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Clinical Utility of Vitamin D3 As Potent Biomarker in Cardiovascular and Liver Disorders

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Abstract

Vitamin D is lipophilic substance needed for calcium and phosphate balance and the regulation of the osteo-metabolic system.The purpose of the study was to look at the possible significance of Vitamin D3 as a biomarker for liver enzymes and cholesterol. 249 cases were analysed, with different combinations of liver enzymes, vitamin D3, and cholesterol.75 clinical samples were processed over the course of the 3year study.46(61.3%) were females and 29 (38.6%) were males.Males were more affected than females.In respect to Vitamin D3, the age group of 41-60 years had a large range of cholesterol levels and liver enzyme values. 11% of cases had high SGOT levels, while 13% had aberrant cholesterol values.Above the age of 60, there was a linear connection between cholesterol and liver enzymes.There was seasonal variations in serum 25-OHD levels.Winter (November-March) indicated a Vitamin D3 deficiency in the blood serum, accounting for 74 cases(66%).Autumn and summer had the best range, with only 0 and 16 cases (14.2%), respectively.Despite wide variability in serum vitamin D levels, the differences were not statistically significant.Vitamin D3 can be an important biomarker in clinical practice since it can aid in the early detection of potential hazards linked with cardiovascular disease and liver dysfunction.

***Keywords:** Vitamin D3, Liver Enzymes, Seasonal Variations, Cholesterol, Biomarker, SGOT, SGPT*

1. Introduction

Vitamin D is an essential lipophilic molecule crucial for maintaining calcium and phosphate balance and regulating the osteo-metabolic system (Barchetta et al., 2011). It is categorized within the class of lipophilic compounds and demonstrates structural analogies to steroids (Bruyère et al., 2007). Through a photochemical conversion process involving UV radiation, it forms a modified ring structure known as a secosteroid(Mheid et al., 2013). Moreover, it plays a diverse role in metabolic functions and mineral homeostasis (Steingrims et al., 2005). The nomenclature of "vitamin D" was assigned to the vitamin found in cod liver oil in accordance with the sequential order of vitamin A, B, and C discoveries (Wolpowitz et al., 2005).

Vitamin D is crucial for bone health, preventing rickets in children and muscle weakness in older individuals. Its active form, 1-25OHD, regulates calcium levels by enhancing absorption and mobilization (Brown et al., 2011). In the human body, vitamin D occurs in two forms: vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol). UVB radiation (290-320 nm) on 7-dehydrocholesterol in the skin produces previtamin D3, which then converts to vitamin D3 through heat. In the liver, vitamin D precursors from sunlight and diet transform into 25-hydroxyvitamin D [25(OH)D] or calcidiol, the primary circulating form commonly used to assess an individual's vitamin D status. Further hydroxylation in the kidneys generates active 1,25-

dihydroxyvitamin D [1,25(OH)2D] or calcitriol. Excessive UVB exposure can convert previtamin D3 to inactive metabolites known as tachysterol and lumisterol (Lips et al., 2006).

The assessment of 25-hydroxyvitamin D (25(OH)D) in serum is the established method for evaluating overall vitamin D status. Clinical categorizations based on 25(OH)D levels are as follows: <20 ng/mL (deficient), 20-30 ng/mL (insufficient), and >30 ng/mL (sufficient) (Holick et al., 2011). However, the precise optimal range for 25(OH)D levels remains unclear. A recent report by the Institute of Medicine suggests that higher levels of 25(OH)D do not consistently provide significantly greater benefits, indicating that levels ≥20 ng/mL may be considered sufficient (Ross et al., 2011). Additionally, the enzyme DHCR7, involved in the conversion of 7-dehydrocholesterol (7DHC) to cholesterol in the skin, potentially competes with UVB photons for the utilization of 7DHC, highlighting its role in vitamin D synthesis and metabolism (Holick et al., 2006).

This suggests a potential competition between UVB photons and DHCR7 for the utilization of 7DHC. As a result, individuals with higher levels of serum 7-dehydrocholesterol may experience decreased efficiency in the synthesis of cholecalciferol (vitamin D3) and elevated skin cholesterol levels compared to their level of sunlight exposure (G.M. Kiebzak et al.,2000). The synthesis of cholecalciferol (vitamin D3) and cholesterol share a common precursor called 7-dehydrocholesterol (7DHC) in the skin (Diffey et al., 2003). Several factors, including hepatic and renal disorders (Zabalawi et al., 2007), thyroid dysfunction (Holick et al., 2008), diabetes (V. Kuan et al. 2013), medications, supplements, and hormonal fluctuations, can impact the levels of cholesterol and 25-hydroxyvitamin D [25(OH)D].

2. Materials and Methods

The present clinical case study aimed to assess the biochemical profiles of individuals presenting symptoms associated with high blood pressure, heart stroke, fatigue, itching, loss of appetite, nausea, vomiting, bone pain or achiness, depression or feelings of sadness, and hair loss. The primary objective of the study was to investigate the potential role of Vitamin D3 as a biomarker for liver enzymes SGPT (Aspartate Transaminase), SGOT (Alanine Transaminase), ALP (alkaline phosphatase) and cholesterol. The study was conducted from the case data available at DNA Labs- A Centre for Applied Sciences, Dehradun, Uttarakhand, from May 2021 to May 2023. Detailed medical histories were noted along with data of clinical examinations performed for all patients and confidentiality of patients was kept as prior importance.

A total of 249 case studiess were done, encompassing various combinations of liver enzymes, Vitamin D3, and cholesterol. From these data available, a subset of 75 cases was selected for comprehensive analysis, which included liver enzymes (SGOT, SGPT, ALP), Vitamin D3, and cholesterol. Furthermore, to explore seasonal variations in Vitamin D3 levels, 112 cases were selected The initial diagnosis was done through various materials and method which included Enzyme-linked immunosorbent assay (ELISA) technique for estimation of Vitamin D3 in serum levels and commercially available Qualisa kit was employed. Additionally, the biochemical profile of liver function test, including liver enzymes (SGOT, SGPT, AP), and cholesterol, was determined using a semi-automated biochemistry analyzer using Erba Kit. This comprehensive analysis encompassed individuals from diverse age groups, ensuring a representative sample for the study.

3. Result and Discussion

During the 3-year duration of this study, a total of 75 clinical samples were processed, which included liver enzymes (SGOT, SGPT, ALP), Vitamin D3, and cholesterol. Among these samples, 46 (61.3%) were females, while 29 (38.6%) were males. The findings revealed that males were more affected 8 (27.5%) compared to females 11 (23.9%). An interesting observation was that all affected females belonged to the age group above 60 years. Furthermore, the age group of (41-60 years) showed a higher percentage of cases 4 (30.7%) with Vitamin D3, liver enzymes, and cholesterol levels either above or below the optimum range in males, while in females, the percentage was 6 (33.3%). On the other hand, the age group of (0-20 years) exhibited optimum levels (Table1) of Vitamin D3, liver enzymes, and cholesterol.

Table 1: Age and Gender Wise Distribution of Vitamin D3, cholesterol and liver enzymes collectively

Age (Years)	Gender		No. of Cases	Above or Below the Optimum Range		Optimum range	
	Male	Female		Cholesterol + Liver Enzymes+ Vit.D3		Cholesterol + Liver Enzymes+ Vit.D3	
				Male	Female	Male	Female
0-20	00	04	04	0	0	00	4

	(0%)	(100%)				(0%)	(100%)
21-40	12 (44.44%)	15 (55.55%)	27	4 (33.3%)	2 (13.3%)	8 (66.6%)	13 (72.2%)
41-60	13 (41.9%)	18(58%)	31	4 (30.7%)	6 (33.3%)	9 (69.2%)	12 (66.6%)
Above 60	4 (30%)	9 (69.2%)	13	0 (00%)	3 (33.3%)	4 (100%)	6 (66.6%)
TOTAL	**29 (38.6%)**	**46 (61.3%)**	**75**	**8 (27.5%)**	**11 (23.9%)**	**21 (72.4%)**	**35 (76%)**

In (Table 2, Figure 2) a more detailed analysis of liver enzymes (SGOT, SGPT, ALP), cholesterol, and their correlation with Vitamin D3. The age group of 41-60 years exhibited a high range of cholesterol levels, as well as liver enzyme levels, in relation to Vitamin D3. Specifically, 11 (35.4%) cases showed abnormal cholesterol levels, 13 (41.9%) cases had elevated SGOT levels, 11 (35.4%) cases had elevated SGPT levels, 13 (41.9%) cases had elevated ALP levels, and 10 (32.2%) cases had abnormal Vitamin D3 levels, all above or below the optimum range. Significantly, the age group above 60 years demonstrated a linear relationship between cholesterol and liver enzymes when considering Vitamin D3 as a biomarker. In this age group, 6 (46.1%) cases had abnormal cholesterol levels, 3 (23%) cases had elevated SGOT levels, 4 (30.7%) cases had elevated SGPT levels, 7 (53.8%) cases had elevated ALP levels, and 6 (41.9%) cases had abnormal Vitamin D3 levels.

Table 2: In-Depth Analysis of Liver Enzymes (SGOT, SGPT, ALP), Cholesterol, and their Correlation with Vitamin D3

		Above or Below the Optimum Range					**Optimum range**				
Age (Years)	**No. Of Cases**	**Chol (130-250 mg/dl)**	**SGOT (14 - 35) IU/L**	**SGPT (14 - 35) IU/L**	**A.P (40-100 IU/L)**	**Vit.D3 (30-100ng/dl)**	**Chol (130-250 mg/dl)**	**SGOT (14 - 35) IU/L**	**SGPT (14 - 35) IU/L**	**A.P (40-100) IU/L**	**Vit. D3(30-100ng/dl)**
0-20	04	0%	0%	0%	0%	0%	100%	100%	100%	100%	100%
21-40	27	6 (22.2 %)	19 (70%)	14 (51.8 %)	7 (25.9 %)	5 (18.5%)	21 (77.7 %)	8 (29.62 %)	13 (48.1 %)	20 (74%)	22(81.4 %)
41-60	31	11 (35.4 %)	13 (41.9 %)	11 (35.4 %)	13 (41.9 %)	10 (32.2%)	20 (64.5 %)	18 (58%	20 (64.5 %)	18 (58%)	21 (67.7%)
Above 60	13	6 (46.1 %)	3 (23%)	4 (30.7 %)	7 (53.8 %)	6 (41.9%)	7 (53.8 %)	10 (76.9%)	9 (69.2 %)	6 (41.9 %)	7 (53.8%)

Analysis from (Table 3) reveals significant seasonal variations in serum Vitamin D3 levels. Winter (November-March) demonstrated the deficit concentration of Vitamin D3 in the blood serum, accounting for 74 cases (66%). Conversely, Autumn and summer exhibited the optimum range, with a mere 0 cases and 16 cases (14.2%) respectively.

Table 3: Seasonal Variations in Serum Vitamin D3 Independent of Age and Gender (2021-2023) Total Cases: 112

Above or Below the Optimum Range			**Optimum range**		
SUMMER (April-August)	**AUTUMN (September-October)**	**WINTER (November-March)**	**SUMMER (April-August)**	**AUTUMN (September-October)**	**WINTER (November-March)**
7 (6.25%)	3 (2.6%)	74 (66%)	16 (14.2%)	0 (0%)	12 (10.7%)

In the context of this research 2 key findings have come to light. Firstly, the study has established that vitamin D3 serves as a significant biomarker for assessing liver enzymes and cholesterol levels. Additionally, it has underscored the presence of pronounced seasonal fluctuations (Table 3, Figure 3) in mean serum 25-OHD (25-hydroxyvitamin D) levels, with particular emphasis on the winter season. Importantly, these fluctuations were observed to be independent of age or sex, (Figure 1) adding a dimension of consistency to their occurrence.

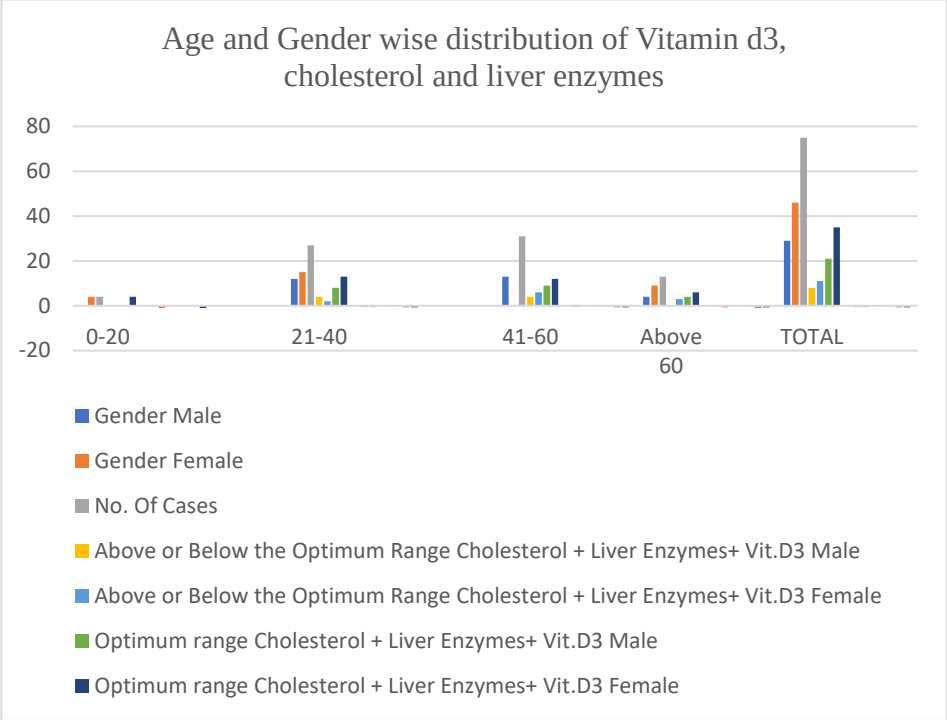

Figure 1: Age and Gender Wise Distribution of Vitamin D3, cholesterol and liver enzymes collectively

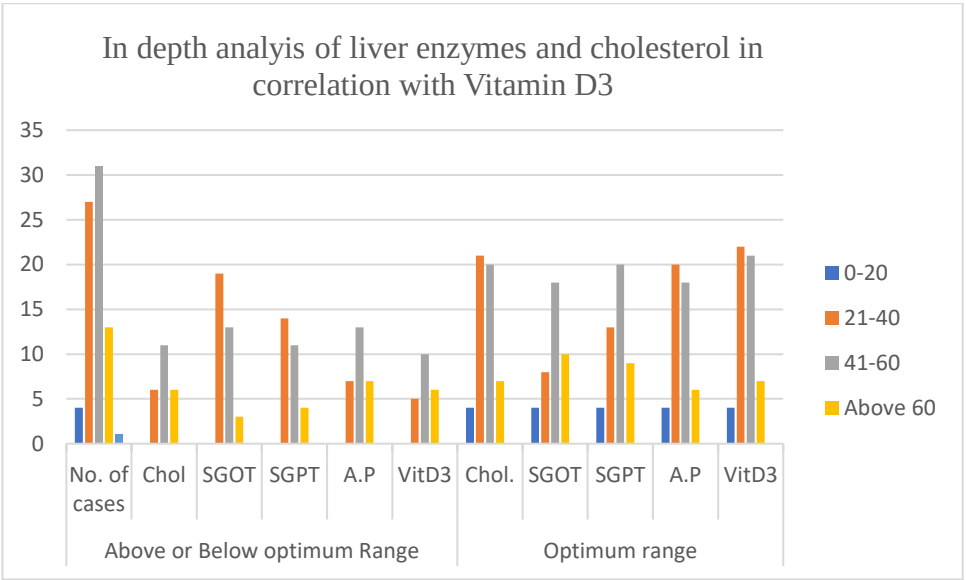

Figure 2: In-Depth Analysis of Liver Enzymes (SGOT, SGPT, ALP), Cholesterol, and their Correlation with Vitamin D3

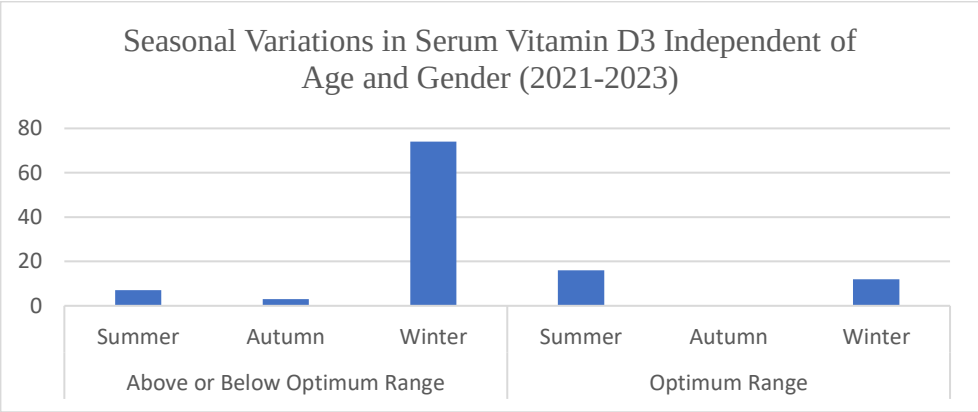

Figure 3: Seasonal Variations in Serum Vitamin D3 Independent of Age and Gender (2021-2023)

The findings of this study are consistent with a number of previously published studies (Costanzo et al., 2011; González et al., 2012; Kashi et al., 2011; Shoben et al., 2011) that looked at the relationship between seasonal variations and vitamin D levels. While some researches have showed decreased levels of serum 25-OHD in the winter, other studies have found that the prevalence of vitamin D deficiency remained steady year-round, regardless of the season (Rajakumar et al., 2011) and some studies stated that vitamin d3 condition worsened in winters as compared to summer and autumn (Hays et al., 2021). These observations suggest that seasonal variations should not be regarded as the sole source of vitamin D variations and that numerous additional factors also contribute to the differences in blood vitamin D throughout the course of the year.However, it's crucial to emphasize that, as of the present scientific landscape, there is a lack of substantial and universally embraced evidence substantiating the notion that males, and females aged above 60 consistently experience heightened susceptibility in comparison to males concerning liver enzyme levels, which include SGPT, SGOT, ALT, cholesterol levels, and vitamin D3 status. The influence of these indicators displays significant variability contingent upon a multitude of factors, encompassing an individual's health status, genetic constitution, lifestyle choices, and the presence of underlying medical conditions.

One noteworthy revelation from this study is the intricate interplay observed within the biosynthesis pathways of vitamin D and cholesterol. (Warren et al., 2021) too have stated the high level of cholesterol leaded to deficient Vitamin d3 level. The implication of this metabolic overlap is the heightened risk of cardiovascular diseases and the concurrent patho- physiological processes associated with atherosclerosis. In addition, the study revealed fluctuations in serum 25-OHD levels that corresponded to different seasons. Compared to the summer and the winter, the serum 25-OHD level was lowest in the autumnal months. Despite the broad variations in serum vitamin D levels, the discrepancies did not approach a significant level.

4. Conclusion

Vitamin D deficiency is becoming more prevalent among Indians, a population that also exhibits higher levels of total cholesterol and lower levels of high-density lipoprotein cholesterol. It is proposed that the enzyme DHCR7, in conjunction with sunlight exposure, may regulate serum 25(OH)D and cholesterol concentrations (Huxley et al., 2011). Additionally, the potential relationship between vitamin D deficiency and liver enzymes such as SGOT (Serum Glutamic-Oxaloacetic Transaminase), SGPT (Serum Glutamic Pyruvic Transaminase), and ALP (Alkaline Phosphatase) remains unclear. Further research is needed to elucidate the possible connections between vitamin D deficiency and liver enzyme alterations in this population (Harinarayan et al., 2009). Furthermore, in individuals with liver failure, there is a notable reduction in the synthesis of 25-hydroxyvitamin D (25-OH vitamin D) due to impaired liver function. However, it should be emphasized that significant impairment of liver function is required for Vitamin D deficiency to manifest. Hence, liver disease can have an impact on the absorption of vitamin D, which may be associated with compromised bile acid production or intestinal edema related to portal hypertension (Nair et al., 2013).

The role of 25-hydroxyvitamin D (25(OH)D) as either a biomarker or a causal factor in disease is still not fully understood. This uncertainty poses a challenge when deciding whether to address low 25 (OH)D levels through supplementation or repletion strategies. Further research is needed to clarify the relationship between 25 (OH)D and disease and guide appropriate management strategies. Vitamin D3 emerges as a noteworthy biomarker for assessing liver enzymes and cholesterol levels due to its intricate interplay within the metabolic

pathways. The evaluation of vitamin D3 levels is crucial in clinical practice, as it provides valuable insights into an individual's health status, especially pertaining to liver function and cholesterol metabolism. Monitoring vitamin D3 levels aids in the early identification of potential risks associated with cardiovascular diseases and liver dysfunction. To optimize vitamin D3 levels, individuals can engage in prudent sun exposure, incorporate vitamin D-rich dietary sources, and consider vitamin D supplements under medical guidance. Ensuring adequate vitamin D3 levels contributes to overall health and well-being, underscoring the significance of its assessment and maintenance in clinical practice.

Conflict of Interest: None

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