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Relationship among Vitamin D3 and Adiponectin and Body Mass Index in diabetes mellitus Type 2 patients

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Abstract

The study was performed on (180) participants and included two groups (120 patients with type 2 diabetes aged (35-65 years) excluding neuropathy, retinopathy, and thyroid dysfunction, and 60 participants aged (32-65 years) as healthy control subjects. Venous blood samples of approximately 5ml were collected from patients and control participants with the approval of the ethics committee of Baghdad Teaching Hospital throughout the period from 1st September 2023 to 15th May 2024.

The results showed p<0.01 for the adiponectin values between each age. The values were increased with increasing age respectively. The results also showed P>0.05 between male and female values of vitamin D and adiponectin. For the mean value of BMI for patients and control groups there was P<0.01 between them. The mean value of vitamin D for patients was significantly lower than that of the control group it was p <0.01 for the values of vitamin D between each age and it decreases with increasing age respectively. The mean value of adiponectin in the patients' group was lower than that of the control group. The mean value of vitamin D for control with normal weight and overweight showed P>0.05 between them. The mean value of adiponectin for normal weight and overweight showed P>0.05 between them. The values of blood urea, and creatinine highly significant differences between patients and control while there is no significant difference in uric acid.

Keywords: Vitamin D3, Adiponectin, Body mass index, diabetes mellitus Type 2.

Introduction

Diabetes is defined as a group of metabolic diseases characterized by hyperglycemia due to impaired secretion and/or insulin action or both. Hereditary predisposition, behavioral, dietary, and environmental risk factors all come together to cause the diverse collection of illnesses known as type 2 diabetes mellitus(T2DM) [1-3]. This widespread endocrine condition affects most people on the planet and can even become a pandemic in certain nations [4]. Multiple abnormalities in the control of protein, lipid, or carbohydrate metabolism, or all of these abnormalities, are characteristics of DM [5], because of this hyperglycemia, hyperlipidemia, and a low nitrogen balance are its defining characteristics. Secondary damage to numerous organ systems, particularly blood vessels, kidneys, eyes, and nerves, may be related to metabolic poor regulation [6]. In individuals with type 2 diabetes, it has been revealed that vitamin D (VD) lowers systolic blood pressure, promotes insulin sensitivity, and avoids rises in the concentration of glucose and insulin resistance [5]. A lot of studies have clarified a connection or relationship between the low concentration of serum 25-hydroxy vitamin D3 [25(OH) D_3] and a higher risk of type 2 diabetes and metabolic syndrome. Outcomes (insulin resistance, insulin secretion, and its regeneration progress β-cell function and glucose

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tolerance [6-7]. Furthermore, insulin secretion and glucose tolerance may be affected by specific alleles differences in the vitamin D-binding protein (DBP) and vitamin D receptor (VDR) [8], Consequently participating in the hereditary risk of type 2 diabetes. Taking that into account vitamin D regulates the insulin production and expression of insulin receptor genes, it is an intriguing environmental potential for the pathophysiology and development of type 2 DM [9]. The hormone adiponectin which is indicated as an adipocytes complement-related protein of 30 KDa, plays a homeostatic role in controlling levels of fat and glucose in the bloodstream [9]. It has been observed that people who suffer from obesity, insulin resistance, and type 2 DM have lower levels of adiponectin. Adiponectin and 25 hydroxyl vitamin D levels have been related to the pathophysiology of prediabetes and T2DM by controlling body weight, energy metabolism, glucose and lipid metabolism, and food intake [10,11]. The liver plays an influential function in vital processes within the body, especially carbohydrate metabolism, as it can save glucose as glycogen and produce glucose from non-carbohydrate sources, high liver enzymes effectiveness such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are indicative of hepatic-cellular injury and also correlated to insulin resistance [12,13].

Material and Methods

Human Vitamin D3 (VD3) ELISA kit observation principle: The ELISA Kit supplied is standard, and Thais procedure with the double-sandwich ELISA technique. Polyclonal antibody tagged with biotin was the detecting antibody, while the precoated antibody was a human VD3 monoclonal antibody. Samples and biotin labeling antibodies were put into ELISA plate wells, and then the mixture was cleaned by either PBS or TBS. ELISA wells were then sequentially filled with avidin-peroxidase conjugates; by using PBS or TBS the reactant was completely removed, with the action of the peroxidase catalytic TMB becomes blue and at last turns into yellow by the effectiveness of the acid. Among samples, there was a significant correlation between the testing factors and the color depth. This experiment follows a technique called the quantitative sandwich enzyme immune assay approach. Standards and samples were pipetted into the wells, and the immobilized antibody bound any ADP that was present. An ADP-specific antibody has been pre-coated on a microplate. ADP-specific biotin-conjugated antibody was put in the wells following the elimination of any unbound materials. A wash was carried out to eliminate any free avidin-enzyme reagent before adding avidin conjugated Horseradish Peroxidase (HRP) to the wells. In the first step color was developed in proportion to the amount of ADP bound after the substrate solution was added to the wells. The color's intensity was measured after stopping color development. Blood sugar was measured manually by a spectrophotometer. 1.0 ml reagent A and 10µl of the standard were added in labeled test tubes, and 1.0 ml reagent and 10µl of serum were added in the test tube and then mixed thoroughly at room temperature (16–25 °C) for 10 minutes, the tubes were incubated, after that at least two hours passed before the color fixed, and the absorbance (A) of the sample and standard was measured at 500 nm.

Statistical analysis:

For the statically presentation of the results (mean and standard deviation) Utilizing the "Statistical Package of Social Science (SPSS) version 26.0," data were updated, coded, and examined. Graphical presentation (Bar graph). Utilizing the independent sample t-test the results will be explained. The P-values represent the significant comparison for any test higher than 0.05 ($P>0.05$) and were reasoned as non-statistically significant (NS), statistically significant(s) when the P-value was less than 0.05 ($P<0.05$).

Results

As shown in Table (1) the correlation between vitamin D concentration and four age groups for both patients and healthy control was higher at (30-39)

years with a mean ± std for vitamin D (16.47±2.07) and (20.32±3.01) for patients and control respectively.

Table (2) Shows the association between Adiponectin concentration which was increased with increasing age respectively (15.98±17.02ng/ml), (18.00±19.39ng/ml), (19.70±23.26ng/ml), (24.85±26.11ng/ml) with a high significant difference <0.01 between the ages. These illustrated results were consistent with (Chen et al., 2013).

whom they found that adiponectin levels were higher with advanced age of men and women healthy subjects and in patients with diabetes. Serum adiponectin levels were significantly and positively associated with age in healthy subjects and patients with diabetes.

Table (3) shows the comparison between VD and adiponectin according to the sex of the participants for two groups of patients and control, it noted the patients' VD for males (14.42±11.37) and females (14.57±11.95) and adiponectin (20.74±22.51) for male and (20.90±23.10) for female and showed no significant difference between male and female P>0.05. The mean value was lower for patients than that of the control group in VD and adiponectin.

As in table (4) the mean value of vitamin D for the control group with normal weight and overweight was (35.04±5.74), (32.57±7.39) respectively with no significant difference between them P>0.05(NS) while for patients (16.62±1.43),(13.88±1.89) normal weight and overweight. Compared between patients and control.

Table (5) Shows the mean value of adiponectin for the control group with normal weight and overweight was (12.52±4.12), (11.05± 4.99) respectively with no significant difference between them P>0.05 (NS) compared with values of patients (10.82±2.31) normal weight and (10.01±1.98) overweight.

Table (6) Shows the mean of blood urea in patient and control (38.88±8.15mg/dl), (30.13±9.87mg/dl) respectively with highly signifycant difference P<0.01 between them. While the mean of creatinine in both patient and control was (0.95±0.28mg/dl), (0.71±0.27mg/dl) respectively with a highly significant difference P<0.01 between them, and the mean value of uric acid for patient and control was (5.44±1.23mg/dl), (5.08±1.25mg/dl) with no significant difference P>0.05 between them.

Table (1): Correlation of Vitamin D concentration in cases of different age groups for patients and control group

Groups of ages (year)	Vitamin D ng/ml mean ± std		**t-test**	**P-Value**	**C.S**
	Patients N=120	Control N=60			
30-39	16.47±2.07	35.32±3.01	13.286	.000	P<0.01(HS)
40-49	13.67±1.35	34.02±2.43	16.663	.000	P<0.01(HS)
50-59	10.20±1.94	32.09±1.89	22.595	.000	P<0.01(HS)
≥60	8.95±2.28	30.25±1.14	26.711	.000	P<0.01(HS)

Table (2): Association between Adiponectin concentration and different age groups for patients and control group.

Groups of ages (year)	Adiponectin ng/ml mean ± std		t-test	P-Value	C.S
	Patients N=120	Control N=60			
30-39	15.98±2.02	20.02±8.06	2.773	.000	P<0.01(HS)
40-49	18.00±1.39	23.02±4.64	11.073	.008	P<0.05(HS)
50-59	19.70±2.26	24.09±2.53	8.241	.001	P<0.01(HS)
≥60	24.85±1.13	26.25±3.34	5.515	.000	P<0.01(HS)

Table (3): Comparison between the values of VD & Adiponectin in Patients and control according to their sex

Groups		Sex	n	Mean ±Std.	t-test	P-Value	C.S
VitaminD ng/ml	Patients (n=120)	Male	59	14.42±1.37	0.070	.944	P>0.05 (NS)
		Female	61	14.57±1.95			
	Control (n=60)	Male	28	31.45±1.99	1.5	.981	P>0.05 (NS)
		Female	32	30.63±2.01			
Adiponectin ng/ml	Patients (n=120)	Male	59	20.74±2.51	0.038	.970	P>0.05 (NS)
		Female	61	20.90±3.10			
	Control (n=60)	Male	28	23.65±1.48	4,589	.928	P>0.05 (NS)
		Female	32	24.43±2.27			

Table (4): The relation between Vitamin D levels of control and patient groups with variable BMI.

BMI Kg/m2		N	Mean±Std. (Vitamin D)	P-Value	t-test	C.S
Control (n=60)	Normal weight	36	35.04±3.74	.152	1.435	P>0.05 (NS)
	Overweight	24	32.57±2.39			
Patients (n=120)	Normal weight	67	16.62±1.43	.112	2.355	P>0.05 (NS)
	Overweight	53	13.88±1.89			

Table (5): the connection of Adiponectin levels for the Control group and patients with variable BMI.

BMI Kg/m2		No.	Mean ±Std. Adiponectin	P-Value	t-test	C.S
Control (n=60)	Normal weight	36	12.52±3.12ng/ml	.152	0.382	P>0.05 (NS)
	Overweight	24	11.05±3.99ng/ml			
Patients (n=120)	Normal weight	67	10.82±2.31	.988	1.83	P>0.05 (NS)
	Overweight	53	10.01±1.98			

Table (6): Comparison between Groups of study Patients and Controls according to kidney function.

Group		Mean± Std.	P-Value	t-test	(CS)
Control(n=60)	BU mg/dl	30.13±3.87	.000	6.319	P<0.01 (HS)
Patients(n=120)		38.88±4.15			
Control(n=60)	Cr mg/dl	0.71±0.27	.000	5.589	P<0.01 (HS)
Patients(n=120)		0.95±0.28			
Control(n=60)	UA mg/dl	5.08±1.25	.067	1.840	P>0.05 (NS)
Patients(n=120)		5.44±1.23			

Discussion

According to the results, the age was divided into 4 groups first (30-39), second (40-49), third (50-59), and fourth (≥60) years. The mean ± std for VD value was (16.47± 12.07ng/ml), (13.67±12.35ng/ml), (10.20±4.94ng/ml) and (8.95±5.28 ng/ml respectively. The results showed that the VD value was decreased with increasing age and with a highly significant difference of p<0.01 between each age which is in agreement with (Wang, et al., 2023). Depending on the fact that lower production and dietary vitamin D intake put older persons at risk for reduced vitamin D levels [14,15]. Interdependence has been noted by epidemiologic studies between low levels of vitamin D and aging-related diseases such as depression, osteoporosis, cardiovascular disease, hypertension, type 2 diabetes, and cancer (Lu, et al., 2021) [16]. These results were compatible with (Sun *et al.*, 2020). They detected that serum adiponectin levels rose in both men and women with diabetes and healthy people with older ages. They cleared that age was positively and strongly interrelated with serum adiponectin levels in both diabetic patients and healthy individuals [17]. This relationship between kidney function, body fat percentage, glucose metabolism, and lipid profiles is

unrelated (AlQuaiz *et al.*, 2018) [18]. Both males and females are facing an increase in body mass and body fat percentage within the interval of age between (40–65 years of age). It has been assumed that decreased insulin sensitivity with age is caused by this age-related rise in adiposity (Chait, et al., 2020) [19]. In the levels of Level of VD and Adiponectin, the results are not in agreement with (Patriota, et al., 2022). Who found that adiponectin in mean and younger adults had a higher prevalence of vitamin D deficiency compared to older participants and females [20]. This is due to many gene variants, located in the loci of genes including DHCR7, CYP2R1, CYP24A1, and GC that are accountable for vitamin D synthesis, hydroxylation, and transport. Besides VDR gene polymorphisms, this may be related to the risk of vitamin D Default. VDR is present in the majority of bodily tissues and cells (Kondratyeva. et al., 2020) [21]. A complex was forming when the active form of vitamin D attaches to VDR via the genomic pathway in cells. This complex interacts with the retinoic acid X-receptor in the nucleus to adjust the transcription of genes that are dependent on vitamin D. Nuclear transcription factor VDR resembles thyroid hormone and steroid receptors (Voltan, et al., 2023). It is encoded by the VDR gene located on chromosome 12 at position 13.11 [22]. Also, the results showed no significant difference between them P>0.05(NS) Adiponectin value between males and females. It's obvious that in boys who were starting puberty, the decline in adiponectin levels contributes to a rise in levels of androgen (Widjaja, et al, 2023), [23]. On the other hand, the body mass index Also this study was in agreement with (Collaboration, 2010). According to what has been reported in many research reports, persons with a BMI of 30 kg/m2 or higher have a significant increase in the chance of developing diabetes throughout life. Although it was a slightly higher BMI is related to the risk of progression of diabetes (Ohno, et al., 2023). This was one of the reasons that lead to obesity turning into diabetes is a gradual inadequacy in insulin secretion accompanied by a gradual increase in insulin resistance [24]. Insulin resistance and imperfection of insulin secretion appear very early in obese patients. Both are similarly aggravated concerning diabetes. Muscle tissues and cells become more resistant to the hormone insulin as excess weight increases (Loos, et al, 2021) [25]. On the contrary, the low blood levels of vitamin D may illustrate the causes of the build-up of vitamin D in the adipose tissue of obese individuals. Obese individuals with a cardiometabolic risk profile are linked to vitamin D insufficiency. The researchers suggest that all overweight and obese people have vitamin D levels less than normal weight (Vranić *et al.*, 2019) [26]. Furthermore, Adiponectin plays a pivotal role in energy metabolism; the concentration of adiponectin decreases in obesity and increases after weight loss. Moreover, the insulin-sensitizing hormone, such as adiponectin in the liver and muscles, even lower levels of adiponectin contribute to peripheral insulin resistance in obesity. Adiponectin levels in the plasma of obese individuals were found to have an inverse correlation with obesity, Obese individuals had plasma adiponectin with lower levels (Luocor, et al 2022) [27].

Conclusions: The results showed that both adiponectin and vitamin D levels decrease in people with DM. However, it has been observed that people of advanced age have a decrease in vitamin D concentration, in contrast to adiponectin levels, which increase. Patients' BMIs were higher than those of the control group.

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