Serum leptin and 25 Hydroxyvitamin D levels in patients with type II diabetes mellitus

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Abstract:

Background: Vitamin D and Leptin appears to play a range of roles in beta cell growth and insulin secretion and most importantly interaction with other hormonal mediators and regulators of energy and metabolism.

Objective: The aim of this study was to measure serum leptin and vitamin D levels and to investigate their relationships with vitamin D and other clinical laboratory parameters in patients with type II diabetes.

Subjects and Methods: Blood samples were taken from 80 patients with type II diabetes mellitus encountered during their attending the Internal Medicine clinic consultancy in Ramadi Teaching Hospital and the National Diabetes Center for Treatment and Research at Al-Mustansiriya University and 60 healthy subject. From December 2014 to November 2015. Investigations included serum Leptin, 25OHD, Insulin, HbA1c using ELISA and biochemical test.

Results: The median concentration of serum 25 OH vitamin D of patients (15.70 ng/ ml) was significantly lower than healthy controls (20.27 ng/ ml). The rate of vitamin D deficiency (VDD) was significantly higher in patients (82.5%) than healthy controls (48.3%). The serum insulin and HOMA-IR were significant increase in patients had vitamin D < 20 ng/ml when compared with an insufficient/normal group. There were no significant differences in leptin levels between type II DM and healthy control.

Conclusion: These results strongly support the role of vitamin D deficiency and serum leptin in pathogenesis of type II diabetes.

Keywords: Type II Diabetes Mellitus (T II D M), Leptin, Vitamin D.

Introduction:

Type II diabetes is a complex disorder characterized by the imbalance between insulin resistance and insulin secretion that induce liver glucose output by preventing glycogen formation and stimulating glycogenolysis and gluconeogenesis then excess rates of liver glucose production result in the development of overt diabetes mellitus, especially fasting plasma glucose (1,2). Type II DM is nowadays ranked among one of the most common non-communicable diseases, in the world. It is responsible for 90 % to 95 % of all cases of diabetes (3). Leptin is a protein (anti-obesity hormone) consists of 167 amino acids and known mainly for regulating appetite control, energy metabolism, and regulation of body weight (4). Secreted by adipose tissue, encoded by ob gene (ob stands for obese). As well to white fat cells (primary), it is also secreted by the placenta (extra-adipose tissues) ovaries, skeletal muscle, stomach, mammary epithelial cells, bone marrow, pituitary gland and liver (5). Vitamin D deficiency and Leptin appears to play a range of roles in islet cell growth and insulin secretion and most importantly interaction with other hormonal Mediators and regulators of energy and metabolism such as insulin, glucagon, growth hormone and glucocorticoids. This finding opens up new avenues in treatments for diabetes (6, 7, 8, 9, and 10). The level of serum leptin correlates with the fat content of the body (11, 12). Significant correlation between vitamins D, leptin and insulin have been identified as regulators of food intake and energy balance (13, 14). The aim of this study was to measure serum leptin, and Vitamin D levels and to investigate their relationships with vitamin D and other clinical and laboratory parameters in patients with Type II DM.

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Subjects and Methods

This case-control study included 80 patients with type II diabetes mellitus encountered during their attending the Internal Medicine clinic consultancy in Ramadi Teaching Hospital and the National Diabetes Center for Treatment and Research at Al-Mustansiriya University and 60 healthy subject controls. During the period from December 2014 to November 2015. The diagnosis of DM was made on the basis of the recommended criteria by **(15)** .Type II diabetic patients were usually of older age and on hypoglycemic tablet treatment. The included diabetic Patients were free of acute illness or infection at the time of the study. Those with known diseases which are associated with glucose metabolism disordered such as Cushing′s disease, acromegaly, chronic pancreatitis, and

pancreatectomy were excluded as well as those with chronic Kidney disease, ischemic heart disease, chronic liver disease and pregnant women . Investigations included serum measurements of leptin, 25OHD, FPG, Insulin, HbA1c and HOMA-IR in all patients and controls. 25-OH Vitamin D total (as the sum of 25-hydroxyvitamin D2+ 25-hydroxyvitamin D3), leptin and insulin were measured with an Enzyme-linked immunosorbent assays by using the kit provided by (Demeditec Company, Germany). Cata. No. (DE1971, DEE007, and DE2935) respectively. Glycated hemoglobin (HbA1c) was measured as a marker of glycemic control in the diabetic patients, using Clover A1c® system. Fasting plasma glucose was estimated by glucose- peroxidase (GODPOD) method. Insulin resistance index (Homeostasis Model Assessment Insulin Resistance-HOMA-IR) was calculated using the formula (16).

Results:

Vitamin D levels differed significantly between type II DM and healthy control subjects (p<0.001) table 1. Vitamin D was significantly higher deficient in 82.5% of patients, insufficient in 17.5% of patients, while in the control group it was deficient in 48.3%, insufficient in 51.7%.There were no significant differences in leptin levels between type II diabetes mellitus and healthy control. Glucose index levels were significantly higher in the type II DM compared to healthy control.

Table 1: The median and mean serum of Vitamin D , leptin and Glucose Index in Type II and Healthy control

Parameter	Controls (n=60)	Type II DM (n=80)
Serum Vitamin D (ng/ml, as median) (Range)	20.27• (12.84 to 42.39)	15.70 (6.69 to 32.1)
Serum Leptin(ng/ml) (as median) (Range)	7.3^{NS} (1 to 24.56)	5.2 (1 to 62.57)
Fasting Blood Glucose (mg/dl) (as Mean±SD)	89±10.2•	239.3±82.9
Serum insulin (uIU/ml) (as Median)	8.39••	10.15
HOMA-IR% (as Median)	1.1•	1.90
HbA1c %	5.4±0.45•	10.40±2.18

Chi-square revealed ●significant differences between type II and controls (p=0.001), ●● significant differences between type II and controls (p=0.036). NS no significant difference between type II DM and controls. HOMA-IR: homeostasis model assessment-insulin resistance.

Table 2 depicts the results of the measured parameters in type II DM patients according to the median value of 25OHD concentrations subgroups (deficient 25OHD group < 20 ng/ml & insufficient/normal 25 OHD group > 20 ng/ml). The deficient group of type II patients had a significant increase of both of serum median values of insulin and HOMA-IR (12.08 uIU/ml, 2.3, respectively) when compared with an insufficient/normal group (8.53 uIU/ml, 1.4 ; p<0.044, p<0.028; respectively) table 2. However, there were no significant differences in other measured parameters between the deficient and insufficient/normal groups.

Table 2: The mean (±SD) and median of selected measurements by Vitamin D deficiency among type-II DM cases.

Parameter	Deficient Vitamin D (<20)ng/ml	
	Normal/insufficient (n=14)	Deficient (n=66)
Serum insulin (uIU/ml) •• (as Median)	8.53	12.08
Insulin resistance (HOMA%)••• (as Median)	1.4	2.3
Hba1c% ^{NS} (as Mean± SD)	10.7±2.13	10.3±2.2
Serum Leptin(ng/ml) ^{NS} (as Median)	3.67	5.98

Chi-square revealed ●● significant differences between type II and controls (p=0.044). ●●● Significant differences between type II and controls (p=0.028).NS no significant difference between type II DM and controls (0.57, 0.07 respectively).

Discussion:

Vitamin D levels differed significantly between type II DM and healthy control subjects (p<0.001) table 1. Vitamin D was deficient in 82.5% of patients, insufficient in 17.5% of patients, while in the control group it was deficient in 48.3%, insufficient in 51.7%. The deficiency in Vitamin D levels are linked to T II D. Such finding is in agreement with that demonstrated by Subramanian et al (17) and Yu et al (18), in addition, Nikooyeh et al (19); Afsaneh et al (20); Nasri et al (21) concluded that supplementation of vitamin D is associated with a lower risk of Type II D. Type II diabetic patients had reduced levels of vitamin D than normal individuals. The insulin resistance is more in vitamin D deficiency. Therefore, vitamin D plays an important role in maintaining normoglycemic condition by influencing insulin secretion. In deficiency state of vitamin D, there is decreased insulin sensitivity and increased insulin resistance (22). Chronic vitamin D deficiency may be a predisposing reason for T II DM. This is supported by the results of the present study that serum VDD showed negative correlations with HOMA-IR and insulin levels (P=0.028, P=0.044) respectively. Vitamin D has been shown to have a role in insulin production, secretion, and IR .In new years it has become apparent that for optimal functioning of several organs and tissues throughout the body need for adequate levels of Vitamin D. Vitamin D receptors are identified in heart, smooth muscle, islets cells of the pancreas which secrete insulin and immune cells (23, 24). It has been also demonstrated that Islets cells of the pancreas and immune cells possess 1 alpha-hydroxylase enzyme required for synthesis of vitamin D, vitamin D receptor, and vitamin D-dependent calcium binding proteins, suggesting an

important role of vitamin D in insulin secretion (25). Witham et al (26) (2010) found out that Vit D intake at different dosage had no effects on IR or on HbA1C. Nagpal et al (27) (2009) also reported that vitamin D supplementation had no effect on the mean of insulin sensitivity but two years treatment with vitamin D did improve HOMA-IR. The current study showed a significant decrease in serum level of leptin in patients compared to the control group (Table 1). The decreased serum leptin in present results may be due to insulin deficiency as a cause for lower leptin levels in diabetics (28). The findings of the present study are in agreement with findings of Abdelgadir et al (29) (2002) the similar result was found by Kraegen et al (30), 2001; Al-Holi (31), 2006; Marjani et al (32), 2010. When related to vitamin D, serum leptin levels was found to be higher in T II patients had VDD < 20 ng/ml .The reduced VitD levels may cause obesity in these individuals as suggested by a previous study (33) . The reduced VitD levels may enhance the capacity of the body to store large amounts of fat as a stress response, to ensure better survival (34). Another study suggests that 25-OH-VitD acts as a negative regulator of leptin secretion (35) . This is consistent with our observations study that individuals with levels of 25-OHVitD > 100 nM/L showed relatively lower leptin levels.

Conclusion:

These results strongly support the role of vitamin D deficiency and serum leptin in pathogenesis of type II diabetes.

Author's contribution:

Thana Ismail Mustafa: Student
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