

## Expanding Role for Vitamin D3 in Diabetic Mellitus and Chronic Kidney Disease

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### ABSTRACT

In between 30% and 50% of people, lack of vitamin D and insufficiency are reputed to be serious health concerns. Diabetes mellitus (DM) and chronic renal disease are both connected with insufficient amounts of vitamin D (CKD). Diabetes' onset and development have both been connected to vitamin D deficiency. But even if there is a connection the relationship between impaired beta cells, insulin resistance, and synthesis of these hormones in patients with diabetes. In modern study, in female the level of Vit D is decreased compared with male, as well as the values of HbA1c were significantly higher in cases than in controls ( $p < 0.01$ ). A lack of vitamin D has been associated with the development of DM. Although there is growing evidence that a vitamin D deficiency the likelihood of getting chronic kidney disease (CKD) and diabetic mellitus (DM) both rises), the relationship between vitamin D, creatinine, and blood urea has been established. As a result, patients with D3 deficiency have higher blood urea levels than controls, which is a significant difference. The level of Creatinine was the highest in the D3 deficiency patients ( $1.689 \pm 0.142$ ) and showed a significant difference when it compared with controls ( $1.000 \pm 0.040$ ) in different significant ( $P \leq 0.01$ ). this study observed that serum creatinine increased in individuals who lack vitamin D and have chronic renal dysfunction and it's widely interpreted as a measure only of renal function.

**Keywords-** cardiovascular disease, chronic kidney disease, diabetes mellitus, vitamin D deficiency.

### I. INTRODUCTION

A hormone that the kidneys make called vitamin D regulates blood calcium levels and has an effect on the immune system. even though Low levels of vitamin D are increased the risk of rickets and fractures, they are linked to cardiovascular disease, cancer, and hypertension as well. Low vitamin D levels are linked to both chronic renal disease and diabetes mellitus (DM). (CKD) (1). In the United States and other Western nations, diabetes-related kidney disease is the primary factor causing chronic renal disease. (CKD). For diabetics, Additionally, it ranks among the long-term problems with the highest rates of morbidity and mortality. In the United States, thirty to forty percent of

all cases of end-stage renal disease are caused by diabetes. [3]. In the United States and other Western nations, diabetes is the most common cause of chronic kidney disease (CKD). In terms of morbidity and mortality, it is also one of the most serious long-term issues for diabetics. In the United States, diabetes accounts for 30 to 40% of all cases of end-stage renal failure. The enzyme 25-hydroxylase converts vitamin D to 25-hydroxyvitamin D (25(OH)D) (CYP2R1). The most common form of vitamin D in circulation is 25(OH) D. The carrier proteins transfer 25(OH)D from the liver to the kidneys [4]. Insulin resistance has long been known as a risk factor for type 2 diabetes. Directly or indirectly, vitamin D may improve insulin responsiveness for glucose transfer, by stimulating the

expression of insulin receptors (Mathieu and Gysemans, [5], or indirectly, via controlling extracellular calcium, making sure calcium is properly absorbed maintaining an adequate intracellular cytosolic calcium (Ca<sup>2+</sup>)<sub>i</sub> pool and passing through cell membranes (Mathieu and Gysemans) [5]. Low vitamin D levels and reduced insulin sensitivity have been linked in cross-sectional studies. [6]. By directly influencing the synthesis and functions of cytokines, vitamin D may increase insulin sensitivity and promote beta-cell survival. Conflicting human research on the connection between type 2 diabetes, systemic inflammation, and calcium or vitamin D levels is lacking. [7]. eGFR), basal metabolic rate, and vitamin D level (25-hydroxyvitamin D3 25(OH)D3) in the blood. However, the most common cause of CKD worldwide being diabetes mellitus [2], Evaluation of the disease's long-term impact on the kidneys is crucial. Glycated hemoglobin is created when glucose is added to hemoglobin in an unenzymatic, permanent process (HbA1c). The average glycemia of the previous 12–16 weeks is represented by the glycated hemoglobin, which remains in RBCs for the duration of their lives [3]. The American Diabetes Association advises that the HbA1c be below 7.0 percent for most patients, whereas the International Diabetes Federation recommends HbA1c readings below 6.5 percent. [4].

## II. MATERIALS AND METHOD

An experimental study was conducted at the private AL Canal Medical Laboratory in Baghdad. A total of (50) patients underwent it. A total of 32 patients—34 women and 16 men—had already been diagnosed with vitamin D3 deficiency, and 18 people without the condition were employed as a control group.

The following tests were performed on each patient and member of the control group: total blood urea, serum creatinine, random blood sugar, HbA1c level, and total 25-hydroxy vitamin D level.

### Samples Collection and Preparation:

Blood samples from both patients and controls were collected. by using a 10 ml syringe to draw blood. They were then divided into two parts: the first part (5 ml) was placed into a vacuum gel test tube with the samples' numbers noted with a permanent marker pen, and the blood was allowed to clot for about 15 minutes before being centrifuged to produce clear serum for the biochemical tests. For the HbA1c level, the second portion (2.5 ml) of the whole blood was put into an EDTA tube.

### Procedures:

French-made SELECTRA PRO M Lite completely automatic biochemistry analyzer accustomed to automatically check the levels of blood urea, serum creatinine, and random blood sugar. Total 25-hydroxyvitamin D levels were estimated in serum using Japanese-made Tosoh AIA-900 automated immunoassay

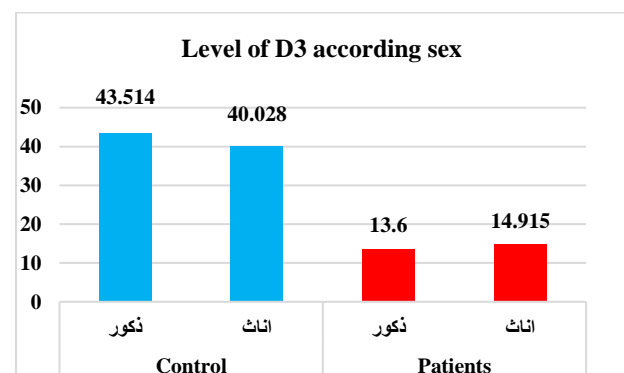
analyzer. American-made Alere Afinion 2 analyzer was used to measure the HbA1c level.

## III. RESULT AND DISCUSSION

In the present research, the level of Vit D (ng/dL) was significantly the lowest in the patients (male) (**13.6±2.356** ng/mL) when it compared with controls (male) (**43.514±9.470**) (P<0.01). While the level of Vit. D in patients (females) also was lowest (**14.915±2.066** ng/mL) than the controls (females) (**40.028±4.042** ng/mL) and significant (P<0.01) as presented in table(1-1), as well as in female the level of Vit D is decreased compared with male in figure 1, table 1.

**Table 1: Level of vit D according to the sex**

Sex groups		Mean±SE
		D3
Control	Male	43.514±9.470
	Female	40.028±4.042
Patients	Male	13.6±2.356
	Female	14.915±2.066
LSD value		16.478
P-value		0.0001*
*P<0.01		



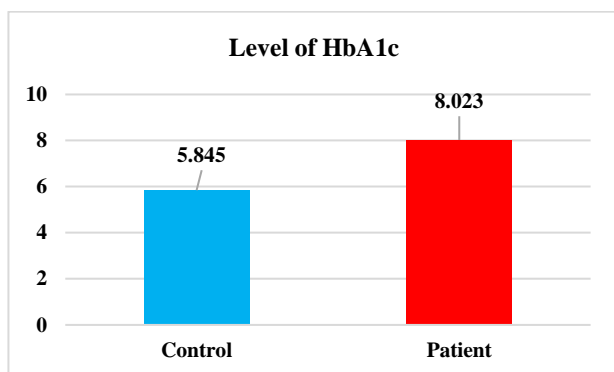
**Figure 1: level of vit D according to the sex**

### Vitamin D and dimities militias relationship (DM)

[Table 2] show the level of HbA1C in D3 deficiency patients were increased then, the outcomes are displayed in control in (figure 2). The values of HbA1c were considerably more in cases than in controls (p< 0. 01). A lack of vitamin D has been associated with the development of DM. While vitamin D levels and diabetes are linked, there is conflicting information regarding how vitamin D levels affect malfunction of - cells, insulin secretion, and insulin resistance in diabetics., Although it is still unknown whether vitamin D insufficiency also increases the risk of death from DM and CKD, A risk factor for DM and CKD may be a vitamin D deficiency (8).

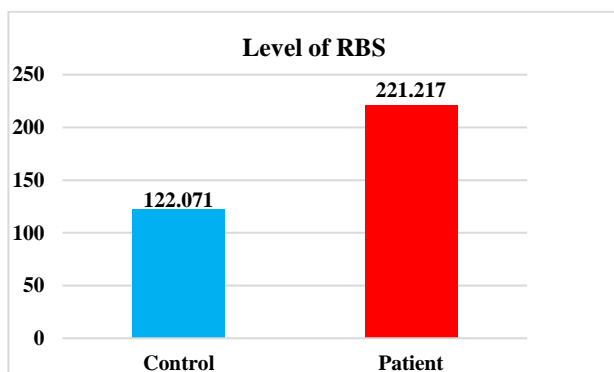
**Table 2: The level of HbA1C in D3 deficiency patients**

Groups	Mean±SE
	HbA1c
Control	5.845±0.087
Patients	8.023±0.336
LSD value	0.621
P-value	0.0001*
*P<0.01	



**Figure 2: The level of HbA1C in D3 deficiency patients**

In this study showed the relation between level D3 and RBS [figure 3] show the level RBS and D3 in DM patients was increased than in control. The values of RBS were substantial increase in cases compared to controls (p< 0. 01).



**Figure 3: The level of RBS in D3 deficiency patients**

Recently, vitamin D3's plays a part in how diabetes develops has received some attention on a global scale (9) Type 2 diabetes and the metabolic syndrome seem to be linked to vitamin D3 insufficiency. The inverse relationship between vitamin D3 levels and glycosylated hemoglobin levels suggests that vitamin D3 may have an impact on glucose homeostasis. Vitamin D3 has both a direct (through its function in sensitive organs and the activation of pancreatic beta-cell) and an indirect (through the controlling calcium hemostasis) favorable influence on insulin secretion and sensitivity

with regard to diabetes. (10). Due to decreased insulin clearance, poor absorption of some diabetic medicines, and impaired renal gluconeogenesis from lower kidney disease, patients with kidney disease that is progressing are at an increased risk for hypoglycemia.

**Vitamin D's impact on chronic kidney disease (CKD)**

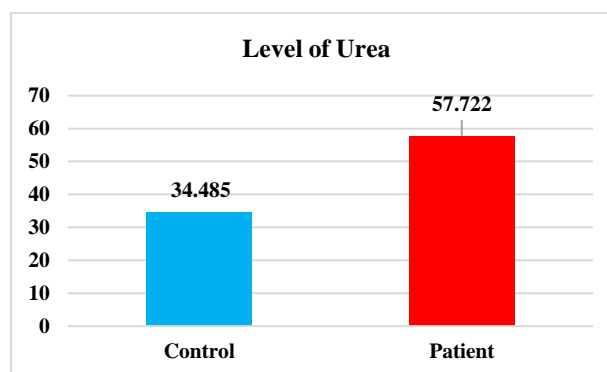
In national studies conducted in the United States, low vitamin D levels have been linked to the advancement of kidney disease and proteinuria. (11).

In this study the level of blood Urea is increased in D3 deficiency patients and showed a significant difference when it compared with controls at \*P<0.01. (table3, figure 4-)

Uncertainty surrounds the pathophysiological mechanism that links high BUN levels to poor renal outcomes. Thought has been given to a number of theories surrounding the association. A clinical feature of CKD that promotes isocyanate synthesis is worsening renal function, which is indicated by a sustained rise in BUN. [12]

**Table 3: The level of blood Urea in D3 deficiency disease**

Groups	Mean±SE
	Urea
Control	34.485±1.544
Patients	57.722±2.850
LSD value	5.951
P-value	0.0001*
*P<0.01	



**Figure 4: The level of blood Urea in D3 deficiency disease**

Randomized clinical studies and a meta-analysis suggest that vitamin D analog therapy may reduce proteinuria in diabetic nephropathy and other proteinuric conditions [13]. Vitamin D may have particularly substantial effects on the kidney, an organ essential to vitamin D metabolism.

The hormone generated actively is 1,25-dihydroxyvitamin D. from cholecalciferol or ergocalciferol, protects kidney injury in animal models by potentially inhibiting the RAS, lowering renal

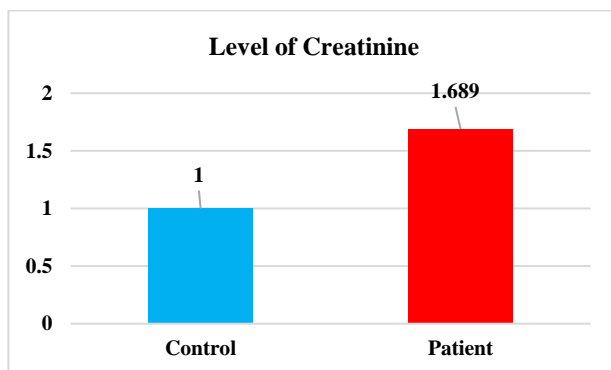
inflammation, and directly promoting podocyte survival [14] Along with RAS inhibitors, these effects lessen albuminuria and glomerulosclerosis. [15]

The level of Creatinine was the highest in the D3 delicacy patients (**1.689±0.142**) and showed a significant difference when it compared with controls (**1.000±0.040**) in different significant ( $P \leq 0.01$ ).

The current results showed high substantial serum elevation creatinine in CKD patients when compared with healthy controls group ( $P \leq 0.01$ ) as presented in [table 4, figure 5]. This is due to the glomerular filtration rate has decreased (GFR) in CKD patients.

**Table 4: The level of Creatinine in CKD patents**

Groups	Mean±SE
	Creatinine
Control	1.000±0.040
Patients	1.689±0.142
LSD value	0.218
P-value	0.0001*
*P<0.01	



**Figure 5: The level of Creatinine in CKD patents**

It's interesting to note that blood creatinine levels may be impacted by vitamin D, which may also alter how much creatinine is produced by muscle. Paricalcitol was given to 16 CKD patients. in an exquisite study by Agarwal et al., and before and after, serial creatinine levels and iothalamate GFRs were assessed. Although the patients' measured GFRs remained unchanged, their creatinine level increased[16].

Creatinine is an endogenous product formed by creatine and creatine phosphate non-enzymatic conversion, 95% percent which the muscle contains. [17]. An uncharged, relatively low-molecular-weight substance is creatinine (113 Da). The glomerulus can filter it freely in the absence of tubular reabsorption. Additionally, the renal tubules only secrete trace amounts of creatinine. [18]. The proportion of as renal function declines, the amount of creatinine expelled through tubular secretion increases. [19]

Increased creatinine can result from either suppression of the active tubular production of creatinine or a reduction in glomerular filtration, which indicates nephron injury and a decline in renal function. These findings supported previous research findings. [20]

Given that renal function declines by 50% before an increase in serum creatinine is seen, serum creatinine may be a later signal of renal impairment. These results agreed with Nisha et al study in (2017) who observed that serum creatinine increased in patients with chronic kidney failure and it's widely interpreted as a measure only of renal function [22].

#### IV. CONCLUSION

The results of our investigation showed a causative association between vitamin D3 levels and diabetes mellitus among patients, according to the findings. It has been found that levels of vitamin D3 are adversely correlated with levels of glycosylated hemoglobin. Low vitamin D levels have been linked to chronic diseases like diabetes and CKD, according to numerous prospective studies.

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