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Full length Research Article

The Effect of Vitamin D Level on Blood Glucose, HbA1c and Some Inflammatory Markers in Sudanese with Type 2 Diabetes Mellitus

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Summary: Diabetes Mellitus are more likely to occur in people with low vitamin D levels. In this study, Sudanese individuals diagnosed with type 2 diabetes mellitus (T2DM) had their serum glucose, HbA1c, vitamin D, and inflammatory markers assessed. In this case-control study, 120 individuals aged 35 to 69 were divided into two groups. The first group, 30 men and 30 women, had been diagnosed with Type 2 diabetes mellitus for a minimum of two years. The second group, the control group, comprised sixty healthy adults, evenly split between 30 males and 30 women. Every participant had a thorough medical history taken, with particular attention to the length of their diabetes, its medical history, and any previous problems. During the clinical examination and laboratory tests, the following parameters were evaluated: total WBC (1,000/ml), ESR (mm/hour), CRP (mg/L), HbA1c (%), and serum vitamin D3 (ng/ml). When 25(OH) vitamin D3 levels were utilized to assess T2DM patients, they showed significantly lower mean blood concentrations than controls: 23 (38.3%) had vitamin D insufficiency, 23 (38.3%) had vitamin D deficiency, and 14 (23.3%) had sufficient vitamin D. Vitamin D-deficient patients had significant increases in HbA1c, glucose, CRP, and total WBC. Additionally, when comparing the mean ESR values of diabetes patients to those of the control group, there was a statistically significant rise. ESR did not significantly alter depending on the controlling level. Males also had a numerically higher level of vitamin D3 than females. Compared to healthy normal controls, individuals with type 2 diabetes have noticeably reduced vitamin D3 levels. Furthermore, in T2DM patients, there was an association between elevated inflammatory markers and HbA1c and insufficiency in vitamin D.

Keywords*: Vitamin D, blood glucose, HbA1c, inflammatory markers, Type 2 diabetes mellitus.*

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INTRODUCTION

Over 80% of cases of diabetes mellitus are type 2 (Ostenson, 2001). It is a heterogeneous condition with a gradual onset that arises from the combination of environmental factors and polygenetic inheritance. The majority of T2DM patients are more susceptible to conditions like atherosclerosis, ischemic heart disease, ischemia, gangrene of the foot, and microangiopathy; diabetic nephropathies, including renal failure and glomerular damage; changes in the eyes, such as diabetic retinopathy and cataract; and neurological abnormalities (Schneider 2009).

Globally, vitamin D insufficiency is prevalent (Abuannai and O'Keefe, 2011). Previuos study indecated that Vitamin D deficiency is associated with a higher chance of complications from diabetes, including cardiovascular disease (CVD) and renal impairment Al-Timimi and Ali (2013),. Moreover, Lappe *et al.* (2007) reported that vitamin D affects innate and adaptive immunity. High vitamin D concentrations may offer protection against inflammatory diseases, (Chu *et al* ., 2010; Elamin *et al* ., 2011). increased concentrations of inflammatory biomarkers, fibrinogen, WBC, or C-reactive protein (CRP). Additionally, vitamin D deficiency increases the risk of cardiometabolic disease and other chronic inflammatory diseases (Hewison 2012).

A combination of diabetes with vitamin D deficiency could result in more complications. Research on vitamin D supplementation for people with type 2 diabetes who are vitamin D deficient has produced conflicting results. Some have reported improved glucose control (Deluca 2004). Moreover, inadequate glycemic control was linked to vitamin D deficiency (Kaya *et al* ., 2018). Moreover, a few studies investigated the correlations between blood vitamin D levels and indicators of inflammation in the broader population (Jorgensen *et al* ., 2010; Ngo *et al* ., 2010).

According to the study, T2DM patients with vitamin D insufficiency had higher ESR than those with adequate vitamin D (Kaya *et al* ., 2018).

In addition to examining the vitamin D levels of the patients with type 2 diabetes, the study aimed to determine how low vitamin D levels related to glycaemic management, HbA1c, and specific inflammatory markers. Through the provision of vitamin D or close observation, the results of this study may improve the management of diabetic patients and avert major complications.

MATERIALS AND METHODS

This case-control study was carried out in the Khartoum state- Sudan. Samples were collected from clinics and hospitals in Khartoum state, such as Jabir Abu Alizz Diabetes Center, Soba University Hospital, and Turkish Teaching Hospital. The study included 60 T2DM patients aged 35–65 and 60 controls matched for age and gender (50% male and 50% female). Cases excluded from this study were pregnant females, renal, hepatic, parathyroid, smokers, alcoholics, cancer patients, and subjects on vitamin D supplementation, calcium, and drugs affecting vitamin D or calcium metabolism. A thorough medical history, including the length of the individual's diabetes, medical history, and history of complications from the disease, was taken from each participant. Accordingly, diabetic subjects were divided into good, moderate, and bad control subjects. Serum vitamin D3, glycated haemoglobin HbA1c, C-reactive protein (CRP), white blood cells (WBC), and erythrocyte sedimentation rate (ESR) were among the parameters examined in the clinical examination and laboratory tests. A trained nurse collected 5.8 ml venous blood samples from each enrolled subject under aseptic conditions. Each blood sample was divided into three parts:
First part: 2 ml were collected in EDTA tubes to measure vitamin D, HbA1c, and TWC.
Second part: 2 ml was collected in a lithium heparin tubes to measure fasting blood glucose and CRP.
Third part: 1.8 ml was collected in an EDTA tubes to measure ESR.
Serum glucose: Glucose concentration was determined by the enzymatic method using a kit (Randox Laboratories Ltd-London).

CRP: C-reactive protein was determined by the CRP-M100 as described by Zong *et al* . (2000).

TWBCs: Total white blood cells was performed in an improved Neubauer haemocytometer using Turk's solution dilution fluid as described by Jain, (1993) by the Mindray BC-6800.

HbA1c: Glycated haemoglobin was determined by immunoassay using Cobas c501 as described by He *et al*. (2021)

Vitamin D: vitamin D was determined by electrochemiluminescence immunoassays using COBAS e411 as described by Yalla *et al* . (2019).

Erythrocyte Sedimentation Rate: The erythrocyte sedimentation rate test was determined by the Westergren method.

Statistical Analysis: Data were analyzed using Statistical Package for Social Science (SPSS). Analysis of variance Analysis of Variance (ANOVA) test (one way) and t-test was used to assess the significant difference among the groups. The differences are considered statistically significant at P value < 0.05. The results were presented as mean ± SD.

RESULTS

Glycemic profile and some inflammatory markers levels: Table (1) shows the two study groups' glycemic profile and some inflammatory markers levels. A significant (P<0.001) increase in the mean Glucose, HbA1c and ESR values in the diabetic patient compared to the control group's values. On the other hand, there was no discernible difference between the two groups' TWBC and CRP levels. When compared to controls, the serum level of vitamin D3 in diabetics was considerably (P<0.01) lower (ranging from 23.62±9.37 ng/ml to 34.85±32.34 ng/ml) Figure (1). Male respondents had significantly greater levels of vitamin D3 than female subjects did as well (Figure 2).

The influence of vitamin D levels on glycemic control and some inflammatory markers in patients with T2DM: The T2DM patients were evaluated based on their 25(OH) D levels; 23 (38.3%) patients had vitamin D deficiency, 23 (38.3%) patients had vitamin D insufficiency, and 14 (23.3%) patients were vitamin D-sufficient. Patients with vitamin D shortage had significantly higher levels of HbA1c, glucose, CRP, and TWB cells (P<0.01) compared to patients with vitamin D insufficiency and vitamin D-sufficient individuals. No significant difference in ESR was found (Table 2).

Table :1
Comparison of glycemic profile and some inflammatory markers.

Parameters	Diabetics (Mean±SD)	Control (Mean±SD)	*P-value*
Glucose (mg/dl)	141.0±56.74	86.28±11.23	0.000
CRP (mg/L)	11.14±12.10	12.72±9.08	0.418
TWC (1,000/ml)	7.25±4.32	6.67±2.44	0.368
ESR (mm/hour)	45.17±14.71	17.80±4.81	0.000
Vitamin D (ng/ml)	23.62±9.37	34.85±32.34	0.011
HbA1c (%)	8.90±2.09	-	-

Table (2):
The influence of vitamin D levels on glycemic control and some inflammatory markers in patients with T2DM

Variables	Mean±SD			*P-value*
	Deficiency	insufficiency	sufficiency	
Sex M/F	12 (40)/11 (37)	12 (40)/11(37)	6 (20)/8 (27)	0.830
HbA1c (%)	10.4±1.84	8.42±1.80	7.15±0.84	0.000
Glucose (mg/do)	190.3±50.99	119.3±39.51	95.78±15.43	0.000
CRP (mg/l)	18.2±3.40	7.93±1.19	4.71±0.74	0.001
TWC (1,000/ml)	8.55±6.20	6.82±2.56	5.81±1.82	0.146
ESR (mm/hour)	43.4±15.57	46.9±12.95	45.07±16.64	0.737

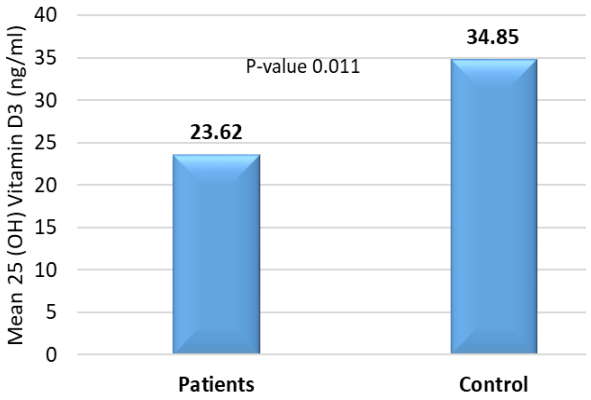

Figure 1:
Serum level of 25 (OH) vitamin D3 in the diabetic and control group

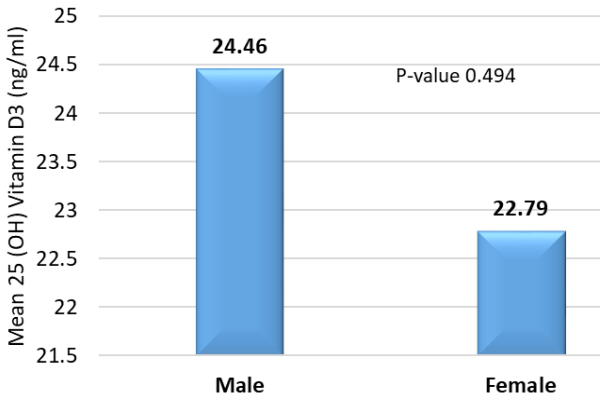

Figure 2:
Relation between gender and Vitamin D3 level in participants (n = 60).

Correlation between vitamin D glycemic control and some inflammatory markers: Table 3 shows the relation between vitamin D and glucose levels, glycemic control, and other inflammatory markers. The following measures showed a strong connection with the vitamin D3 level: TWBC (r= -0.308, p=0.017), HbA1C (r= -0.605, p=0.000), CRP (r= -0.500, p= 0.000), and glucose (r= -0.655, p= 0.000). However, no correlation could be seen between ESR and vitamin D3 (r=0.100, p= 0.455).

Influence of the diabetic's control on the blood glucose level, HbA1c and inflammatory markers: Table 4 shows that the diabetic subjects were divided into 3 subgroups according to glycemic control: 10 (16.7%) patients had good control, 15 (25.0 %) patients had moderate control, and 35 (58.3%) patients had inadequate control. HbA1c, Glucose, CRP, and TWB cells were considerably higher (P<0.001) in patients with bad control than in moderate and good control; however, there was no significant difference in ESR regarding the controlling level.

Table (3):
Correlation of vitamin D with clinical and laboratory parameters in patients with T2DM.

Variables	R-value	P-value
Glucose (mg/dl)	-0.655**	0.000
HbA1c (%)	-0.605**	0.000
CRP (mg/l)	-0.500**	0.000
TWC (1,000/ml)	-0.308*	0.017
ESR (mm/hour)	0.100	0.455

DISCUSSION

The current finding indicated a significantly low serum level of vitamin D3 in diabetic patients compared to the control values. The vitamin D3 level directly influenced the glucose and HbA1c levels in the current result. This finding is expected so that vitamin D3 plays a role in body homeostasis. Also, vitamin D3 directly and indirectly influences the β-cell in the pancreas.). Earlier studies have discovered a link between low levels of vitamin D and metabolic syndrome, a known risk factor for diabetes and other major causes of death in the US (Forrest and Stuhldreher, 2011; Binkley *et al* ., 2012; Fung *et al* ., 2012). It also plays a critical role in adult osteoporosis prevention. Further research has revealed that vitamin D involves more than maintaining calcium homeostasis.

Table (4):
Influence of the diabetic's control on the blood glucose level, HbA1c and inflammatory markers

Variables	Mean ± SD			*P-value*
	Good control	Moderate control	Bad control	
HbA1c (%)	6.66 ±0.29	7.24 ±0.26	10.3 ±1.72	0.000
Glucose (mg/do)	98.6 ±20.97	100.7 ±21.06	170.4 ±56.17	0.000
CRP (mg/l)	4.39 ±2.12	5.31 ±2.08	15.6 ±2.41	0.002
TWC (1,000/ml)	5.58 ±2.08	6.30 ±2.16	8.13 ±5.23	0.160
ESR (mm/hour)	48.10 ±13.17	46.07 ±14.68	43.94 ±15.37	0.713

It is also vital for immune system function and cell proliferation (Christakos *et al*., 2007), inhibits carcinogenesis, and delays the onset of other inflammatory diseases like T2D and cardiovascular disease (Roth 2007; Drake and Ng, 2010; Anagnostis *et al* ., 2010). Morover, it has been revealed that vitamin D affects the development of insulin resistance, type 2 diabetes, and β-cell activity. Even though maintaining calcium homeostasis is the most well-known use of vitamin D, it is also believed to affect β-cell activity. This effect may be achieved by circulating 1, 25-dihydroxy vitamin D binding to the β-cell receptor (Peechakara and Pittas, 2008). As an alternative, 1-alpha-hydroxylase, expressed in β-cells, could activate 25(OH)D in response to vitamin D (Peechakara and Pittas, 2008). Vitamin D can also influence insulin secretion, a calcium-dependent function, by controlling extracellular calcium levels and calcium influx through β-cells (Sheshadri and Tamilselvan, 2011). The function of β-cell secretory may be adversely affected by any alterations in calcium flux (Pittas *et al* ., 2006; Palomer *et al* ., 2008).

The present study indicated that patients with vitamin D deficiency had significantly higher HbA1c and glucose levels compared to those with sufficient vitamin D and those with insufficient vitamin D. According to Badawi *et al* . (2014), vitamin D deficiency in type 2 diabetes may have an effect on beta cell function and the onset of type 1 diabetes. Vitamin D deficiency and HbA1C are significantly correlated, and there is an inverse association between vitamin D and insulin resistance, according to Yiu *et al* . (2011). Forouhi *et al* . (2014). These authors pointed out that when there was baseline vitamin D insufficiency, there was a ten-year risk of higher glucose concentrations while fasting, glucose concentrations throughout the two hours, and a metabolic syndrome risk factor score. Similar findings were reported by the majority of prospective studies on young people recently diagnosed with diabetes (Daa *et al* ., 2014).

The research findings indicate a statistically significant rise in the average ESR values among individuals with diabetes mellitus in contrast to the control group. On the other hand, Table 1 indicates that there was no remarkable difference in TWBC and CRP levels between the two groups. Compared to patients with vitamin D insufficiency and those with adequate vitamin D, those with vitamin D deficit had significantly higher CRP and TWBC levels. Compared to individuals with moderate and well-managed blood sugar, those with poorly controlled blood sugar had significantly higher levels of CRP and TWBC (Table 4). Nonetheless, there was no discernible variation in ESR concerning the controlling level. This research supports a prior meta-analysis of prospective studies that discovered a substantial correlation between CRP and the risk of type 2 diabetes (T2DM) (Wang *et al* ., 2013).

Lymphocytes and insulin levels correlate positively (Ryder *et al* ., 2014). A comprehensive review and meta-analysis found a clear correlation between higher WBC counts and a higher risk of type 2 diabetes (Gkrania-Klotsas *et al* ., 2010). Further research yielded some results indicating that inflammation plays a role in the onset of diabetes. Diabetes mellitus and ESR did not significantly correlate, according to Schmidt *et al* . (1999).

Increased risk of cardiometabolic disease and other chronic inflammatory disorders has been associated with elevated levels of inflammatory biomarkers, such as C-reactive protein (CRP), white blood cell count (WBC), or plasma fibrinogen (Hewison 2012). High vitamin D concentrations may offer protection against inflammatory diseases, according to certain research (Chu *et al* ., 2010; Elamin *et al* ., 2011). The findings of this investigation contradict with those of a few other studies (Ostenson 2001; Ngo *et al* ., 2010) that looked at the relationships between inflammatory markers and blood vitamin D levels. The current study's findings conflict with another study that found T2DM patients with vitamin D insufficiency had higher ESRs than those with adequate vitamin D. ESR and vitamin D levels were inversely correlated (Kaya *et al* ., 2018).

Males had considerably greater levels of vitamin D3 than females in the current investigation. This could be attributed to the habits of dressing and less exposure to the sun for females in the Middle East and North Africa. Previous studies showed how clothing (long sleeves and pants), sunscreen (applied liberally and frequently), and behaviour (seeking shade) can reduce the amount of skin surface area that is exposed to solar UVB ray penetration and consequently limit the amount of vitamin D3 synthesis that occurs on the skin (Matsuoka *et al* ., 1987; Matsuoka *et al* ., 1992).

Furthermore, this study indicated that the poorly controlled blood sugar group had significantly higher HbA1c and glucose levels compared to the individuals with moderately and well-managed blood sugar, those with. Regarding diabetes self-management, it is crucial to have reliable and valid measures (McNabb 1997). Several self-care behaviors in individuals with diabetes are associated with positive outcomes. These encompass nutritious dietary choices, regular physical activity, blood sugar monitoring, adherence to prescribed medications, effective problem-solving abilities, healthy coping mechanisms, and behaviors aimed at reducing risk (Shrivastava *et al* ., 2013). These behaviors demonstrated a positive correlation with effective glycemic control, a decrease in complications, and an enhancement in quality of life (Deakin *et al* ., 2005)

In conclusion, the current investigation found that T2DM patients had considerably lower levels of 25(OH) vitamin D3 compared to healthy controls. The low levels of 25(OH) vitamin D3 elevated inflammatory markers. Vitamin D supplements may be helpful in the prevention and treatment of type 2 diabetes since vitamin D levels have been related to glycemic control in diabetics. Further research is needed to fully understand the benefits of including vitamin D supplements in the type 2 diabetes treatment plan.

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participated in preparing the manuscript. All authors revised and approved the final version of the manuscript.

Ethics approval:
Ethical approval was granted from Khartoum State- Ministry of Health- Research Department

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent.

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