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Vitamin D and Insulin Resistance in Metabolic Syndrome

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Authors' contributions

This work was carried out in collaboration between both authors. Author MAM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author EME managed the analyses of the study and managed the literature searches. Both authors read and approved the final manuscript.

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ABSTRACT

Poor vitamin D status is frequently linked with nearly all elements of the metabolic syndrome. There is insufficient evidence of beneficial effect to recommend vitamin D supplementation as a means of improving insulin resistance. The aim of this study was to determine the relation between vitamin D deficiency and insulin resistance in patients with metabolic syndrome.

Materials and Methods: Ninety patients with metabolic syndrome received 200,000 IU vitamin D intramuscularly every 4 weeks for 12 weeks. Serum 25-hydroxy vitamin D [25(OH)D], fasting blood sugar, Hb A1c, homeostasis model assessment of insulin resistance(HOMA IR), serum lipid profiles anthropometric factors and blood pressure were assessed before and after intervention.

Results: After intervention, Serum 25-hydroxy vitamin D [25(OH)D] concentration increased in all subjects (14.5 ± 2.2 vs. 32 ± 5.5 (P .0001)]. There was a significant decrease of HOMA-IR (3.05 ± 0.34 vs 2.08 ± .25(P=0.003) in patients with vitamin D deficiency before supplementation.

In conclusion vitamin D supplementation improve IR in patients with metabolic syndrome with vit D deficiency. So, vitamin D supplementation based on baseline [25(OH)D] is recommended.

Keywords: Insulin resistance; vitamin D; metabolic syndrome; HOMA IR.

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1. INTRODUCTION

Vitamin D, in addition to its role in calcium and bone metabolism, has pleiotrophic effects in many cell types in many life forms. These include a potential role in the actions of insulin and development of obesity. Thus, not surprisingly hypovitaminosis D has been linked with hypertension, atherogenic dyslipidaemia and increased CVD risk [1]. Low skin exposure to sunlight, low dietary intake of vitamin D, high body mass index (BMI), and genetic predispositions may contribute to the occurrence of Hypovitaminosis D [2]. Measurement of Serum 25-OH-vitamin D is the generally accepted tool to assess vitamin D status [2]. Although suboptimal vitamin D levels almost always asymptomatic, population based screening for vitamin D deficiency is not recommended, but test for vitamin D deficiency in patients with high-risk conditions such as osteoporosis, chronic kidney disease, hyperparathyroidism, or a malabsorption syndrome is recommended [3].

Obesity is one of the leading global health risk factors for morbidity and mortality, accounting for 4.8% of deaths worldwide [4]. Insulin resistance (IR) indicates decreased response to insulin-mediated cellular actions [5] with subsequent reduction in tissue glucose uptake and impairment in insulin suppressive effect on hepatic glucose output [6], in addition to its effect on protein and lipid metabolism and on vascular endothelial function and genes expression [7]. IR is the most common metabolic alteration related to obesity [8], representing a significant link between obesity and other metabolic risks such as cardiovascular diseases [9].

HOMA is a vastly used clinical and epidemiological tool to assess β-cell function and insulin resistance [10]. Although, if used appropriately, it closely mirrors the glucose clamp technique in the assessment of insulin sensitivity [11], it only shows what is occurring with glucose homeostasis in the fasting state [10]. There is conflicting data about the role of vitamin D supplementation on HOM -IR as a reflection of insulin resistance.

1.1 Aim of the Study

The aim of this study was to determine the effect of vitamin D supplementation on insulin resistance in patients with metabolic syndrome.

2. MATERIALS AND METHODS

A prospective study was conducted in Alfayum University on 90 patients with metabolic syndrome were recruited from the outpatient clinic of internal medicine during the period from January 2015 to January 2016, with the approval of the local ethics committee. Written informed consent was obtained from the participants.

Inclusion criteria for participants with metabolic syndrome are: the presence of any three of the following five traits [12]:

- Abdominal obesity, defined as a waist circumference in men ≥102 cm (40 in) and in women ≥88 cm (35 in)
- Serum triglycerides ≥150 mg/dL
- Serum HDL cholesterol <40 mg/dL in men and <50 mg/dL in women
- Blood pressure ≥130/85 mmHg
- Fasting plasma glucose (FPG) ≥100 mg/dL

Patients were excluded if they were pregnant, lactating, taking any glucose lowering medications, using any anti-hypertensive or lipid lowering medications or had chronic liver or renal disease.

BMI was calculated as weight/height^2 (kg/m^2). Resting systolic blood pressure (SBP) and diastolic BP (DBP) were measured while the participants were seated using a standard sphygmomanometer with an appropriate size cuff. Lipid profile (total cholesterol, triglycerides, HDL-C and LDL-C) were assessed. Fasting morning blood was drawn for measurement of glucose, insulin, calcium, phosphorus, HbA1c, and 25-hydroxyvitamin D [25(OH)D] and IR was assessed on the basis of the homeostasis model assessment of IR (HOMA-IR), using the following formulae: HOMA-IR = [fasting insulin (mU/l) × fasting glucose (mg/l)/405]. Patients were assigned to consume vitamin D supplements (200,000 IU) by intramuscular injection every 4 weeks for 12 weeks. Follow up of serum calcium, phosphorus levels were done regularly. The level of serum 25-hydroxy vitamin D [25(OH)D] was measured at the beginning and end of the study. Plasma total [25(OH)D] concentrations were measured in duplicates by using IDS enzyme immunoassay (IDS-EIA, Immunodiagnostic Systems INC., Scottsdale, AZ). We used the cut-off value for deficiency of [25(OH)D] levels below

20 ng/ml following the Endocrine Society Clinical Practice guidelines [13].

2.1 Statistical Analysis

All collected data were expressed as mean± SD and analyzed by using SPSS version 12 using the following tests: Student t test, Chi-square test, P > 0.05 was considered no significant, P < 0.05 was considered significant P <0.001 was considered highly significant.

3. RESULTS

Of the 90 obese patients included in the study; 40(44.4%) were males and 50(55.6%) were females, with a mean age of 55.6± 8 years, 20 patients of the studied 90 patients (22.22%) were vitamin D deficient (25-hydroxyvitamin D <20 ng/ml).

Comparing with the baseline, plasma [25(OH)D] level significantly increased in the all studied subjects who received vitamin D (14.5 ± 2.2 vs. 32 ± 5.5 (P .001), however, there was no significant effect on HOMA –IR nor TG (as shown in Table 1). In vitamin D deficient patient HOMA-IR showed a decrement pattern [3.05 ± 0.34 vs 2.08±0.25 (P=0.003)], in addition to a significant change in TG concentration (p < 0.04) after 12 weeks of vitamin D supplementation, as shown in Table 2.

Also, there was statistically significant decrease in HBA1C levels after vitamin D supplementation for 12 w in all participants [5.7 ± 0.08 vs 5.6 ± 0.13 (P=0.01)], in addition to patients with vitamin D deficiency [5.8 ± 0.12 vs 5.6 ± 0.2 (P=0.03)] (as shown in Tables 1 and 2).

4. DISCUSSION

Our analyses revealed that vitamin D deficient patients with low serum [25(OH)D] concentrations at baseline and increases in serum [25(OH)D] concentrations during follow up contribute to decrement pattern of HOMA-IR.

Kayeniyil et al. [14] Gagnon et al. [15], Skaaby [16] observations were consistent with our observation of the effect on baseline serum [25(OH)D] on metabolic syndrome as they reported low probability for onset of metabolic syndrome with increase in baseline [25(OH)D] concentrations.

Table 1. Different variables of all participants before and after vitamin D supplementation

	Before	After	P value
Vit D (ng/ml)	17.2±1.2	39.5±7.2	0.001
Weight (kg)	88.7±20.2	77.1 ± 17.5	0.01
Waist (cm)	101.3 ± 18.2	100.2 ± 16.8	0.72
BMI	34.7 ± 2.7	34.4 ±3.2	0.31
SBP (mm HG)	136±19.7	133±18.2	0.62
DBP (MM hg)	85.3 ± 7.2	84 ± 7.7	0.75
HBA1C	5.7 ± 0.08	5.6 ± 0.13	0.01
T Cholesteol (mg/ dl)	188 ± 22.7	187.5 ± 20.2	0.81
TG (mg/dl)	179.2 ± 52	164.3 ± 20	0.12
HOMA IR	2.9 ±0.49	2.7 ± 0.36	0.5

Table 2. Different variables of patients with vitamin D deficiency before and after vitamin D supplementation

	Before	After	P value
Vit D (ng/ml)	14.5± 2.2	32.00± 5.2	0.001
Weight (Kg)	88.2± 41	87.5±22.6	0.16
Waist (cm)	101.2± 23.5	99.8 ± 16.8	0.72
BMI	34.7 ± 2.7	34.4 ±3.2	0. ±42
SBP (mm HG)	132±11.2	130±17.2	0.42
DBP (mm HG)	83.3±7.8	82.2±6.9	0.72
HBA1C	5.8 ± 0.12	5.6 ± 0.2	0.03
T Cholesterol (mg/dl)	192±19.2	190±18.3	0.62
TG (mg/ dl)	194±38	164±13	0.04
HOMA IR	3.05 ± 0.34	2.68 ± 2.5	0.03

Moreover, Belenchia et al. [17] and Kelishadi et al. [18] concluded that the correction of poor vitamin D status may be effective in treatment of obesity and its associated insulin resistance.

Some of the proposed mechanisms for vitamin D's role in improving insulin resistance in obesity include inflammation reduction [19] and improving peripheral and hepatic uptake of glucose, [20] in addition, vitamin D modulates nuclear peroxisome proliferative activated receptor (PPAR) which has a key factor in the IR [21].

In contradiction to our results; Carrillo E et al. [22] found that vitamin D supplementation in adults induced an early improvement in peak power, and elevated vitamin D status was associated with reduced waist-to-hip ratio inspite of insignificant effect on HOMA-IR.

Moreover, Mousa, et al. [23] Harris, et al. [24] Wamberg, et al. [25] Salehpour, et al. [26] and Beilfuss, et al. [27] concluded that neither measures of insulin resistance, secretion nor glycaemic indices were influenced by vitamin D supplementation. This provides evidence that vitamin D supplementation has no significant effect on glucose and insulin metabolism in overweight and obese individuals.

In addition, two meta-analyses [28,29] reported nonsignificant effect of vitamin D supplementation on IR.

In line with these results, we observed statistically significant decrease in HBA1C levels after vitamin D supplementation for 12 weeks in all participants, in addition to patients with vitamin D deficiency. These results come in agreement with the meta-analysis done by Poolsup et al. [29] who confirmed an improvement in HbA1c levels after vitamin D supplementation in pre-diabetics. On the other hand, another meta-analysis [30] could not confirm this effect but in diabetic patients.

These conflicting results may be explained by the variability in the analytic approach, follow up time, consideration of confounders, and baseline serum [25(OH)D] concentrations.

Our study also revealed improvement in triglyceride concentrations after vitamin D supplementation in vitamin D deficient patients only, a finding which was not present on comparing all the studied subjects after vitamin D supplementation.

These results are in agree with Ford et al. [31] Saedisomeolia et al. [32] and Chaudhuri et al [33] who reported a negative correlation between serum levels of [25(OH)D] and triglycerides levels in patients with metabolic syndrome and type 2 diabetes.

Suggested mechanisms include positive effect of vitamin D on serum calcium with subsequent reduction of hepatic triglyceride production [34], reduction in parathyroid hormone level with increase in triglyceride tissue uptake [35], upregulation of VLDL cholesterol gene receptors [33] and reduction of insulin resistance via reduction of pro-inflammatory cytokines [36].

On contrary, Ponda et al. [37] Saeidlou et al. [38] Rusconi et al. [39] and Andersen et al. [40] could not confirm any correlation between vitamin D supplementation and improvement of triglyceride levels neither in obese children nor in adults.

5. CONCLUSION AND RECOMMENDATIONS

Vitamin D supplementation improves IR in patients with metabolic syndrome with vit D deficiency. So, vitamin D supplementation based on low baseline [25(OH)D] is recommended.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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