The Egyptian Journal of Hospital Medicine (July 2023) Vol. 92, Page 6863- 6869

Correlation between Vitamin D Level and The Degree of Insulin Resistance in Patients With Metabolic Syndrome

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ABSTRACT

Background: Indicators of the metabolic disorder known as metabolic syndrome (MS) include resistance to insulin, poor glucose tolerance, diabetes mellitus (DM), obesity, accumulation of abdominal fat, dyslipidemia, and hypertension.

Objective: For evaluation the relationship between intake of vit D and the degree of insulin resistance in MS patients.

Patients and Methods: A cross-sectional study was done in Benha University and Teaching Hospital's outpatient clinic. Adult patients with metabolic syndrome who were 18 years of age or older who attended to the outpatient clinic were the subjects of this study. **Results:** Our findings demonstrated that vitamin D levels of the diabetic and non-diabetic participants were equivalent, but there was a statistically significant relation between DM and HOMA-IR since diabetic patients had considerably higher levels of HOMA-IR than non-diabetics (P<0.001).

Conclusion: According to our findings, vit D had a substantial negative correlation with HOMA-IR in both the general population and diabetes patients, with a greater vit D level resulting in a lower HOMA-IR level, as well as a significant negative link with BMI and WC.

Keywords: Vit D, Insulin resistance, Metabolic syndrome.

INTRODUCTION

According to the WHO, MS is a pathologic condition characterised by abdominal obesity, resistance to insulin, high blood pressure, and hyperlipidemia. Other names for it include syndrome X and insulin resistance. Various healthcare organisations have slightly different definitions, but they are not significantly different [(1)].

According to current estimates, MS affects thirty percent of the global population and is associated with 2-to-3-fold increased risk of illness and death compared to healthy individuals [(2)].

Uncertainty surrounds the complex pathogenic pathways underlying MS. It is still debatable whether each MS component represents a separate pathology or the symptom of just one pathogenic process. Environment and social variables, such as excessive intake of calories and inactivity, are significant as probable contributing factors because of the vast regional variance in the incidence of MS and the present "catch up" in the developing world. The discovery that the majority of pathways connected to MS include visceral fat as a fundamental trigger emphasises the significance of elevated intake of calories as a significant causal component [(3)].

(VDD), which affects roughly fifty percent of the world's population, affects people of all ages and races [(4)]. Numerous authors have explored the probable connection between vit deficits and metabolic disorders like MS [(5)]. The impact of vit D on MS components has been linked to a number of pathophysiologic mechanisms. One tenable hypothesis is that vit D influences insulin production and sensitivity, two critical MS-related processes. The vit D receptor is expressed by cells in the pancreas, musculoskeletal tissues, and adipose tissue, among other peripheral organs. A vit D shortage can reduce cells' ability to convert pro-insulin into insulin [(6)].

This investigation looked at the relationship between vit D status and the degree of resistance to insulin in MS patients.

PATIENTS AND METHODS

This cross-sectional study was held in the outpatient clinic of Benha University and Teaching Hospital. This study was conducted on adult patients aged 18 or older with metabolic syndrome attending an outpatient clinic as well as inpatients.

Exclusion criteria: Patients with type 1 diabetes, those with parathyroid gland disorders, those with renal or hepatic impairment, those who have a history of cancer, and those who take medications that can affect how responsive the body is to insulin (such as anti-diabetic drugs, glucose-raising agents, antineoplastic and anti-retroviral drugs, adrenal cortical steroids, selective estrogen receptor modulators, parathyroid hormone and its analogues, antiandrogens, and aroma).

Demographics: Demographic data including age, gender, duration of MS medical history (including treatment history), history of smoking and consumption of alcohol and co-morbidities (e.g., cardiac, hepatic or renal pathology).

Clinical examination: Weight in kilogrammes (Kg) and height in centimetres (cm) were measured as part of the anthropometric evaluation. The (WC) was measured at two points: the iliac crest and the lowest rib border. A suitable-sized cuff was used to take the patient's blood pressure after at least five minutes of relaxation and with them sitting upright. After three measurements, the average of the second and third measurements was recorded and used in the study.

Laboratory investigations: FPG levels, Lipid profile: plasma levels of TC, TG, and HDL-C, FPI, and HOMA-IR were all measured. For the determination of

Received: 26/03/2023
Accepted: 23/05/2023

25-hydroxyvitamin D in plasma by high performance liquid chromatography (HPLC), plasma levels of 25(OH)D3 were measured using (HPLC; Immundiagnostik AG, Germany). Five-part differential CBC by CELL-DYN Ruby, Haematology Analyzer (USA) [(7)]. Kidney function test with (Urea, Cr, and Uric Acid) by ARCHITECT Ci4100 Integrated System Instrument (Clinical Chemistry Analyzer and Immunoassay Analyzer) [(8)]. Clinical chemistry analyzer and immunoassay analyzer, ARCHITECT Ci4100 integrated system device, CRP [(9)].

Ethical approval:

The study received permission from Benha University Faculty of Medicine's Ethics Committee (IRB No. MS-1-10-2021). All individuals agreed to participate in the study after being fully informed of its objectives. The entire process of conducting the study adhered to the Helsinki Declaration.

Statistical Analysis

Using SPSS V. 24.0 for Windows, all data were collected, tabulated, and statistically evaluated. The Shapiro Wilk test was employed to determine whether the data distribution was normal. Frequencies and relative percentages were employed to depict qualitative data. Quantitative data were presented as median and interquartile range (IQR) and were compared by Mann-Whitney test. A P-value of 0.05 or less was used to designate significant data.

RESULTS

As shown in Table (**1**, this cross-sectional study included 200 participants (37 males and 163 females) with 48 years as median age. The median BMI of participants was 35.92 kg/m^2. Half of the 200 participants had DM type 2.

Table (1): Demographic data of all the studied participants

		Study participants (n=200)
Age (years)	**Median**	48
	IQR	44 – 54
	Min-Max	18 - 60
BMI (kg/m^2)	**Median**	35.92
	IQR	33.06 – 39.54
	Min-Max	24.69 – 56.19
WC (cm)	**Median**	95
	IQR	90 – 111.5
	Min-Max	85 - 124
Gender	**Male**	37 (18.5%)
	Female	163 (81.5%)
Diagnosis	**No risk factors**	68 (34%)
	DM type 2	100 (50%)
	HTN	18 (9%)
	Hypothyroidism	8 (4%)
	IHD	6 (3%)

IQR: Interquartile range, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance.

According to table 2, the patients in the study had median HOMA-IR levels of 3.65 and median vitamin D levels of 12.8 ng/millilitre.

Table (2): HOMA-IR and vit D evaluation of the studied participants

		Study participants (no=200)
HOMA-IR	**Median**	3.65
	IQR	1.8 – 5.2
Vitamin D (ng/mL)	**Median**	12.8
	IQR	11.6 – 19.15

Median and IQR: non parametric test. IQR: Interquartile range, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance.

As shown in table 3, there was no statistical significance relationship between DM and BMI or sex distribution, but there was a statistically significant link between DM and age and WC because diabetic patients showed significant higher WC than non-diabetics and were older.

Table (3): Relation between demographics and DM type 2

		DM type 2		P value
		Yes (no=100)	**No (no=100)**	
Age (years)	Median	54	44.5	**<0.001***
	IQR	45 – 55	31 – 49.75	
BMI (kg/m^2)	Median	36.21	35.92	0.264
	IQR	33.59 – 39.54	32.87 – 39.06	
WC (cm)	Median	95	95	**0.029***
	IQR	95 – 112	90 - 110	
Sex	Male	21 (21%)	16 (16%)	0.467
	Female	79 (79%)	84 (84%)	

The levels of HOMA-IR in diabetic patients showed higher statistically significant level than in non-diabetic participants, however, the two groups showed similar vit D levels (Table 4).

Table (4): Relation between demographics and DM type 2

		DM type 2		P value
		Yes (n=100)	**No (n=100)**	
HOMA-IR	Median	4.95	2.9	**<0.001***
	IQR	3.2 – 6.6	1.4 – 3.9	
Vit D (ng/mL)	Median	12.8	12.6	0.065
	IQR	12.5 – 25.8	10.8 – 18.4	

Median and IQR: nonparametric test. IQR: Interquartile range, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance.

Vit D level was found to have a significant negative connection with HOMA-IR (rs= -0.602, P<0.001), BMI (rs= -0.335, P<0.001), and WC (rs= -0.373, P<0.001) when 100 diabetic individuals were studied individually (Figures 1-3). But, age and vit D level relation showed no statistical significant difference.

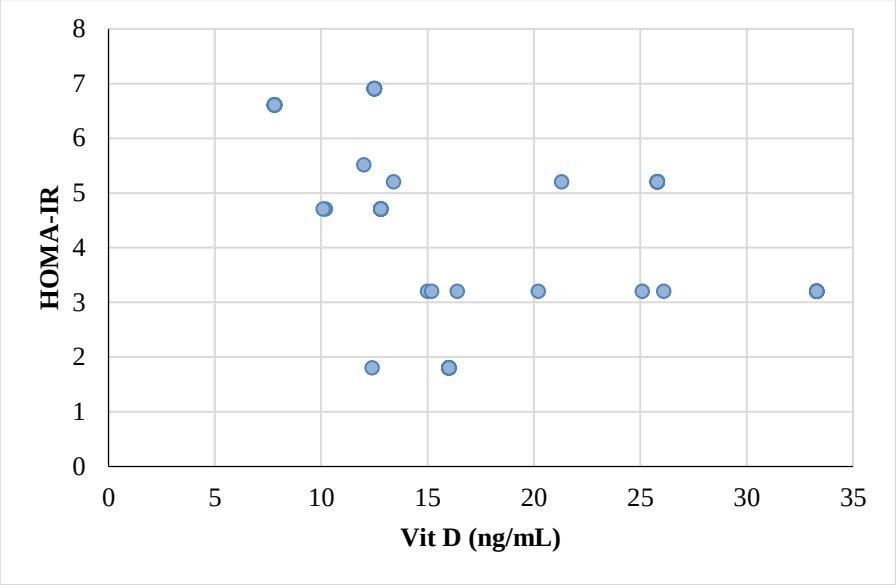

Fig (1): Vitamin D and diabetic patients' HOMA-IR correlation

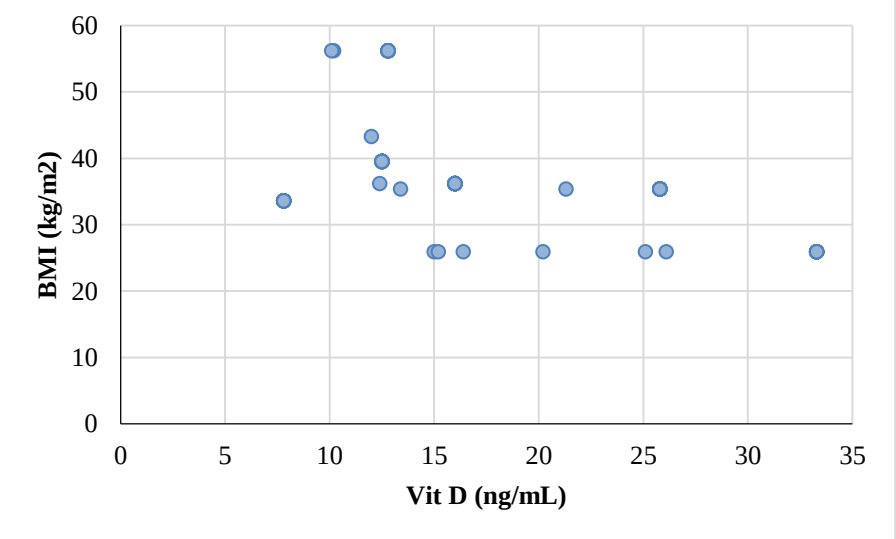

Fig (2): Vitamin D and diabetic patients BMI correlation

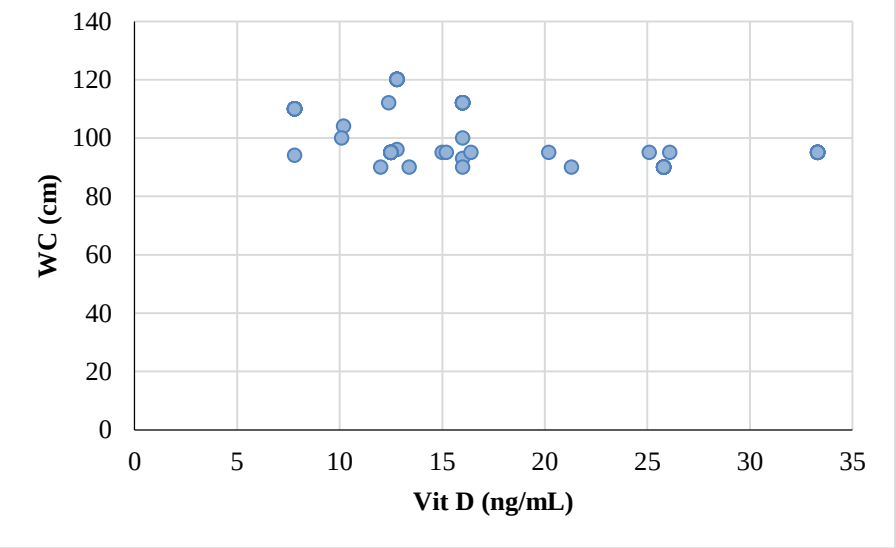

Fig (3): Vitamin D and diabetic patients WC correlation

In non-diabetic patients, there was a substantial positive association between Vit D level and age (rs= 0.421, P<0.001) and there was a significant inverse relationship between Vit D level and WC (rs= -0.366, P<0.001) (Figures 4-6). BMI and vitamin D levels did not exhibit any statistically significant correlation.

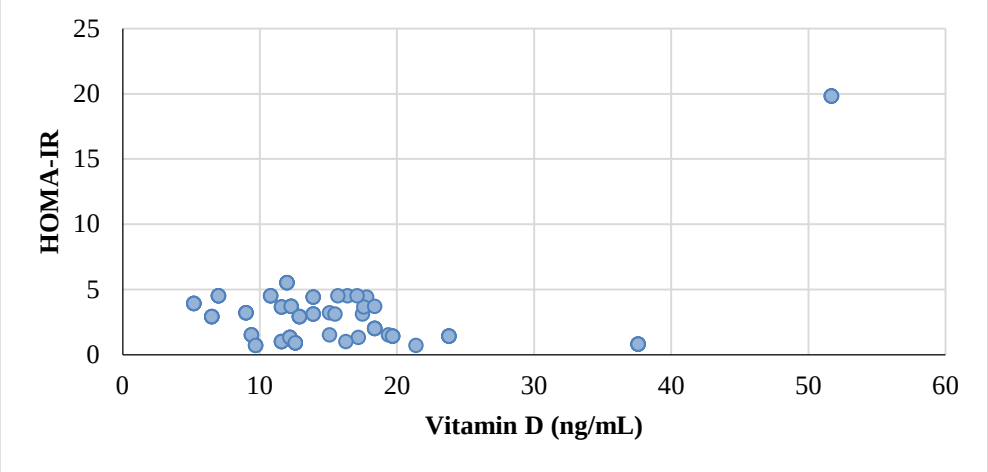

Fig (4): Vit D and HOMA-IR of the non-diabetic participants correlation

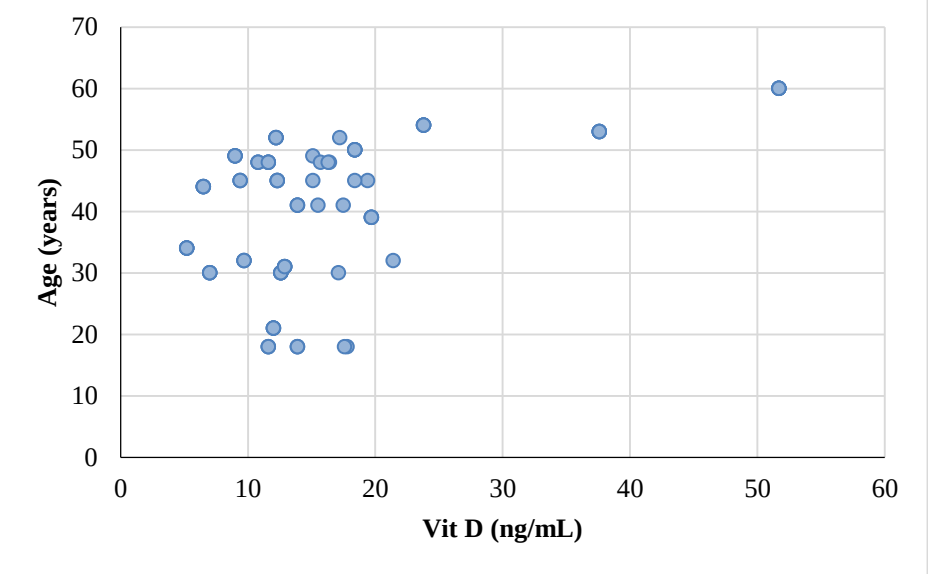

Fig (5): Vit D and non-diabetic participants age correlation.

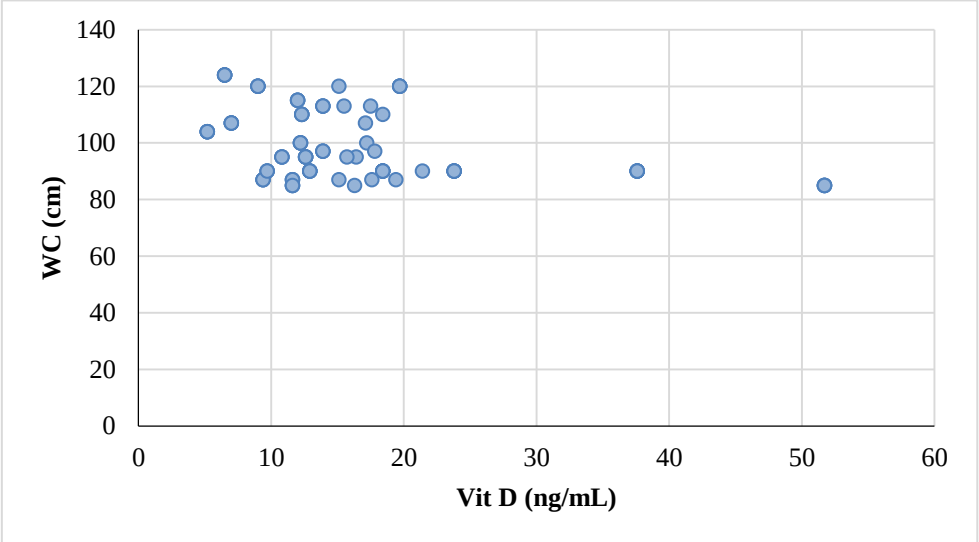

Fig (6): Vit D and non-diabetic participants WC correlation.

DISCUSSION

Many earlier research have suggested a link between low vit D levels and MS and reduced insulin secretion, but other investigations have not supported this finding [10].

The results of our study revealed that the median age of the 200 participants —163 women and 37 men— was 48 years old, with an interquartile range (IQR) of 44 to 54 yrs. The participants' median waist circumference was 95 cm, with an IQR of 90 to 111.5 centimeters, and their median BMI was 35.92 kilograms/m^2, with an IQR of 33.06 to 39.54 kilograms/m^2.

Our study found that half of the 200 participants had DM type 2, along with nine percent hypertension, four percents hypothyroidism, and three percent IHD. The study's participants had median levels of vit D of 12.8 ng/millilitre and HOMA-IR of 3.65, respectively, with interquartile ranges (IQR) of 11.6 to 19.15 ng/millilitre and 1.8 to 5.2, respectively.

The study by **Talaei *et al.*** [11] found that the mean HOMA-IR level was 3.573.18 and vit D level mean was 43.03±19.28 ng/millilitre, which was in agreement with this. After receiving vit D treatment for 8 weeks, they discovered that the mean of the HOMA IR changed to 2.89±3.28. In England, where diabetes incidence was rising with age, a similar trend was also seen. With men (15.7 percent) and women (10.4 percent), age range of 65 to 74 years has the highest diabetic incidence [12].

According to a study by **Suastika *et al.*** [13] on the people of Bali, the frequency of IFG and T2DM was around two times higher in the elderly than in the younger age group. IFG and T2DM have a tendency to occur more frequently as we become older. In 2000, the prevalence of DM and IFG among older Chinese people in Taiwan was 16.9 percent and 25.5 percent, respectively, according to research by **Peng *et al.*** [14] over a 5-year follow-up, the cumulative prevalence of DM and IFG was 23.7 percent and 27.9 percent, respectively. 6.8 percent of people with diabetes with recent onset had the disease in the prior five years. Overt proteinuria, IFG, and high total cholesterol were independent risk factors for newly diagnosed DM [14].

Because diabetic patients had significantly higher HOMA-IR readings than non-diabetics (P<0.001), our results showed a statistically significant link between DM and HOMA-IR. While vit D levels were comparable in diabetics and non-diabetics.

This was in line with earlier studies, which showed that Saudi T2DM patients had blood insulin levels that were much greater than those of healthy controls [15]. Additionally, **Khan *et al.*** [16] found that HOMA-IR was significantly greater in T2DM patients compared to controls, which was supported by earlier research on Saudi T2DM patients [17]. In the **Khan *et al.*** [16] study, severe IR (HOMA-IR > 10) affected 34.04 percent of DM and 5.216 percent of non-diabetic controls. In another study of 107 T2DM patients and 101 controls, an IR frequency of 46.7 percent in diabetic patients and 5.9 percent in controls was discovered [17].

A statistically minor variation in vitamin D levels between MS patients and seemingly healthy people without MS was discovered in **Shamy *et al.*'s** [18] investigation. This outcome was consistent with research by **Rudvan *et al.*** [19], conducted on 191 MS patients, which discovered no statistically significant difference in vit D levels between MS patients and controls.

Vitamin D had a significant negative connection with HOMA-IR (rs= -0.179, P=0.001), BMI (rs= -0.15, P=0.034), and WC (rs= -0.377, P<0.001) in the current investigation, with the greater the vit D level, the lower was the HOMA-IR degree. On the other hand, age and vit D levels significantly correlated positively (rs=0.346, P0.001). Vit D level was found to have a significant negative connection with HOMA-IR (rs= -0.602, P<0.001), BMI (rs= -0.335, P<0.001), and WC (rs= -0.373, P<0.001) when 100 diabetic individuals were studied individually. However, age and vit D levels correlations showed no statistically significant difference.

Type 2 DM, dyslipidemia, and CVD increased risk have all been associated to insulin resistance. Research has examined the relationships between MS onset, insulin resistance, and vit D deficiency. The majority of past research's findings supported the link between vit D deficiency and the emergence of insulin resistance and dyslipidemia, despite certain results from those studies being inconclusive [19].

Numerous studies revealed that vit D insufficiency was inversely associated to HOMA-IR [18-20], and some studies revealed that vit D treatment may assist patients with T2DM improve their insulin resistance and moderate their glycemic response [21-23].

Additionally, especially in some ethnic groups, VDR polymorphisms are linked to insulin resistance and aberrant glucose metabolism [22]. Additionally, the **Gannagé-Yared *et al.*** [23] study demonstrates a substantial negative association between vit D levels and HOMA IR in the general population.

Additionally, **Szymczak-Pajor *et al.*** [24] demonstrated that serum vit D levels correlated with the values of metabolic parameters such as BMI, HOMA-IR, TG, HDL, LDL, TC, and HbA1c, indicating that hypovitaminosis D favours the development of insulin resistance.

Currently, studies have established a direct link between vit D3 and resistance to insulin. Because of this, maintaining higher vit D3 levels is important to prevent resistance to insulin within a particular range, and this finding provides a therapeutic treatment prescription [25].

Talaei *et al.* [11] showed glucose homeostasis and vit D supplementation effects. The findings

demonstrated that vit D treatment in individuals with T2DM significantly reduced blood FPG, insulin, and HOMA-IR.

HOMA-IR dramatically decreased after vit D supplementation, although **Witham *et al.*** [26] found that vit D intake had no effect on either resistance to insulin or HbA1c. Vit D treatment for two years enhanced HOMA-IR, although **Nagpal *et al.*** [27] found that vit D intake had no effect on the average degree of sensitivity of insulin.

One of the mechanisms for vit D effects is that it increases insulin receptor gene transcription while suppressing the renin gene. Other mechanisms include the presence of vit D receptors on pancreatic cells, the expression of vit D activating 1 hydroxylase in pancreatic cells, the presence of a vitamin D response element in the insulin gene, and the presence of a vit D receptor in skeletal muscle. The following has been proposed as a possible target for diabetes treatment: lowering the renin levels that hyperglycemia causes in cells in the pancreas and preventing the activity of renin-angiotensin [28].

Due to its anti-inflammatory effects, effects on the metabolism of calcium and phosphorus, and alteration of the insulin receptor gene, vit D may help prevent diabetes. It seems that vit D raises the calcium levels within cells, which then makes it easier for glucose to enter muscle. Nuclear PPAR (Peroxisome proliferative activated receptor), which is crucial for insulin sensitivity, is also under the influence of vit D. Vit D deficiency is linked to an increase in inflammation. ILs, IL-1, IL-6, TNF-a, and other proinflammatory cytokines linked to insulin resistance are expressed less when vit D is present, and NF-Kb activity is similarly downregulated [29].

Regarding WC, which is a cornerstone in the diagnosis of MS, a study obtained no significant correlation between vitamin D level and WC [30], which is in disagreement with **Shamy *et al.*** [18] study. Another study done by **Kavarić *et al.*** [31] demonstrated a significant and inverse relation between vitamin D level and WC. Thus, this field needs more future studies on a large number of patients to make this correlation, if it exists, clearer and more reasonable.

In non-diabetic patients, our results showed a strong positive correlation between age and level of vit D ($rs= 0.421$, $P<0.001$). While there was a weak negative connection ($rs= -0.366$, $P<0.001$) between vitamin D levels and WC. The levels of vitamin D and HOMA-IR and BMI did not show any statistically significant association.

In accordance with our findings, according to **AlHewishel *et al.*** [32] diabetes patients had a higher rate of vit D deficiency than non-diabetic patients. They also discovered that the prevalence of vit D insufficiency varied by age group. Compared to groups of individuals aged twenty-one to forty and between the ages of forty and sixty, the prevalence of vit D deficiency was lower in the group of adults over the age of 60. This could be explained by the idea that these people might regularly take vit D as a prophylactic precaution in addition to osteoporosis treatment. Adequate vit D levels may aid in maintaining bone health and preventing osteoporosis in older individuals, non-ambulatory seniors who find it challenging to exercise, postmenopausal women, and patients undergoing long-term steroid therapy.

Another study on 126 healthy individuals discovered that low vit D levels had a detrimental effect on pancreatic beta-cell activity and that there was a clear correlation between 25(OH)D levels and insulin sensitivity [33]. A 20-year follow-up study of 4,843 patients with T2DM demonstrated a link between vitamin D intake and a decreased incidence of the disease [34].

CONCLUSION

According to our findings, vitamin D had a substantial negative correlation with HOMA-IR in both the general population and diabetes patients, with a greater vitamin D level resulting in a lower HOMA-IR level, as well as a significant negative link with BMI and WC.

RECOMMENDATIONS

Treatment for type 2 diabetes should include vitamin D supplements.

Sponsoring financially: Nil.
Competing interests: Nil.

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