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Vitamin D supplementation influence in insulin resistant pre-diabetic obese patients

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Abstract

Obese adults often have low blood levels of 25-hydroxyvitamin D (25OHD). There is mounting evidence that vitamin D has immunomodulatory and anti-adipogenic properties. The purpose of this research was to determine how vitamin D supplementation affects insulin resistance and internal analysis in obese participants who were also pre -diabetic and vitamin D deficient.

forty-two pre-diabetic, obese participants with insulin resistance and vitamin D deficiency (25OHD <20 ng/ml) were randomly assigned to a vitamin D group (a weight-reduction diet plus a weekly dose of 50 000 IU vitamin D for two months followed by 25 000 IU for one month) or a weight reduction diet only group for 3 months (12 weeks). Before and after the intervention, weight, 25OHD blood levels, insulin resistance, fat mass, and muscle mass were evaluated.

When compared to the baseline values in the vitamin D group, vitamin D supplementation significantly increased the blood 25OHD level (P <0.001) and significantly decreased HOMA-IR. Both groups lost weight, BMI, and insulin resistance (P< 0.05). After the intervention with vitamin D supplementation compared to the other group, there were considerable weight loss, substantial growth in blood 25OHD concentrations, and substantial reductions insulin resistance and in triglycerides levels.

Conclusions: The increase in vitamin D status in pre–diabetic insulin resistant obese participants with vitamin D deficiency was followed by a reduction in weight and insulin resistance

Thus weight reduction and vitamin D administration may work together to enhance glucose metabolism in insulin resistant pre diabetic obese people.

Key words: pre-diabetic; obese; 25(OH)D ;fat mass; insulin resistance.

1. Introduction

An elevation in body fat encourages adipose tissue malfunction and aberrant fat mass physical forces, which has a negative impact on metabolism, biomechanics, and psychosocial health. Obesity is a persistent, progressive, relapsing, and curable multifactorial, neurobehavioral disorder. It is regarded as the second most prevalent etiology of cancer and may soon surpass cigarette smoking as the most prevalent avoidable cause of the disease [1].

Since its occurrence has risen in the previous several decades, over half of individuals in the United States (48.5%) are pre diabetics or diabetics, and more than two thirds of adults (70.2%) are overweight or obese. Due to the most recent statistics from the Globe Health Organization, type 2diabetes and obesity both pose serious public health problems across the world (WHO report 2020 and 2021) [2].

Continuously consuming too much energy causes impairs insulin secretion due to interactions with the insulin signaling cascade and enhances apoptosis of pancreatic beta cells and hypertrophy of adipocytes due to extreme triglyceride storage in the liver and muscle tissues [3]. This condition is identified as Insulin Resistance. Insulin resistance is a systemic metabolic disorder characterized by decreased insulin sensitivity, which then progresses to a decrease in insulin action. [45]

When nutrition storage pathways that have evolved to enhance efficient energy consumption are exposed to persistent energy surpluses, insulin resistance develops. [46] Ectopic lipid buildup in the liver and skeletal muscle activates signaling pathways that compromise insulin signaling, decreasing hepatic glycogen production and muscle glucose absorption. [47] Ectopic lipid in the muscles causes muscle insulin resistance, which develops before liver insulin resistance and directs ingested glucose to the liver, increasing hepatic de novo lipogenesis and hyperlipidemia.[49] White adipose tissue (WAT) is then invaded by macrophages, increasing lipolysis, which in turn causes an elevation in hepatic

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triglyceride production and hyperlipidemia because of an elevation in fatty acid esterification [4].

Pre-diabetes, a phase in between having normal blood glucose levels and having type 2 diabetes, described by impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) terms,is more common than type 2 diabetes worldwide across all ages, sexes, and racial/ethnic groups. it is usually linked to obesity and other aspects of metabolic disorder where preventive lifestyle modification measures have been demonstrated to be beneficial in postponing or avoiding the development of diabetes in pre-diabetes [5].

In turn, obesity is often linked to hypovitaminosis-D because adipose tissue may store 25(OH) D, making it physiologically inaccessible [6].

Low levels of blood 25(OH)D, calcitriol [1,25(OH)2D] and elevated parathyroid hormone (PTH), may all lead to a rise in intracellular calcium in adipocytes,which could promote lipogenesis and make a patient more likely to gain weight and develop diabetes [7].

Researchers have found that your body has vitamin D receptors all around, even in the pancreas, which makes insulin and is crucial in the development of diabetes [5]

Numerous case controlling and cross-sectional investigations indicate a negative correlation between type 2 diabetes, glucose intolerance, and vitamin D levels [8]. This could occur as a result of the distribution of vitamin D receptors (VDR) on skeletal muscle, adipose tissue, and pancreatic beta cells. Insulin secretion or sensitivity may be affected by vitamin D levels. [48] Variations in the intracellular calcium content of beta cells may act as a mediator for the action of vitamin D on insulin production [9].

By acting as an anti-inflammatory, vitamin D increases insulin responsivity. Interleukin 1 and 6, TNF-alpha, and other proinflammatory cytokines that contribute to insulin resistance (IR) are downregulated by vitamin D, which in turn decreases NF-Kappa b function [10].

By raising parathyroid hormone (PTH) concentrations, vitamin D insufficiency reduces insulin sensitivity [11].

It is anticipated that a rise in blood 25OHD values would decrease fat mass and meta-inflammation in obese people because of the link between vitamin D deficiency and excess weight and as meta-inflammation is a major factor in the pathophysiology of obesity. This investigation was designed to compare the effect of vitamin D3 supplementation (50 000 IU/week for 2 weeks followed by 25 000 IU/week) and a diet regimen to a diet regimen only on obesity induced insulin resistance, weight and fat mass in pre-diabetic obese patients with vitamin D deficiency throughout a 12-week weight loss diet program. It was what an impact a vitamin D dosage and a low-calorie diet could have on insulin resistance in people who are obese pre-diabetics and have low vitamin D levels.

Patients and Methods

Study design and subjects

Forty- two vitamin D deficient insulin resistant pre-diabetic obese patients presented in obesity unit of Physical medicine, Rheumatology and Rehabilitation department in Ain Shams University Hospitals, Cairo, Egypt in the period from December 2019 to until the end of July 2021.Males and females between the ages of 30-50 years, with BMI 30-40 kg/m2, Pre- diabetics with insulin resistance diagnosed by Fasting blood sugar: 100-125mg/dl or HbA1C: 5.7-6.4 % and homeostatic model assessment- insulin resistance (HOMA-IR) > 3.i.e Participants who were willing to take part in the experiment and had moderate to severe insulin resistance**,** along with a blood 25OHD level below 20ng/ml, were sought out. Data collection was done in randomly chosen days every week.

Patients with diabetes mellitus, sun light allergies, any medical condition that may lead to secondary obesity as(Polycystic ovary syndrome, Hypothyrodism and Cushing syndrome),any medical condition that could possibly affect vitamin D level(Parathyroid disease, Hepatic or renal disease,malabsorption syndrome) or those taking medications that may alter weight as tricyclic antidepressant, valproate, carbamazepine, steroids and oral contraceptive pills or medications that would affect vitamin D levels as orlistat, statins, steroids, Thiazide diuretics, antiepileptics, anti- diabetics, rifampicin and calcium supplementation together with pregnant or cancer patients were excluded from the trial.

The Ain Shams medical ethics committee authorized the trial. Patients who consented to participate in the research and completed the eligibility requirements were given a general description of it before they signed an informed consent form.

The community and public health department of the college of medicine at Ain Shams University, under the direction of a statistics specialist, established the sample size.

The sample size was 21participants in every group.

Two groups of individuals were randomly assigned: a vitamin D + diet regimen group in which vitamin D pills (50 000 IU cholecalciferol followed by 25,000 IU cholecalciferol) were given to each week for 12 weeks,while the other group were given the same diet with no vitamin D. Throughout the trial, weight reduction programs were given to both groups. For the purpose of tracking their weight, the

participants visited once each week. Based on the unique features of the patients, a weight reduction diet was created with a daily calorie restriction target of 500 kcal fewer than the Mifflin formula-calculated total energy needs (TEE).

Variations in insulin resistance were the trial's main finding, while variations in vitamin D levels, weight, fat and muscle mass, and lipid profiles were its secondary findings.

Measurements

With light clothing and no shoes, length and weight were estimated to the closest 0.1 cm and 0.1 kg on a calibrated stadiometer-scale (Seca, Hamburg, Germany). Weight (kg) divided by length (m2) was used to compute BMI. Using a body analyzer and following the instructions in the manufacturer's handbook, overall body fat and muscle mass were assessed (model Inbody 720, Japan).

After fasting for 12 hours A 10-mL sample of venous blood was drawn, and the seum was separated by centrifugation and kept at -20°C until the day of analysis. Serum concentrations of intact PTH and 25-OH vitamin D and fasting insulin were measured utilizing a high sensitivity enzyme-linked immunosorbent assay (ELISA) kit from Crystal Day in Shanghai, China. Fasting blood glucose and HbA1C was measured by glucose oxidase method and synchron cx5 respectively. Insulin resistance was calculated by the following equation

Homeostatic Model Assessment of Insulin Resistance (HOMA- IR):

Fasting Insulin (µIU/mL) × Fasting Blood Glucose (mg/dL)/405

Colorimetric enzymatic analysis used to assess calcium and the lipid profile, The investigations were done in accordance with the instructions from the manufacturer.

The patients' dietary intakes were evaluated using a 24-hour food recall or food diary. Participants provided thorough answers to a series of questions to record details about their time spent in the sun. The participants were asked to recollect minutes or hours spent outside, clothing pattern and nature of work during the previous seven days., participants also filled out some physical activity questions of the last 7 days, and on the answers basis, physical activity was rated as, sedentary, light, moderate, or very active.

Statistical analysis

Data were reported as frequencies (percentage), whereas numerical values were provided as mean ±standard deviation (SD). Since all of the data had a normal distribution, parametric tests were carried out; the baseline data for the two groups were compared using the independent samples t test (continuous parameters) and the chi-square test (categorical parameters), and the intragroup variations were evaluated using the paired samples t test before and after the research.

At the conclusion of the trial, between-group variations were examined using analysis of covariance (ANOVA) corrected for baseline values and covariates. Statistical significance was defined as a P value ≤ 0.05. Pearson correlation coefficients were established with the continual values depending on the distribution of the variables. Substantial data was defined as $p \leq 0.05$.

IBM-SPSS-Statistics Ver. 20.0 was used to conduct all statistical analyses.

RESULTS

All the forty two volunteers continued the study till the end of the experiment finished the experiment; No substantial adverse effects connected to the weight reduction program or vitamin D3 supplementation were discovered in the groups. Table 1 displays the baseline features of the research population. Throughout the course of the study, no adverse effects or symptoms were documented. Between the two groups, there were no considerable variations.

The effects of vitamin D3 supplementation on anthropometric and laboratory findings are shown in table 2 After supplementation, the laboratory parameters of both groups were as follows. Following vitamin D_3 supplementation serum 25(OH)D increased significantly ($p < 0.001$)in both groups and a significant decrease in weight and body mass index in both groups. ($p < 0.001$), TG levels decreased significantly (p :0.010*) only in group one(vitamin d +diet).

In both groups mean FBG levels decreased and HOMA-IR values significantly decreased m ($p < 0.001$; for both groups.

Changes in all parameters from baseline to post-supplementation levels were compared (Δp). After supplementation, serum vitamin D levels increased in both groups, yet the increment was more in group one. While the weight, BMI, FBS value, and HOMA-IR levels decreased in both groups ($p < 0.001$). However, the changes were larger in favour of group one.

Table 1:Baseline demographic and medical data of the study participants (both groups):

		Groups					
		Group I(n=21)		**Group II(n=21)**		**t**	**P-value**
Age						-0.593	0.557
	Mean ±SD	36.000 ± 3.834		36.857 ± 5.406			
Height(cm)						-0.365	0.442
	Mean ±SD	166.45 ±10.22		164.55± 11.27			
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**
Sex	**Male**	3	14.29	1	4.76	1.105	0.293
	Female	18	85.71	20	95.24		
Occupation	**Worker**	15	71.43	10	47.62	2.471	0.116
	Not-Worker	6	28.57	11	52.38		
Hypertension	**Positive**	2	9.52	3	14.29	0.227	0.634
	Negative	19	90.48	18	85.71		
Smoking	**Positive**	2	9.52	1	4.76	0.359	0.549
	Negative	19	90.48	20	95.24		
Family history of diabetes mellitus	**Positive**	10	47.62	12	57.14	0.382	0.537
	Negative	11	52.38	9	42.86		
Ischemic heart disease	**Positive**	0	0.00	1	4.76	1.024	0.311
	Negative	21	100.00	20	95.24		
Sun exposure	**Non**	15	71.43	10	47.62	2.533	0.282
	10 Min-1 Hour	4	19.05	8	38.10		
	>1 Hour	2	9.52	3	14.29		
Physical activity	**Sedentary/no**	17	80.95	13	61.90	1.867	0.172
	Light	4	19.05	8	38.10		

a P value for $\chi 2$-test. b Mean ± SD c P value for Independent-Samples t-Test between means.

Table 2:Comparative study between the baseline **(**mean± SD) and the 12 weeks post intervention (mean± SD) values of the anthropometric and laboratory findings in the same group

Variable (Mean± SD)	**Group 1(Vitamin D+ diet) (**n **=21)**			**Group 2 (Diet)(**n **= 21)**		
	Baseline	**12 wks Post intervention**	P**-value**	**Baseline**	**12 wks Post intervention**	P**-value**
Weight [kg]	96.12±10.63	90.50±10.237	<0.001*	92.719 ±10.553	88.59 ±10.465	<0.001*
BMI [kg/m^2]	35.143±3.135	33.00±3.112	<0.001*	35.190±3.341	33.457±3.306	<0.001*
Fat mass[kg]	33.752±2.541	32.495±2.303	0.137	34.024±2.285	33.176±2.601	0.365
Muscle mass[kg]	39.433±2.138	40.000±2.704	0.444	39.414±20226	39.786±1.949	0.530
Waist hip ratio (W/H)(WHR)	0.968±0.044	0.964±0.056	0.824	0.980±0.035	0.975±0.050	0.703
25(OH)D [ng/ml]	12.690±3.827	30.929±4.393	< 0.001*	12.443±3.585	24.495±4.240	< 0.001*
FBS[mg/dl]	112.952±8.429	106.307±7.778	0.001*	114.095±8.282	112.270±8.335	< 0.001*
Fasting insulin[µIU/ml]	14.270±2.049	12.450±1.958	< 0.001*	13.851±1.653	13.048±1.588	< 0.001*
HOMA-IR	3.976±0.628	3.251±0.396	< 0.001*	3.914±0.642	3.629±0.607	< 0.001*

Variable (Mean± SD)	Group 1(Vitamin D+ diet) (n =21)			Group 2 (Diet)(n = 21)		
	Baseline	12 wks Post intervention	P-value	Baseline	12 wks Post intervention	P-value
HbA1c	6.005±0.220	5.893±0.209	0.056	5.976±0.202	5.922±0.193	0.141
TG [mg/dl]	276.619±74.819	237.952±72.602	0.010*	289.476±67.450	289.238±68.958	0.975
HDL[mg/dl]	40.976±8.971	41.395±4.907	0.855	44.138±9.890	44.429±7.080	0.894
LDL[mg/dl]	153.514±27.426	150.838±22.489	0.715	151.481±28.531	147.295±37.200	0.619

* $p \leq 0.05$ indicates statistical significance. Mean± SD:mean and standard deviation.
# Comparison of baseline and 12 weeks post intervention **(**Mean± SD) in both groups.
BMI – body mass index, WHR – waist-hip ratio, 25(OH)D –25-hydroxy vitamin D, FBG – fasting blood glucose, HOMA-IR – homeostasis model assessment of insulin resistance., TG – triglyceride, LDL– low-density lipoprotein cholesterol, HDL – high-density lipoprotein.

Table 3: Comparative study of the change(mean difference) of the studied variables between both groups

Variable	Group 1 Change.(mean difference)	Group2 Change(mean difference)	P-value#
ΔWeight [kg]	5.619±2.251	4.129±1.711	0.020*
ΔBMI [kg/m^2]	2.143±0.323	1.733±0.146	<0.001*
ΔFat mass[kg]	1.257±3.722	0.848±4.190	0.739
ΔMuscle mass[kg]	-0.567±3.326	-0.371±2.662	0.835
ΔWaist hip ratio (W/H)	0.004±0.077	0.005±0.056	0.964
Δ25(OH)D [ng/ml]	-18.238±2.637	-12.052±2.601	<0.001*
ΔFBS [mg/dl]	6.646±7.712	1.826±1.366	0.007*
Δ Fasting insulin[µIU/ml]	1.820±0.747	0.803±0.271	<0.001*
ΔHOMA-IR	0.725±0.399	0.286±0.077	<0.001*
ΔHbA1c	0.112±0.252	0.054±0.162	0.384
ΔTG [mg/dl]	38.667±61.828	0.238±33.733	0.017
ΔHDL[mg/dl]	-0.419±10.380	-0.291±9.861	0.967
ΔLDL[mg/dl]	2.676±33.144	4.186±38.010	0.892

* $p \leq 0.05$ indicates statistical significance.
# Comparison of the change of variables between both groups.
BMI – body mass index, WHR – waist-hip ratio, 25(OH)D –25-hydroxy vitamin D, FBG – fasting blood glucose, HOMA-IR – homeostasis model assessment of insulin resistance., TG – triglyceride, LDL– low-density lipoprotein cholesterol, HDL – high-density lipoprotein.

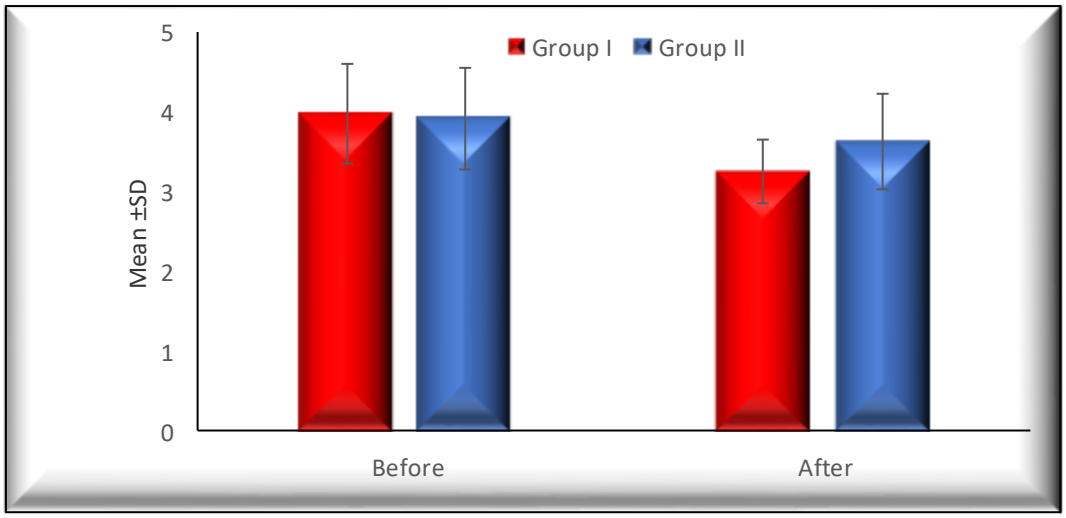

Fig (1): Showing the baseline and post intervention HOMA-IR results in both groups

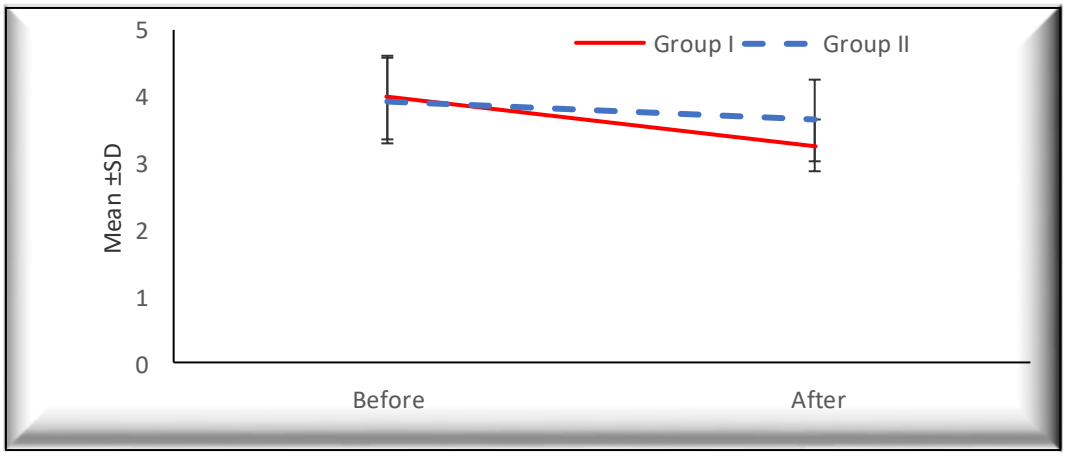

Figure (2): Showing Comparison between the two groups in the change (baseline to post intervention levels) of HOMA-IR

Table 4:Correlation study between the change of serum vitamin D (Δ25(OH)D) value with the change values of other variables.

Correlations		
change of variables (Δ)	Δ25(OH)D	
	R	**P-value**
ΔHOMA-IR	-0.332	0.032*
ΔTriglycerides	-0.359	0.020*
ΔHDL	-0.112	0.482
ΔLDL	-0.009	0.957
ΔWeight	-0.406	0.008*
ΔBMI	-0.636	<0.001*
ΔFBG	-0.276	0.077
Δ Fasting insulin	-0.463	0.002*
ΔHbA1c Change	0.036	0.820
ΔFat mass (kg)	-0.246	0.116
ΔMs mass (kg)	0.206	0.191
ΔW/H	0.229	0.145

Significant Pearson correlation, *

* $p \leq 0.05$ indicates statistical significance.# relative change of variables (Δp).

25(OH)D – 25-hydroxy vitamin D,, HOMA-IR – homeostasis model assessment of insulin resistance. TG – triglyceride, HDL – high-density lipoprotein, LDL– low-density lipoprotein cholesterol,BMI – body mass index, FBG – fasting blood glucose,W/H -waist hip ratio.

A statistical substantial negative correlation was found between vitamin D change and HOMA-IR change, triglycerides level change and fasting insulin change of P value 0.032,0.020 and 0.002 and with r value -0.332,-0,359 and -0.463 respectively(.shown in table 4)

A statistical substantial negative correlation was found between vitamin D change and weight and BMI change of P value 0.008 and <0.001* and with r value-0,406 and -0.636 respectively. (Shown in table 4).

DISCUSSION

Obesity pandemic and vitamin D levels relationship gains interest**,** there is an association between obesity, which is characterized by low-grade inflammation, and vitamin D [12].

Boucher [13] revealed a definite connection between vitamin D status and overweight, with reports indicating that obesity alters vitamin D metabolism and reduces vitamin D absorption in obese people.

Some investigations have shown a negative link between blood vitamin D values and insulin resistance because pancreatic -cells contain receptors for the active form of vitamin D and the local synthesis of 1α, 25(OH)2D3 may be a crucial modulator of islet activity [14].

It is believed that taking vitamin D supplements may regulate insulin resistance in obese people at a low cost via both preventive and therapeutic measures [15].

The demographic data did not show any statistically substantial differences in the two groups. Our demographic data gives a detailed results compared to Ahmed et al. [16] studying the impact of vitamin D3 on insulin sensitivity in prediabetes with hypovitaminosis D; however, factors influencing vitamin D metabolism, such as diet, sunshine exposure, physical activities, and others, were not taken into account;

In our results both groups lost weight, on Comparison between the two groups the change (baseline to post intervention levels) of weight shows a statistically substantial decrement between the two groups of P-value 0.020 in favor of group one, Moreover, the relative change (baseline to post intervention levels) of BMI shows a statistically substantial variation between the two groups of P-value:0.001 in favor of group one.

In addition, our results showed a statistically substantial negative connection between vitamin D change and weight and BMI change of P value 0.008 and <0.001* and with r value-0,406 and -0.636 respectively.

In regards to the impact of vitamin D on the anthropometric parameters (BW, BMI and WHR), Our results is matched with Vigna et al. [17] studying the impacts of vitamin D dosage on the results of a low-calorie diet in workers who were obese or overweight and came to the conclusion that higher vitamin D rates were linked to higher weight loss

Our intervention lasted long enough, along with dosages of 50,000 IU per week for two months, followed by 25,000 IU per week for one month, to cause detectable increases in blood vitamin D levels. Given that group 1's median serum 25(OH)D level grew considerably and group 2's vitamin D status underwent substantial alterations there was a statistically substantial variation between the two groups.

Our findings are consistent with those of Buscemi et al. [18], who established that obese people had decreased vitamin D values that return to normal after major weight reduction. Our results are also matched with Lotfi-Dizaji et al. [19] who studied 44 obese participants with vitamin D deficiency were randomly allocated to the vitamin D group (a reducing weight diet plus a bolus weekly dose of 50 000 IU vitamin D) or the placebo group (a weight loss diet plus edible paraffin weekly) for 12 weeks to determine the effects of vitamin D dosage along with weight loss diet on meta-inflammation and fat mass., It was shown that vitamin D supplement significantly increased serum 25OHD levels (P< 0.001). Both groups saw a loss in weight, BMI, and fat mass (P <0.05). Conclusion: Advancement in vitamin D status in obese subjects with vitamin D deficiency in combination with weight loss diet led to weight and fat mass. Between the groups, there were substantial decreases in weight and fat mass as well as substantial growth in serum 25OHD levels after intervention with vitamin D dosage compared to placebo (P< 0.05). by Duan et al. [20] they showed that despite the increase of serum vitamin D level, the obesity indices (BMI.,WHR)didn’t improve significantly although there were notable improvement in serum vitamin D level after supplementation.

Numerous writers have hypothesized a connection between low vitamin D levels and metabolic malfunction, specifically insulin resistance and its associated characteristics. Diagnostic criteria for the metabolic disorder, formerly known as the "Insulin resistance Disorder," include elevated insulin resistance, higher risks of eventual cardiovascular

disease, T2DM, or both, and anomalies in each of the variables [13].

In agreement with our results Imga et al. [21] stated that HOMA-IR level changes are predicted by changes in 25(OH)D level and their study showed a decrease in HOMA-IR value after vitamin D supplementation in obese premenopausal women. Also, Niroomand et al. [22] showed that Serum 25-hydroxyvitamin D levels in the experimental group were considerably greater at 6 months (36 ng/ml versus 16 ng/ml, P value 0.001) on a total of 162 patients, 83 of whom completed the 6-month follow-up (44 in the experimental group and 39 in the control group). The vitamin D group's HOMA-IR score was much lower, but there was no substantial change in FPG between the two groups.

Also, Lerchbaum et al., [23] and Hajhashemy et al. [24] studied the impact of vitamin D supplement on 192 obese vitamin D deficient insulin resistant patients for 13 and 12 weeks respectively, resulted in significant improvement of insulin and glucose metabolism together with abdominal obesity and dyslipidemia in while Safarpour et al. [25] study on 85 Iranian obese vitamin d deficient insulin resistant supplemented for 8 weeks showed significant improvement in insulin and glucose metabolism and non-significable improvement in abdominal obesity and dyslipidemia [26].

Gaskill et al. [27] revealed that a lifestyle interference in addition to vitamin D3 at 25,000 and 50,000 for three months or more enhanced insulin sensitivity in adults with obesity and vitamin D insufficiency. Vitamin D3 intake in excess of the suggested daily allowance RDA for three months or more corrected vitamin D status in obese adults.

Zhang et al. [28] study showed that Vitamin D receptor polymorphism (such as Apa 1 and Fok 1) and insulin sensitivity are racially distinct, and regular vitamin D treatment for 6 months has been shown to drastically lower HOMA-IR readings in vitamin d deficient pre diabetic south Asian women residing in New Zealand.

It was understood that vitamin D dosage—low or high—supplementation frequency—daily or weekly—and vitamin D form—alone or as a co-supplement—all had a significant impact on glucose homeostasis. For modest dosages of vitamin D (≤4000 IU/d), it was hypothesized that HOMA-IR reduced. This could be the outcome of higher compliance or more consistent vitamin D3 absorbed in the stomach [29], However, Gaskill et al. [27] stated that Along with a lifestyle change, high dosage vitamin D3 for three months or longer improved vitamin D status in obese people and improved insulin sensitivity.

Our results go in accordance with Ahmed et al. [16] study of insulin response to vitamin D3 dosage Sensitivity in prediabetes with hypovitaminosis D: a randomized placebo-controlled trial in which patients achieved vitamin D sufficiency (25(OH)D > 30 ng/mL) by taking 60,000 IU of vitamin D3 soft gels once a week for 12 weeks. The vitamin D levels in the placebo group did not significantly alter. Following the therapy of hypovitaminosis D, the study's findings demonstrated an enhancement in insulin sensitivity, as measured by the OGIS (oral glucose insulin sensitivity) index at 120 minutes.

On the contrary to our results, in a recent meta-analysis, which only included the outcomes of controlled studies, vitamin D supplementation had no effect on patients' fasting glucose, fasting insulin, or serum HOMA-IR levels [30],[31].

The investigators of that study hypothesized that a number of variables might account for these conflicting findings, including the varied follow-up time of vitamin D treatment, vitamin D supplement alone or in combination with other micronutrients.

Boucher [13] showed that in a meta-analysis of 28 earlier trials, supplementation was found to have no overall benefits for reducing the risk of developing type 2 diabetes, reducing insulin resistance, or reducing fasting blood sugar. However, subgroup analyses utilizing stratified data discovered substantial drops in insulin resistance in participants achieving a 25(OH)D of >30ng/ml(>75nmol/l) and substantial reduction in fasting blood glucose in participants whose 25(OH)D had been <30 ng/m [32].

When vitamin D was administered to pre-diabetics participants without calcium, subgroup analysis showed that T2DM risk was substantially decreased by 16–18% with dosages of vitamin D >2000 IU/day [13],[32].

Rasouli et al., [33] studying obese and overweight prediabetic persons are randomized to receive daily doses of vitamin D3 4000 IU or a matched placebo for a period of 24 months to determine the impact of vitamin D supplements on insulin sensitivity and secretion in prediabetes and it showed that it didn’t improve b cell function this could be attributed to the low supplementation treatment dose given to those obese prediabetic patients.

Wallace et al. [34] conducted a double-blind study of Vitamin D supplementation has little impact on insulin in the population of people with prediabetes, according to research on how it affects insulin resistance and b cell function.

Our study showed a statistically substantial negative connection between vitamin D change and HOMA-ir change, triglycerides level change and fasting insulin change of P value 0.032,0.020 and 0.002 and with r value -0.332,-0,359 and -0.463 respectively, emphasized by Schleu et al. [35] study

that revealed that HOMA-IR values and VITD levels were inversely correlated and Vigna et al., [17] stated that when BMI > 30 kg/m2 is used as the criterion for obesity. After adjusting for BMI, [25(OH)D] still had a substantial negative correlation with the Homeostatic Model Assessment for Insulin Resistance. Furthermore, [25(OH)D] no longer associated with weight or body fat.

On the contrary, Alsheikh and Almubayadh, [36] in a randomized control clinical experiment found no relation between high levels of vitamin D and insulin resistance.

Ehrampoush et al. [37] study revealed a strong negative relationship between vitamin D values and insulin resistance, fasting plasma glucose. Meta-Analysis and Meta-Regression of Rafiq and Jeppesen, [38] demonstrated a rising negative connection between vitamin D level and insulin resistance in non-diabetic subjects as their BMI rose. The strength of correlation (r=-0.229, CI 95%=-0.322 to -0.131) is the highest in the quartile with a BMI value more than 30.

Our results regarding the connection between vitamin d levels and fasting blood sugar was similar to Alsheikh and Almubayadh [36] study which indicates that although vitamin D administration raises FBG, it has no effect on insulin levels.

In Zhang et al., [28] study in prediabetics without restrictions on BMI, oral vitamin D treatment has been demonstrated to have higher impact in improving FBG and HBA1.

Yu et al. [39] study supported that Contradicting our findings, low blood vitamin D levels elevated the chance of developing prediabetes but did not significantly affect alterations in HBA1C, FBG, or HOMAIR between those with prediabetes managed with vitamin d and those receiving a placebo.

Rajabi-Naeeni et al.,[40] studying the impact of omega-3 and vitamin D co-supplementation on glycemic control and lipid levels in reproductive-aged women with pre-diabetes and hypovitaminosis showed that vitamin D and omega-3 co-supplementation have good impacts on fasting plasma insulin, glucose and HDL-C levels, HOMA-B, waist measurement, and weight in women of fertility age with pre-diabetes and hypovitaminosis.

Regarding lipid profiles, several investigations suggested that dyslipidemia may result from low 25(OH)D levels. In Imga et al., [21] study, with low vitamin D levels exhibited increased LDL-C levels. And after taking vitamin D supplements, both patients who were overweight and those who were obese showed a decrease in LDL-C. Contradicting our results that shows a non-significant reduction in LDL results.

Despite the LDL reductions, no substantial variation was found in HDL-C levels matching our results of the post supplementation HDL values ((mean: 40.976±8.971 vs 41.395±4.907) (P-value: 0.855).

Our study showed a significant decrease in TG level after vitamin D supplementation which was highlighted by the Endocrine Society Guidelines who recommended taking a 50,000 IU vitamin D3 dose once a week for eight weeks [41].

According to the findings of Xue et al., [31] meta-analysis, supplementing with a little amount of vitamin D was sufficient to lower triglyceride values.

Our results showed decrease in TG in the vitamin D group with no substantial variation in HDL and LDL, after taking vitamin D supplements, LDL-c and TG dramatically decreased and in Naharci et al., [42] HDL-c increased significantly.

In a related research, LDL-c and TG rose dramatically whereas TC and HDL-c declined substantially after eating supplements of vitamin D at levels of 300 IU/d for three years [43] and according to Wang et al. [44]**'s** meta-analysis of vitamin D supplementation's impact on lipid profiles Only LDL was substantially altered after the intervention.

More research is required in the future since the findings regarding the impact of vitamin D on lipid profiles are often inconsistent.

The findings imply that vitamin D administration, particularly in individuals who are overweight, may be preventive against potential dyslipidemia and insulin resistance.

Our research has a number of drawbacks. First, we looked at baseline and 3-month assessments of the variables; repeated, long-term observations may be more useful for assessing the outcomes. Second, this research focused on a specific age group and was a randomized controlled trial. Third, we looked at the factors in the population of obese people. The quickie approach is more accurate, however the fat accumulation product and/or the triglyceride/glucose index may be employed as predictors of insulin resistance in clinical practice, thus we chose the HOMA-IR index instead.

CONCLUSIONS

The improvement in vitamin D status in obese participants with vitamin D deficiency was accompanied by a reduction in weight and insulin resistance.

Following vitamin D administration, 25(OH)D levels showed a negative correlation with HOMA-IR, LDL-C, and triglycerides. In insulin resistant pre-diabetic obese people, weight reduction plus vitamin D treatment may work in concert to enhance glucose metabolism. Further To establish the benefits of vitamin D supplementation on insulin resistance and dyslipidemia in obese people, longer and bigger trials are required.

Equations

Homeostatic Model Assessment of Insulin Resistance (HOMA- IR):

Fasting Insulin (μIU/mL) × Fasting Blood Glucose (mg/dL)/405

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Conflicts of interest

"There are no conflicts to declare".

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