

## Original Article

# Vitamin D Deficiency as a Risk Factor for Metabolic Syndrome: Insights from a Case-Control Study

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Received: 14/11/2024 | Accepted: 23/11/2024 | Published: 11/12/24 | DOI: <https://doi.org/10.26719/LJMR.18.2.11>

## ABSTRACT

**Purpose:** Vitamin D deficiency disproportionately affects women, posing significant health concerns because of its pivotal role in bone and tooth health and immunity as well as its potential protective effects against certain cancers. Aim: This study investigates the disproportionate impact of vitamin D deficiency on women's health, with a specific focus on metabolic syndrome.

**Methods:** This case-control study examines the correlation between vitamin D levels and various metabolic parameters such as waist circumference, blood pressure, fasting glucose, and lipid profiles. Blood samples were collected to measure serum vitamin D levels, and participants were assessed for components of metabolic syndrome conducted at Misurata Medical Center. A sample of 132 participants aged 18-60 years, including 71 individuals diagnosed with metabolic syndrome and 61 healthy controls with adequate vitamin D levels was used in this study.

**Results:** The study found that 69.01% of women with metabolic syndrome exhibited severe vitamin D deficiency, while 22.53% showed insufficient levels. A significant negative correlation ( $r = -0.871^{**}$ ,  $p < 0.01$ ) was observed between vitamin D deficiency and insulin resistance. Moreover, a positive association ( $r = 0.796^{**}$ ,  $p < 0.014$ ) was detected between vitamin D deficiency and high-density lipoprotein (HDL) levels, while a negative correlation ( $r = -0.769^{**}$ ,  $p < 0.017$ ) was found with triglycerides and FBS ( $r = -0.274^{**}$ ,  $p < 0.018$ ). Among the healthy controls, only 6.81% exhibited metabolic syndrome indicators.

**Conclusions:** Vitamin D deficiency significantly increased metabolic syndrome indicators in the group with the condition, while these indicators remained stable in the control group. This highlights the association between low vitamin D levels and the development of metabolic syndrome. Most participants had severe deficiency, which negatively correlated with insulin resistance and weight, and positively with HDL levels. This emphasizes the need for targeted interventions to address vitamin D deficiency, particularly among women at risk of metabolic syndrome.

**Keywords:** Vitamin D deficiency, metabolic syndrome, women's health, insulin resistance, high-density lipoprotein, triglyceride.

### How to cite this article:

Elaswdi HA, Elbbakush RM, Elbahloul MA, Mustafa AB, Elgenaidi AR, Hamad SS. Vitamin D deficiency as a risk factor for metabolic syndrome: Insights from a case-control study. *Libyan J Med Res.* 2024;18:65-72.

## INTRODUCTION

Metabolic syndrome is a complex disorder characterized by central obesity, insulin resistance, dyslipidemia, and hypertension, which collectively increase the risk of cardiovascular diseases and type diabetes presents a significant health challenge in Arab populations.<sup>1,2</sup> Key diagnostic criteria include fasting blood glucose levels  $\geq 100$  mg/dl or insulin resistance; HDL cholesterol levels  $< 40$  mg/dl for men and  $< 50$  mg/dl for women; triglyceride levels  $\geq 150$  mg/dl; blood pressure  $\geq 85/130$  mmHg; and waist circumference  $> 95$  cm for men and  $> 80$  cm for women.<sup>3</sup> The prevalence of metabolic syndrome is notably high in Arab countries, with obesity being a significant contributing factor. In these nations, obesity rates exceed 16%, with Libya ranking 16th globally in prevalence.<sup>4,5</sup> The rising incidence of metabolic syndrome, particularly among young individuals and females, necessitates urgent public health interventions to address these disorders in the region.<sup>6</sup>

Globally, metabolic syndrome is prevalent among women, especially in the Middle East. The components of this syndrome increase the risk of cardiovascular diseases. Vitamin D is critical for various bodily functions, affecting organs such as the kidneys and heart. Its deficiency is linked to a heightened risk of osteoporosis and metabolic disorders. In a study conducted in Misurata, Libya, the prevalence of metabolic syndrome was found to be 12.5% among women aged 18 to 60 years. The study also found that 65% of these women had vitamin D deficiency. This finding is significant as it highlights the need for comprehensive strategies to address these issues in Arab populations and beyond.<sup>13</sup>

Vitamin D deficiency is a significant factor influencing metabolic syndrome, playing a critical

role in insulin resistance and glucose metabolism dysregulation.<sup>14</sup> Low vitamin D levels are associated with an increased risk of metabolic syndrome, characterized by elevated blood pressure, abnormal cholesterol levels, excess abdominal fat, and high blood sugar.<sup>15</sup> The prevalence of diabetes has quadrupled since 1980, with over 500 million cases reported in 2016.<sup>14</sup> Studies indicate a strong correlation between vitamin D deficiency and insulin resistance, emphasizing the importance of managing vitamin D levels.<sup>16</sup> A study found that vitamin D supplementation for over three months reduced HbA1c levels in individuals with type 2 diabetes mellitus.<sup>17</sup> Understanding vitamin D's role in metabolic pathways may enhance therapeutic strategies, making further research essential.

## MATERIALS AND METHODS

### Study Design, Site and Period

The case-control study involved collecting blood samples to measure serum vitamin D levels and assessing participants for metabolic syndrome components as per IDF criteria during their regular follow up into therapeutic Nutrition Clinic at MMC from July to September 2023.

### Sample of Study

The study followed the ethical standards set by the Libyan Academy of Graduate Studies. A total of 132 participants aged 18 to 60 years were randomly selected from the nutrition clinic at Misurata Medical Centre during their regular followups. Eligibility was determined for individuals diagnosed with metabolic syndrome who were residing in Misurata. Participants were then divided into two groups: 71 patients diagnosed with metabolic syndrome and 61 healthy controls with adequate vitamin D levels. This division allowed for a comparative analysis of the impact of vitamin D deficiency on metabolic syndrome indicators.

### Ethical Consideration

Data were collected from patients using a structured questionnaire, and blood samples were obtained following the receipt of informed consent from the participants. This approach ensured the ethical treatment of subjects and adherence to research protocols.

### ***Data Collection Procedures***

Data collection was conducted from July to September 2023. Each patient underwent measurements for height, weight, and blood pressure after a 15-minute resting period. Waist circumference was recorded in centimeters, and Body Mass Index (BMI) was calculated. Additionally, fasting blood glucose, HDL cholesterol, and triglyceride levels were assessed. Comprehensive patient data, including age, occupation, marital status, parity, and medical history, were obtained through a structured questionnaire. Insulin resistance was evaluated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), which involved the measurement of serum insulin levels.

### ***Blood Samples Collection and Analysis***

Blood samples were collected following a 12-hour fasting period using a sterile 10 ml needle. A total of 8 ml was drawn into two clot-free tubes, adhering to standard protocols for blood collection to minimize contamination and ensure sample integrity. Tubes were labeled appropriately to avoid misidentification.

### ***Transportation of Samples***

Samples were transported to the laboratory under controlled conditions, ensuring they were kept at room temperature or refrigerated, depending on the specific analysis requirements. Transport time was minimized to reduce the risk of degradation or alteration of analysis.

### ***Assessment of Insulin Resistance***

Insulin resistance was assessed via the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) method. Insulin levels were quantified using the Cobas e411 analyzer, which employs Electrochemiluminescence technology (ECL 15D0-01). Fasting blood glucose (FBS) values were determined using the Cobas Integra 400 plus analyzer from Rosh Germany, utilizing Enzyme and Substrate Absorbance photometry. The HOMA-IR value was calculated by multiplying the FBS result by the insulin result and dividing by 405. Samples were centrifuged in plastic tubes without anticoagulants for 5 minutes at 3000 revolutions per minute, and 500 microliters of serum were extracted for analysis.

### ***Lipid Level Measurements***

For the measurement of lipid levels, including triglycerides, HDL, and LDL, the Rosh-Germany Cobas Integra 400 plus analyzer was utilized, also employing Enzyme and Substrate Absorbance photometry principles. Samples were placed in clot-free tubes, and serum was obtained through centrifugation for 5 minutes at 3000 revolutions per minute, with 500 microliters of serum withdrawn for analysis. All procedures adhered to international standards for laboratory analysis, ensuring accuracy and reliability of results.

### ***Analysis of Data***

To perform calculations for statistical analysis, SPSS Statistical Version 24 and Graphs were used. Descriptive statistical methods: represented in the Frequency and Percent as well as Pie Chart. Pearson Correlation was used to study the relationship between variables. The relationship between two variables is significant if P-value is less than 0.05. Chi square was used to assess the variation between variables.

## **RESULTS**

Participants included 71 individuals diagnosed with metabolic syndrome, representing 55.08% of the sample, and 61 healthy controls with adequate vitamin D levels. Among the healthy controls, only 6.81% exhibited metabolic syndrome indicators. Participants had an average age of 35.14 years. Most were married (71.83%), and about 53.51% had three children. Regarding health conditions, 29.57% experienced high blood pressure, and 46.47% had fasting blood sugar levels over 100 mg/dl. Additionally, 63.38% had triglyceride levels above 150 mg/dl, and 77.46% had low HDL levels. The study revealed that 69.01% had severe vitamin D deficiency (<20 ng/dl), 22.53% had insufficient levels (20-30 ng/dl), and only 8.45% had adequate levels ( $\geq 30$  ng/dl).

A significant variation ( $p=0.014$ ) of vitamin D between among all participants, the average Vitamin D level for all cases was  $17.7458 \pm 7.292$ , this is rejection of the null hypothesis and acceptance of the alternative hypothesis regarding the suggestion of a prevalence of Vitamin D deficiency among those with insulin resistance syndrome.

**Table 1.** Displays the mean and standard deviation.

	FBS		TG		HDL		LDL	
	Case	Control	Case	Control	Case	Control	Case	Control
<b>Mean</b>	105.251	88.907	155.056	123.943	47.087	55.008	103.180	105.325
<b>N</b>	71	61	71	61	71	61	71	61
<b>SD</b>	33.3758	10.2815	47.6824	46.8404	14.8968	7.3217	30.8221	7.3217

**Table 2.** Displays the mean, standard deviation and level of vitamin D in sample.

Parameter	Status	N	Mean	SD
Vitamin D	Good	10	17.7458	7.29222
	Insufficient	12	39	2.19
	Deficiency	49		
				<b>Maximum/mean</b>
Control	Sufficient	61	79/ 39.9302	32.4/ 9.93027

**Table 3.** Displays the chi-square test and *P*-value.

Pearson Chi square	P value
<sup>a</sup> 138.114	0.0014

The study reveals a prevalence of Vitamin D deficiency among patients with Insulin Resistance Syndrome, totaling 71 individuals included in the study. Among these patients, 49 cases suffer from severe deficiency of Vitamin D, representing 69.01% of the total, while 16 cases have insufficient levels of Vitamin D, accounting for 22.53% of the total. Only 6 individuals have adequate levels of Vitamin D, representing just 8.45% of the total, indicating a widespread deficiency of Vitamin D among these patients. Additionally, Figure 1 illustrates the results of the Vitamin D analysis compared across different age in case groups.

In the study cohort, 67.6% of individuals exhibited had insulin resistance. Additionally, 69.01% of the subjects were found to have a deficiency in Vitamin D.

Notably, individuals with Vitamin D deficiency displayed heightened levels of insulin resistance. The analysis revealed a robust negative correlation between Vitamin D levels and insulin resistance, as demonstrated by the Pearson correlation coefficient ( $r = 0.871^{**}$ , significant at  $p < 0.01$ ).

Moreover, the Spearman and Kendall correlation coefficients were employed, yielding a correlation coefficient of  $0.815^{**}$  with statistical significance ( $p < 0.01$ ). This signifies a compelling inverse association between Vitamin D deficiency and insulin resistance. The prevalence of insulin resistance exceeded 2.5% was observed in 84.5% of the study population, with 57.7% exhibiting high insulin resistance levels surpassing 3%.

In conclusion, the study underscores the significant inverse relationship between Vitamin D status and insulin resistance levels, supporting the rejection of the null hypothesis in favor of the alternative hypothesis. Pearson correlation coefficient indicated that the relationship between

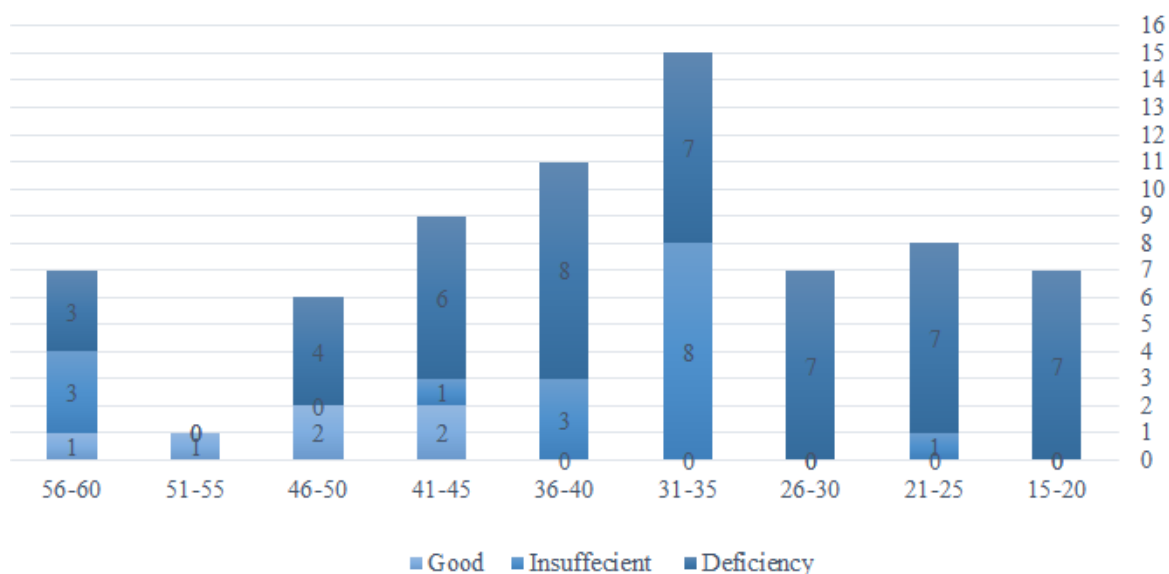


Fig 1. Illustrates the results of the Vitamin D analysis compared across different age groups.

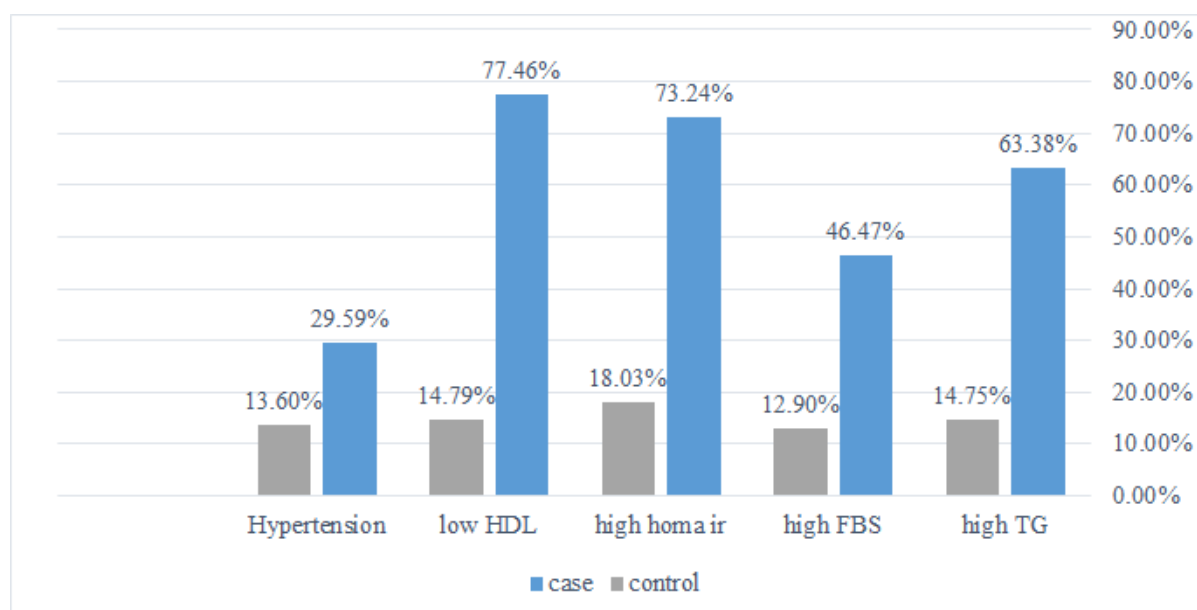


Fig 2. Illustrates the incidence rates of elevated triglycerides, fasting glucose, insulin resistance, reduced HDL, and hypertension.

Vitamin D levels and triglycerides coefficient of  $-0.769^{**}$  was significance value ( $p < 0.017$ ). This underscores a robust inverse association between the two variables. Additionally, employing the Pearson correlation coefficient between Vitamin D levels and HDL cholesterol revealed a coefficient of  $0.796^{**}$  with a significance value of  $p < 0.017$ , surpassing the threshold of 0.01 for statistical significance, thereby confirming a strong positive correlation between the variables.

The analysis demonstrates a significant inverse correlation between Vitamin D levels and triglycerides, as well as a strong positive correlation ( $r = 0.796^{**}$ ) between Vitamin D levels and HDL cholesterol. These findings contribute valuable insights into the intricate relationship between Vitamin D status and lipid profiles.

## Discussion

Studies related to metabolic syndrome are scarce in Libya despite the prevalence of metabolic syndrome. Results have shown that patients with metabolic syndrome suffer from low levels of vitamin D, which may exacerbate the severity of the condition. Reviewing previous studies conducted in different locations to assess the levels of vitamin D in individuals with metabolic syndrome revealed studies with statistically similar results to our study. Two studies showed low levels of vitamin D in approximately 80% of participants, with 20% having sufficient levels of vitamin D.<sup>18,19</sup> Another study in Beijing found that only 78% had vitamin D levels below 20 nanograms, with vitamin D levels negatively correlated with fat percentage and insulin resistance.<sup>20</sup> A study in Qatar revealed a significant deficiency in a large proportion of individuals with metabolic syndrome, with around 64% of participants experiencing a lower-than-normal level of vitamin D.<sup>21</sup> A study in Kuala Lumpur in 2011 assessed vitamin D levels in adult patients with metabolic syndrome, showing that approximately 87% of female participants suffered from a deficiency in vitamin D levels, while 41% of male participants experienced a deficiency in vitamin D levels.<sup>22</sup>

The results of these studies may help in reducing the prevalence of metabolic syndrome and minimizing the severity of the condition in affected individuals. In addition to the primary role of vitamin D in calcium and phosphorus balance and bone health, vitamin D plays a crucial role in regulating various cells in the body, including beta cells in the pancreas. Through the calcium channels present in beta cells, vitamin D receptor (VDR) receptors influence insulin secretion, explaining how a deficiency in vitamin D levels may lead to health issues, such as disruptions in blood sugar levels.<sup>23</sup>

Our findings are consistent with a study conducted in India, which found an inverse relationship between vitamin D and insulin resistance. Using HOMA IR analysis, the study concluded that vitamin D plays a significant role

in glucose metabolism and suggested that a deficiency in vitamin D increases the risk of type 2 diabetes.<sup>24</sup> Another study evaluated the relationship between vitamin D and insulin resistance, indicating an inverse relationship between vitamin D and insulin resistance. The study highlighted that maintaining a good level of vitamin D helps reduce the risk of diabetes. This is attributed to the role of vitamin D receptor (VDR) in stimulating insulin receptors in the cell and aiding in glucose metabolism. A deficiency in vitamin D may also lead to increased rates of fat synthesis.<sup>25</sup> While our study results differed, a study conducted in Norway in 2009 indicated no impact of vitamin D levels on triglycerides and insulin resistance even after administering vitamin D doses to patients.<sup>26</sup> The actual effect of vitamin D supplements in reducing insulin resistance may not be clear; however, the impact of vitamin D, in other words, the damages that may result from vitamin D deficiency may not be effectively treated with vitamin supplements.

In our study, the results did not show a significant correlation between age and vitamin D levels. This lack of association could be attributed to the relatively small sample size, with not large numbers in each age group. Additionally, the distribution of metabolic syndrome incidence varies among specific age groups. Our findings differed from a study conducted in Iran, which demonstrated a statistically significant relationship between vitamin D and age. The study suggested that the reason behind this difference might be related to issues with vitamin D synthesis due to dermatological problems.<sup>27</sup>

A study was conducted on 287 participants to assess the level of vitamin D and its impact on weight gain and the severity of metabolic syndrome. The study confirmed our results regarding the effect of vitamin D on weight, finding an inverse relationship between vitamin D levels and triglycerides. However, the results differed regarding the impact of vitamin D levels on waist circumference, as the study showed a statistically significant relationship between vitamin D levels and waist circumference, while

our research found no statistically significant relationship.<sup>28</sup>

The results also differed regarding the effect of vitamin D levels on insulin resistance, with the study showing a strong inverse relationship between vitamin D levels and triglycerides. While previous research has highlighted the significant impact of triglycerides on insulin sensitivity, the study suggests a need for further investigation into the effect of insulin resistance.<sup>29</sup>

Regarding blood pressure, our results aligned with another study conducted in 2018, showing no statistically significant relationship between vitamin D levels and blood pressure. A study indicated that the effect of vitamin D levels remains unclear, and the impact of vitamin D supplements on renin synthesis requires further research due to conflicting results.<sup>30</sup>

This underscores the need for additional studies to understand the broader and deeper effects of vitamin D on various health factors, including weight, triglycerides, insulin resistance, and blood pressure, which could contribute to improving prevention and treatment of metabolic syndrome.

## CONCLUSION

This study revealed that, Vitamin D deficiency significantly increased metabolic syndrome indicators in the group with the condition, while these indicators remained stable in the control group. This highlights the association between low vitamin D levels and the development of metabolic syndrome. Most participants had severe deficiency, which negatively correlated with insulin resistance and weight, and positively with HDL levels. This emphasizes the need for targeted interventions to address vitamin D deficiency, particularly among women at risk of metabolic syndrome.

## ACKNOWLEDGMENT

The authors would like to express their sincere thanks to all the participants who participated in the study. They also convey their sincere thanks to the management of Misurata Medical Center for permitting them to carry out the study in these places. The authors have no conflict of interest to declare. No funding was received for this study.

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