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Original Article

Association of Vitamin D Deficiency with Risk of Metabolic Syndrome: Evidence from a Case-Control Study in South India

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ABSTRACT

Background: Metabolic syndrome (MetS) is a growing public health challenge in India, characterised by a cluster of cardiometabolic risk factors. Emerging evidence suggests that vitamin D deficiency may contribute to its development.
Objectives: To assess vitamin D status in patients with MetS compared to healthy controls, and to evaluate the association between vitamin D deficiency and risk of MetS in a South Indian population.
Methods: A hospital-based case–control study was conducted at MES Medical College, Kerala, from March 2013 to March 2014. Seventy-three patients with MetS (defined by NCEP ATP III criteria) and 73 age- and sex-matched controls were recruited. Serum 25-hydroxyvitamin D [25(OH)D] was measured by chemiluminescent immunoassay. Vitamin D status was classified as deficient (<20 ng/ml), insufficient (20–29 ng/ml), or sufficient (≥30 ng/ml). Data were analysed using chi-square tests and independent t-tests; odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.
Results: Mean serum vitamin D was significantly lower in cases than controls (14.5 ± 5.3 vs. 19.8 ± 4.0 ng/ml, $p < 0.001$). Vitamin D deficiency was more prevalent among cases (91.6%) than controls (64.4%). Participants with vitamin D deficiency had nearly six-fold higher odds of MetS (OR = 5.99, 95% CI: 2.29–15.7).
Conclusion: Vitamin D deficiency is strongly associated with MetS in this South Indian cohort. Routine screening and correction of vitamin D deficiency may help prevent and manage MetS in similar populations.

Keywords*: Vitamin D, 25-hydroxyvitamin D, Metabolic syndrome, Case-control study, South India*

INTRODUCTION

Metabolic syndrome (MetS) is widely recognised as one of the most pressing health challenges of the 21st century [1]. It is not a single disease but rather a collection of interconnected abnormalities—abdominal obesity, elevated blood glucose, high blood pressure, and dyslipidemia—that together multiply the risk of cardiovascular disease and type 2 diabetes mellitus (T2DM) [2]. The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) defines the syndrome as the presence of at least three of these risk factors [3]. By that definition, nearly a quarter of adults worldwide are estimated to be affected. In India, reported prevalence rates range from 8% in rural areas to almost 20% in urban populations, reflecting the rapid lifestyle transitions across the country [4].

Traditionally, insulin resistance and obesity have been regarded as the central mechanisms driving MetS [5]. In recent years, however, attention has turned to other factors that may influence its development, particularly vitamin D [6]. Once thought to be essential only for maintaining bone health, vitamin D is now recognised as a hormone-like compound with far-reaching effects on human physiology [7]. Vitamin D receptors have been identified in pancreatic β-cells, adipose tissue, vascular smooth muscle, and immune cells, suggesting that the vitamin regulates insulin secretion, lipid metabolism, blood pressure, and inflammation [8]. These discoveries have opened new avenues of research into its role in non-skeletal disorders.

Observational studies worldwide have reported an inverse relationship between circulating 25-hydroxyvitamin D [25(OH)D] and MetS [9]. Lower vitamin D levels have been linked to insulin resistance, poor glycemic control, adverse lipid profiles, and higher blood pressure [10]. Some prospective studies even suggest that individuals with adequate vitamin D are less likely to develop diabetes or hypertension [11]. On the other hand, randomised trials of vitamin D supplementation have produced mixed results, and the strength of the association appears to vary across populations. This inconsistency highlights the need for population-specific studies that can account for local variations in genetics, lifestyle, and environment.

India presents an interesting paradox in this context. Despite abundant sunlight for most of the year, vitamin D deficiency is widespread, with estimates suggesting that 50–90% of the population may be affected [12]. The reasons are multifactorial—darker skin pigmentation that reduces vitamin D synthesis, traditional clothing that limits sun exposure, indoor lifestyles, and diets low in vitamin D-rich foods. Kerala, a state in southern India with a relatively advanced healthcare system and high literacy rates, is not exempt from this paradox. The coexistence of widespread vitamin D deficiency with the rising burden of MetS in this region is a concern that has not been adequately explored in scientific literature [13].

Against this background, the present study investigated the relationship between vitamin D status and metabolic syndrome in a South Indian population. It specifically sought to compare serum vitamin D levels between patients with MetS and healthy, age— and sex-matched controls, and to evaluate whether vitamin D deficiency increases the odds of developing MetS. By addressing this gap in regional data, the study aims to contribute to a broader understanding of vitamin D's extracellular functions and to highlight its potential role in public health strategies to prevent cardiometabolic diseases.

Materials and Methods

Study design and setting: This was a hospital-based case–control study conducted at MES Medical College, Kerala, between March 2013 and March 2014. The institution serves a mixed urban and rural population in the Malabar region, providing an appropriate setting to explore vitamin D status in relation to metabolic syndrome. Ethical clearance was obtained from the Institutional Ethics Committee before initiation of the study, and informed consent was secured from all participants.

Study population: Seventy-three patients diagnosed with metabolic syndrome (cases) and an equal number of age- and sex-matched apparently healthy volunteers (controls) were recruited. Diagnosis of MetS was made according to the NCEP ATP III criteria, which require the presence of at least three of the following:

- Central obesity (waist circumference >102 cm in men, >88 cm in women)
- Triglycerides ≥150 mg/dl or on treatment for hypertriglyceridemia
- HDL cholesterol <40 mg/dl (men) or <50 mg/dl (women)
- Blood pressure ≥130/85 mmHg or on antihypertensive treatment
- Fasting plasma glucose ≥100 mg/dl or on treatment for diabetes

Inclusion and exclusion criteria: Men and women aged 20–60 years were eligible. Patients with chronic hepatic, renal, cardiac, skeletal, or endocrine diseases (other than diabetes mellitus), those with acute illness, pregnant or lactating women, and individuals on calcium or vitamin D supplementation were excluded.

Data collection: Sociodemographic and clinical information were recorded using a structured questionnaire. According to standardised protocols, anthropometric measurements included weight, height, and waist circumference. Body mass index (BMI) was calculated as weight (kg)/height (m^2). Blood pressure was measured in the sitting position after five minutes of rest using a mercury sphygmomanometer; the average of two readings was taken.

Laboratory investigations: After an overnight fast, 5 mL of venous blood was collected from each participant. Serum was separated and analysed for the following parameters:

- **Vitamin D:** Serum 25-hydroxyvitamin D [25(OH)D] measured using a chemiluminescent immunoassay (Vitros 5600, Ortho Clinical Diagnostics). Vitamin D status was defined as deficient (<20 ng/ml), insufficient (20–29 ng/ml), or sufficient (≥30 ng/ml).
- **Glycemic indices:** The glucose oxidase-peroxidase method measures fasting blood sugar (FBS).
- **Lipid profile:** Triglycerides and total cholesterol measured enzymatically; HDL cholesterol measured after precipitation of other lipoproteins; LDL cholesterol calculated using the Friedewald equation.
- **Calcium and phosphorus:** Estimated using standard colourimetric methods (Arsenazo III and Fiske-Subbarow).

Statistical analysis: Data were analysed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD), and group comparisons were performed using independent t-tests. Categorical variables were analysed using chi-square tests. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to assess the association between vitamin D deficiency and metabolic syndrome. A p-value of <0.05 was considered statistically significant.

Results

A total of 146 participants were included, comprising 73 patients with metabolic syndrome (cases) and 73 age—and sex-matched controls.

Baseline characteristics: Cases had significantly higher waist circumference, fasting blood sugar, triglycerides, and systolic blood pressure than controls, while HDL cholesterol was significantly lower. Mean serum 25(OH)D levels were also markedly lower in the case group (14.5 ± 5.3 ng/ml) than in controls (19.8 ± 4.0 ng/ml; $p < 0.001$). Diastolic blood pressure showed no significant difference between groups. Table 1 summarises the baseline characteristics of the two groups.

Table 1: Baseline characteristics of cases and controls

Parameter	Cases (n=73) Mean ± SD	Controls (n=73) Mean ± SD	p-value
Waist Circumference (cm)	99.7 ± 9.1	89.4 ± 9.8	<0.001
Fasting Blood Sugar (mg/dl)	120.1 ± 24.2	92.1 ± 9.6	<0.001
Triglycerides (mg/dl)	176.9 ± 37.1	110.9 ± 32.2	<0.001
HDL Cholesterol (mg/dl)	39.2 ± 9.5	50.6 ± 7.8	<0.001
Systolic BP (mmHg)	133.7 ± 17.8	117.0 ± 9.0	<0.001
Diastolic BP (mmHg)	85.4 ± 8.7	90.8 ± 9.2	0.609
25(OH)D (ng/ml)	14.5 ± 5.3	19.8 ± 4.0	<0.001

Vitamin D status in cases and controls: Vitamin D deficiency (<20 ng/ml) was present in 91.6% of MetS cases compared to 64.4% of controls, a highly significant difference ($p < 0.001$). Only one individual in the control group had sufficient vitamin D (≥30 ng/ml), while none of the cases met sufficiency criteria (**Table 2**).

(**Table 2**)

Vitamin D Status	Cases (n=73) n (%)	Controls (n=73) n (%)	p-value
Deficient (<20 ng/ml)	67 (91.6%)	47 (64.4%)	<0.001
Insufficient (20 - 29 ng/ml)	6 (8.2%)	25 (34.2%)	
Sufficient (≥ 30 ng/ml)	0 (0%)	1 (1.4%)	

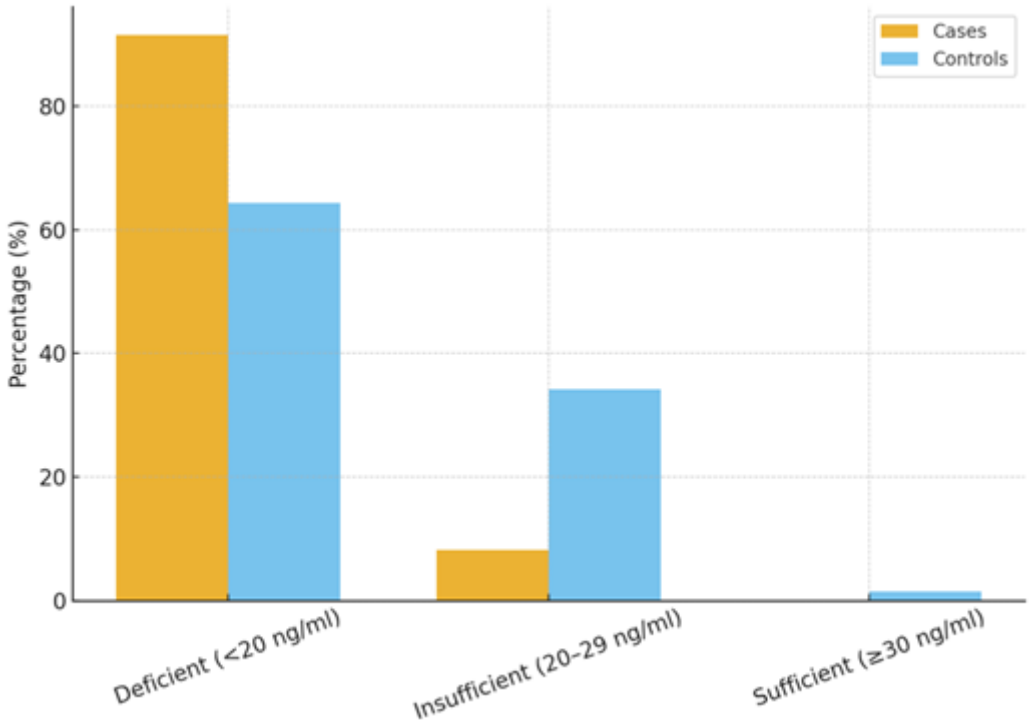

Figure 1. Distribution of vitamin D status in cases and controls

Association between vitamin D deficiency and MetS: When participants were grouped into deficient (<20 ng/ml) and non-deficient (≥20 ng/ml) categories, those with vitamin D deficiency had nearly six-fold higher odds of having MetS (OR = 5.99, 95% CI: 2.29–15.7, $p < 0.001$) (**Table 3**).

(**Table 3**)

Vitamin D Level	Cases (n=73)	Controls (n=73)	Odds Ratio (95% CI)	p-value
<20 ng/ml	67 (91.6%)	47 (64.4%)	5.99 (2.29 – 15.7)	<0.001
≥20 ng/ml	6 (8.2%)	26 (35.6%)	Reference	

Vitamin D and metabolic components: Correlation analysis revealed significant inverse associations between serum vitamin D levels and waist circumference ($r = –0.19$, $p = 0.022$), fasting blood sugar ($r = –0.31$, $p < 0.001$), triglycerides ($r = –0.24$, $p = 0.004$), and systolic blood pressure ($r = –0.33$, $p < 0.001$). No significant association was observed with HDL cholesterol ($r = 0.14$, $p = 0.105$).

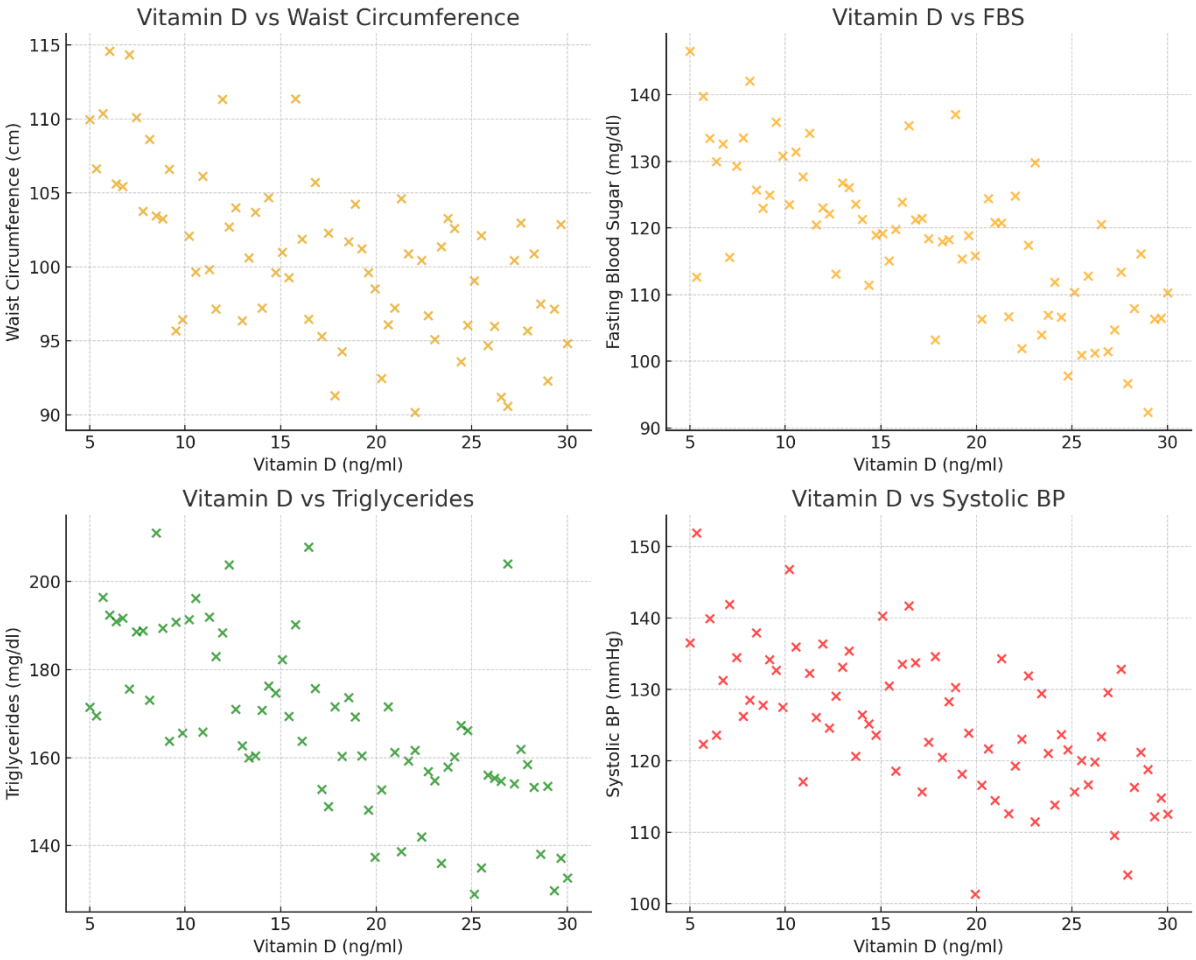

Figure 2 Correlation with metabolic components

Discussion

In this hospital-based case–control study, we observed a strikingly higher prevalence of vitamin D deficiency among patients with metabolic syndrome (91.6%) than among age— and sex-matched healthy controls (64.4%). The mean serum 25(OH)D concentration was significantly lower in cases, and individuals with vitamin D deficiency were nearly six times more likely to have MetS. These findings strongly suggest that hypovitaminosis D may play an important role in the pathogenesis of MetS in this South Indian population.

Our results are consistent with previous epidemiological evidence linking vitamin D deficiency to MetS [14]. Data from the Third National Health and Nutrition Examination Survey (NHANES III) in the United States demonstrated an inverse association between serum vitamin D levels and MetS prevalence, independent of age, sex, and ethnicity [15]. Similar associations have been reported in European and East Asian populations, where lower vitamin D status correlated with higher rates of obesity, hyperglycemia, and dyslipidemia [16]. In the Indian context, Sharma et al. reported that vitamin D deficiency was significantly associated with MetS in an urban North Indian cohort, echoing the findings from Kerala.

Multiple mechanisms support biological plausibility for this association. Vitamin D has been shown to enhance insulin secretion by pancreatic β-cells and improve insulin sensitivity in peripheral tissues by upregulating insulin receptors. It also influences adipocyte function and modulates inflammatory cytokine production, both of which are central to the

pathogenesis of MetS. Furthermore, vitamin D may regulate the renin–angiotensin system and vascular tone, contributing to blood pressure control. The observed inverse correlations in our study between vitamin D and waist circumference, fasting blood sugar, triglycerides, and systolic blood pressure lend further support to these mechanistic pathways.

Interestingly, our study did not demonstrate a significant correlation between serum vitamin D and HDL cholesterol, although other studies have reported such an association. This discrepancy may reflect differences in sample size, population characteristics, or lifestyle factors such as diet and physical activity. It is also possible that vitamin D influences lipid metabolism more strongly through triglyceride pathways than through HDL modulation.

One notable finding in our study was that despite widespread vitamin D deficiency, serum calcium and phosphorus levels remained within the normal range. This suggests that secondary hyperparathyroidism or compensatory mechanisms may preserve calcium–phosphorus balance in the short term, even in the presence of low vitamin D levels. However, the long-term consequences may include adverse skeletal outcomes and metabolic disturbances. Future studies should include parathyroid hormone (PTH) and other bone turnover markers to clarify these interactions.

Our findings have important implications for public health. Both MetS and vitamin D deficiency are highly prevalent in India, and their coexistence may compound the risk of diabetes and cardiovascular disease. Screening for vitamin D deficiency in high-risk groups, food fortification strategies, and lifestyle interventions promoting safe sun exposure could be cost-effective approaches to mitigate this risk. Randomised controlled trials are also warranted to determine whether vitamin D supplementation can improve metabolic outcomes in Indian populations.

This study has certain limitations. Given the hospital-based setting, the findings may not be fully generalizable to the community. The cross-sectional design precludes causal inference, and residual confounding by factors such as dietary habits or physical activity cannot be excluded. Additionally, we did not assess PTH levels, which might have provided further insights into calcium–vitamin D homeostasis. Nevertheless, the study is strengthened by its case–control design, standardised biochemical measurements, and focus on a relatively under-researched region of South India.

In summary, our study demonstrates a strong association between vitamin D deficiency and metabolic syndrome, with deficient individuals having almost six-fold higher odds of MetS. These findings reinforce the growing evidence that vitamin D is vital beyond bone health, influencing cardiometabolic risk. Addressing hypovitaminosis D through public health measures may offer an additional strategy for reducing the burden of metabolic diseases in India and similar settings.

Conclusion

This case–control study demonstrates a strong association between vitamin D deficiency and metabolic syndrome in a South Indian population. Patients with MetS had significantly lower serum 25(OH)D levels than healthy controls, and those with deficiency were nearly 6 times more likely to have MetS. The findings suggest that hypovitaminosis D is highly prevalent and essential to cardiometabolic risk in this region.

Recommendations

Given the dual burden of metabolic syndrome and vitamin D deficiency in India, routine screening for vitamin D status in high-risk individuals should be considered. Public health measures such as dietary fortification, supplementation programs, and education on safe sun exposure may help reduce the prevalence of deficiencies. Larger, population-based prospective studies and interventional trials are needed to establish causality and evaluate whether vitamin D deficiency correction can lower the burden of MetS and related diseases.

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Conflict of interest: The authors declare no conflict of interest related to this study.
Data availability: The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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