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Original Research Article

Association between Vitamin D Deficiency and Hyperbilirubinemia in Jaundiced Patients

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Abstract: ***Background***: Jaundice, characterized by elevated serum bilirubin levels, reflects underlying hepatic dysfunction, which may impair vitamin D metabolism. Vitamin D deficiency is increasingly recognized as a frequent complication in liver disorders, but its prevalence and association with jaundice are not well established. ***Aim of the Study*:** The present investigation aimed to assess the frequency of vitamin D deficiency among individuals diagnosed with jaundice and to explore the correlation between vitamin D status and serum bilirubin concentrations. ***Methodology***: The study enrolled 150 patients with jaundice confirmed through clinical and biochemical assessments, alongside 50 healthy control subjects. Serum levels of 25-hydroxyvitamin D [25(OH)D] and total bilirubin were quantitatively measured and analyzed. Serum-vitamin D ranks were stratified into three-groups: deficiency (<20 ng/mL), insufficiency (20–29 ng/mL), and sufficiency (≥30 ng/mL). ***Results***: Vitamin D-deficiency was significantly more predominant among jaundiced patients compared to controls (72% vs. 38%, $p < 0.001$). Patients with insufficient vitamin D were identified in 18% of patients and 34% of controls, while only 10% of patients had sufficient levels compared to 28% of controls. An inverse and statistically significant relationship was identified between serum bilirubin and vitamin D levels ($r = -0.42$, $p < 0.001$), showing that greater bilirubin levels were linked with lower serum vitamin D concentrations. ***Conclusions***: Vitamin D-deficiency is extremely predominant in jaundiced patients and correlates inversely with the severity of hyperbilirubinemia. Regular assessment of vitamin D-status in jaundiced people could support timely therapeutic strategies and enhance overall patient prognosis.

Highlights:

1. Impact of vitamin D deficiency and its relationship with hyperbilirubinemia in Jaundiced Patients.
2. The importance of investigation of Vitamin D level in jaundiced patients as deficiency correlates inversely with the severity of hyperbilirubinemia.
3. Investigation of Vitamin D could maintain suitable therapeutic schemes and improve the prognosis in Jaundiced patients.

Keywords: Jaundice, Vitamin D Deficiency, 25-Hydroxyvitamin D, Bilirubin, Hepatic Metabolism, Fat-Soluble Vitamins.

INTRODUCTION

Jaundice manifests as a clinical syndrome distinguished by icteric discoloration of the skin, mucous membranes, and sclera, attributable to hyperbilirubinemia [1]. Bilirubin a "yellow-hued pigment", arises from the physiological catabolism of heme, primarily derived from senescent erythrocytes (RBC). In normal-circumstances the liver processes bilirubin which is then excreted through bile into the digestive tract [2]. However, when this process is disrupted due to various causes, bilirubin accumulates in the body, leading to jaundice.

Jaundice can be categorized into three-main-types based on its underlying cause: prehepatic-hyperbilirubinemia (hemolytic), hepatic-hyperbilirubinemia (hepatocellular) and posthepatic-hyperbilirubinemia (obstructive jaundice). Pre hepatic jaundice results from increased destruction of erythrocytes (RBC) whereas hepatic jaundice arises from liver-diseases such as hepatitis or cirrhosis and post-hepatic-jaundice is often due to "obstruction of bile flow" and commonly caused by gallstones or tumors [3].

The severity and symptoms of hyperbilirubinemia (Jaundice) depend on its cause and period [4]. In some cases, jaundice may be accompanied by fatigue, dark urine, pale stools, itching and

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abdominal-pain. Early-diagnosis and management are essential to determine the underlying condition and prevent-complications [5].

Cholecalciferol, a lipid-soluble vitamin D form, is vital for regulating calcium and phosphate homeostasis and supporting proper skeletal mineralization [6]. Distinct from most vitamins, endogenous synthesis of vitamin D is initiated in the skin upon exposure to ultraviolet-B (UVB) radiation from sunlight. This photochemical process converts 7-dehydrocholesterol to pre-vitamin D3, which subsequently undergoes isomerization to form cholecalciferol, the active form of vitamin D3 [7]. Vitamin D can also be acquired through dietary intake such as fat of fish and nutritional supplements [8].

Vitamin D, whether synthesized endogenously or obtained through diet, requires two hydroxylation-steps to be transformed into its active hormonal-form. The first occurs in the liver, The conversion results in the synthesis of 25(OH)D, the main circulating metabolite and the most reliable biomarker for assessing an individual's vitamin D levels. The second hydroxylation step takes-place mainly in the kidneys generating 1,25-dihydroxyvitamin D [$1,25(OH)_2D$], the biologically active hormone that mediates its effects via the vitamin D receptor (VDR) [9].

As well as Vitamin D classical role in bone-metabolism, emerging evidence suggests that Vitamin D also has immunomodulatory, anti-inflammatory, and potential anticancer properties [10, 11]. Deficiency in vitamin D may be connected to a variety of health-complications, including "rickets in children", "osteomalacia and osteoporosis in adults", increased susceptibility to infections, autoimmune diseases, cardiovascular disorders, and metabolic syndromes [12, 13].

Deficiency of vitamin D is recognized as a widespread public health problem across the world, predominantly observed in populations characterized by reduced exposure to ultraviolet radiation and higher melanin levels in the skin, malabsorption syndromes, chronic kidney or liver diseases, and certain genetic polymorphisms affecting vitamin D metabolism [14, 15]. Screening and appropriate supplementation are key strategies in preventing and managing deficiency-related complications. The present investigation endeavors to elucidate the prevalence of vitamin D deficiency in individuals presenting with jaundice and to delineate the correlation between serum vitamin D concentrations and the magnitude of hyperbilirubinemia. Additionally, the study aims to evaluate vitamin D status within this cohort to inform and optimize targeted therapeutic interventions.

MATERIAL AND METHODS

The present descriptive cross-sectional study was complemented by at General-hospital of Samawah, Iraq, from June 2024 to April 2025. Ethical clearance was granted for the study, with written-informed consent collected from all members or their authorized guardians prior to their enrollment.

A total of 150 patients diagnosed with clinical jaundice were consecutively recruited. Inclusion-criteria including Age 18 years and above, clinical evidence of jaundice confirmed by yellow discoloration of the sclera and skin, and laboratory confirmation increased serum total bilirubin concentrations exceeding 2.0 mg/dL. Exclusion-criteria included patients with chronic-kidney-disease, liver failure, or malignancies also including those receiving vitamin D supplementation within the previous three months or consumption of drug that influence vitamin D-metabolism, notably anticonvulsants and corticosteroids, women during pregnancy or lactation and patients experiencing malabsorption syndromes or long-standing gastrointestinal illnesses Additionally, a control-group of "50 age- and sex-matched healthy individuals" without jaundice or known liver disease was enrolled for comparative analysis.

Samples Collection and Laboratory Procedures

Demographic data (age, sex) and clinical history (comorbidities, medication use) were collected using a structured questionnaire and review of medical records. Clinical examination confirmed the presence of jaundice and assessed associated symptoms.

Following a minimum of 8 hours of fasting, 5 mL of venous blood was obtained from each individual enrolled in the study. The samples were collected in plain-tubes, allowed to clot for 30 minutes, and subsequently centrifuged at 3000 rpm for 10 minutes to isolate serum. Serum aliquots were kept at −20°C until analysis [16, 17]. Serum total bilirubin was measured using the diazo method on an automated chemistry analyzer (EasyBil-P, India).

Serum of 25-Hydroxyvitamin-D [25(OH)D] was Quantified via "chemiluminescent immunoassay" (CLIA) using the Cobas-e411 analyzer (Roche Diagnostics, Germany) [18]. The assay demonstrated intra- and inter-assay coefficients of variation below 6%. Vitamin D status was categorized according to Endocrine Society criteria as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics, version 20. The distribution of continuous variables was examined employing the Shapiro–Wilk test to assess normality. Descriptive data were reported as means with standard deviations for continuous variables, while categorical variables were

expressed as frequencies and corresponding percentages. Intergroup comparisons between jaundiced patients and control subjects were conducted using the independent samples t-test for normally distributed continuous data, and the Chi-square test was utilized to evaluate associations among categorical variables [19]. A p-value ≤ 0.05 was considered the threshold for statistical significance.

RESULTS AND DISCUSSION

This study recruited 150 individuals diagnosed with jaundice (mean age: 45.2 ± 13.8 years; 88 males, 62 females) and 50 age- and sex-matched healthy controls (mean age: 43.7 ± 12.5 years; 29 males, 21 females). The groups were comparable in terms of age and sex, with no statistically significant differences detected ($p > 0.05$).

The observed differences in vitamin D status are unlikely to be confounded by demographic variables such as age or sex. Age-related changes in vitamin D metabolism have been previously reported, with older individuals often exhibiting lower serum vitamin D levels due to decreased cutaneous synthesis, reduced dietary intake, and impaired renal conversion [20]. However, the relatively similar mean ages in both groups minimize the potential influence of age on the study Results.

Regarding gender, previous studies have reported inconsistent findings [21]. Some suggest that females may have poorer vitamin D ranks due to cultural, behavioral or hormonal factors, while others report no significant gender differences [22]. In our study, both males and females among jaundiced patients exhibited high prevalence of vitamin D deficiency, indicating that hepatic dysfunction may be a stronger determinant of vitamin D status than gender-related factors. The balanced gender distribution further strengthens the internal validity of our findings by reducing the risk of gender-related confounding.

The frequency of vitamin D-deficiency (<20 ng/mL) among jaundiced patients was significantly higher compared to controls (72.0% vs. 38.0%, $p < 0.05$). Vitamin D insufficiency (20–29 ng/mL) was observed in 18% of jaundiced patients and 34% of controls, while sufficient levels (≥30 ng/mL) were found in only 10% of patients compared to 28% of controls as showing in Table-1).

Table 1: Vitamin D Status in Jaundiced Patients and Controls

Vitamin D Status	Jaundiced Patients (n = 150)	Controls (n = 50)	p-value
Deficient (<20 ng/mL)	108 (72.0%)	19 (38.0%)	< 0.001
Insufficient (20–29 ng/mL)	27 (18.0%)	17 (34.0%)	0.02
Sufficient (≥30 ng/mL)	15 (10.0%)	14 (28.0%)	0.005

The mean serum total bilirubin level in jaundiced patients was 5.8 ± 2.1 mg/dL, significantly higher than in controls (0.8 ± 0.3 mg/dL, $p < 0.001$). A statistically significant inverse relationship was established between serum bilirubin-levels and vitamin-D concentrations ($r = -0.42$, $p < 0.001$), indicating that higher bilirubin levels were linked with lower vitamin D levels (Figure 1).

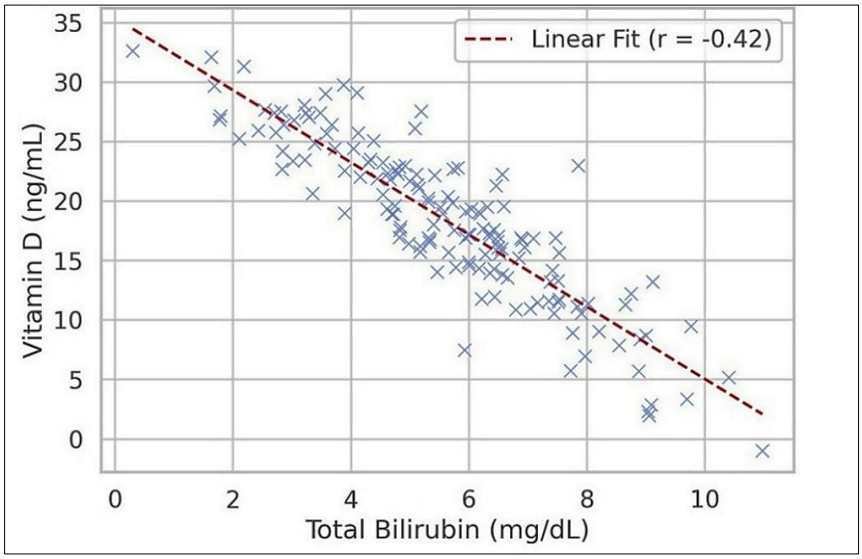

Figure 1: Showing the negative correlation between serum bilirubin and vitamin D levels

This study reveals a notably high incidence of vitamin D deficiency in individuals diagnosed with jaundice, with approximately 72% of the cohort exhibiting deficient serum 25(OH)D levels. Moreover, a

significant inverse relationship was observed between serum bilirubin and vitamin D concentrations, suggesting a potential interaction between hepatic dysfunction and impaired vitamin D metabolism.

Results of this study are consistent with previous-studies indicating that liver disease can significantly compromise vitamin D homeostasis [23]. The liver plays a crucial role in the first hydroxylation step required to convert vitamin D into its active form [24]. Hepatic dysfunction, as observed in jaundiced individuals, may therefore impair this metabolic pathway, leading to reduced circulating 25(OH)D levels [25]. Moreover, cholestasis and biliary obstruction impair the intestinal absorption of fat-soluble vitamins such as vitamin D, thereby intensifying the deficiency [26].

The observed negative correlation between bilirubin and vitamin D levels supports the hypothesis that worsening hepatic dysfunction, reflected by elevated bilirubin, is associated with more pronounced vitamin D deficiency [27,28]. This relationship may have clinical implications, as vitamin D has been implicated in modulating immune function, inflammation, and hepatic fibrosis progression. It is also important to consider that jaundiced patients may have reduced sun exposure and dietary intake due to illness-related lifestyle changes, which could further contribute to their vitamin D deficiency.

CONCLUSION

This study exhibits that deficiency of vitamin D is extremely prevalent between patients with jaundice, significantly exceeding its prevalence in healthy individuals. The significant inverse correlation between serum bilirubin levels and vitamin D concentrations suggests that worsening hepatic dysfunction may impair vitamin D metabolism and absorption. Given the crucial-role of D vitamin in immune-regulation, inflammation, and overall health, routine assessment and "early-correction" of "vitamin D deficiency" in jaundiced patients may be clinically beneficial. Further longitudinal studies are warranted to explore the therapeutic impact of vitamin D supplementation in improving outcomes for this patient population.

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