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Association of Serum 25-Hydroxyvitamin D with Metabolic Syndrome Severity in Adults: A Tertiary Care Observational Study

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ABSTRACT

Background: Metabolic syndrome (MetS) is a significant challenge in the world health that is defined by a complex of metabolic dysfunctions, such as central obesity, dyslipidemia, hypertension, and poor glucose metabolism. The role of vitamin D in the pathogenesis of metabolic disorders has been recently discovered as a consequence of its action on insulin resistance and inflammation.

Objective: To evaluate the relationship between serum 25-hydroxyvitamin D [25(OH)D] concentrations and severity of metabolic syndrome in adults visiting a tertiary care hospital.

Methods: This cross-sectional observational study is done between June 2023 and June 2025 in the teaching hospital attached to Bakhtawar Amin Medical and Dental College, Multan. One hundred and thirty adults diagnosed with metabolic syndrome using the NCEP ATP III criteria were recruited. ELISA was used to determine the level of serum 25(OH)D and placed into the following classes: deficient, insufficient, and sufficient. The severity of metabolic syndrome was identified according to the number of diagnostic elements. Correlation and multivariate regression were used in the statistical analysis.

Results: Vitamin D deficiency was found in 62.3% of respondents. The levels of serum 25(OH)D were also significantly inversely correlated with the measures of waist circumference, fasting glucose, triglycerides, and insulin resistance ($p<0.05$). The more severe metabolic syndrome participants would have much lower vitamin D levels. Low vitamin D was found in the multivariate analysis to be an independent predictor of the severity of the disease.

Conclusion: Low levels of serum 25(OH)D are found to be a significant determinant of severity of metabolic syndrome. The clinical practice of early risk stratification may use a tool like vitamin D assessment.

Keywords: Vitamin D, 25-hydroxyvitamin D, metabolic syndrome, insulin resistance, obesity, dyslipidemia, Pakistan

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INTRODUCTION

Metabolic syndrome (MetS) is a complex clinical syndrome defined as a group of interrelated metabolic abnormalities, such as central obesity, insulin resistance, dyslipidemia, and hypertension [1]. It is a significant international health issue because it has been closely linked to type 2 diabetes mellitus, heart disease and higher mortality rates in general. During the last 20 years, the morbidity of metabolic syndrome has increased significantly, especially in low and middle-income countries. South Asia, with Pakistan not being an exception, has a marginally high rate, being fueled by intense urbanization processes, sedentary living, changes in diets, and rising obesity rates [2,3].

Having long been considered a vital action mediator in calcium homeostasis and skeletal health, vitamin D is a fat-soluble secosteroid hormone. Nonetheless, new findings have demonstrated that it is more involved in other metabolic and endocrine processes [4]. It is believed that serum 25-hydroxyvitamin D [25(OH)D] is the best biomarker of vitamin D status because it has a relatively long half-life and has a stable circulating level. There is widespread expression of VDRs in several metabolically active tissues, such as pancreatic 8-cells, fat tissue, skeletal

muscle, and vascular endothelium, indicating that it plays an important role outside the bone metabolism [5].

The connection between vitamin D deficiency and the metabolic disorders has been drawing increasing attention of recent researches. Hypovitaminosis D has been linked to insulin secretion, insulin sensitivity, chronic low-grade inflammatory reaction, and lipid metabolism. Such pathophysiological processes play a leading role in the pathogenesis and the course of metabolic syndrome. Vitamin D is supposed to tune the insulin signaling pathway, calcium flux in the pancreatic 8 cells, and pro-inflammatory cytokines, thus affecting the glucose and lipid homeostasis [6,7].

A number of epidemiological studies have shown that there is an inverse relationship between serum 25(OH)D levels and the constituents of metabolic syndrome such as abdominal obesity, high level of fasting glucose, hypertriglyceridemia, and low level of HDL cholesterol [8]. Furthermore, people who have lower vitamin D levels are proved to have a higher prevalence and severity of metabolic syndrome. Although these results were achieved, even the nature of this association is complicated and there is lack of regional information, especially on the Pakistan population [9].

Vitamin D deficiency in Pakistan is very widespread among various population groups including young and elderly individuals, despite the country being sun rich, which is a result of low exposure to sunlight, cultural dressing, nutritional unbalanced food and indoor lifestyle in the urban areas. This general lack, in conjunction with the increase in the prevalence of metabolic syndrome, highlights the importance of seeking the possible connection between the two issues in the local population [10].

The current study was conducted to analyze the relationship between the levels of serum 25-hydroxyvitamin D and the severity of metabolic syndrome in a sample of adults at a tertiary care hospital. The analysis sought to determine whether the states of vitamin D could be used as a clinical useful biomarker in the determination of the metabolic risk and severity of the disease, and hence, adding to the improved approach of early detection and management [11].

MATERIALS AND METHODS

The study was an observational cross-sectional investigation spanning two years between June 2023 and June 2025 at the teaching hospital of Bakhtawar Amin Medical and Dental College, Multan, Pakistan. The study was initiated after the consent of the Institutional Review Board (IRB Ref No: ERC/2023/0117) had been obtained. Everything was done in harmony with the principles of the Declaration of Helsinki. All participants signed informed consent before participation.

The study used a non-probability consecutive sampling technique to employ 130 adult participants with ages ranging between 30 and 65 years. All the respondents had met the diagnostic criteria of metabolic syndrome according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III). Based on these criteria, a diagnosis of metabolic syndrome was made whenever at least three of the following components were met: central obesity (waist circumference 102 cm in males and 88 cm in females), excessive fasting blood glucose (100 mg/dL or pre-known diabetes), hypertension (130/85 mmHg), high triglycerides (150mg/dL) and low levels of high-density lipoprotein cholesterol (HDL-C <40mg/dl in men and

The study excluded participants with chronic liver disease, chronic kidney disease, endocrine diseases like thyroid dysfunction or Cushing syndrome, malignancy or acute or chronic inflammatory diseases. Those that were given vitamin D supplements or corticosteroids, lipid-lowering drugs, and drugs that are likely to affect glucose or calcium metabolism in the past three months were excluded as well to reduce confounding factors. This did not include pregnant and lactating women.

Each participant was evaluated clinically. Age, gender, and medical history were also captured as demographic data. Standardized procedures were used in the anthropometric measurements. A calibrated digital scale was used to measure body weight, and a stadiometer was used to measure height to determine body mass index (BMI, kg/m 2). The waist circumference was done at the mid point between the lower rib margin and iliac crest by use of non-stretchable measuring tape. A calibrated sphygmomanometer was used to measure blood pressure within the participant who had at least 5 minutes of rest.

The samples were sampled by veins that had fasted overnight (810 hours) and in aseptic conditions. Fasting blood glucose, lipid profile (total cholesterol, triglycerides, HDL-C, and LDL-C), fasting insulin and serum 25-hydroxyvitamin D [25(OH)D] were analyzed in serum. The level of serum 25(OH)D was determined by a standardized enzyme-linked immunosorbent assay (ELISA) procedure. The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was used to assess insulin resistance, and computed as: fasting insulin (ug/mL) fasting glucose (mg/dl)/405.

The serum 25(OH)D levels were used to classify the status of vitamin D as deficient (<20 ng/mL), insufficient (2030 ng/mL), and sufficient (>30 ng/mL). The intensity of metabolic syndrome was determined by the number of diagnostic features (three, four, and five components) and the more the better the severity of metabolic syndrome.

All the data collected were inputted and interpreted under the Statistical Package of Social Sciences (SPSS) 25. The variables that are continuous were presented as mean and standard deviation, whereas categorical variables were expressed in frequencies and percentages. Before analysis, the data distribution was tested on the normality. The correlation between the level of serum vitamin D and

metabolic parameters was assessed by Pearson correlation analysis. One-way analysis of variance (ANOVA) was used to compare the mean level of vitamin D between the various severity groups of the metabolic syndromes. The analysis was conducted by multiple linear regression analysis to determine independent predictors of the severity of metabolic syndrome after correcting the possibility of occurrence of confounding variables like age, gender, and BMI. The p-value was considered to be significant with a less value of 0.05.

RESULTS

The final analysis involved 130 participants with metabolic syndrome. The statistical age of the population of study was 47.6 years of average with a majority being females (55.4%) as opposed to males (44.6%). The population was predominantly obese with a mean body mass index (BMI) of 31.2 ± 4.6 kg/m². Most of the participants had central obesity and the mean waist circumference was 103.8 ± 9.4 cm. Table 1 describes the baseline demographic and clinical profile of the study population.

The serum 25-hydroxyvitamin D levels assessment indicated that the proportion of those with hypovitaminosis D was high among the participants. It was determined that there were 81 patients (62.3) deficient in vitamin D and 32 (24.6%) insufficient and only 17 (13.1%) were sufficient in vitamin D. The average level of serum 25(OH)D in the total group was 21.3 ± 6.8 ng/mL. These results reveal the rampant prevalence of vitamin D deficiency among patients with metabolic syndrome (Table 2).

A subsequent analysis showed that there was a significant negative correlation between serum levels of 25(OH)D and the major metabolic parameters. The lower levels of vitamin D were related to the larger waist circumference ($r = -0.45$, $p = 0.001$), the higher levels of fasting blood glucose ($r = -0.38$, $p = 0.002$), the stronger levels of triglycerides ($r = -0.41$, $p = 0.001$), and the greater levels of insulin resistance as estimated by HOMA-IR ($r = -0.47$, $p = 0.001$). The results show that low levels of vitamin D are strongly associated with the deterioration of the metabolic dysfunction (Table 3).

The participants were also stratified based on the number of diagnostic components present to determine the level of severity of metabolic syndrome. Of the study population, 39 patients (30.0) were found to have three components, 52 (40%) to have four components and 39 (30%) to have all five components of metabolic syndrome. As the metabolic syndrome became more severe, a gradual reduction of serum levels of vitamin D was noted. The mean of vitamin D level among patients with three components is 27.8 ± 5.6 ng/mL; however, the mean of vitamin D among patients with four and five components is 22.4 ± 4.9 ng/mL, and 18.2 ± 4.3 ng/mL, respectively with the level of significance of $p < 0.001$ as demonstrated in Table 4.

A multivariate linear regression analysis was conducted to further assess the independent relationship between vitamin D and severity of metabolic syndrome after controlling the possible confounding factors such as age, gender, and BMI. The level of serum 25(OH)D was still an important independent predictor of the severity of the metabolic syndrome ($\beta = -0.34$, $p = 0.001$). Moreover, BMI and waist circumference were also significantly correlated, but the strength of the correlation was not as high as for vitamin D levels (Table 5).

The findings of this study shows the existence of an inverse relationship between serum 25-hydroxyvitamin D levels and severity of metabolic syndrome that is clear and statistically significant. Reduced vitamin D was repeatedly linked with the deterioration of metabolic parameters, an augmented insulin resistance, and an elevated count of elements of metabolic syndrome, which validates the prospective use of vitamin D as a biomarker in estimating the risk of metabolism.

Table 1: Baseline Demographic and Clinical Characteristics of Participants (n = 130)

Variable	Value
Age (years)	47.6 ± 10.2
Male, n (%)	58 (44.6%)
Female, n (%)	72 (55.4%)
BMI (kg/m²)	31.2 ± 4.6
Waist circumference (cm)	103.8 ± 9.4
Systolic BP (mmHg)	136.5 ± 12.8
Diastolic BP (mmHg)	86.2 ± 8.7

Table 2: Distribution of Vitamin D Status Among Participants

Vitamin D Status	Frequency (n)	Percentage (%)
Deficient (<20 ng/mL)	81	62.3%
Insufficient (20–30 ng/mL)	32	24.6%
Sufficient (>30 ng/mL)	17	13.1%

Table 3: Correlation of Serum 25(OH)D with Metabolic Parameters

Parameter	Correlation Coefficient (r)	p-value
Waist circumference	-0.45	<0.001
Fasting blood glucose	-0.38	0.002
Triglycerides	-0.41	0.001
HOMA-IR	-0.47	<0.001

Table 4: Serum Vitamin D Levels According to Metabolic Syndrome Severity

Number of MetS Components	Participants (n)	Vitamin D (ng/mL)
3 components	39	27.8 ± 5.6
4 components	52	22.4 ± 4.9
5 components	39	18.2 ± 4.3

Table 5: Multivariate Linear Regression Analysis for Predictors of Metabolic Syndrome Severity

Variable	β Coefficient	p-value
Serum 25(OH)D	-0.34	0.001
BMI	0.21	0.015
Waist circumference	0.26	0.009
Age	0.08	0.210
Gender	0.05	0.340

DISCUSSION

The current study shows that serum 25-hydroxyvitamin D [25(OH)D] levels have a significant negative correlation with the severity of metabolic syndrome in adults [12]. It was also observed that a significant percentage of the participants were vitamin D deficient and that deficiency was closely associated with deteriorating metabolic values such as central obesity, hyperglycemia, dyslipidemia and insulin resistance. These results support the accumulating number of studies indicating that vitamin D has a significant role in metabolic control in addition to its traditional skeletal role [13].

A significant result of this study would be the high rate of hypovitaminosis D in people with a metabolic syndrome. Over a half of the population in the study had inadequate levels of vitamin D as it is reported in the South Asian populations where vitamin D deficiency is incredibly high in spite of the fact that ample sunlight is available [14]. This paradox is commonly found to be caused by a lack of sun exposure, indoor living, air pollution, skin pigmentation and cultural clothing habits, which restrict effective exposure to ultraviolet B radiation required to produce vitamin D [15].

The inverse relationship between serum 25(OH)D and the waist circumference observed shows that there is a strong association between central obesity and vitamin D deficiency. It has been observed that adipose tissue serves as a storage of fat-soluble vitamins, which result in the seizure of vitamin D and decreased bioavailability in the bloodstream [16]. Also, chronic low-grade inflammation is a result of obesity by itself, and it can further worsen the metabolism and action of vitamin D. Vitamin D deficiency and obesity can both be the cause and result of the other through this bidirectional relationship, which eventually leads to an increasing metabolic dysfunction [17].

It was also displayed in the study that low vitamin D levels were strongly connected to insulin resistance judged by an increase in HOMA-IR. This substantiates the hypothesis that vitamin D participates in glucose homeostasis in more than one way, one of them being the enhancement of the insulin receptors expression, the regulation of intracellular calcium levels in pancreatic 8-cells, and the control of insulin secretion [17]. In addition, vitamin D has the potential of enhancing peripheral insulin sensitivity through the regulation of skeletal muscle and adipose tissue gene expression. These pathways may be impaired when there is a deficiency in vitamin D, and be involved in the occurrence of hyperglycemia and type 2 diabetes which are found in the spectrum of the metabolic syndrome [18].

The other significant observation is that there is an inverse correlation between the serum triglycerides and the vitamin D levels [19]. The lipid metabolism is also found to be affected by vitamin D because it regulates the lipase activity of lipoprotein and the lipid synthesis in the liver. When the levels of vitamin D decrease, there is a possibility that it causes the dysregulation of lipid metabolism and thus encourages hypertriglyceridemia which is an essential constituent of metabolic syndrome [20].

The fact that the levels of vitamin D gradually reduced with the number of metabolic syndrome components in the study is another evidence that it is related to the severity of a disease. Those who had more metabolic abnormalities always had a low level of serum 25(OH)D. Such a graded relationship indicates that the deficiency of vitamin D is not only linked to the occurrence of metabolic syndrome but also to the strength and course of the latter [19,21].

The potential clinical utility of serum vitamin D levels is evidenced by its independent predictive value to the severity of the metabolic syndrome, as shown by the regression analysis. Vitamin D was an important determinant of the severity of the diseases even after the confounding variables like age, sex and BMI have been adjusted. This observation implies that vitamin D can provide an effective biomarker to stratify clinical practice with regard to metabolic risk [13,14].

Pathophysiologically, vitamin D has anti-inflammatory activity as it inhibits the pro-inflammatory cytokines including interleukin-6 and tumor necrosis factor-alpha, which increase in metabolic syndrome. A key pathophysiology that contributes to insulin resistance and endothelial dysfunction is chronic inflammation. Thus, vitamin D deficiency can be a factor in the pro-inflammatory state, which is why it promotes the process of metabolic degradation [11,17].

Regardless of these important findings, one should note that there are some drawbacks of the study. The cross-sectional design does not allow one to determine causal relationship between the lack of vitamin D and metabolic syndrome [5]. Moreover, other variables like dietary intake, sunlight, and seasonal change were not quantitatively

examined and this could affect serum vitamin D levels. Longitudinal and interventional studies are needed in the future to establish whether vitamin D supplementation can be effective in improving the metabolic outcomes and decreasing the disease burden [19,20].

CONCLUSION

This study will provide evidence that there is a strong negative relationship between the level of 25-hydroxyvitamin D in the blood and the intensity of metabolic syndrome in adults. The deficiency of vitamin D was extremely widespread and closely linked to the central obesity, insulin resistance, dyslipidemia, and a higher number of metabolic syndrome factors. Reduced levels of vitamin D were an independent predictor of increased severity of the disease marking vitamin D as a potentially important biomarker in clinical risk assessment of metabolic risk. Regular assessment of vitamin D status can contribute to the earlier identification of the high-risk group and the preventive measures could be provided. Additional prospective and interventional studies of large scale are justified to study the therapeutic inferences of vitamin D in management of metabolic syndrome.

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Authors' Contributions:

S.H. conceptualized and designed the study, supervised data collection, and drafted the manuscript. A.M. contributed to study design refinement, performed statistical analysis, interpreted the data, and critically revised the manuscript for intellectual content. Both authors approved the final version of the manuscript and are accountable for all aspects of the work.

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Data Availability: The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request.

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