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THE EFFECT OF VITAMIN D SUPPLEMENTATION ON HBA1C IN TYPE 2 DIABETIC PATIENT IN DIABETIC CENTERS IN TAIF CITY, SAUDI ARABIA

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Abstract:

Introduction: *Type 2 diabetes mellitus has a high prevalence rate among our population in Saudi Arabia. Vitamin D deficiency was more familiar among T2DM patients in different populations.*

Aim of work: *This study aims to assess the effect of vitamin D supplementation on HbA1c in type 2 diabetic patient.* ***Methodology:*** *A retrospective study conducted in diabetic centres in Taif city, Saudi Arabia in the past year (January 2018 to December 2018). The reviewed data was socio-demographic, HbA1c, vitamin D supplementation. SPSS program version 22 was used for data analysis.*

Results: *250 T2DM patients participated in the present study; half of them had vitamin D deficiency (<30 ng/ml).Supplementation with Vitamin D did not lead to significant effect in total weight or change in BMI in T2DM patients.84.4% of T2DM patients in the present study were suffered from other comorbidities included; Hyperlipidemia/dyslipidemia (59.2%), Hypertension (41.6%), Thyroid disorders (17.6%), Chronic Kidney disease (15.6%), Chronic liver disease (11.6%), and Malabsorption disease (2.8%). Supplementation with Vitamin D significantly (P=0.024) improve the 4th HbA1C reading and also improve thyroid disorders (P=0.002) in T2DM patients.*

Conclusion: *Supplementation with Vitamin D has no significant effect on total weight or BMI in T2DM patients. The majority of T2DM patients in the present study were suffered from other chronic disorders. Supplementation with Vitamin D significantly improve the 4th HbA1C reading and also improve thyroid disorders in T2DM patients.*

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INTRODUCTION:

Type 2 diabetes mellitus has a high prevalence rate among our population in Saudi Arabia (25.4%)[1], more awful a systematic study conducted from 1989 to 2009 reports an alarming increase in prevalence of Type 2 Diabetes Mellitus from 10.6% up to 32.1%[2], and this percentage is expected to be 45.6% in 2030[3]. This dramatic changes in disease progression require more attention to the treatment of Type 2 Diabetes Mellitus to prevent further macrovascular or microvascular complications. However, (HbA1c) now used as a significant predictor for diabetes control in which high updated mean (HbA1c) is associated with a high risk of morbidity and mortality and vice versa. Interestingly a prospective observational study, reports that any reduction in updated mean (HbA1c) by 1% is associated with approximate reduction by fifth in mortality related to diabetes, more than tenth for myocardial infarction and more than third for microvascular complications [4]. For that, researchers highlight on achieving optimal updated mean (HbA1c) to minimize further risk of hyperglycemia [5].

Unfortunately, Type 2 Diabetes Mellitus is hard to control due to polypharmaceutical treatment includes lifestyle modification and polymedicinal remedies.

Moreover, oral antidiabetic drugs and insulin injection are associated with risk of coma and developing obesity [5], despite that many patients in developing countries cannot overcome the cost of newer antidiabetic analogues. Hence, researchers try to include other modifiable factors such as vitamin D in Type 2 Diabetes Mellitus management. Vitamin D deficiency among different Saudi population is common 81.0% [6], and currently, seems to be linked with Type 2 Diabetes Mellitus and other metabolic syndromes [7]. A systematic review revealed that Type 2 Diabetes Mellitus risk is increased with low vitamin D levels <14 nmol/L while risk decreased when vitamin D levels >25 nmol/L[8]. In addition to that vitamin D deficiency was more common among T2DM patients in different populations[9][10], also vitamin D deficiency had been reported to be associated with increases in updated mean (HbA1c) levels in diverse communities; Asians[10], Americans[11] and Caucasians[12]. In 2010, a retrospective study was done on South Asian Type 2 Diabetes Mellitus patients with vitamin D inadequacy to assess the effect of vitamin D replacement concurrent with calcium replacement therapies on updated mean (HbA1c) with a low sample size (N:50) that a show a positive impact of vitamin D and calcium replacements on (HbA1c)[13]. Also in 2011, a randomized clinical trial was performed in Shahrekord University of Medical Sciences for the impact of vitamin D replacements (5000IU/week for 12 weeks) on (HbA1c), results show a decrease in (HbA1c) after treatment with vitamin D replacements [14]. Another randomized clinical trial was performed in "Besat Diabetes Clinic" in Rasht, North of Iran in 2016 for the same reason but with higher sample size N:90 compared to N:60 but for the lesser duration (5000IU/week for eight weeks), same results were observed[15]. In Switzerland, a prospective randomized clinical trial was performed on 55 patients with Type 2 Diabetes Mellitus for more than 10 years but with a high dose of vitamin D supplements (300000 IU IM for 6 months), and they found (HbA1c) positively decreased in the conventional group compared to the placebo group[16]. In Saudi Arabia, daily replacement with cholecalciferol 5000 IU was associated with improvement in vitamin D status and B cell activity but neither for HbA1c and insulin resistance [17].

AIM OF WORK:

Our aim of the present study is to assess the effect of vitamin D supplementations on (HbA1c) throughout a retrospective study in type 2 diabetic patient.

Methods

A retrospective study was conducted. Files of type 2 diabetic patients were reviewed in the past year (January 2018 to December 2018) in diabetic centres in Taif city. Data reviewed from files of the patients in the predetermined period were socio-demographic, HbA1c, vitamin D supplementation. SPSS program version 22 was used for data analysis. Approval was taken from the medical college of Taif university to conduct the research. Also, approval was taken from administrators of diabetic centres to collect data. The collected data was used for research purposive only (Confidentiality).

RESULTS:

Table (1): Descriptive statistics of the participant's T2DM patients.

	Description (n=250)
AGE	
Range	29 - 88
Mean ± SD	51.7 ± 11.7
AGE	
≤ 40 years	45 (18)
41-50 years	80 (32)
51-60 years	67 (26.8)
> 60 years	58 (23.2)
Gender	
Male	134 (53.6)
Female	116 (46.4)
BMI	
Underweight	8 (3.2)
Normal weight	41 (16.4)
Overweight	146 (58.4)
Obese	55 (22)
Social Status	
Single	34 (13.6)
Married	169 (67.6)
Divorced	23 (9.2)
Widow	24 (9.6)
Social class	
Low	40 (16)
Middle	143 (57.2)
High	67 (26.8)
Residence	
Urban	160 (64)
Rural	90 (36)

Table 1 shows that 250 diabetic patients were participated in the present study and divided into two groups according to vitamin D supplementation. The participant's age range was 29-88 years, and the mean of their age was 51.7 ± 11.7. More than half of participants (53.6%) were males, overweight (58.4%), had a middle social class (57.2%) and urban residence (64%).

Table (2): Clinical data of the T2DM patients

	Description (n=250)
Vitamin D level	
<30 ng/ml	125 (50)
>30 ng/ml	125 (50)
Diabetes Type	
Type 2 DM	250 (100)
Medication	
Insulin	124 (49.6)
OHGD	87 (34.8)
Insulin + OHGD	39 (15.6)
Anti-DM Dosage	
Low	90 (36)
High	160 (64)

Table 2 shows that all of our participant (250) had T2DM and half of them had vitamin D deficiency (<30 ng/ml). Approximately half (49.6%) of participated patients were taking insulin medication, 43.8% were taking OHGD while 15.6% were taking Insuline+OHGD. Nearly two- thirds of participants (64%) had high Anti-DM dosage

Table (3): HbA1C readings of the studied T2DM patients.

	Description (n=250)
1st HbA1C reading	
Range	7 - 14
Mean ± SD	10.2 ± 1.6
2nd HbA1C reading	
Range	7 - 13.8
Mean ± SD	10 ± 1.6
3rd HbA1C reading	
Range	6.8 - 13.8
Mean ± SD	9.9 ± 1.6
4th HbA1C reading	
Range	6.5 - 13.6
Mean ± SD	9.7 ± 1.6

Table (4): Vitamin D supplementation of the studied T2DM patients.

	Description (n=250)
Vitamin D supplements	
Yes	102 (40.8)
No	148 (59.2)
Vitamin D Dosage	
<600 IU/day	31 (30.4)
>600 IU/day	71 (69.6)
Duration of Vitamin D supplements	
< 3 ms	13 (12.7)
3-6 ms	30 (29.4)
6-9 ms	25 (24.5)
9-12 ms	23 (22.5)
> 12 ms	11 (10.8)

Table 4 shows that only 40.8% of participant's T2DM patients were taking Vitamin D supplements; while 59.2% of them did not. 71 patients were taking >600 IU/day of vitamin D, and 31 patients were taking <600 IU/day

Table (5): comorbidities associated with T2DM.

	Description (n=250)
Other comorbidities	
Hyperlipidemia/dyslipidemia	148 (59.2)
Hypertension	104 (41.6)
Thyroid disorders	44 (17.6)
Chronic Kidney disease	39 (15.6)
Chronic liver disease	29 (11.6)
Malabsorption disease	7 (2.8)
No other chronic disease	39 (15.6)

Table 5 shows that in the present study 84.4% of T2DM patients were suffered from other comorbidities included; Hyperlipidemia/dyslipidemia (59.2%), Hypertension (41.6%), Thyroid disorders (17.6%), Chronic Kidney disease (15.6%), Chronic liver disease (11.6%), and Malabsorption disease (2.8%)

Table (6): Comparison of Vitamin D supplements regarding demographic data

	Vitamin D supplements		P value
	Yes (n=102)	No (n=148)	
AGE			
Range	32 - 78	29 - 88	
Mean ± SD	52.5 ± 10.5	51.1 ± 12.4	0.346#
AGE			
≤ 40 years	13 (12.7)	32 (21.6)	0.073*
41-50 years	38 (37.3)	42 (28.4)	0.139*
51-60 years	25 (24.5)	42 (28.4)	0.497*
> 60 years	26 (25.5)	32 (21.6)	0.476*
Gender			
Male	52 (51)	82 (55.4)	0.491*
Female	50 (49)	66 (44.6)	
BMI			
Underweight	4 (3.9)	4 (2.7)	0.719*
Normal weight	14 (13.7)	27 (18.2)	0.343*
Over weight	60 (58.8)	86 (58.1)	0.910*
Obese	24 (23.5)	31 (20.9)	0.628*
Social Status			
Single	13 (12.7)	21 (14.2)	0.743*
Married	74 (72.5)	95 (64.2)	0.165*
Divorced	4 (3.9)	19 (12.8)	0.068*
Widow	11 (10.8)	13 (8.8)	0.598*
Social class			
Low	16 (15.7)	24 (16.2)	0.911*
Middle	54 (52.9)	89 (60.1)	0.259*
High	32 (31.4)	35 (23.6)	0.175*
Residence			
Urban	62 (60.8)	98 (66.2)	0.379*
Rural	40 (39.2)	50 (33.8)	

*Chi square test, #t-test.

Table 6 shows that supplementation with Vitamin D did not lead to significant effect in total weight or change in BMI in T2DM patients.

Table (7): Comparison of Vitamin D supplements regarding clinical data

	Vitamin D supplements		P value
	Yes (n=102)	No (n=148)	
Vitamin D level			
<30 ng/ml	98 (96.1)	27 (18.2)	0.000*
>30 ng/ml	4 (3.9)	121 (81.8)	
Medication			
Insulin	49 (48)	75 (50.7)	0.682*
OHGD	35 (34.3)	52 (35.1)	0.893*
Insulin + OHGD	18 (17.6)	21 (14.2)	0.459*
Anti-DM Dosage			
Low	33 (32.4)	57 (38.5)	0.319*
High	69 (67.6)	91 (61.5)	

Table 7 shows that supplementation with Vitamin D significantly (P= 000.0) affect the serum vitamin D level (<30 ng/ml). While it had no significant effect on the type of diabetic medication or Anti-DM Dosage.

Table (8): Comparison of Vitamin D supplements regarding HbA1C level

	Vitamin D supplements		P value
	Yes (n=102)	No (n=148)	
1st HbA1C reading			
Range	7.5 - 13.6	7 - 14	
Mean ± SD	10.4 ± 1.6	10 ± 1.6	0.089#
2nd HbA1C reading			
Range	7.2 - 13.1	7 - 13.8	
Mean ± SD	10.1 ± 1.6	10 ± 1.7	0.554#
3rd HbA1C reading			
Range	6.8 - 12.7	7 - 13.8	
Mean ± SD	9.8 ± 1.5	9.9 ± 1.7	0.478#
4th HbA1C reading			
Range	6.5 - 12.5	6.5 - 13.6	
Mean ± SD	9.4 ± 1.5	9.9 ± 1.7	0.024#

*Chi square test, #t-test.

Table 8 shows that supplementation with Vitamin D significantly (P=0.024) improve the 4th HbA1C reading in T2DM patients.

Table (9): Comparison of Vitamin D supplements regarding the presence of co-morbidities

Other comorbidities	Vitamin D supplements		P value
	Yes (n=102)	No (n=148)	
Hyperlipidemia/dyslipidemia			
Yes	60 (58.8)	88 (59.5)	0.920*
No	42 (41.2)	60 (40.5)	
Hypertension			
Yes	39 (38.2)	65 (43.9)	0.370*
No	63 (61.8)	83 (56.1)	
Thyroid disorders			
Yes	9 (8.8)	35 (23.6)	0.002*
No	93 (91.2)	113 (76.4)	
Chronic Kidney disease			
Yes	14 (13.7)	25 (16.9)	0.498*
No	88 (86.3)	123 (83.1)	
Chronic liver disease			
Yes	13 (12.7)	16 (10.8)	0.639*
No	89 (87.3)	132 (89.2)	
Malabsorption disease			
Yes	2 (2)	5 (3.4)	0.504*
No	100 (98)	143 (96.6)	
No other chronic disease			
Yes	18 (17.6)	21 (14.2)	0.459*
No	84 (82.4)	127 (85.8)	

*Chi square test, #t-test.

Table 9 shows that among all the comorbidities associated with T2DM, Thyroid disorders was significantly (P=0.002) improved by Vitamin D supplementation in T2DM patients.

DISCUSSION

In the Middle East and North Africa, vitamin D deficiency is startlingly high as compared to other geographical regions (18). Specifically, in Saudi Arabia, where the sunlight is paradoxically directly proportional to the prevalence of vitamin D deficiency, hypovitaminosis D has been related not only to osteoporosis among apparently healthy males and post-menopausal females but also significantly related to cardiometabolic risk factors in both children and adults. Interestingly, there is an alarming prevalence of chronic non-communicable diseases in KSA, including T2DM, obesity, metabolic syndrome, and cardiovascular diseases (19).

Al-Daghri et al. reported that vitamin D supplementation is most beneficial to individuals who are at risk for osteoporosis and other bone-related diseases and also to those who are deficient and have other extraskeletal chronic disorders, such as diabetes T2DM and cardiovascular disease (19).

The current study shows that 250 diabetic patients were participated in the present study and divided into 2 groups according to vitamin D supplementation. The participant's age range was 29-88 years, and the mean of their age was 51.7 ± 11.7. More than half of participants (53.6%) were males, overweight (58.4%), had a middle social class (57.2%) and urban residence (64%).

Previous studies have shown vitamin D deficiency among healthy young Saudi women of age 25 to 35 years was 30% and 55% in women of 50 years or more, indicating that it is common in young and postmenopausal women (20). In another study on male population from Saudi Arabia, the prevalence of vitamin D deficiency was found to between 28% and 37% (21). Researchers have shown that vitamin D deficiency is highly prevalent among healthy Saudi women as well as men and primarily attributed to obesity, reduced exposure to sunlight, inadequate dietary vitamin D supplementation, sedentary lifestyle, lack of education and older age; which in turn affects BMD and bone turnover markers (21). Previous studies have shown Vitamin D deficiency among young and middle age Saudi Arabian males may lead to serious health consequences as high prevalence of a vitamin D deficiency occurs in Saudi Arabians despite having adequate exposure to sunlight and reported sufficient intake of dairy products (22).

The present study shows that all of our participant (250) had T2DM and half of them had vitamin D deficiency (<30 ng/ml). Approximately half (49.6%) of participated patients were taking insulin medication, 43.8% were taking OHGD while 15.6% were taking Insuline+OHGD. Nearly two-thirds of participants (64%) had high Anti-DM dosage Alhumaidi et al. (2013) found that the mean serum vitamin D in the diabetic patients was 15.7 + 7.5 ng/mL as compared non-diabetic group having 11.1 + 5.9 ng/mL and a total of 340 patients (98.5%) from both groups were observed to be deficient in vitamin D level which is the highest reported so far in Saudi Arabia. The population in the Southern Region of Saudi Arabia is generally insufficient in vitamin D irrespective of the presence of T2DM, and there is a greater need for supplementation of vitamin D in this population. Vitamin D deficiency has been implicated in inhibited insulin secretion and increased insulin resistance, and more recently with the development of T2DM (23).

The current study shows that only 40.8% of participant's T2DM patients were taking Vitamin D supplements; while 59.2% of them did not. 71 patients were taking >600 IU/day of vitamin D, and 31 patients were taking <600 IU/day

Alhumaidi et al. in 2013 found that 98.5% of his study population in Saudi Arabia had vitamin D deficiency with no significant difference in vitamin D level between a patient with diabetes and without diabetes. However specifically comparing only the deficiency of 25OHD with levels less than 20 ng/mL, 76.6% of the patients with diabetes as compared to 58.1% patients from non-diabetic population had a vitamin D deficiency which was a statistically significant difference with a p-value less than 0.0005 (23).

The current study shows that supplementation with Vitamin D did not lead to significant effect in total weight or change in BMI in T2DM patients.

Al-Zahrani et al. (24) reported that supplementation with vitamin D did not lead to significant reductions in total weight or change in BMI. The previous studies discussing the effect of vitamin D supplementation on weight are few, and the results are conflicting. Holick et al. found that on 65 men aged 61-65 years, a significant weight loss of 1.1 kg was observed in the treatment group after 12 weeks given 0.75 mg alphacalcidol than the placebo group (25). Additionally, in a long-term study of 18 months, Lind et al. observed that alphacalcidol caused a small but significant weight loss (0.9 kg) in a group of 14 middle-aged men (26). On the other hand, treatment for one year with either 2000 IU cholecalciferol, 0.25 mg alphacalcidol, or 0.25-

0.50 mg calcitriol did not affect body weight when compared with placebo among 238 post- menopausal women (27).

Furthermore, Trivedi et al. on men and women aged 65 years or above, cholecalciferol in a dose of 100000 IU or placebo was given every four months and, in a subgroup analysis on 238 subjects, there was no significant difference in body weight between the two groups after five years (28). It was considered it highly unlikely that supplementation with

cholecalciferol has a significant effect on weight. This is also supported by a recent study where a 2000 IU cholecalciferol daily for seven days among ten healthy young men had no impact on weight and fat metabolism (29).

On the other hand, Alfawaz et al. (30) reported that the overall prevalence of vitamin D deficiency was 78.1% in women and 72.4% in men, and 25(OH) vitamin D was significantly correlated to increasing age and weight (p-values < 0.0001 and 0.005, respectively).

84.4% of T2DM patients in the present study were suffered from other comorbidities included; Hyperlipidemia/dyslipidemia (59.2%), Hypertension (41.6%), Thyroid disorders (17.6%), Chronic Kidney disease (15.6%), Chronic liver disease (11.6%), and Malabsorption disease (2.8%). Interestingly, thyroid disorders were significantly (P=0.002) improved by Vitamin D supplementation in T2DM patients.

It was reported that vitamin D deficiency might play a role in the incidence of chronic disorders such as hypertension, CVD, obesity tumors and type 1 diabetes (T1DM). Vitamin D deficiency was associated with acute coronary events in men and increased mortality in the general population (31).

It was reported that supplementing with high-dose vitamin D have shown benefits in many medical conditions including fibromyalgia where 61% of diagnosed fibromyalgia women had 25OHD insufficiency. Vitamin D deficiency was associated with various illnesses like insulin resistance, allergic disease, multiple sclerosis and cancers and its possible role in the treatment of these conditions are in evolution (32).

Our finding shows that supplementation with Vitamin D significantly (P=0.024) improve the 4th HbA1C reading in T2DM patients.

Talaei et al. (33) was reported some mechanisms for the effects of vitamin D on T2DM included; presence of vitamin D receptors on pancreatic β cells, vitamin D activating 1α hydroxylase is expressed in pancreatic β cells, presence of vitamin D response element in the insulin gene, presence of vitamin D receptor in skeletal muscle, the fact that vitamin D increases the transcription of insulin receptor genes, and also inhibits the renin gene reducing hyperglycemic-induced increases in renin levels in pancreatic β cells and blockade of renin- angiotensin activity has been proposed as a novel target for diabetes management.

Previous studies have demonstrated higher HbA1c levels in patients with vitamin D deficiency. Tahrani *et al*. (34) show a high incidence of hypovitaminosis D in South Asians with T2DM, particularly in women. Abnormal vitamin D concentration was more common in South Asians with T2DM compared with those without T2DM control.

Nasri et al. (35) found that serum HbA1c value was significantly less than that of the control group in male interventional group. It means that vitamin D therapy has a beneficial effect on the control of blood sugar in male diabetic patients.

Strobel et al. (36) made a randomized, placebo-controlled intervention study with nearly 2 000 IU cholecalciferol per day demonstrates that insulin levels correlate markedly after six months of VD although the underlying insulin resistance persisted. After six months of medication, 78% of patients achieved a 25OHD concentration of >20 ng/ml. Their HbA1c was markedly lower at baseline (p=0.008) and after medication (p=0.009) than in patients with 25OHD <20 ng/ml.

CONCLUSION:

Supplementation with Vitamin D has no significant effect on total weight or BMI in T2DM patients. The majority of T2DM patients in the present study were suffered from other chronic disorders. Supplementation with Vitamin D significantly improve the 4th HbA1C reading and also improve thyroid disorders in T2DM patients.

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