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The study of inter-relationship among secondary hyperparathyroidism and vitamin D3 deficiency in obese diabetics and obese non-diabetic patients

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ABSTRACT

Background: Adiposity is connected to vitamin D3 (Vit. D3) deficiency and hyperthyroidism. Type 2 diabetes (T2D) is associated with Vit. D3 deficiency. Our study aims to assess the inter-relationship among Vit. D3 deficiency and secondary hyperparathyroidism in obese diabetic and non-diabetic patients.

Methods: Our study included 90 patients (45 obese type 2 diabetics and 45 obese non-diabetics as control). Serum Vit. D3, serum parathyroid hormone (PTH), calcium, leptin, fasting blood sugar (FBS), serum insulin, insulin resistance (HOMA-IR), hemoglobin A1C (HbA1c), and body mass index (BMI) were measured.

Results: The levels of Vit. D3 deficiency were 100% in obese diabetics and non-diabetic patients 17.43 ±3.94 and 13.95 ±4.60, respectively. The association was inversely related to BMI in the obese diabetic patients (r=-0.36, P=0.01) and non-diabetic (r=-0.18, P=0.23). While the correlation was positive as well as significant (r=0.49, P<0.001) between PTH levels with BMI in obese diabetic subjects with a mean of 44.10 ±14.01, 13.3**%** have elevated PTH levels, the correlation was positive and no significant with BMI (r=0.06, P<0.6) through obese non-diabetics the mean was 57.19 ±1**7.71**, and 35.5% of them had a high level of PTH. Our results showed a very weak and no significant negative correlation between Vit. D3 and PTH in each of the obese diabetics and obese non-diabetic groups (r=-0.12, P=0.4) and (r=-0.24, P=0.1), respectively. Serum concentration of leptin has significantly associated with body mass index (r=0.94, P<0.001) in obese diabetic through (r=0.3, P=0.04) in control. The most surprising finding is the very strong association between HOMA-IR with BMI in non-diabetics (r=0.87, P <0.001).

Conclusion: Adiposity is a risk factor for T2D related to Vit. D3 deficiency and high level of PTH. The correlation between Vit. D3 deficiency and PTH is inverse and insignificant.

Keywords: *Obesity; vitamin D3; parathyroid hormone; type 2 diabetes*

J Popul Ther Clin Pharmacol Vol 30(4):e249–e262; 14 March 2023.

INTRODUCTION

The expansion of obesity has grown worldwide in the past five decades, reaching pandemic levels[1]. Adiposity rises the danger of many diseases like T2D, fatty liver disease, high blood pressure, heart attack, osteoarthritis, and cancers [2]. It also has a detrimental effect on the mental health of individuals, depression, stress, and poor sleep quality [3]. WHO revealed that in 2008 the worldwide spread of overweight and adiposity was about 1.5 billion and 500 million adults, respectively[4]. World Health Organization (WHO) has proposed 3 types of adiposity depending on BMI, which is extracted using the mathematical equation of $\frac{weight(Kg)}{height(m^2)}$ kg/m2. Individuals with a BMI ≥ 25 are considered overweight, individuals with a BMI ≥ 30 are obese, and those with a BMI over 40 are considered morbidly obese [5]. Increased white adipose tissue mass (adiposity), which derives from an imbalance between energy intake and energy expenditure, is the key morphological characteristic of obesity [6]. Obesity is caused by a chronic energy imbalance resulting from increased calorie intake versus decreased energy consumption [7]. Metabolism mechanisms influence long- and short-term energy homeostasis, including adipokines, cytokines, thermogenic adipose tissue, and hunger and satiety hormones [8]. One or more of these regulatory disruptions can lead to obesity [9]. Genes may have a lesser-known influence on the emergence of obesity. Lean people have more active thermogenic adipose tissue, whereas obese people have less of it [10]. The impairment of the pancreatic islet cells, which results in a loss of blood glucose regulation, is the pathophysiology of diabetes. If insulin resistance coexists with the failure of pancreatic beta-islet cells, diabetes development is more likely to occur. Type 1 and type 2 diabetes are on the rise, and their occurrence is mainly attributed to obesity and body mass[11]. Vit. D3 is a fat-soluble secsteroid, historically regarded as a crucial regulator of bone metabolism, calcium, and phosphorous balance [12]. It is essential in white adipose tissue physiology and glucose homeostasis, often dysregulated in people afflicted by obesity [13]. Vit. D3 deficiency involves numerous pathologies, including endocrine pathology, immune disorders, diabetes mellitus, hypertension, cardiovascular disease, and obesity [14]. In recent years, avoiding sunlight reduced serum 25 hydroxy-vitamin D (25[OH]D) levels [15]. In the exposure of ultraviolet B (UVB) radiation from sunshine, the skin produces the majority of Vit. D3, which is then sequentially hydroxylated in the liver and kidneys to form 25(OH) Vit. D3 and 1,25(OH)2 Vit. D3, respectively[16]. Vit. D3 can also be obtained from some food [17]. All tissues contain intracellular Vit. D3 receptors and the 1-hydroxylase enzyme, indicating that, Vit. D3 serves a variety of activities [18]. In a study done in the city of Karbala, one of the cities in Iraq, Hypovitaminosis D was found in higher than (85%) of (postmenopausal women), higher than (65%) of women of reproductive age, higher than (60%) of youth males aged (25-49) years, and roughly (82%) of males aged (50-70) years [19]. Studies have indicated that, Vit. D3 might have an essential role in developing adiposity [20]. 1,25(OH)2D3 which is the strongest physiologically effective circulating metabolite is produced by humans. Due to the abundance of Vit. D3 receptors (VDR) on adipocytes, there is a fluctuation in the active form of Vit. D3 levels in obese people[21]. Many theories have been put out as to why obese people have lower 25(OH)D levels, including adipose tissue's sequestration of Vit. D3 [22]. The risk of prediabetes was correlated with Vit. D3 status. [23]. The pathways of Vit. D3 that affect islet function may be implicated in numerous aspects. First, the VDR was articulated in pancreatic beta cells, and Vit. D3 can exert its action by directly attaching to the VDR [24]. Second, pancreatic cells express 25(OH)D-1-hydroxylase (CYP27B1), an enzyme that enables 25OHD transformation into active 1,25(OH)2D3. Third, intracellular calcium Ca2+ concentrations are required for insulin action. Vit. D3 helps to regulate Ca2+ flow in pancreatic cells [25]. Fourth, Vit. D3 can affect insulin sensitivity by acting on pancreatic cells and insulin-sensitive tissues such as white adipose tissue, muscle, and liver [26]. PTH is important in controlling calcium and phosphate equilibrium [27]. Reduction in Ca2+ stimulates the release of PTH from the parathyroid glands. In reaction, Ca2+ and Mg2+ reabsorption in the renal tubule is increased, but Pi and HCO3- reabsorption is decreased [28]. However, osteoclastic activity is stimulated in the bones as well as increasing intestinal absorption of calcium by activating Vit. D3 resulting in raised serum calcium [29]. In

J Popul Ther Clin Pharmacol Vol 30(4):e249–e262; 14 March 2023.

obese individuals, higher PTH levels comparing to non-obese individuals provide indicating that calcium and Vit. D3 balance is disrupted [22]. Because visceral fat deposition and leptin may also be a causative factor for hyperparathyroidism, severe obesity-related hyperparathyroidism is not only caused by Vit. D3 insufficiency [30].

MATERIAL & METHODS

Subjects

The subject included 90 patients from Iraqis have obesity aged over 18 years (31 women and 59 men) who participated in this study after they were diagnosed with obesity using body composition analyzer to measure a body mass index (BMI) ≥30 Kg/ m2. The process was done in the Iraq Specialized Laboratory; under supervision of Razi University in Iran, Faculty of Chemistry. Participants were organized into two groups based on T2D, n = 45 patients and non-diabetic n=45 patients. Before sampling, each participant was informed of the study aims for scientific and ethical integrity.

Blood collection and measurements

Phlebotomy of each subject was conducted using 3× 4 ml vacutainer. After overnight fasting, blood was divided into two parts, one serum tube in normal form and one with EDTA as an anticoagulant. Following the standard procedure, the blood in the plain tube was separated after 30 minutes at room temperature and kept at 20°C. Blood samples in EDTA were used directly to measure glycated hemoglobin. Insulin assay, Vit. D3, PTH, and leptin were measured by COBAS e 411 (ROCH, Germany), and calcium and HbA1c were measured using COBAS E311 (Electrochemiluminescence (ECL) technology, Germany). The normal reference range for serum calcium was 8.4–10.4 mg/dL. PTH levels in the blood ranged from 15 to 65 pg/mL. Serum Vit. D3 levels were split into four statuses: Severe Vit. D3 deficiency: 5-10 ng/mL, Vit. D3 deficiency:10-20 ng/mL, Vit. D3 insufficiency 20-30 ng/mL, and optimal vitamin: 30-100 ng/mL.

Exclusion criteria

The exclusion criteria used for the participants in the study are as follows: Type 1 diabetes patients, pregnant women, persons on the anti-obesity drug, comorbid conditions such as chronic obstructive pulmonary disease, HIV, COVID-19, and tuberculosis, and those with BMI less than 30 kg/m2.

Statistical analysis

The statistical package for social sciences (SPSS) software was used for the statistical analyses (SPSS Version 26, Chicago, USA). Before statistical analysis, the histogram and Kolmogorov-Smirnov method were used to verify the normality of the distributions. Categorical variables are expressed as numbers (%), and all continuous variables as mean SD. To examine the variances between the means of continuous variables, the student's t-test and one-way anova were used. calcium serum concentration, PTH, and Vit. D3 were utilized as explanatory factors in linear regression with the entering technique to investigate the relationship between BMI as a dependent variable and these variables. A P value of 0.05 or less was regarded as statistically significant.

RESULTS

Our study included 90 obese patients, 50% of them have diabetic type 2 (62.2% male and 37.7% female), and 50% of obese non-diabetic (68.8% male and 31.1% female). All obese individuals had a BMI greater than 30 kg/m2. They were divided into three groups: class one (low-risk) obesity for 28.8% ranged between 30-34.7 kg/m2, class two for 42.2%, ranged between 35–39.8 kg/m2, and class three, for 28.8% of them, ranged between 41–53.9 kg/m2. The mean BMI in the obese diabetic group was 37.98 kg/m2 and in the obese non-diabetic group, was 38.1 kg/m2. The total mean BMI in the female group was 40.35 kg/m2 and in the male group, was 36.9 kg/m2. Our data showed the mean and std. deviation of the age of obese diabetic patients was 46.35 ±7.97, while in obese non-diabetic was 43.42 ±8.95. The rate of Vit. D3 deficiency (Vit. D3 levels<30 ng/ml) was 100% in both the obese with diabetes and non diabetes patients 17.43 ±3.94 and 13.95 ±4.60, respectively.

Comparison parameters involved in the current study in obese diabetics and non `diabetics by gender

In the female group, the current results showed a significant drop in the level of PTH in obese diabetic patients compared to obese non-diabetics. In comparison, a significant increase was observed in the concentrations of HOMA-IR, insulin, and HbA1c in obese diabetic patients compared to obese non-diabetics. The male group showed a significant increase in HOMA-IR, Vit. D3, PTH, insulin, and HbA1c concentrations in obese diabetic males compared to obese non-diabetics males. While other parameters (BMI, Ca+2, and leptin) did not show significant differences for both groups at P value < 0.05, as indicated in Table 1.

TABLE 1: Comparison parameters in obese diabetics and obese non-diabetics by gender:

Hormones	Female		P value	Male		P value
	Obese Diabetic	Obese non-diabetic		Obese Diabetic	Obese non-diabetic	
BMI (kg/m2)	39.8 ± 5.52	40.9 ± 8.79	0.687	36.8 ± 5.39	37.0 ± 5.72	0.89
PTH (pg/ml)	44.78±16.49	58.46±18.88	0.04	43.68±12.85	56.62±17.45	0.02
Vit-D3 (ng/ml)	17.11± 3.83	14.24 ± 5.25	0.08	17.63 ± 4.14	13.81 ± 4.41	0.01
Homo-IR	4.27 ± 1.26	1.50 ± 0.45	<0.001	3.52 ± 1.07	1.37 ± 0.35	<0.001
Insulin sensitivity	0.25± 0.01	0.32±0.01	<0.001	0.25± 0.01	0.32±0.01	< 0.001
HbA1c (%)	9.50 ± 1.35	6.63 ± 1.21	<0.001	8.36 ± 1.59	6.26 ± 1.06	< 0.001
FBS (mg/dl)	181.8 ± 49.9	94.9 ± 18.7	<0.001	163.0 ± 46.2	88.8 ± 18.6	< 0.001
Insulin(micIU/ml)	52.3 ± 13.2	14.6 ± 2.96	<0.001	58.1 ± 17.9	15.1 ± 2.88	< 0.001
Leptin (µg/ml)	19.56±5.25	24.11±8.66	0.1	17.45±5.08	17.70±6.17	0.86
Ca+2 (mg/dl)	8.10 ± 1.35	8.40 ± 1.10	0.49	8.42 ± 1.44	8.40 ± 1.10	0.95

Comparison of HbA1c level in obese diabetics and obese non-diabetics with BMI groups

The current results illustrated that HbA1c increases with increasing BMI in obese diabetics, but in the obese non-diabetics, non-significant was noted according to BMI categories. As indicated in Table 2, there was a significant rise in obese diabetics compared to the corresponding group of obese non-diabetics at a P value < 0.05, as shown in Table 2.

TABLE 2: Estimation of HbA1c levels in obese diabetics and obese non-diabetics with BMI groups

BMI (kg/m2)	Cases	Obese Diabetic	Obese Non-diabetic	t-test P value
		HbA1c (%) Mean ± SD		
Class 1	13: 17	8.16 ± 1.42	6.12±1.31	< 0.001
Class 2	19: 14	8.53 ± 1.30	6.30±0.50	< 0.001
Class 3	13: 14	9.79 ± 1.45	6.76±1.24	< 0.001
P value		0.011	0.27	t-test P value
LSD		1.0: 1.1	Non-Sig	

* Cases: Number of individuals in the both of two groups (diabetic: non-diabetic).

Comparison of HOMA-IR level in obese diabetics and obese non-diabetics with BMI groups

Our results clarified the HOMA-IR increase significant difference in obese diabetics and obese non-diabetics groups with BMI categories. In contrast, we recorded a significant increase in the obese diabetics compared with the match group of obese non-diabetic at a P value < 0.05, as seen in Table 3.

TABLE 3: Estimation of HOMA-IR level in obese diabetics and obese non-diabetics by BMI groups

BMI (kg/m2)	Cases	Diabetic	Obese Non-diabetic	t-test P value
		HOMA-IR Mean ± SD		
Class 1	13: 17	3.60 ± 0.82	0.51 ± 0.44	< 0.001
Class 2	19: 14	3.26 ± 0.65	1.20 ± 0.66	< 0.001
Class 3	13: 14	4.83 ± 1.29	2.61 ± 1.10	< 0.001
P value		< 0.001	< 0.001	t-test P value
LSD		Sig	Sig	

*Cases: Number of individuals in the both of two groups (diabetic: non-diabetic).

Comparison of PTH levels in obese diabetics and obese non-diabetics with BMI Groups

The current results indicated a significant difference in levels of PTH in the obese diabetics according to BMI categories and no effect on the control group. While in the group of obese diabetics our results were clarified a significant increase in (class1 and class 2 categories) compared to the corresponding groups of obese non-diabetics, but non-significant differences in the class 3 category when compared with the corresponding group of obese non-diabetics at P value < 0.05 as seen in Table 4.

TABLE 4: Comparison of PTH levels in obese diabetics and obese non-diabetics with BMI Groups

BMI (kg/m2)	Cases	Diabetic	Obese Non-diabetic	t-test P value
		PTH (pg/ml) Mean ± SD		
Class 1	13: 17	36.53 ± 7.1	57.9 ± 16.2	<0.001
Class 2	19: 14	42.88 ± 13.0	56.0 ± 16.7	0.02
Class 3	13: 14	53.45 ± 16.4	57.3 ± 14.9	0.53
P value		0.04	0.960	t-test P value
LSD		Sig	Non-Sig	

*Cases: Number of individuals in the both of two groups (diabetic: non-diabetic).

Comparison of Vit. D3 level in obese diabetics and obese non-diabetics with BMI groups

According to BMI categories, we did not find significant differences in the level of Vit.D3 in diabetic patients and control. While there is a significant difference in class 2 and class 3 categories in obese diabetic patients compared with the match group of obese non-diabetics, no significant difference was recorded in the class 1 category at P value < 0.05, as seen in Table 5.

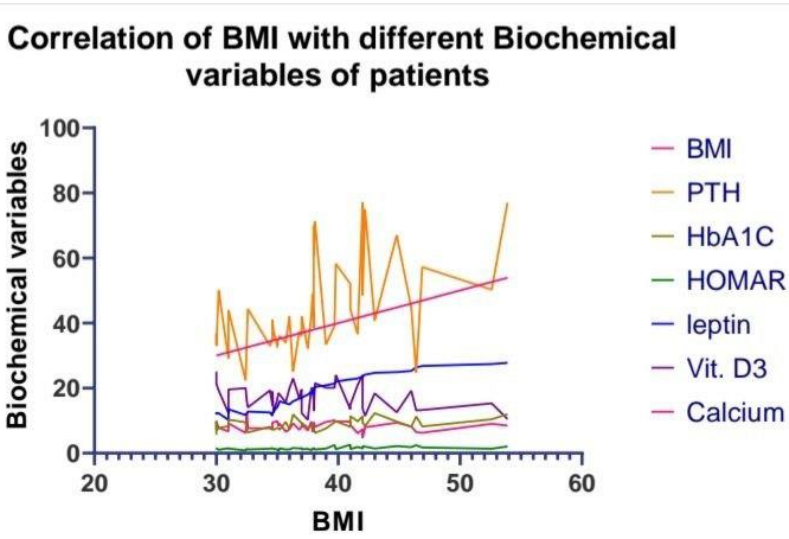
TABLE 5: Estimation of Vit. D3 level in obese diabetic and non-diabetic according to BMI groups

BMI (kg/m2)	Cases	Diabetic	Control	t-test P value
		Vit. D3 (ng/ml) Mean ± SD		
Class 1	13: 17	18.28± 4.17	14.77± 5.34	0.06
Class 2	19: 14	18.21 ± 3.56	14.68 ± 3.83	0.01
Class 3	13: 14	15.4± 4.00	12.21± 4.31	0.05
P value		0.10	0.24	t-test P value
LSD		Non-Sig.	Non-Sig.	

*Cases: Number of individuals in the both of two groups (diabetic: non-diabetic).

Pearson correlation coefficient of BMI with different biochemical variables of patients in the obese diabetic group

The current study showed a significant positive association among BMI and PTH (r=0.49, P<0.001), HbA1C (r = 0.49, P<0.001), HOMA.IR (r=0.53, P<0.001), and leptin (r=0.94, p<0.001) while invers correlation with vit. D3 (r =-0.36, P=0.01), but no significant association with calcium (r=-0.11, P=0.4) as seen in Figure 1.

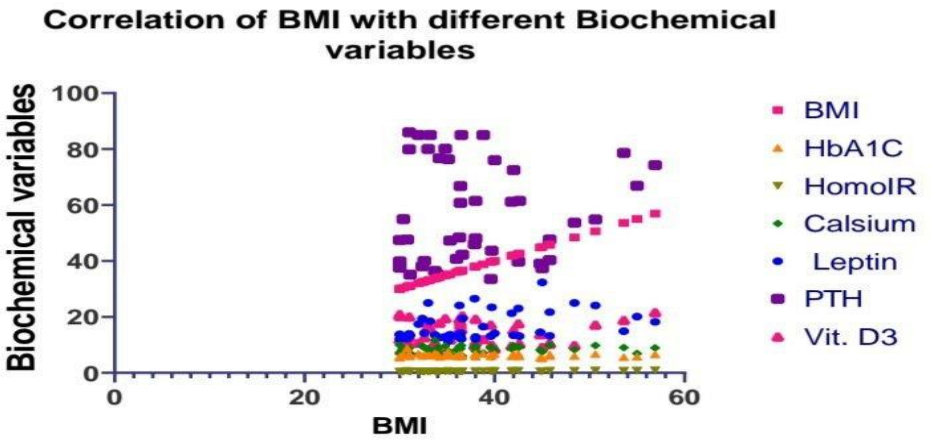


	BMI Vs. HbA1c	BMI Vs. HOMA.IR	BMI Vs. PTH	BMI Vs. Vit. D3	BMI Vs. Leptin	BMI Vs. Calcium
r	0.49	0.53	0.49	- 0.36	0.94	-0.11
P value	0.001	0.001	0.001	0.0149	<0.001	0.43

FIGURE 1: Pearson correlation coefficient among BMI with different biochemical variables in obese diabetic patients.

Pearson correlation coefficient of BMI with different biochemical variables in the obese non-diabetic group

The current study indicated a positive association among BMI and PTH (r=0.06, P<0.6), HbA1C (r =0.16, P=28), HOMA.IR (r=0.87, P< 0.001) and leptin (r=0.3, P=0.04) while invers association with Vit. D3 (r =- 0.18, P= 0.23) and calcium (r =-0.14, P=0.36) as seen in Figure 2.



	BMI Vs. HbA1c	BMI Vs. Homo.IR	BMI Vs. PTH	BMI Vs. Vit. D3	BMI Vs. Leptin	BMI Vs. Calcium
r	0.16	0.87	0.06	- 0.18	0.3	- 0.14
P value	0.28	<0.001	0.6	0.23	0.04	0.36

FIGURE 2: Pearson correlation coefficient among BMI with different biochemical variables in obese non-diabetic group.

Inter-relationship among hyperparathyroidism and Vit. D3 deficiency in obese diabetic and obese non-diabetic patients

Depending on Vit. D3 statuses, our results showed a non-significant difference in the level of PTH in diabetic patients and non-diabetic individuals, where in the diabetic patients the mean of PTH was lower in the status of Vit. D3 deficiency than the status of Vit. D3 insufficiency (43.71±12.4), (45.05±18.2) respectively. While in the non-diabetic group, the mean of the PTH was lower in both of the status of severe Vit. D3 deficiency and insufficiency (52.75 ± 13.65), (52.50 ± 21.85) respectively, but higher in the status of Vit. D3 deficiency (59.46 ± 18.06), as shown in Table 6 and Figure 3. In contrast, we only found a significant difference in the concentration of PTH in obese diabetics compared with the non-diabetic group according to Vit.D3 deficiency. At the same time, other statuses had no significant difference recorded at P value<0.05.

TABLE 6: Estimation of PTH levels in obese diabetics and obese non-diabetics according to Vit.D3 statuses

Vit.D3 (ng/ml)	Cases	Obese Diabetic	Obese Non-Diabetic	t-test P value
		PTH (pg/ml) Mean ± SD		
Sever Vit.D3 Deficiency	0: 9	0	52.75 ± 13.65	NO
Vit.D3 Deficiency	32: 30	43.71 ± 12.4	59.46 ± 18.06	0.01
Vit.D3 Insufficiency	13: 6	45.05 ± 18.2	52.50 ± 21.85	0.44
P value		0.77	0.48	t-test P value

LSD	Non-Sig	Non-Sig	

*Cases: Number of individuals in the both of two groups (diabetic: non-diabetic).

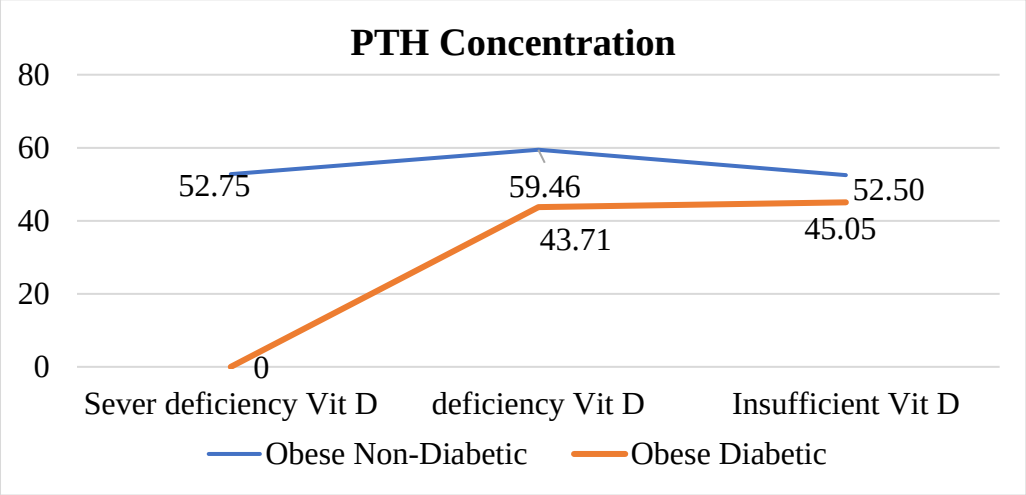


FIGURE 3: Effecting of Vit. D3 cases on the levels of PTH.

Correlation of PTH with Vit. D3 and Leptin in obese diabetics and obese non-diabetics group

Figures 4 and 5 show a weak inversely correlation and no significant between hyperparathyroidism with Vit. D3 deficiency in obese diabetics (r =- 0.12, P=0.4), while positive correlation in the obese non-diabetics (r =- 0.1, P=0.4). While a clear and significant positive association between PTH with leptin in obese diabetics (r = 0.54, P<0.001), in contrast, non-significant differences in obese non-diabetics (r = 0.24, P=0.1).

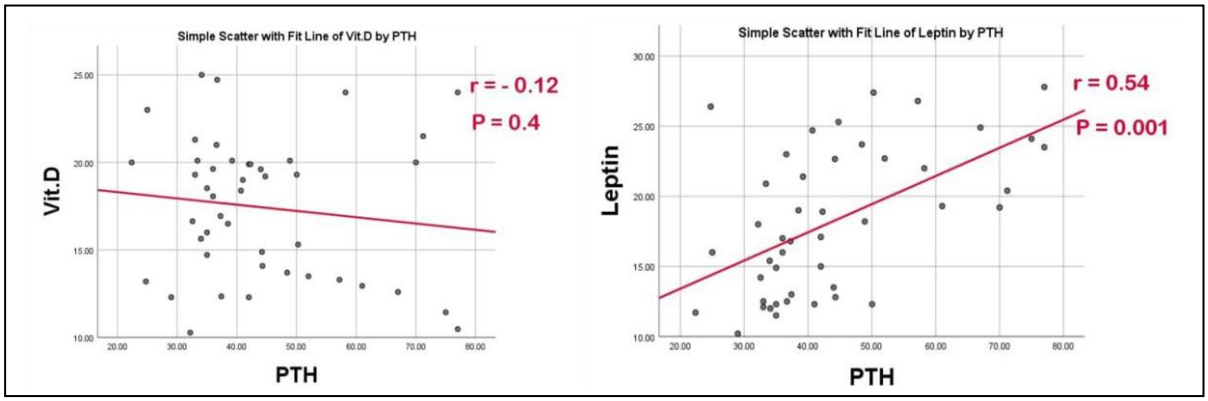


FIGURE 4: Correlation of PTH with Vit. D3 and Leptin in the obese diabetic group.

J Popul Ther Clin Pharmacol Vol 30(4):e249–e262; 14 March 2023.

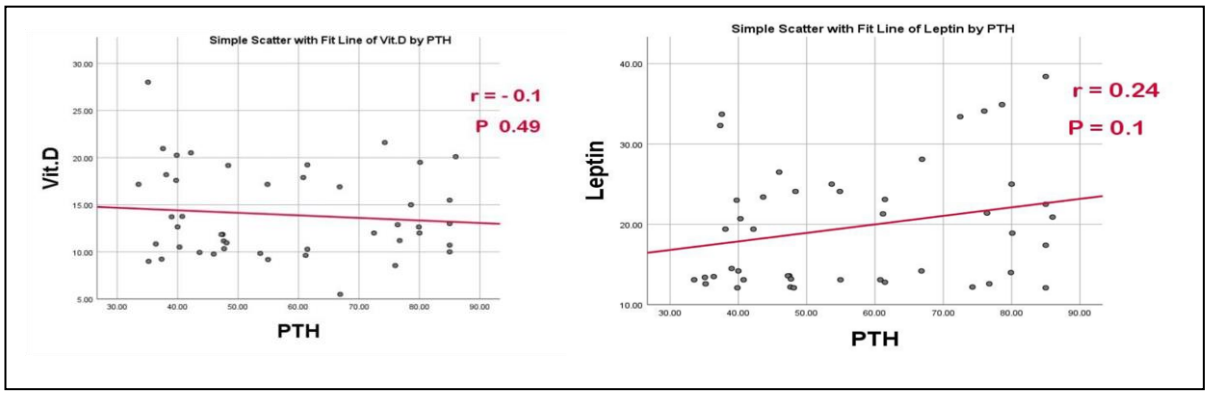


FIGURE 5: Correlation of PTH with Vit. D3 and Leptin in obese non-diabetic group.

DISCUSSION

Adiposity is a chronic, complicated, and degenerative condition affecting one out of 5 people in 2025[31]. Obesity is an indicator of T2D [32]. This study assesses the inter-relationship among secondary hyperparathyroidism and Vit. D3 deficiency in obese diabetics and obese non-diabetic patients. Our results illustrated the levels of HbA1c increase with increasing BMI in obese diabetic patients. At the same time, in control, non-significant was noted according to BMI categories, while a significant difference between Homo.IR with BMI according to BMI categories in the the obese diabetics and obese non-diabetics groups were observed, our results indiated significant differences in concentration of HbA1c and Homo.IR in obese diabetics compares with obese non-diabetics. And a significantly positively correlation among HOMA-IR and HbA1C with body mass index (r=0.49, P=0.001) (r=0.53, P=0.001), respectively in obese diabetic patients. But in control, the correlation of HbA1C with BMI was lower and insignificant (r=0.016, P=0.28). This result is in agreement with several studies [33-35]. The most surprising finding is the powerful association between Homo.IR with BMI in obese non-diabetic (r=0.87, P<0.001), we consider this to reveal the significant risk factor for type 2 diabetes. Adiposity is an indicator of type-2 diabetes. Jiajia Jiang and his colleagues discovered that non-esterified glycerol, fatty acids, hormones, and inflammatory cytokines that may contribute to the emergence of insulin resistance are generated by adipose tissue. These were the greatest indications related with markers in obesity [36]. Since obesity is the accumulation of fat on cells and tissues, so it can distort the receptors for the hormone insulin. Macrophages are major mediators of adiposity-induced insulin resistance. This behavior is attributable to direct as well as signaling pathways from M1 traditionally-activated macrophages but M2 conversely-activated macrophages fail to elicit these effects [37].

According to gender, our results documented significantly lower levels of Vit. D3 in diabetics patients compared to the control in the male group, while non-significant differences according to the female group, as shown in Table 1.

Perhaps the reason is due to the similar lifestyle of women in Iraq, due to the social traditions that oblige women to stay at home permanently. This results in not being exposed to sunlight naturally, unlike men. This result is similar to a study by LK Johnson and his colleagues [38], which differs from the influence of Abudawood, Manal, et al.[39].

So, according to BMI classifications, the results showed no significant differences among levels of Vit. D3 in either obese diabetes patients or obese non-diabetic patients. A considerable increase in the diabetic patients compared with the match group of control except for the obesity1 category. In obese diabetics, we discovered a significant negative relationship (r=-0.36, P 0.01) between serum levels of 25(OH) D and BMI; in contrast, we discovered a very weak inversely correlation (r=0.005, P=0.9) no significant in obese non-diabetics patients[40], the common factor between the two groups is obesity. The difference between the two

groups is type 2 diabetes. However, this association was more clearly in obese diabetic individuals [41] [42]. The reasons that Vit. D3 levels not significantly with obesity groups may be the intake of Vit. D3 supplements by some patients or the effect of other diseases such as kidney disease or decreased intestinal absorption or small samples[43, 44]. The immune system's cells also affect the production of specific enzymes 25-1a-hydroxylase) that regulate the balance of Vit. D3 in the body [45].

Vit. D3 has mild effects on insulin flowing, HbA1c, and insulin resistance, according to certain randomized clinical studies [46]. Obesity and Vit. D3 deficiency are both highly associated with type 2 diabetes [47]. It has been noted that the interaction between Vit. D3 deficiency and adiposity can lead to the development of insulin resistance [48]. Many studies have concluded this inverse correlation between obesity with Vit. D3 [13, 49, 50]. Several factors cause Vit. D3 deficiency in obese people, Including Not enough exposure to the sun because of their lifestyle and lack of activity, and the blocking of Vit. D3 in adipose tissue[51]. Despite the sunny climate in Iraq, Vit. D3 deficiency is prevalent due to the traditions and religious beliefs prevailing in this area: wearing clothes that cover the entire body, living in closed houses, and avoiding the heat of the sun[52, 53]. The dispersion of 25(OH)D into a wider volume of whole body tissues may be the source of the decreased serum 25(OH)D, especially if 25(OH)D was effectively sequestered in many other tissues [54]. Moushira Zaki and colleagues investigated 201 obese Egyptian women with Vit. D3 deficiency in the study. They found that a decrease in Vit. D3 in obese patients is associated with abnormal metabolic components and inflammatory biomarkers. Moreover, VDR polymorphisms are essential in immune and inflammation status[55]. The distribution of VDR distribution in skeletal muscle, adipose tissue, and pancreatic cells is the primary cause of vitamin Insulin sensitivity is also influenced by 1 hydroxylase in β cells and the Vit. D3 responsive region in the human insulin androgen receptor promoter [56].

Compared to the obese non-diabetics group, the obese diabetics group in our study had a stronger positive correlation between PTH and adiposity ($r=0.49$, $P<0.001$) and ($r=0.06$, $P=0.6$), respectively. So, we found a significant difference in the level of PTH with increasing degrees of obesity in the obese diabetic according to BMI categories and no significance in the obese non-diabetic group. As far as we knowledge, the presence of diabetes factors in obese individuals is the reason for the significant differences between the two groups[57, 58]. Gender was also considered a considerable variable in this study as it revealed a significant increase according to females and males in obese diabetics compared with obese non-diabetics [59]. Our results of increased levels of PTH in adiposity agree with other researches [60]. Through some processes, including a reduction in the action of the lipoprotein enzyme in grown fat tissues, serum PTH level has been strongly associated with obesity and fat deposition [61].

Our study clarified a weak, non-significant negative correlation between Vit. D3 levels and PTH. This result matches with the result reported by Stephen Hewitt [62]. According to Vit. D3 statuses, our results showed that the levels of PTH were non-significant in either obese diabetics or obese non-diabetics [59].

The high sPTH was unrelated to the low Vit. D3. Other researchers have pointed out that sPTH levels in obesity are independent of Vit. D3 levels. Additionally, 20% of patients had elevated sPTH one year following bariatric surgery, although normal s25OHD levels [63]. As a result, our findings support the concept that the negative association between PTH and Vit. D3 in obesity is not causative. Still, the biochemical changes directly affect adiposity itself. The occurrence of an inverse correlation between PTH and Vit. D3 cannot be taken to determine the presence of Vit. D3 deficiency in adiposity. This result agrees with Jumaahm M.K and his colleagues' findings [64]. Because leptin and visceral fat deposition may also contribute to hyperparathyroidism in severely obese people, Vit. D3 deficiency is not the only factor that to be considered [30]. However, we disagree with the findings of a study by Ashley Lotito et al., which concluded that (1000 IU) Vit-D supplementation reduces serum PTH concentration in the obese and overweight population [65]. However, their study ignored the effect of the leptin hormone on obesity. Also, it did not include the interaction of diabetes and insulin resistance on the biochemical relationship with Vit. D3 in obesity, while our study included.

There is a strong positive relationship between leptin with body mass index (r = 0.94, P = 0.001) and PTH (r =0.54, P<0.001) which was indicated in our results. It was interesting and significant in obese diabetic group. In contrast, a significant association was observed in obese non-diabetic group with BMI (r =0.3, P=0.04) and non-significant with PTH (r=0.24, P = 0.2). We believe this relationship is causal. Hoang et al. demonstrated that leptin administration increased parathyroid PTH secretion in parathyroid explants, whereas leptin receptor blockade inhibited this phenomenon [66]. Another theory proposes an influence of adipokine on PTH and a positive association between leptin and PTH [59]. A high leptin level is closely associated with obesity, as indicated in some studies [67, 68]. In contrast, in some other articles have been mentioned that, leptin resistance is marked by decreased satiety, excessive nutrient consumption, and increased total body mass. Obesity is frequently the result of this[69]. The effect of the type 2 diabetes factor was clear in the relationship between obese diabetic patients and obese non-diabetic individuals. Growing evidence suggests that leptin is also critical for glycaemic control[70].

Our data showed a higher deficiency in calcium level by the mean and std. deviation 8.30±1.39 (r=-0.11, P 0.43) in obese diabetics than in non-diabetics obese 8.41±1.08 (r=0.14, P 0.36) [71]. Still, there is no significant difference between the two groups [59], [72]. So, we did not find a significant difference between the two comparing groups, female and male.

Vit. D3 has traditionally acted as the primary regulator of blood calcium metabolism, directly or indirectly, through the PTH. However, many tissues, such as gut, adipose tissue, cardiac and skeletal muscles, and β-cells, contain VDR [73]. Negative feedback processes like intestine absorption, kidney reabsorption, and bone storage can regulate the body's calcium metabolism. Several concepts have been put up regarding the metabolic impact of calcium on adipose tissue in treating obesity. PTH is released in response to low serum calcium levels and mobilizes calcium from bone to stabilize serum calcium levels. Additionally, PTH controls the transformation of 25(OH)D3 into its active form, calcitriol, which enhances calcium absorption [74] [75].

CONCLUSION

Adiposity is a risk factor for T2D related to Vit. D3 deficiency and high level of PTH. The correlation between Vit. D3 deficiency and hyperthyroidism is inverse and insignificant, and it should not be considered as causative. Instead, the disorder is caused by biochemical abnormalities as a reaction to obesity.

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