			
Gender	**35-44 years n=19**	**45-54 years n=28**	**55-64 years n=27**	**Statistically significant**
Male	44.77 ± 4.23	39.72 ± 3.98	21.39 ± 13.9	**SS**
Female	31.6 ± 6.25	10.87 ± 3.89	07.24 ± 1.30	**SS**
Statistically significant	**SS**	**SS**	**SS**	

SS: statistically significant by one-way ANOVA test. Vitamin D in males and females was significant at $P<0.01$ in the different three groups. Vitamin D levels in males and females were significant at $p<0.01$

Table 3: Distribution of the cases according to vitamin D level and glucose level

Parameters	Mean ± SD	r
Vitamin D in ng/dl	22.75 ± 14.97	-0.8
Glucose in mg/dl	150.58 ± 63.82	
	Negatively correlated	

Correlation coefficient for vitamin D and glucose levels. Vitamin D was negatively correlated with serum glucose levels (r=-0.8)

Table 4: Distribution of the cases according to vitamin D and HbA1c

Parameters	Mean±SD	r
Vitamin D (ng/dl)	22.75 ± 14.97	-0.8
HbA1c (%)	07.90 ± 8.48	
	Negatively correlated	

Pearson correlation coefficient for vitamin D and HbA1c levels. Vitamin D was negatively correlated with HbA1c levels (r=-0.8)

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Table 5: Distribution of the cases according to vitamin D and body mass index

Parameters	Mean ± SD	r
Vitamin D (ng/dl) **BMI (kg/m²)**	22.75 ± 14.97 26.55 ± 4.10	- 0.5
	Negatively correlated	

Pearson correlation coefficient for vitamin D and BMI. Vitamin D was negatively correlated with BMI (r=-0.5)

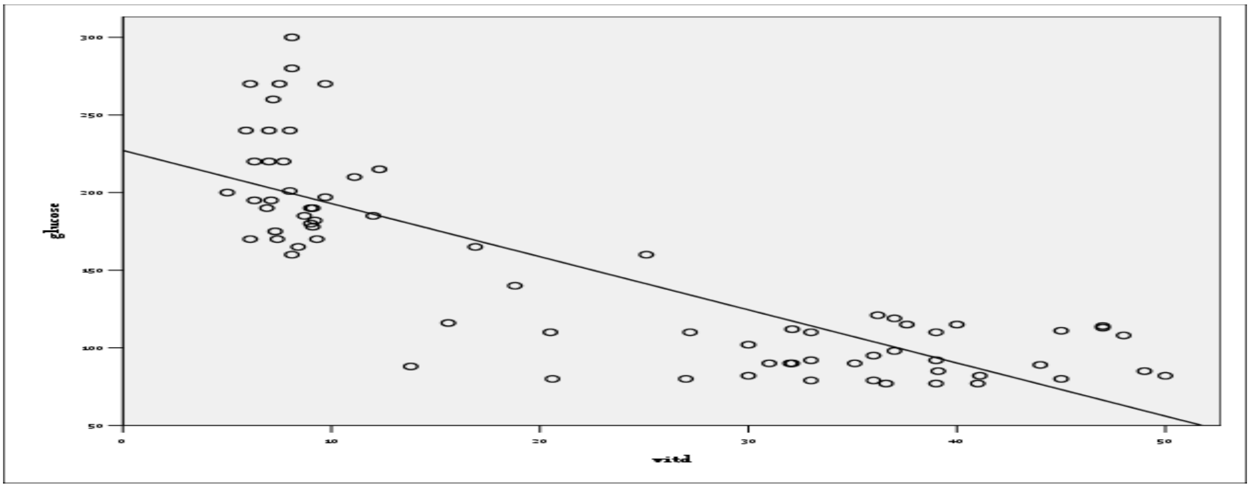

Figure 1: Correlation of vitamin D and glucose level (r=-0.8, P<0.001)

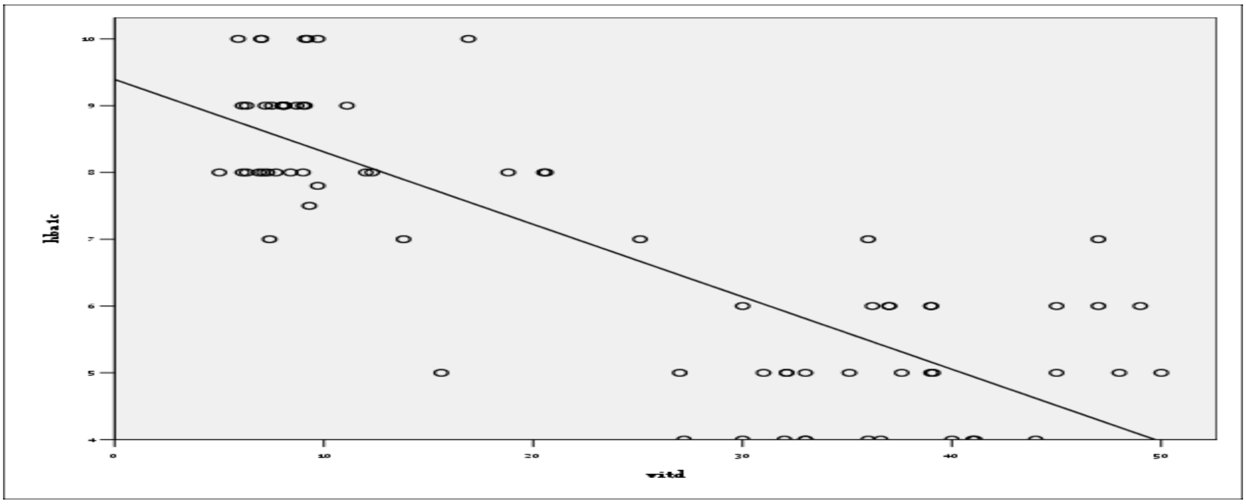

Figure 2: Correlation of vitamin D and HbA1c concentration (r=-0.8, p<0.001)

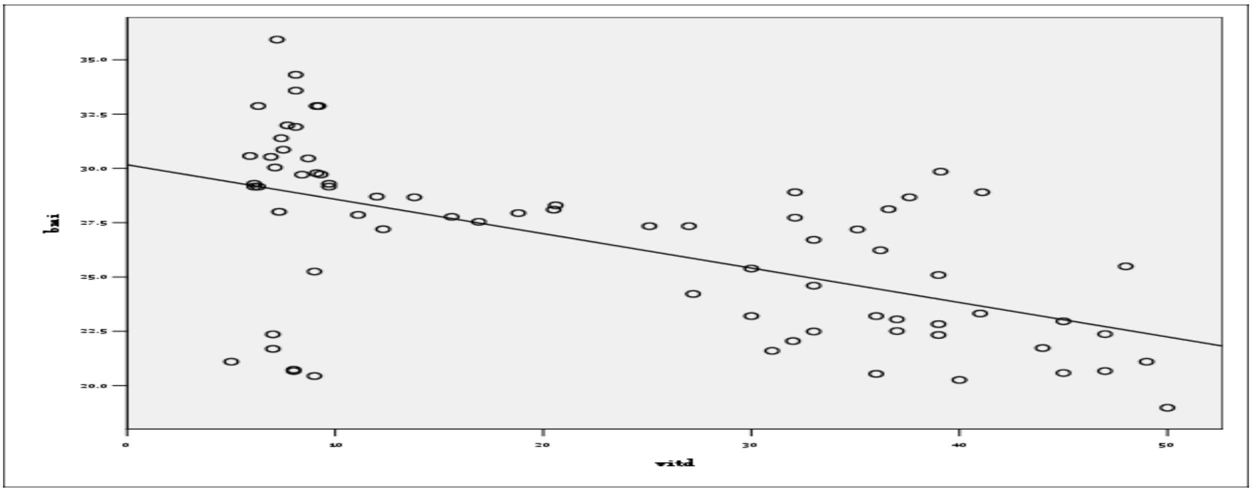

Figure 3: Correlation of vitamin D and body mass index (r=-0.5, p<0.01)

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Discussion

In the present study which has been conducted in the southwest region of Libya where all the subject's exposed to adequate sunlight throughout the year. Thus, the present findings showed about half of type II diabetic patients had vitamin D deficiency or insufficiency (Out of which 25.0% were males and 85.0% were females). Indeed, the total mean of vitamin D levels was 22.75±14.97 ng/dl (males were two-fold of the females). This is supported by the previous study which revealed that half of the diabetic patients had vitamin D deficiency [18]. Another study also showed half of diabetic patients had vitamin D deficiency [19]. Moreover, the present study reported that women were more susceptible to vitamin D deficiency and some of them were in the menopause stage. The study was in good agreement with the previous study which revealed that a high prevalence of hypovitaminosis D was among Brazilians with type II diabetes and it was more related to female gender who counted for about 75.0% and most of them were nonwhite persons [20]. The current study reported that elderly ages (>45 years) had an inverse effect on vitamin D levels for both male and female patients but, it was more prevalent with the elderly female gender. The study was consistent with a study that demonstrated a very high of diabetic women had vitamin D deficiency or insufficiency regardless of the abundance of sunshine and hypovitaminosis was more prevalent in the postmenopausal than premenopausal women [21]. Vitamin D deficiency may be attributed to inadequate vitamin D intake, social and religious behaviors, covering clothes and wearing a hijab which could be a main blocker of exposure to sunlight which leads to the disruption of vitamin D synthesis [22, 23]. During menopause stage there is a decline in estrogen production. Estrogen is responsible for increasing the activity of 1-α hydroxylase (expressed in the kidneys) and regulates vitamin D receptors. Therefore, estrogen activates and regulates vitamin D levels by activating 1-α hydroxylase enzyme and vitamin D receptors [24-26]. Aging has an inverse effect on vitamin D status as kidney function efficiency is diminishing in older ages than young individuals. Therefore, older individuals are less able to convert vitamin D into active form [27]. Additionally, the effectiveness of producing vitamin D through exposure to sunlight can be affected by skin color. Melanin pigment of darker skin reduces the absorption of sunlight. Therefore, people with darker skin show lower levels of vitamin D [28, 29]. The current study revealed a difference in glucose and HbA1c levels between males and females. Thus, vitamin D levels were inversely correlated with serum glucose and HbA1c levels. Serum glucose and HbA1c levels were significantly higher in subjects having vitamin D deficiency and vitamin D was inversely correlated with serum glucose and HbA1c levels [30]. It is consistent with a study conducted in Turkey which showed a strong relation of lower vitamin D with worse diabetic regulation in DM II subjects [31]. Vitamin D plays an important role in the metabolism of glucose and it directly stimulates insulin secretion from beta cells of the pancreas and enhances insulin synthesis. Moreover, vitamin D improves insulin sensitivity [6]. Vitamin D deficiency may increase blood glucose by decreasing insulin sensitivity, glucose uptake of peripheral tissues and increasing insulin resistance [32, 33]. Vitamin D might improve insulin sensitivity by lowering inflammatory responses [34]. The study reported that a high percentage of the subjects were not healthy weight (43.24% overweight and 18.91% obese). Furthermore, the study showed a negative correlation between vitamin D and BMI levels. Sequestering of vitamin D in adipose tissues and altered vitamin D metabolism in obese individuals can be the reasons for vitamin D deficiency in obese individuals [35-37]. In obesity, storing vitamin D in adipose tissues makes it unavailable which results in depletion of calcitriol and rise in parathyroid hormone (PTH). This in turn increases intracellular calcium in adipocytes stimulating lipogenesis which leads to impaired glucose intolerance [8]. Thus, it should be recommended that regular measurement of serum vitamin D among patients with diabetes mellitus, particularly, elderly aged individuals. National strategies are needed to raise public awareness of the importance and necessity of vitamin D. All efforts must be dedicated to educating the community on how to prevent hypovitaminosis D through adopting proper lifestyle practices focused on maintaining adequate sun exposure and increasing their dietary intake of vitamin D.

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Conclusion: The study concludes that vitamin D deficiency is negatively correlated to glucose, HbA1c and BMI which all contribute to the development of type II diabetes mellitus due its effect on glucose homeostasis, insulin secretion and insulin sensitivity. Vitamin D supplementation can improve glycemic status in diabetic patients which might help in improving the overall health of the individuals.

Author contributions: Both authors contributed equally.
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Ethical issues: Including plagiarism, informed consent, data fabrication or falsification and double publication or submission were completely observed by the authors.
Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.
Author declarations: The authors confirm that all relevant ethical guidelines have been followed and any necessary IRB and/or ethics committee approvals have been obtained.

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