Section: Internal Medicine

Original Research Article

ASSOCIATION OF SERUM VITAMIN D LEVELS AND METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) IN PATIENTS WITH METABOLIC SYNDROME: A CROSS-SECTIONAL STUDY

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Abstract

Background: Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) is a prevalent condition globally, often associated with Metabolic Syndrome (MetS), characterized by insulin resistance, obesity, and hypertension. Vitamin D has been implicated in various physiological processes including metabolic and liver function. The relationship between Vitamin D deficiency and MASLD, especially in MetS patients, remains underexplored. This study aims to assess the association between serum Vitamin D levels and MASLD severity in MetS patients. The specific objectives include comparing Vitamin D levels between cases and controls and exploring the relationship between Vitamin D deficiency and liver steatosis, cholesterol, and glycemic control. **Materials and Methods:** A cross-sectional study was conducted at BRD Medical College, Gorakhpur, from April 2023 to March 2024. A total of 130 patients with MASLD and MetS were randomly selected. Serum Vitamin D levels were measured alongside clinical parameters, and liver steatosis was assessed using FibroScan. Data were analyzed using SPSS v25, with $p < 0.05$ considered statistically significant. **Result:** Vitamin D deficiency was found in 15.4% of participants, with 26.1% having insufficient levels. A significant inverse correlation was observed between Vitamin D levels and MASLD severity ($r = -0.661$, $p < 0.001$). Lower Vitamin D levels were associated with higher cholesterol ($p = 0.05$) and triglycerides ($p = 0.025$), though no significant relationship was found with HbA1c ($p = 0.736$). **Conclusion:** Vitamin D deficiency is strongly associated with MASLD severity in MetS patients. Lower Vitamin D levels are linked to more severe liver steatosis and adverse lipid profiles. Routine monitoring and potential supplementation of Vitamin D may benefit this population.

INTRODUCTION

Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) is the most common chronic liver disease worldwide, affecting approximately 25% of adults, with a rising incidence due to increasing rates of obesity and diabetes. MASLD encompasses a range of liver conditions, from simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis.[1-3] Metabolic Syndrome (MetS), characterized by central obesity, insulin resistance, dyslipidemia, and hypertension, significantly raises the risk of MASLD and type 2 diabetes. Lifestyle factors, including poor diet and sedentary behavior, are key drivers of both MetS and MASLD, though genetic predisposition also plays a role. Vitamin D, a pleiotropic hormone, influences not only bone health but also immunity, inflammation, and cell proliferation.[4,5] Vitamin D receptors are found in key metabolic tissues, including the liver.[6] Deficiency in Vitamin D is prevalent, with 30–50% of the global population affected, and is strongly associated with conditions like obesity, MetS, insulin resistance, and MASLD.[7] In MASLD, inflammation and oxidative stress, exacerbated by adipokines and cytokines,

contribute to liver damage. Addressing inflammation and metabolic dysfunction is crucial in managing MASLD and its progression. Although some studies have linked low Vitamin D levels to MASLD severity, others have found no independent relationship. Evidence from large population-based studies remains limited, and the link between Vitamin D deficiency and MASLD progression, particularly steatosis and fibrosis stages, needs further exploration. Vibration-Controlled Transient Elastography (VCTE) has been shown to be a non-invasive and effective tool for assessing liver steatosis and fibrosis, in contrast to invasive procedures like liver biopsy.[8,9]

Aim and Objectives

The aimed to investigate the association between serum Vitamin D levels and Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) in adults with Metabolic Syndrome (MetS), with liver steatosis serving as a key marker of liver damage. The study seeks to assess the prevalence of Vitamin D deficiency in the population, evaluate the correlation between Vitamin D levels and the severity of liver steatosis, and analyze the relationship between Vitamin D status and metabolic markers such as cholesterol, triglycerides, and HbA1c. These objectives will provide insight into the role of Vitamin D in the progression of MASLD in individuals with MetS.

MATERIALS AND METHODS

A cross-sectional study was conducted from April 2023 to March 2024 at the Department of General Medicine, BRD Medical College, Gorakhpur. Participants were selected via simple random sampling from patients diagnosed with MASLD attending the outpatient department. A total of 130 patients were included based on sample size calculations, with prevalence of MASLD in India considering 30% (Krishnamoorthy Y et al (2022) [10]. A pre-structured proforma was used to collect sociodemographic data, clinical profiles, and laboratory investigations. Vitamin D levels were assessed through serum 25-hydroxyvitamin D (25(OH)D) tests, with <20 ng/mL considered deficient, 20-30 ng/mL insufficient, and >30 ng/mL normal. Data were analyzed using SPSS version 25. Association tests (Chi-square, ANOVA) and correlation coefficients were calculated to explore relationships between Vitamin D levels and clinical parameters. Statistical significance was set at $p < 0.05$.

RESULTS

The clinical profile of the study participants (N=130), the mean age of the participants was 53.31 ± 11.1 years. The gender distribution included 91 females (70%) and 39 males (30%). The mean Body Mass Index (BMI) was 31.43 ± 4.73. The average waist circumference measured 92.25 ± 7.51 cm. Hemoglobin (Hb) levels averaged 11.52 ± 1.61 g/dL, while HbA1c levels averaged 7.21 ± 1.31%. Fasting blood sugar levels were 105.54 ± 10.20 mg/dL. The mean systolic blood pressure was 137.77 ± 5.52 mmHg, and the mean diastolic blood pressure was 84.62 ± 8.06 mmHg. Regarding lipid profile, the average serum cholesterol level was 199.38 ± 41.10 mg/dL, and the mean serum HDL level was 42.31 ± 6.64 mg/dL. The mean serum triglyceride level was 149.80 ± 34.62 mg/dL. Total bilirubin levels averaged 0.79 ± 0.54 mg/dL. Liver function tests showed an average SGOT level of 48.70 ± 13.25 IU/L and an average SGPT level of 35.15 ± 9.29 IU/L. The average alkaline phosphatase (ALP) level was 240.08 ± 99.65 IU/L [Table 1]. The distribution of Vitamin D levels among the 130 study participants revealed that 15.4% (n = 20) were Vitamin D deficient, with serum levels below 20 ng/mL (mean = 17.17 ± 7.03 ng/mL). A total of 26.1% (n = 34) of the participants had insufficient Vitamin D levels, ranging from 20 to 30 ng/mL (mean = 23.38 ± 10.55 ng/mL). The majority of the participants, 58.4% (n = 76), had normal Vitamin D levels, with serum concentrations above 30 ng/mL (mean = 26.81 ± 11.72 ng/mL). This distribution highlights that a significant proportion of the study population exhibited suboptimal Vitamin D levels, with over 40% falling into either the deficient or insufficient categories [Table 2]. Participants with Vitamin D deficiency had significantly higher total cholesterol levels (209 ± 43.69 mg/dL) compared to those with normal Vitamin D levels (202.79 ± 41.58 mg/dL) ($p = 0.05$). Similarly, higher triglyceride levels were observed in Vitamin D-deficient participants (166.90 ± 34.75 mg/dL) compared to those with normal levels (149.38 ± 35.60 mg/dL) ($p = 0.025$) [Table 3]. There was no significant association between Vitamin D levels and glycemic control as measured by HbA1c and fasting blood sugar. The mean HbA1c for Vitamin D-deficient participants was 7.10 ± 1.11%, compared to 7.22 ± 1.20% in participants with normal Vitamin D levels ($p = 0.736$). A similar non-significant association was observed for fasting blood sugar ($p = 0.07$) [Table 4]. The association between Vitamin D levels and blood pressure was borderline significant for systolic blood pressure ($p = 0.07$) but statistically significant for diastolic blood pressure ($p = 0.02$). Participants with Vitamin D deficiency had a mean diastolic blood pressure of 87.60 ± 6.14 mmHg compared to 83.05 ± 8.79 mmHg in those with normal Vitamin D levels [5]. The association between Vitamin D levels and the severity of Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD), measured by the Controlled Attenuation Parameter (CAP) score, revealed a significant inverse correlation. Participants with mild MASLD (S1) had the highest mean Vitamin D levels at 26.81 ± 11.72 ng/mL. Those with moderate MASLD (S2) had lower Vitamin D levels,

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averaging 23.38 ± 10.55 ng/mL. The lowest Vitamin D levels were observed in participants with severe MASLD (S3), with a mean of 17.17 ± 7.03 ng/mL. Statistical analysis showed a significant association between Vitamin D levels and MASLD severity, with a p-value of 0.02, indicating that as MASLD severity increases, Vitamin D levels tend to decrease [Table 6]. The association between the MASLD CAP score grade and the hepatic profile of the study subjects (N=130). Among the subjects with CAP Grade S1, classified as mild (N=64), the mean serum glutamic-oxaloacetic transaminase (SGOT) was recorded at 48.31 ± 11.02 U/L, while the mean serum glutamic-pyruvic transaminase (SGPT) was 36.22 ± 11.61 U/L, and the mean alkaline phosphatase (ALP) was 224.42 ± 80.37 U/L. For those in CAP Grade S2, representing moderate steatosis (N=48), the mean SGOT increased slightly to 50.44 ± 16.37 U/L, with a mean SGPT of 35.40 ± 5.89 U/L and an ALP mean of 237 ± 82.75 U/L. In the severe category, CAP Grade S3 (N=18), the mean SGOT decreased to 45.44 ± 11.01 U/L, while the mean SGPT further declined to 30.67 ± 11.31 U/L, and the mean ALP surged to 304 ± 164.92 U/L. The p-values for SGOT, SGPT, and ALP were 0.377, 0.197, and 0.142, respectively, indicating no statistically significant differences among the groups. The correlation between serum Vitamin D3 levels and CAP score (MASLD severity) among the study subjects. The correlation coefficient (r) is -0.661, indicating a strong negative correlation between Vitamin D3 levels and CAP score. The p-value is reported to be highly significant, <0.001, which underscores the robustness of this relationship. This correlation suggests that as Vitamin D3 levels decrease, MASLD severity as measured by the CAP score tends to increase. This finding implies a potential role for Vitamin D3 in influencing the severity of MASLD [Table 8].

Table 1: Clinical Characteristics of the Study Population (N=130).

S.no	Particulars		Mean ± SD / n (%)
1	Age (in years)		53.31 ± 11.1
2	Gender	Female	91 (70)
		Male	39 (30)
3	Body Mass Index (BMI)		31.43 ± 4.73
4	Waist circumference		92.25 ± 7.51
5	Hemoglobin (Hb)		11.52 ± 1.61
6	HbA1c		7.21 ± 1.31
7	Fasting Blood Sugar		105.54 ± 10.20
8	Systolic Blood Pressure		137.77 ± 5.52
9	Diastolic Blood Pressure		84.62 ± 8.06
10	Serum Cholesterol		199.38 ± 41.10
11	Serum HDL		42.31 ± 6.64
12	Serum Triglyceride		149.80 ± 34.62
13	Total Bilirubin		0.79 ± 0.54
14	Serum Glutamic Oxaloacetic Transaminase (SGOT)		48.70 ± 13.25
15	Serum Glutamic Pyruvic Transaminase (SGPT)		35.15 ± 9.29
16	Alkaline Phosphatase (ALP)		240.08 ± 99.65
17	Vitamin D3		24.65 ± 16.11

Table 2: Distribution of Vitamin D Levels Among Participants (N=130)

Vitamin D Status	Deficient (<20 ng/mL)	Insufficient (20-30 ng/mL)	Normal (>30 ng/mL)
Number of Participants	20 (15.4%)	34 (26.1%)	76 (58.4%)
Mean Vitamin D (ng/mL)	17.17 ± 7.03	23.38 ± 10.55	26.81 ± 11.72

Table 3: Association Between Vitamin D Levels and Cholesterol/Triglycerides

Parameter	Vitamin D Deficiency (<20 ng/mL)	Normal Vitamin D (>30 ng/mL)	p-value
Cholesterol (mg/dL)	209 ± 43.69	202.79 ± 41.58	0.05
Triglycerides (mg/dL)	166.90 ± 34.75	149.38 ± 35.60	0.025

Table 4: Association Between Vitamin D and Glycemic Control (HbA1c and Fasting Blood Sugar)

Parameter	Vitamin D Deficiency (<20 ng/mL)	Normal Vitamin D (>30 ng/mL)	p-value
HbA1c (%)	7.10 ± 1.11	7.22 ± 1.20	0.736
Fasting Blood Sugar (mg/dL)	104.40 ± 7.34	103.79 ± 7.68	0.07

Table 5: Association Between Vitamin D and Blood Pressure

Blood Pressure (mmHg)	Vitamin D Deficiency (<20 ng/mL)	Normal Vitamin D (>30 ng/mL)	p-value
Systolic BP	139.60 ± 4.75	136.91 ± 5.71	0.07
Diastolic BP	87.60 ± 6.14	83.05 ± 8.79	0.02*

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Table 6: Association Between Vitamin D Levels and MASLD Severity (CAP Score) (N=130)

CAP Grade (MASLD Severity) (n)	Vitamin D (ng/mL)	p-value
S1 (Mild) (64)	26.81 ± 11.72	0.02*
S2 (Moderate) (48)	23.38 ± 10.55	
S3 (Severe) (18)	17.17 ± 7.03	

Table 7: Association between MASLD CAP score grade and Hepatic profile of study subjects (N=130)

CAP Grade (n)	SGOT Mean ± SD	SGPT Mean ± SD	ALP Mean ± SD
S1 Mild (64)	48.31 ± 11.02	36.22 ± 11.61	224.42 ± 80.37
S2 Moderate (48)	50.44 ± 16.37	35.40 ± 5.892	237 ± 82.75
S3 Severe (18)	45.44 ± 11.01	30.67 ± 11.31	304 ± 164.92
P-value	0.377	0.197	0.142

S- Steatosis

Table 8: Correlation between Vitamin D3 and CAP Score (MASLD)

Variable	Correlation Coefficient "r"	p value
CAP Score	-0.661*	<0.001**
S. Vitamin D3		

*Negative correlation, **Highly significant (p<0.001)

DISCUSSION

This study investigated the relationship between serum Vitamin D levels and the severity of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in patients with Metabolic Syndrome (MetS). The findings demonstrated a significant inverse correlation between Vitamin D deficiency and MASLD severity, as well as associations with lipid profiles, while no significant relationship was observed with glycemic control. Our results showed that lower Vitamin D levels were significantly associated with more severe steatosis, as assessed by CAP scores using FibroScan. Participants with severe MASLD (S3) exhibited markedly lower Vitamin D levels compared to those with mild or moderate MASLD ($p < 0.001$). These observations align with previous research, which has highlighted the protective role of Vitamin D in liver health, particularly in modulating hepatic inflammation and fibrosis. Ji et al,[11] (2023) found a strong link between reduced Vitamin D levels and increased liver fibrosis in MASLD patients, while Liu et al,[12] (2020) similarly reported a significant association between Vitamin D deficiency and advanced fibrosis in MASLD patients. These studies suggest that Vitamin D may influence the progression of MASLD, possibly through its anti-inflammatory and metabolic regulatory properties.

The current study also identified a significant relationship between Vitamin D deficiency and elevated lipid levels. Participants with deficient Vitamin D had higher cholesterol ($p = 0.05$) and triglyceride levels ($p = 0.025$) compared to those with normal Vitamin D levels. These findings are consistent with prior research. Bennouar et al,[13] (2021) demonstrated that Vitamin D deficiency was associated with dyslipidemia, particularly elevated triglycerides, in MASLD patients. Similarly, Liu et al,[12] (2020) reported that Vitamin D supplementation improved lipid profiles in MASLD patients by regulating lipid metabolism and reducing hepatic fat accumulation. This underscores the potential role of maintaining adequate Vitamin D levels to mitigate the lipid abnormalities frequently observed in MASLD patients with MetS.

In contrast to some studies, we did not find a significant association between Vitamin D levels and glycemic control, as measured by HbA1c and fasting blood sugar. The mean HbA1c and fasting blood sugar levels were comparable across participants with deficient, insufficient, and normal Vitamin D levels, with no statistically significant differences ($p > 0.05$). These results diverge from findings such as those of Aludwan et al,[14] (2020) who identified an inverse relationship between Vitamin D levels and HbA1c in MASLD patients with type 2 diabetes. However, studies such as Yu-Lei et al,[15] (2024) also reported non-significant associations between Vitamin D and glycemic control, indicating that the impact of Vitamin D on glucose metabolism may be less pronounced in populations without severe diabetes. Furthermore, a significant association was found between Vitamin D deficiency and diastolic blood pressure ($p = 0.02$), with Vitamin D-deficient participants showing higher diastolic pressures. This finding is consistent with the work of Heo et al,[16] (2021) who demonstrated a link between Vitamin D deficiency and elevated blood pressure in MASLD patients.

Overall, this study's findings are consistent with the broader literature, reinforcing the role of Vitamin D in the management of MASLD. However, the variability in the significance of Vitamin D's impact on glycemic control across different studies may be due to differences in study populations, baseline Vitamin D levels, or metabolic characteristics. For example, studies such as Hoseini et al,[17] (2020) and Bennouar et al,[13] (2021) focused on specific subgroups, such as elderly women or individuals with advanced metabolic disturbances, which may account for the differing outcomes regarding Vitamin D's influence on glucose metabolism. Further research is needed to clarify these

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relationships and explore the potential therapeutic role of Vitamin D in this patient population.

Limitations: This study's cross-sectional design limits the ability to establish causal relationships. Furthermore, the study population was limited to patients from a single center, potentially limiting the generalizability of the findings. Longitudinal studies and randomized controlled trials are necessary to establish a clearer understanding of the potential therapeutic benefits of Vitamin D supplementation in MASLD.

CONCLUSION

This study highlights a significant association between Vitamin D deficiency and the severity of MASLD in patients with MetS, particularly in relation to lipid profiles and diastolic blood pressure. Regular monitoring of Vitamin D levels and supplementation may provide beneficial effects in managing MASLD and metabolic disturbances.

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