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COMPARISON OF SERUM VITAMIN D LEVELS IN PATIENTS WITH AND WITHOUT GALLSTONE

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ORIGINAL ARTICLE

ABSTRACT

Background: The current lifestyle and epidemiological studies have definitively identified gallstone disease (GD) as a complex, metabolic disease prone to gene-environment interactions for development, but its relationship with vitamin D deficiency still remains unexplained.
Objective: We aimed to explore the associations of serum 25-hydroxyvitamin D [25(OH) D] levels with gallstone disease and correlated metabolic indexes in this cross-sectional study.
Methods: This study was cross-sectional, case-control design which was carried out between May 2023 and April 2024 in a tertiary care hospital. One hundred and sixty subjects (age group: 25-65 years) participated. Group constituted of newly diagnosed 80 cholelithiasis patients which were confirmed by ultra-sound as Group A and other was consist of healthy control subjects 80, not previously known as case in biliary or gallbladder diseases (group B) were explored for their vitamin D status. Demographic, medical history, and lifestyle data to account for age and sex- matched participants, a standardized questionnaire was used.
Results: The BMI, triglyceride and total cholesterol levels were significantly higher than in cases with gallstones compared to controls ($p < 0.001$). Vitamin D levels were significantly lower in patients with gallstones than in the control group. In contrast, a marked negative correlation between serum 25(OH) D levels and BMI, triglycerides and total cholesterol was observed.
Conclusion: Low vitamin D levels, lower value of the serum vitamin D was associated significantly with increased risk for gallstone disease and unfavorable Metabolic Syndrome profile and may have role in etiopathogenesis**.**

Keywords: Gallstone, Vitamin D deficiency, 25(OH) D, BMI and Lipid profile.

Article received: 02-04-2025
Revised: 12-05-2025
Accepted: 19-06-2025

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INTRODUCTION: Gallstone disease, also called cholelithiasis, is one of the most common digestive system diseases requiring hospitalization and occurs mainly in middle-aged and elderly people worldwide. It results from a multifactorial origin, genetic [1] and hormonal agents being the predisponet factors with female gender, obesity, rapid weight loss, high fat diet and sedentary lifestyle identified as risk factors. Most important pathogenesis for gallstone formation is related to both, cholesterol supersaturation and biliary stasis.

So far gallstones have been strongly associated with other metabolic pathologies like dyslipidemia and insulin resistance [2]. In this context, scientific interest has garnered concerning the impact of micronutrients on gallbladder physiology and bile metabolism and vitamin D in particular [2]. Over the last years, an increasing number of studies have been probing new ways that vitamin D may be

involved in both classical and non-classical metabolic and immunological processes. [1] And this kind of receptors is widespread in tissues with the liver and gallbladder [3].
Recent studies have found that low serum vitamin D levels could contribute to changes in cholesterol homeostasis as well as gallbladder bile stasis and inflammation, enhancing the likelihood of developing GSD [4]. However the link between vitamin D status and cholelithiasis among a population afflicted with prevalent hypovitaminosis D has remained unresolved.
Our study aimed at comparing serum vitamin D in subjects with and without gallstones (GS), examining its independent associations with several metabolic markers, as well as morphometric parameters.

METHODOLOGY: This was a case-control cross-sectional study conducted from May 2023 to March 2024 at the Department of Surgery in a multispecialty tertiary care hospital.
Participants: 160 people aged 25-65 years.
The study included:
Cases: 80 cases of gallstones detected by abdominal ultrasonographies (Group A).
Control: 80 healthy control individuals with no ultrasonographic or previous clinical evidence of stones (Group B)
Matching: Age (±3 years) and sex of all participants were matched to avoid confounding.

Inclusion Criteria:
Adults aged 25-65 years
Incident cholelithiasis (for case group)
No vitamin D supplements in the preceding 6 months

Exclusion Criteria:
Prior liver or kidney disease
Current pregnancy or lactation
Malabsorption syndromes
Active infections (including HIV and hepatitis B or C)
Pharmacologic agents which influence vitamin D metabolism (e.g. steroids, anticonvulsant)

Data Collection: The demographic variables, dietary habits and physical activities were recorded through an epidemiological survey and medical history through a food-interview. BMI was calculated by the measured height and weight. All participants provided:
Serum 25-hydroxyvitamin D [25(OH) D] levels
Profile hospitality (total cholesterol LDL HDL triyglicerides)
Fasting blood glucose
Vitamin D status: Sufficient: ≥30 ng/mL, insufficient: 20-29 ng/mL and deficient: <20 ng/mL
Laboratory Analysis: The serum 25 (OH) D levels were measured with the chemiluminescent immunoassay (CLIA) and is one of the most sensitive methods available. Enzymatic assays were performed for estimation of plasma lipids and glucose levels.
Statistical Analysis: The data analysis was done with SPSS. Independent samples t-tests within normal data (mean ± standard deviation [SD]) and continuous variables. Chi-square tests served for this purpose, to the extent that dependent variables were ordinal and categorical variables. Table 2 showed the results of the correlations based on measured vitamin D values from data to other variables using Pearson correlation. P≤0.05 was considered to denote statistical significance.

RESULTS: Vitamin D deficiency was found to be significantly more prevalent among patients with gallstone (73.8 %) than in those without the disease (38.7 %) [p≤0.001]. Importantly, it was stressed in the review that other vitamin D related pathologies were not assessed because of time constraints. -0.42, p ≤0.001) between 25(OH) D levels and BMI -0.27, p=0.01), as well as with TG (r = -0.23; P= 0. 25(OH) D levels were not significantly correlated also with fasting glucose.

TABLE 1: THE DEMOGRAPHIC DETAILS AND CLINICAL DATA OF THE STUDY POPULATION

Parameter	Gallstone Group (n=80)	Control Group (n=80)	p-value
Age (years)	45.6 ± 9.8	44.1 ± 8.7	0.31
Female (%)	72.5%	70.0%	0.71
BMI (kg/m²)	28.7 ± 3.6	25.3 ± 2.9	<0.001

Parameter	Gallstone Group (n=80)	Control Group (n=80)	p-value
Triglycerides (mg/dL)	168.2 ± 44.3	139.7 ± 37.5	<0.001
Total cholesterol (mg/dL)	202.1 ± 31.9	187.6 ± 29.4	0.002
25(OH)D level (ng/mL)	15.4 ± 6.8	24.9 ± 7.2	<0.001

DISCUSSION: According to our findings, vitamin D deficiency is associated with gallstone disease. Conclusions In matched healthy M1 subjects, the present study provide a strong support to the hypothesis that vitamin D status might affect gallbladder and bile composition on the basis of significantly lower 25(OH)D levels in cholelithiasis.

Vitamin D and Gallstone Formation Physiological Effects of Vitamin DVitamin D has multiple physiological roles which might account for adverse health outcomes.

Vitamin D Receptors (VDRs) in Bile Acid Metabolism VDR expression in hepatocyctes and cholangiocytes indicates a broader role of VDR, even in bile acid metabolism regulated at the level of basal gene transcription. Recently it has been reported that VDR activation regulates not only bile acid biosynthesis but also the cholesterol trafficking, both crucial processes for gallstone formation [5, 6].

Effects on immunomodulation and inflammation: Vitamin D also has immune regulation properties, and its deficiency could lead to produce low-grade chronic inflammatory process that may interfere in the ability of gallbladder contraction causing improvement development of sludge [7].

Role in smooth muscle function: VDRs on the smooth muscle cells could be implicated in promoting gallbladder motility. Bile stasis subsequently ensues due to decreased contractility, and this further leads to precipitation of cholesterol crystals [8].

Generally there are generally numerous functional effects with regard to the person of 25 oh Ve had insufficiency, meant for occasion a great abnormal lipid metabolism, using greater triglyceride values an important gallstone risk-factor [9].

Together, these mechanisms provide a biologic rationale for an association between vitamin D deficiency and cholelithiasis, but causality has not been convincingly demonstrated.

Other studies have also reported similar findings large population based study Kim et al found more gallstones in those with vitamin D deficiency (controlling for BMI and age) [10]. Zhang et al. had done a case- control study also reported an inverse relationship between gallstones and vitamin D levels also emphasized the effect of vitamin D on lipid metabolism in blood by quoting the regulation of cholesterol, which synthesizes bile salts [11].

On the other side, various other researches have suggested that gallstone disease was not associated with levels of vitamin D if they adjusted related risk factors such as obesity and metabolic syndrome [12]. While our study did attempt to account for these confounders using matched sampling and statistical adjustments, this is always difficult to get right.

Assuming if gallstone formation is one role of vitamin D deficiency, probably it can be screened and correct in high risk group and decrease burden of cholelithiasis. This relationship should be further clinically investigated, e.g. in consideration of the significant worldwide prevalence of hypovitaminosis D (in particular found in South Asia and Middle East).

Limitations:

Cross-sectional design precludes establishing causality.

Ewell et al. 1995 Sunlight exposure and dietary intake not exactly quantified

The current study was a retrospective, single-center study of Japanese patients and lacked diversity in ethnic composition.

However, it has been essential advance studies need to be carried out to determine the impact of vitamin D supplementation in preventing gallstone.

CONCLUSION: This study reveals a significant association of vitamin D deficiency with gallstone disease. After adjusting for age and sex, patients with cholelithiasis had significantly lower levels of serum 25(OH)D compared with control subjects. Future studies are required but this preliminary data suggest that 1 dose of 300,000 IU oral cholecalciferol may be an intervention trial for a potential modifiable risk factor in gall stone pathogenesis. Our findings suggest that the possibility of preventing strategies may have been considered by examining how to develop preventive measures

for reducing the risk of gallstone disease through vitamin D status maintenance because maintaining vitamin D sufficiency could be a simple and inexpensive strategy.

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How to cite this:
Bukhari D, Hussain F. Comparison of serum vitamin D levels in patients with and without gallstone. J Med All Sci Hyd. 2025;1(1):15-18

Authors Contribution

Dr. Dua Bukhari	*Concept and design*
Dr. Fareed Hussain	*Acquisition of data*