

## The Correlation between Vitamin D and Clinical Implications for Obesity-Related Type 2 Diabetes Mellitus

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### Abstract

**Background:** Obesity and type 2 diabetes have both rapidly raised during the last periods and are ongoing to increase at a disturbing rate universal. Several clinical and epidemiological researches demonstrated a reverse association between circulating vitamin D levels, central adiposity and the progress of insulin resistance and diabetes.

**Objective:** The target of this work was to elucidate the complex role of vitamin D and the clinical implications of diabetes on metabolic defects related with obesity.

**Subjects and Methods:** This study encompassed 90 diabetic patients (45 obese and 45 non obese) who were attending the National Diabetic Center/ Al-Mustansiriyah University during the period from June 2019 to January 2020; their age range was (35-60) years. All participant underwent clinical and biochemical examinations.

**Results:** A substantial rise ( $p= 0.01$ ) in waist/hip ratio, body mass index, fasting serum glucose, total cholesterol, triacylglycerol, and low density lipoprotein cholesterol in obese diabetic patients as paralleled to non-obese group. Moreover, there was an elevation in glycated hemoglobin, serum insulin, and homeostasis model assessment for insulin resistance in obese group, but it was not significant. A substantial decrease ( $p= 0.01$ ) in serum high density lipoprotein cholesterol and vitamin D3 were detected in obese diabetic patients as paralleled to non-obese group.

Also, obese diabetic patients had the higher percent (61%) of D3 deficiency as paralleled to non-obese patients.

**Conclusions:** In the present study, it is found that there is significant increase in blood sugar in the individuals with decreased vitamin D levels, which was related with insulin resistance, decreased  $\beta$ -cell function, and obesity.

**Keywords:** Diabetes Mellitus, Obesity, Insulin Resistance, Vitamin D3.

### Introduction

Type 2 diabetes mellitus (T2DM) is a progressive and chronic disease manifested by  $\beta$ -cell dysfunction and improved insulin resistance (IR), defined as the insufficient response of liver, skeletal muscle, and adipose tissue to endogenous insulin secretions and few medications improve IR (1).

Vitamin D deficiency is a crucial factor in the progress of T2DM. Vitamin D is supposed to advance the body's sensitivity to insulin and thus diminish the risk of IR. It can also regulate the production of insulin in the pancreas through control of the insulin receptor gene. However, the relation between vitamin D status and diabetes still remains poorly understood (2).



Vitamin D is nature's own product; it is produced in the skin through the action of sunlight on 7-dehydrocholesterol (3). Vitamin D has been proposed to have a great role in global health not only in the musculoskeletal system but also in immune system modulation, cellular proliferation and differentiation, inhibition of rennin synthesis and erythropoiesis (4).

Humans get vitamin D via the sun and through their diet. When people are exposed to sunlight, 7-dehydrocholesterol converts to pre-vitamin D<sub>3</sub>, which is quickly converted to vitamin D<sub>3</sub> that enters the circulation. Most vitamin D<sub>3</sub> is transported in the blood by binding to vitamin D binding protein (85-88)% or albumin (12-15)%. In the diet, vitamin D mainly comes from animal derived food, where it is metabolized by 25-hydroxylase to 25-hydroxyvitamin D (25-(OH)D<sub>3</sub>), which is the main circulating metabolite and a determinant of a patient's vitamin D status. However, 25-(OH)D<sub>3</sub> has little biological activity and needs to be transported to the kidney for further hydroxylation to its active form, 1,25-dihydroxyvitamin D (1,25-(OH)<sub>2</sub>D<sub>3</sub>) (5).

Obesity rises the risk of vitamin D deficit, and adipose tissue is of excessive concern as a determinant of vitamin D requests and bioavailability. The reverse association between vitamin D status and adiposity is well-known (6). Adipose tissue also metabolizes vitamin D, thus each steps of this process need hormonal activation of vitamin D and degradation (7). So, as a predictor of vitamin D inadequacy, obesity has been suggested to be following to little sun exposure (8). This may have significant consequences for obesity-associated health effects, given that vitamin D hormone has physiological and biochemical mechanistic influences as well as the prospective to decrease obesity-associated risks of tissue damage (9).

It is commonly putative that obesity denotes a worldwide health problematic since it is related with comorbidities, such as DM, hypertension, metabolic syndrome, renal disease, cardiovascular disease, skeletal modifications, and cancer. Furthermore, obesity is also frequently related with low vitamins levels, comprising vitamin B1 (thiamine), folate, and vitamin D (10). All treatment includes vitamin D with calcium (Ca<sup>2+</sup>) were used to compensate the deficiency (11).

The target of this work was to elucidate the complex role of vitamin D and the clinical implications of diabetes on metabolic defects related with obesity.

## Material and Methods

Current study encompassed 90 patients with T2DM (45 obese and 45 non obese) who were attending the National Diabetic Center/ Al-Mustansiriyah University during the period from June 2019 to January 2020; their age range was (35-60) years. All participant underwent clinical and biochemical examinations.

Waist to hip (W/H) ratio was estimated and body mass index (BMI) was deliberate as weight (Kg) divided by height (m<sup>2</sup>). Fasting venous blood samples were collected from all the subjects after 10-12 hours fasting. Laboratory assessments were down, which encompassed fasting serum glucose (FSG), glycated hemoglobin (HbA1c), lipid profile comprising: total cholesterol (TC), triacylglycerol (TAG), low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C). They were measured using a chemical analyzer. While, serum insulin was measured using enzyme linked immuno Sorbent assay



(ELISA). Furthermore, vitamin D3 measured using the assay principle combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA) by (Minividas, Biomerix kit, France). Hypovitaminosis is defined by most experts as a serum 25(OH)D level < 20 ng/ml, whereas a serum 25(OH)D level of > 30 ng/ml is deliberated to be normal and a level of 20–30 ng/ml describes vitamin D insufficiency (12).

Insulin resistance representing by homeostasis model assessment-2 for insulin resistance (HOMA2-IR) is calculated using Microsoft downloaded freely.

### Statistical Analysis

All statistical calculations were done using computer programs SPSS (Statistical Package of Social Science) program, version 17 software. Study analysis of data are done as mean  $\pm$  SD. Student-t test was approved to equate the significance variance in the mean values between two groups. The *p*-value < 0.05 was deliberated substantial.

### Results

Study characteristic of patients and controls are shown in Table (1). There was an elevation in age, W/H ratio, BMI, HbA1c, insulin, and HIMA-IR2 in diabetic patients as paralleled to the controls, but it was not important. Moreover, there was a substantial rise (*p*= 0.01) in FSG, TC, TAG, and LDL-C in diabetic patients as paralleled to the controls. While, a substantial decrease (*p*= 0.01) in serum HDL-C and vitamin D3 in patients as paralleled to the controls.

Table (1): Study characteristic of patients and controls

Parameters	Means $\pm$ SD		<i>p</i> -value
	T2DM (n=90)	Control (n=45)	
Gender (M/F)	(43/47)	(21/24)	-
Age (Years)	48.08 $\pm$ 4.73	45.01 $\pm$ 3.40	0.35
W/H ratio	1.24 $\pm$ 0.04	0.83 $\pm$ 0.01	0.50
BMI (Kg/m <sup>2</sup> )	28.69 $\pm$ 3.63	25.01 $\pm$ 4.40	0.75
FSG (mg/dl)	174.23 $\pm$ 13.42	87.29 $\pm$ 2.25	0.01
HbA1c (%)	8.18 $\pm$ 1.29	4.48 $\pm$ 0.82	0.05
Insulin ( $\mu$ U/ml)	18.85 $\pm$ 1.44	11.74 $\pm$ 3.26	0.05
HOMA2-IR	5.45 $\pm$ 2.87	2.40 $\pm$ 0.23	0.05
TC (mg/dl)	210.50 $\pm$ 13.40	160.22 $\pm$ 10.46	0.01
TAG (mg/dl)	189.13 $\pm$ 10.06	120.28 $\pm$ 3.90	0.01
HDL-C (mg/dl)	42.36 $\pm$ 5.02	57.78 $\pm$ 2.94	0.01
LDL-C (mg/dl)	102.80 $\pm$ 6.34	78.91 $\pm$ 4.03	0.01
Vitamin D3 (ng/ml)	18.84 $\pm$ 3.59	34.14 $\pm$ 3.25	0.01

*p* < 0.05: significant, *p*= 0.01: highly significant.



Anthropometric, clinical, and biochemical factors among patients groups are presented in Table (2). A substantial rise ( $p= 0.01$ ) in W/H ratio, BMI, FSG, TC, TAG, and LDL-C in obese diabetic patients as paralleled to non-obese group. Furthermore, there was an elevation in HbA1c, serum insulin, and HOMA-IR in obese group, but it was not significant.

A substantial decrease ( $p= 0.01$ ) in serum HDL-C was detected in obese diabetic patients as paralleled to non-obese group.

**Table (2): Anthropometric, clinical, and biochemical factors among patients groups**

Parameters	Means±SD		p-value
	Obese (n= 45)	Non-obese (n=45)	
Gender (M/F)	(20/25)	(23/22)	-
Age (Years)	49.82±3.53	46.31± 5.94	0.69
W/H ratio	1.80±0.02	0.68±0.05	0.01
BMI (Kg/m <sup>2</sup> )	34.86±4.98	22.52±2.29	0.01
FSG (mg/dl)	196.73±7.47	151.73±6.15	0.01
HbA1c (%)	9.54±1.06	6.83±1.53	0.05
Insulin (μU/ml)	14.13±2.99	9.35±3.53	0.05
HOMA2-IR	6.85±3.34	4.06±2.40	0.05
TC (mg/dl)	225±15.50	196.42±12.25	0.01
TAG (mg/dl)	207.46±16.90	171.95±7.65	0.01
HDL-C (mg/dl)	36.62±2.70	48.11±4.35	0.01
LDL-C (mg/dl)	118.0±8.34	87.12±4.33	0.01

$p < 0.05$ : significant,  $p= 0.01$ : highly significant.

Additionally, there was a substantial decrease ( $p= 0.01$ ) in serum vitamin D3 in obese diabetic patients as paralleled to non-obese group, Table (3).

Comparison of vitamin D3 deficiency among male and female diabetic patients was shown in Figure (1). Also, obese diabetic patients had the higher percent (61%) of D3 deficiency as paralleled to non-obese patients, Figure (2).

**Table (3): Serum vitamin D3 among diabetic patients groups**

Parameters	Means±SD		p-value
	Obese (n=45)	Non-Obese (n=45)	
Vitamin D3 (ng/ml)	14.19±3.53	23.5 ±3.66	0.01

$p = 0.01$ : highly significant.



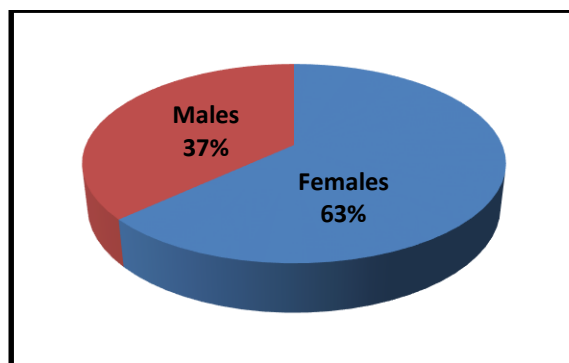


Figure (1): Comparison of vitamin D3 deficiency among diabetic males and females

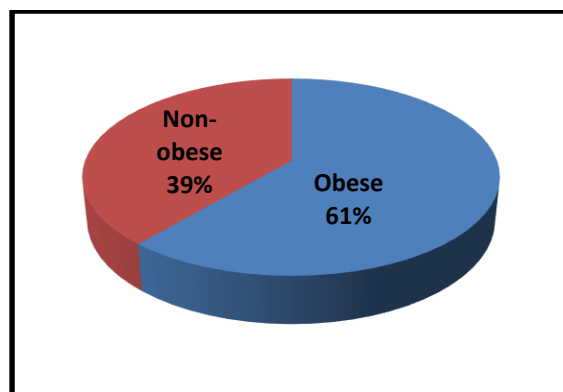


Figure (2): Comparison of vitamin D3 deficiency among obese and non-obese patients

## Discussion

Vitamin D deficiency has strong argument in its effect on pathogenicity and development of T2DM. The varied influence of vitamin D on glucose and  $\text{Ca}^{+2}$  homeostasis has made it an ideal contender to know its role in glycemic control in T2DM. So, this study was conducted to clarify vitamin D status in diabetic patients and its relation to glycemic control and different biochemical parameters (13).

Body mass index showed a significant rise in obese group when paralleled to non-obese with further significant increase in W/H ratio in those patients. Also, there is a substantial elevation in the levels of FSG, fasting insulin, and HOMA2-IR in obese patients as paralleled to their levels in non-obese group, which is in agreement with earlier study (14).

Obesity impairs adipocyte function where hypo perfusion and hypoxia in adipose tissues results in impairment in the formation of adipokines (15).

One possible mechanism for the dysregulation of adipocyte is inflammatory reaction. High nutrient milieu may stimulate circulating macrophages that could lead to chronic lower inflammatory state, this results in marked dysfunction in the accumulated lipid both in adipose tissue and the liver with subsequent chronic inflammatory state which is a characteristic feature of obesity (16).

In obese group there is significant hyperinsulinemia and hyperglycemia as compared to normal control group, IR in obese persons leads to a lessened clearance of blood glucose beside an increased in hepatic glucose output, both combining to result in elevated blood glucose this is referred to as the adipoinsulin axis (17).

Obesity as a triggering factor with its characteristic hyperglycemia because of impairment in glucose uptake in the muscle and liver addition to IR with diminished antilipolytic effect of insulin that increase hepatic cholesterol formation and decreased HDL-C can result in significant increase in TC, TAG, LDL-C, and significant diminution in HDL-C in obese group paralleled to control (18).

Accumulating evidence demonstrated vitamin D stimulates the islet  $\beta$ -cells to secrete insulin through its active form 1,25-(OH)<sub>2</sub>D<sub>3</sub>. It is believed that vitamin D might regulate insulin signal transduction and glucose-induced insulin secretion by this pathway (19). (20) designated in multiethnic model that vitamin D was considerably interrelated to IR and  $\beta$ -cell function. They proposed that decreased vitamin D concentrations may play a considerable role in the pathogenesis of T2DM. It has been assessed that adults > 18 years of age revealed a mechanistic association between serum vitamin D levels, glucose homeostasis, and the progress of DM (21).

Previous work confirmed the presence of vitamin D receptor (VDR) in pancreatic islet  $\beta$ -cells and showed impaired insulin secretion in mice lacking functional VDR. These data suggest vitamin D regulates insulin secretion via VD (22). A meta-analysis of 16 studies comprised of 18096 individuals aids the theory that prenatal vitamin D status is related with children birth weight (23). It has been indicated that reduced maternal 25(OH)D levels may also donate to the longer-term risk of obesity in children. It has been documented rises in numerous adiposity indices in preschool-aged children (4 and 6 years) born to mothers with reduced 25(OH)D levels (24). One study (25) indicated that increasing serum vitamin D levels to normal led to a 55% relative lessening in the risk of T2DM progress.

It is probable that vitamin D could have benefits in patients with hyperglycemia and/or IR. It has been postulated that vitamin D reduces both glucose output and hepatic lipid formation, and through IR (26). A meta-analysis of up to 22 researches provided some indication for vitamin D-associated declines in HbA<sub>1c</sub> and fasting glucose, but only among T2DM patients with decreased 25(OH)D levels (27).

Another study after a follow-up period of 22 years indicated women have lower serum vitamin D levels than men and the incidence of T2DM in men is 72% less than women. These data suggest higher vitamin D levels prevent incidence of T2DM especially among females. In the present study, female sex was significantly related with lesser vitamin D status which was in accordance with Zhang *et al.*, (28) and in contrary to many previous studies who document a not significant difference between men and women (29,30). This can be explained by the fact that in the Arabic world, women had lower outdoor activities and wore their traditional clothes which reduced the surface area exposed to direct sunlight (31).

## Conclusions





In the present study, it is found that there is significant increase in blood sugar in the individuals with decreased vitamin D levels. Exposure to early morning sunlight is one of the largest prospective to study the influence of vitamin D supplementation on correlation of blood sugar levels. Low vitamin D status can be caused by number of influences. Low blood levels of its main metabolite, vitamin D, have been linked to poor health outcomes such as DM. Decreased vitamin D also related with IR, decreased  $\beta$ -cell function, and obesity.

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