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Exploring relationships between Lipid parameters and Serum Vitamin-D deficiency.

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Abstract

Background: Vitamin D deficiency is a prevalent global health concern. To investigate the relationship between serum vitamin D levels and lipid parameters.

Methodology: A prospective observational cohort study was carried out at Sindh Government Hospital Liaquatabad from October 2021 to February 2022. The study included a total of 171 participants, comprising both males and females aged 18 years or older, with vitamin D levels falling below 30 ng/ml. Participant selection employed a consecutive non-probability sampling method. Serum vitamin D levels were quantified using the COBAS method. Dyslipidemia and hypertriglyceridemia were defined based on established clinical guidelines. Exclusion criteria encompassed individuals with specific medical conditions and those currently using medications. Statistical analysis was conducted using SPSS version 22.0.

Results: Out of the 171 participants, the majority were female, constituting 129 (75.43%), while 42 (24.56%) were male. Interestingly, a higher prevalence of vitamin D deficiency was observed among younger patients, with the age group of 30-39 years displaying the highest rate of vitamin D deficiency. Regarding lipid profiles, dyslipidemia was significantly more common in female patients (50.87%) compared to their male counterparts (5.26%). However, it's noteworthy that male patients exhibited higher triglyceride levels (167.21 ± 89.64 mg/dl) than females.

Conclusion: This study reveals a strong relationship between vitamin D deficiency and lipid parameters.

Keywords

Vitamin D, Dyslipidemia, Hypertriglyceridemia, Vitamin D Deficiency

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Introduction

Vitamin D, also known as calciferol, is a vitamin soluble in fat and a steroid according to the chemical classification[1,2]. The main source of the vitamin is Dietary and endogenous synthesis. The other type of vitamin D is vitamin D2 (ergocalciferol), which is obtained from plant sources; however, a very small quantity of vitamin D3 is provided by food derived from animals. The main source of this vitamin is skin synthesis after exposure to sunlight (ultraviolet-B). Regardless of its source, vitamin D is metabolized as hydroxylated in the liver into the 25 Hydroxyvitamin D [25 (OH) D] and later converted into 1,25 dihydroxy vitamin D in the kidneys, which is its inactive form. The levels of serum 25 hydroxyvitamin D commonly addressed in laboratory investigations is the total reflection of vitamin D in the body[3,4].

Several studies have highlighted the prevalence of vitamin D deficiency among patients due to different confounding factors worldwide[2]. Several known and unknown factors have been taken into consideration for the relevancy of serum vitamin D deficiency; however, the impact of vitamin D deficiency leads to multiple complications[5]. The inordinately high rates of vitamin D deficiency in the South Asian adult population have been well documented; vitamin D deficiency in this population is thought to be multifactorial with variables such as nutrition or dietary habits, socioeconomic status, age, gender, time of year, presence of comorbid and genetics all playing some role in its pathophysiology[6]. Yet, even as the knowledge about vitamin D deficiency evolves, no singular predisposing or precipitating factor has been identified as of writing.

Vitamin D deficiency itself has been associated with and identified as a risk factor for several disease processes, such as asthma, cardiovascular diseases, polycystic ovarian syndrome, immunocompromised states, and severe COVID-19 pneumonia, to name a few[7]. However, the causal relationship between these pathologies and vitamin D deficiency remains unproven.

One exception to this is the relationship of vitamin D deficiency with dyslipidemia. An inverse correlation between the two has been thoroughly researched and published in recent times[8-10]; high serum vitamin D levels were associated with favorable lipid profiles, and conversely, suboptimal serum vitamin D levels were associated with suboptimal lipid levels. Despite these extensive records, the causal relationship between the two remains unascertained, as is the case with so many other conditions associated with vitamin D deficiency[11].

The deficiency of Vitamins is fully linked with dyslipidemia and multiple other abnormalities; however, the elevated levels of TC and low-density lipoproteins (LDL) and high-density lipoproteins (HDLs) cholesterols are of great attention. Besides elevating the cholesterol levels of HDLs and LDL, the deficiency is associated with cardiovascular diseases. Mendelian randomization studies or random controlled trials are awaited to fully evaluate this phenomenon.

The data on various aspects of vitamin D deficiency and dyslipidemia or hypertriglyceridemia is scarce locally; despite being the topic of attention, only a few studies have been conducted locally and worldwide. Only a handful of studies from Pakistan have been published in the last few decades, to the best of our knowledge. In this cohort, we have analyzed the prevalence of dyslipidemia and hypertriglyceridemia in patients with vitamin D deficiency, ascertaining the magnitude of these ailments.

Methodology

A prospective observational cohort study was carried out at Sindh Government Hospital Liaquatabad from October 2021 to February 2022. The study included male and female patients aged 18 years or older with vitamin D levels ≤ 30 ng/ml. A consecutive non-probability sampling method was employed. Ethical approval was obtained from the hospital's ethical review board, and informed consent was obtained from all participants.

Serum 25-hydroxyvitamin D levels were assessed using the immunoassay with a detection limit of 7.5 to 175 nmol/L via the COBAS method by Roche Diagnostics, Mannheim, Germany. Vitamin D deficiency was defined as levels below 30 ng/ml. The 2018 AHA/ACC Guidelines were used to define hypertriglyceridemia and dyslipidemia. Patients with lipid-altering medications, vitamin D or calcium supplements, rheumatological diseases, osteoarthritis, bone trauma, pathological fractures, chronic systemic diseases, or malignancy were excluded.

Hypertriglyceridemia was defined as fasting triglyceride (TG) levels ≥ 200 mg/dl, and dyslipidemia was defined as fasting high-density lipoprotein cholesterol (HDL-C) levels < 40 mg/dl for men, < 50 mg/dl for women, or fasting low-density lipoprotein cholesterol (LDL-C) levels ≥ 160 mg/dl for both genders.

Statistical analysis was performed using SPSS version 22.0. Categorical factors were expressed as frequencies and percentages, while continuous variables, including vitamin D, TGL, HDL-C, and LDL-C, were presented as mean and standard variation. Gender, age groups, and the prevalence of dyslipidemia and hypertriglyceridemia in male and female cohorts were reported as frequency and percentage.

Results

A total of 171 patients were included in the study. Patients were predominantly female; the female-to-male ratio in our study was noted as 3:1. Mean age of the patients was 39.12±8.67 years, representing a relatively younger population suffering from vitamin D deficiency; the largest number of participants belonged to the age group of 30-39 years. The gender and age distribution of patients is summarized in table 1.

Table 1: Patient baseline characteristics & frequency of metabolic syndrome (n=257).

Variables		N(%)
Gender	Female	129(75.43)
	Male	42(24.56)
Age; Mean ± SD (years)		39.12 ± 8.67
Age groups	18-29 years	15(8.77)
	30-39 years	93(54.38)
	40-49 years	57(33.33)
	≥50 years	6(3.5)

The prevalence of hypertriglyceridemia was overall low. Males demonstrated higher levels of TGLs compared to females; younger male patients showed lower levels of serum TGLs compared to older ones; the data is presented in table 2.

Table 2: Serum lipid profile comparison between men and women.

Variables	Total	Men	Women	Mean Difference
Serum TG levels (mg/dl)	145.50±84.01	167.21±89.64	123.8±78.39	43.41
Serum HDL-C (mg/dl)	40.63±9.59	47.59±6.53	33.68±12.66	13.91
Serum LDL-C (mg/dl)	142.05±33.74	151.2±40.11	132.9±27.38	18.30

Dyslipidemia was highly prevalent in female patients compared to men; a high proportion of the female patients had suboptimal (≤50 mg/dl) HDL-C levels rather than high (>160 mg/dl) LDL-C levels. The various aspects of the prevalence of dyslipidemia and hypertriglyceridemia in men and women in patients with vitamin D deficiency are summarized in table 3.

Table 3: Prevalence of lipid abnormalities in men and women.

Variables		Men	Women
Prevalence of hypertriglyceridemia*		15(8.77)	6(3.5)
Prevalence of Dyslipidemia	**HDL-C****	9(5.26)	126(50.87)
	LDL-C***	6(3.5)	6(3.5)
Overall prevalence******		105(61.04)	

HDL-C: High Density Lipid Cholesterol, LDL-C: Low Density Lipid Cholesterol
*Serum fasting triglyceride level of ≥200 mg/dl.
**Serum fasting level of high-density lipid cholesterol of ≤40mg/dl for men and ≤50mg/dl for women.
***Serum fasting level of low-density lipid cholesterol of ≥160 mg/dl for either gender.
****Some patients had more than one variant of dyslipidemia.

Discussion

The relationship between dyslipidemia and vitamin D deficiency showed an inverse relationship between the two variables[12]; therefore, it was not unexpected to find such a high prevalence of dyslipidemia in our study as all cohorts had significantly reduced serum levels of vitamin D. Female subjects constituted over three-quarters of all patients in our analysis, demonstrating not only a higher prevalence (and lower means) of pathologically low serum vitamin D levels but also significantly lower serum levels of HDL-C compared to men, these findings also parallel previous reports[13].

Suboptimal levels of serum HDL-C were more commonly observed, especially in women, compared to serum LDL-C and triglycerides levels; hypertriglyceridemia was rarely encountered in women, whereas it was the most common abnormality recorded in men. Our results are quite similar to the ones published in which they demonstrated significantly increased levels of HDL-C with higher or therapeutic levels of serum vitamin D[13]. However, they also reported a correlation for triglycerides. Our sample size was small, and we did not encounter a large number of patients exhibiting hypertriglyceridemia; even when hypertriglyceridemia was seen, it usually overlapped with low HDL-C levels; as such, no inference can be made from our data in this aspect specifically. A possible explanation of differential findings regarding vitamin D deficiency could be due to the differential assay methods used for serum levels, the current study used cutoff levels of laboratory values however a study reported using the electrochemiluminescence assay showed a slight difference in the results of 250 HD levels[14].

Previous studies have also not identified any significant association between high or low levels of serum vitamin D levels and the risk of substantially raised LDL-C levels, similar to the findings of our study[15]. Our results also did not show significant levels of suboptimal LDL-C levels; the prevalence was extremely low for both men and women. However, it is difficult for us to make any definitive statements as we registered only four patients with suboptimal levels of LDL-C, and as the case was in patients with hypertriglyceridemia, there was significant overlap with suboptimal HDL-C levels. Even with such a small sample size, however, it is apparent that serum vitamin D levels impact HDL-C serum levels more than serum LDL-C or triglyceride levels, similarly found in the study[16].

We recorded an inordinate number of female patients presenting with suboptimal levels of serum vitamin D and HDL-C; all but one patient had HDL-C levels of ≤50 mg/dl. Regional data has shown prevalence rates for suboptimal HDL-C levels ranging from 50-90% without any predilection for vitamin D levels; ranges were higher among women and those belonging to the sub-continent[17]. Ergo, it is not unusual to come up against exceedingly high rates of dyslipidemia in the local population; hypovitaminosis D is likely to further exacerbate these percentages giving some explanation for the high prevalence seen in our study.

It is hard to correlate dyslipidemia with hypovitaminosis D when, by some estimates, up to 90% of the general population harbors some variant of suboptimal cholesterol blood levels in Pakistan[16]. Concordantly, exceptionally high rates of vitamin D deficiency have been reported all across Pakistan by multiple authors; all studies showed vitamin D deficiency disproportionately affected women[18-20]. Whenever patients with hypovitaminosis D have dyslipidemia, these tend to affect HDL-C levels more than LDL-C or triglyceride levels; the most common variant of dyslipidemia in the local population is due to aberrant HDL-C levels. Perhaps there is a causal relationship between these two variables. Our sample size was too small and confounded by the non-randomized nature of the study; as such, we are unable to make any definitive statements regarding this matter.

The pleiotropic effect of vitamin D on the cardiovascular system, immunity, adipose tissue, glucose, and lipid metabolism is being reviewed and studied in ever greater detail in modern times[21], with evidence emerging for an inverse correlation between vitamin D levels and leptin or resistin, and a similar correlation with adiponectin levels[22,23]. It also has paracrine, endocrine, and autocrine effects, which can affect several organs beyond the musculoskeletal system[23]; whether these properties of vitamin D affect lipid metabolism is still being explored. Most of the data that is available on the topic and that which was discussed and referenced in our article is retrospective. Randomized prospective studies in humans are lacking and are necessary to evaluate the exact mechanisms by which vitamin D levels affect lipid levels, if at all.

As clinicians, it would be reasonable to extrapolate that reduced vitamin D levels are associated with suboptimal lipid levels, which in turn are associated with adverse cardiovascular outcomes, and optimization and supplementation should lead to better cardiovascular outcomes. However, such an assumption would be inaccurate. Similarly, the Meta-analyses of randomized control trials have demonstrated that markers of cardiovascular disease, including inflammatory enzymes and metabolites, hypertension, and arterial endothelial thickness, are largely unaffected by vitamin D levels; similar Mendelian randomization studies have also concurred that genetic reduction of vitamin D levels does not increase cardiovascular risk[24-26]. More vitamin D supplementation did not improve cardiovascular outcomes[27,28]. However, this should not deter clinicians from optimizing serum vitamin D levels in patients either through supplementation or improved nutrition and lifestyle changes, as improvement in vitamin D levels is beneficial to other aspects of health, including bone mineral homeostasis, insulin resistance, glucose metabolism, fertility in women, reduce cancer risk, enhanced immunity, improved gene expression and function[29-34].

Limitations

Due to the nature of the study, there were some significant shortcomings encountered, mostly due to the unavailability of data. The metabolic and anthropometric profiles of the patients, along with comorbidities, were not recorded nor analyzed in this study. Concordantly, nutritional status, daily caloric intake, daily medical use, history of addiction(s), and history of smoking or smokeless tobacco usage were also not recorded.

Conclusion

The study revealed a notable prevalence of hypertriglyceridemia and dyslipidemia among female patients, particularly in the younger age groups, in comparison to their male counterparts. However, it's essential to acknowledge that the exceptionally high prevalence of suboptimal vitamin D levels within the general population adds complexity to accurately establishing clinical correlations between these variables. Given the existing data limitations, certain relevant factors remain unrecorded and warrant further exploration in future research to provide a more comprehensive understanding of these interrelated health concerns.

Conflicts of Interest

The author(s) have no conflicts of interest.

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