Research Article

Comprehensive analysis and correlation of Serum 25-Hydroxyvitamin D3 Levels with glycemia and cardiometabolic risk factors: A tertiary care hospital-based study

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Keywords

HbA1c, dyslipidemia, lipid profile, vitamin D deficiency

Abstract

Background: Role of Vitamin D is not limited to skeletal health but it acts as a potential modulator of metabolic homeostasis. Studies have shown its influence on insulin secretion and cardiometabolic risk factors. This study was conducted to evaluate correlation of serum 25-hydroxy vitamin D3 (25OH VitD3) levels with glycemic status and lipid profile parameters in a tertiary care hospital setting.

Methods: A cross-sectional observational study was conducted taking 173 adults (>18 years) attending outpatient department of a tertiary care hospital between April and December 2025. Participants were categorized based on HbA1c levels according to American Diabetes Association criteria into non-diabetic, pre-diabetic, and diabetic. 25OH VitD3, total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were estimated from fasting serum sample. Statistical analyses were performed and statistical significance was set at $p<0.05$.

Results: Vitamin D deficiency and insufficiency were observed in more than 65% of participants (mean 25OH VitD3: 27.8±16.16 ng/mL). Patients with diabetes mellitus showed significantly higher TG, VLDL, TG/HDL and TC/HDL ratios and lower HDL levels ($p<0.05$). 25OH VitD3 showed a weak statistically significant negative correlation with HbA1c ($\rho = –0.186$, $p=0.014$) but no significant correlation with lipid parameters. Regression models revealed moderate explanatory power (R^2: 23.9–28.4%), with classical metabolic markers contributing more than vitamin D.

Conclusion: A high prevalence of vitamin D deficiency was detected. Vitamin D demonstrated a weak correlation with glycemia and no correlation with lipid parameters. Vitamin D may function as a metabolic modulator rather than a primary determinant of dysglycemia and dyslipidemia.

Introduction

Exploration of the functional role of vitamin D beyond its classical involvement in calcium homeostasis and skeletal health has generated considerable interest in recent years. Traditionally recognized for its importance in bone mineralization and prevention of rickets and osteomalacia, vitamin D is now increasingly acknowledged as a pleiotropic hormone with wide-ranging effects on multiple organ systems [1]. The discovery of vitamin D receptors (VDRs) in diverse tissues - including the pancreas, liver, adipose tissue, vascular smooth muscle, and immune cells - has significantly expanded the understanding of its biological functions. The active form of vitamin D, calcitriol (1,25-dihydroxyvitamin D), exerts genomic as well as non-genomic effects through its interaction with VDRs, thereby influencing cellular proliferation, differentiation, immune modulation, and metabolic regulation [2].

Particularly noteworthy is the presence of VDRs in pancreatic beta cells, which play a central role in insulin synthesis and secretion. Experimental and clinical studies suggest that vitamin D may modulate insulin secretion directly by binding to VDRs in beta cells and indirectly by regulating intracellular calcium flux, which is essential for insulin exocytosis. In addition, vitamin D has been implicated in improving insulin sensitivity in peripheral tissues such as skeletal muscle and adipose tissue. It may also exert anti-inflammatory effects that help mitigate insulin resistance, a key pathogenic mechanism underlying type 2 diabetes mellitus [3,4]. Thus, vitamin D appears to contribute to metabolic homeostasis not only through its endocrine functions but also via its immunomodulatory and anti-inflammatory properties.

Diabetes mellitus is characterized by chronic hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both. Persistent disturbances in glucose metabolism are frequently accompanied by dyslipidemia, which significantly enhances cardiovascular risk. In patients with diabetes, increased hepatic lipogenesis and altered lipid metabolism lead to elevated triglyceride levels and reduced high-density lipoprotein (HDL) cholesterol concentrations. This dyslipidemic pattern promotes the formation of small dense low-density lipoprotein (LDL) particles, which are more susceptible to oxidative modification and more atherogenic than larger LDL particles [5,6]. The coexistence of hyperglycemia and atherogenic dyslipidemia accelerates endothelial dysfunction, oxidative stress, and chronic low-grade inflammation, all of which contribute to the progression of atherosclerosis and heightened cardiometabolic risk [7].

Emerging evidence suggests that vitamin D deficiency may be associated with adverse glycemic status and unfavorable lipid profiles. Low serum 25-hydroxyvitamin D3 [25(OH) D3] levels have been linked to poor glycemic control, higher HbA1c levels, insulin resistance, and an increased prevalence of metabolic syndrome. Moreover, vitamin D deficiency has been correlated with elevated triglycerides and reduced HDL cholesterol, further amplifying cardiovascular risk [8]. However, the findings across different populations remain inconsistent, possibly due to variations in ethnicity, lifestyle, dietary habits, sunlight exposure, and genetic factors affecting vitamin D metabolism.

In the Indian context, vitamin D deficiency is highly prevalent despite abundant sunlight, owing to factors such as skin pigmentation, urban lifestyle, limited outdoor activity, and dietary insufficiency. Studies have reported significantly high prevalence of hypovitaminosis D across different regions of India [9–11]. Nevertheless, studies examining the relationship between serum 25-hydroxyvitamin D3 levels, glycemic indices, and lipid parameters in the Indian population are relatively limited. Given the growing burden of diabetes and cardiovascular disease in India, understanding these associations is of considerable clinical relevance.

Therefore, the present study was undertaken to analyze the correlation of serum 25-hydroxyvitamin D3 levels with glycated hemoglobin (HbA1c) and lipid profile parameters. By evaluating these relationships, the study aims to provide further insight into the potential role of vitamin D in modulating glycemic control and cardiometabolic risk factors among individuals with altered glucose metabolism.

Materials and Methods

A cross-sectional observational study was conducted in a tertiary care teaching hospital after obtaining approval from the Institutional Ethics Committee. A total of 173 patients aged more than 18 years who attended the outpatient department of the hospital attached to a medical sciences institute were enrolled between April 2025 and December 2025 after obtaining written informed consent. The study was carried out in accordance with the ethical principles outlined in the Declaration of Helsinki and its subsequent revisions concerning biomedical research involving human subjects.

Non-diabetic, pre-diabetic and patients with diabetes mellitus, were assigned with group 1, 2 & 3 respectively. Diagnosis of diabetic state was made based on the glycated hemoglobin (HbA1c) value according to American Diabetes Association (ADA) criteria [12]. HbA1c was measured in a high-performance liquid chromatography (HPLC) based fully automatic analyser (Arkray - ADAMS HA 8180T, Japan). Any patients who were on therapy of lipid lowering agents and/or vitamin D3 supplementation, patients who refused to give consent were excluded in the study.

Recruited participants were instructed for 12 hours overnight fast. In the morning, 04 mL of venous blood was collected in plain vacutainer tube with gel separator under aseptic precaution. Blood was allowed to clot for 30 minutes and serum was separated by centrifugation at 1200g for 15 minutes. Fasting serum samples were analysed for 25-Hydroxyvitamin D3 (25OH Vit D3), total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL) and high-density lipoprotein (HDL) in fully automated analyser (Vitros 5600 integrated

system, QuidelOrtho, USA) with intra- and inter-assay coefficients of variation (CV) of 5.1 & 6.8, 1.1 & 1.5, 1.0 & 1.8, 1.5 & 2.9, 1.0 & 2.1 for the parameters respectively. Patients' demographic and clinical details were noted. Data was compiled using Microsoft Excel 2019 (Microsoft Corp., Redmond, WA) and statistical analysis was performed using Jamovi for Windows, version 2.6.26. Normality was assessed using the Shapiro–Wilk test. Normally distributed variables were analysed using Student's t-test or ANOVA, while non-parametric variables were analysed using Mann–Whitney U test or Kruskal–Wallis test. Spearman's rank correlation was used for association analysis. Multivariate linear regression models were constructed to evaluate independent predictors. Statistical significance was set at p value <0.05.

Results

Table 1 shows descriptive statistics and normality assessment of the study participants' data. Values of age, TC, LDL and non-HDL cholesterol followed normal distribution while the other parameters such as HbA1c, HDL, TG, VLDL, TG/HDL ratio, TC/HDL ratio, LDL/HDL ratio and 25OH Vit D3 values did not follow the normal distribution pattern. Non-parametric statistical tests were used to analyse the data which did not follow the normal distribution [13].

Table 1: Descriptive statistics and assessment of normality of the data.

Parameters	N	Mean	Standard Deviation	Shapiro-Wilk Test	
				W	p
Age (Years)	173	47.94	16.25	0.984	0.046
HbA1c (%)	173	6.67	1.94	0.709	<.001
Serum Total Cholesterol (mg/dL)	173	180.62	45.87	0.988	0.133
Serum HDL (mg/dL)	173	45.91	15.38	0.842	<.001
Serum LDL (mg/dL)	173	116.27	42.08	0.984	0.052
Serum Triglycerides (mg/dL)	173	153.83	79.49	0.843	<.001
Serum VLDL (mg/dL)	173	30.91	16.58	0.816	<.001
Triglyceride to HDL Ratio	173	3.85	2.81	0.779	<.001
Total Cholesterol to HDL Ratio	173	4.21	1.4	0.94	<.001
LDL to HDL Ratio	173	2.74	1.2	0.957	<.001
Non-HDL Cholesterol (mg/dL)	173	134.71	43.67	0.985	0.066
Serum 25-OH Vitamin D3 (ng/mL)	173	27.8	16.16	0.921	<.001

Table 2 shows comparison of parameters between female and male study participants. We found statistically significant lower concentration of HDL in male compared with female (p<0.05) while higher levels of TG/HDL ratio, TC/HDL ratio and LDL/HDL ratio in male compared with female (p<0.05). Other parameters were not statistically different among male and female study participants (p>0.05).

Table 2: Comparison of study participants as per gender.

Parameters	Female (n=103)		Male (n=70)		p value
	Mean / Median	SD / IQR	Mean / Median	SD / IQR	
Age (Years)*	46.99	15.15	49.34	17.77	0.352
HbA1c (%)†	5.9	1.05	6.1	1.8	0.11
Serum Total Cholesterol (mg/dL) *	181.82	45.75	178.86	46.32	0.678
Serum HDL (mg/dL)†	48	17.5	40	11.75	<0.001
Serum LDL (mg/dL) *	115.92	41.83	116.78	42.75	0.896
Serum Triglycerides (mg/dL)†	129	65	143.5	83.96	0.185

Parameters	Female (n=103)		Male (n=70)		p value
	Mean / Median	SD / IQR	Mean / Median	SD / IQR	
Serum VLDL (mg/dL)†	26	13.1	28.5	19.65	0.185
Triglyceride to HDL Ratio†	2.64	2.48	3.63	2.84	0.008
Total Cholesterol to HDL Ratio†	3.74	1.64	4.37	1.88	0.002
LDL to HDL Ratio†	2.38	1.55	2.85	1.52	0.009
Non-HDL Cholesterol (mg/dL) *	134	60.05	133	67.25	0.538
Serum 25-OH Vitamin D3 (ng/mL)†	23.7	19.95	23.4	21.92	0.924

**For parameters following normal distribution: Mean, SD and p value of student's t-test;*

† For parameters not following normal distribution: Median, IQR and p value of Mann-Whitney U test.

Table 3 shows comparison of parameters between non-diabetic, pre-diabetic and diabetic study participants classified as per ADA criteria. We found statistically significant difference in age, HbA1c, HDL, TG, VLDL, TG/HDL ratio, TC/HDL ratio and non-HDL cholesterol values among study groups ($p<0.05$). Other parameters did not show statistically significant difference.

Table 3: Comparison of study participants based on the diabetic status.

Parameters	Non-Diabetic (n=53)		Pre-Diabetic (n=63)		Diabetic (n=57)		p value
	Mean / Median	SD / IQR	Mean / Median	SD / IQR	Mean / Median	SD / IQR	
Age (Years) *	36.45	16.19	47.81	14.20	58.77	10.01	<0.001
HbA1c (%)†	5.5	0.2	5.9	0.3	7.8	3.3	<0.001
Serum Total Cholesterol (mg/dL) *	171.45	39.12	189.98	42.32	178.79	53.64	0.053
Serum HDL (mg/dL)†	47	13	46	14.5	40	18	0.006
Serum LDL (mg/dL) *	108.48	37.33	123.54	38.68	115.48	48.69	0.109
Serum Triglycerides (mg/dL)†	111	92	135	67	146	78	0.004
Serum VLDL (mg/dL)†	22	18.4	27	13.4	29.2	16	0.004
Triglyceride to HDL Ratio†	2.28	2.61	2.88	1.96	4.03	2.62	<0.001
Total Cholesterol to HDL Ratio †	3.61	1.19	3.92	1.62	4.71	1.92	0.004
LDL to HDL Ratio†	2.38	1.14	2.56	1.39	3.01	1.88	0.065
Non-HDL Cholesterol (mg/dL) *	121.74	39.25	143.08	40.25	137.53	48.86	0.016
Serum 25-OH Vitamin D3 (ng/mL)†	23.7	21	24	19.1	22.8	18.4	0.63

**For parameters following normal distribution: Mean, SD and p value of ANOVA test;*

† For parameters not following normal distribution: Median, IQR and p value of Kruskal-Wallis test.

Table 4 shows comparison of parameters between participants having deficiency, insufficiency and sufficiency as per serum 25OH VitD3 levels. There was no statistically significant difference in all the parameters ($p>0.05$) except 25OH VitD3 levels ($p<0.05$) among study groups.

Table 4: Comparison of study participants based on the Serum 25-OH Vitamin D3 levels.

Parameters	Deficient (<20 ng/mL) (n=62)		Insufficient (20-30 ng/mL) (n=52)		Sufficient (30-100 ng/mL) (n=59)		p value
	Mean / Median	SD / IQR	Mean / Median	SD / IQR	Mean / Median	SD / IQR	
Age (Years)*	45.66	16.45	48.67	17.4	49.69	14.93	0.357
HbA1c (%)†	5.8	2.56	5.95	1.15	5.9	1.15	0.855
Serum Total Cholesterol (mg/dL)*	172.42	46.39	189.54	45.89	181.37	44.51	0.147
Serum HDL (mg/dL)†	41	19.75	46.5	14.25	45	10	0.202
Serum LDL (mg/dL)*	109.51	40.07	121.26	44.19	118.98	42.03	0.271
Serum Triglycerides (mg/dL)†	133.5	85.75	142	78.5	129	77.5	0.339
Serum VLDL (mg/dL)†	26.5	17.15	28.2	15.7	26	15.5	0.338
Triglyceride to HDL Ratio†	2.79	3.22	3.53	2.42	2.93	2.04	0.694
Total Cholesterol to HDL Ratio †	3.99	1.65	4.17	1.81	3.92	1.64	0.643
LDL to HDL Ratio†	2.56	1.44	2.86	1.26	2.45	1.59	0.912
Non-HDL Cholesterol (mg/dL)*	129.4	44.92	141.42	45.69	134.37	40.34	0.375
Serum 25-OH Vitamin D3 (ng/mL)†	13.75	5.47	23.6	4.7	43.2	13.85	<0.001

**For parameters following normal distribution: Mean, SD and p value of ANOVA test;*

† For parameters not following normal distribution: Median, IQR and p value of Kruskal-Wallis test.

Table 5 shows Spearman's correlation matrix heatmap among parameters. We found significant positive correlation between age vs HbA1c, age vs TG, age vs VLDL, age vs TG/HDL ratio, HbA1c vs TG, HbA1c vs VLDL, HbA1c vs TG/HDL ratio, HbA1c vs TC/HDL ratio, HbA1c vs LDL/HDL ratio, TC vs HDL, TC vs LDL, TC vs TG, TC vs VLDL, TC vs TC/HDL ratio, TC vs LDL/HDL ratio, TC vs non-HDL, LDL vs TG, LDL vs VLDL, LDL vs TC/HDL ratio, LDL vs LDL/HDL ratio, LDL vs non-HDL, TG vs VLDL, TG vs TG/HDL ratio, TG vs TC/HDL ratio, TG vs LDL/HDL ratio, TG vs non-HDL, VLDL vs TG/HDL ratio, VLDL vs TC/HDL ratio, VLDL vs LDL/HDL ratio, VLDL vs non-HDL, TG/HDL ratio vs TC/HDL ratio, TG/HDL ratio vs LDL/HDL ratio, TG/HDL ratio vs non-HDL, TC/HDL ratio vs LDL/HDL ratio, TC/HDL ratio vs non-HDL and LDL/HDL ratio vs non-HDL ($p<0.05$). We found significant negative correlation between HbA1c vs HDL, HbA1c vs 25OH VitD3 (also shown in Figure 1), HDL vs TG, HDL vs VLDL, HDL vs TG/HDL ratio, HDL vs TC/HDL ratio and HDL vs LDL/HDL ratio ($p<0.05$). Remaining correlations were not statistically significant.

Table 5: Spearman's correlation matrix heatmap among parameters (n=173).

Parameters		Age	HbA1c	TC	HDL	LDL	TG	VLDL	TG/HDL	TC/HDL	LDL/HDL	Non-HDL	25OHD
Age	rho (ρ)	—											
	p-value	—											
HbA1c	rho (ρ)	0.565*	—										
	p-value	<.001	—										
TC	rho (ρ)	0.041	0.028	—									
	p-value	0.593	0.714	—									
HDL	rho (ρ)	-0.055	-0.266*	0.297*	—								
	p-value	0.47	<.001	<.001	—								
LDL	rho (ρ)	0.013	0.025	0.890*	0.094	—							
	p-value	0.862	0.741	<.001	0.219	—							
TG	rho (ρ)	0.160*	0.256*	0.310*	-0.305*	0.224*	—						
	p-value	0.036	<.001	<.001	<.001	0.003	—						
VLDL	rho (ρ)	0.157*	0.257*	0.309*	-0.305*	0.224*	1.000*	—					
	p-value	0.039	<.001	<.001	<.001	0.003	<.001	—					
TG/HDL Ratio	rho (ρ)	0.157*	0.329*	0.087	-0.676*	0.122	0.890*	0.890*	—				
	p-value	0.04	<.001	0.256	<.001	0.11	<.001	<.001	—				
TC/HDL Ratio	rho (ρ)	0.102	0.281*	0.499*	-0.617*	0.626*	0.535*	0.535*	0.690*	—			
	p-value	0.183	<.001	<.001	<.001	<.001	<.001	<.001	<.001	—			
LDL/HDL Ratio	rho (ρ)	0.061	0.201*	0.537*	-0.525*	0.750*	0.383*	0.383*	0.534*	0.947*	—		
	p-value	0.429	0.008	<.001	<.001	<.001	<.001	<.001	<.001	<.001	—		
Non-HDL	rho (ρ)	0.072	0.112	0.940*	0.036	0.935*	0.416*	0.415*	0.292*	0.717*	0.740*	—	
	p-value	0.346	0.144	<.001	0.637	<.001	<.001	<.001	<.001	<.001	<.001	—	
25OH VitD3	rho (ρ)	0.062	-0.186*	0.095	0.146	0.096	0.021	0.022	-0.056	-0.086	-0.05	0.069	—
	p-value	0.415	0.014	0.214	0.055	0.208	0.779	0.777	0.466	0.263	0.515	0.367	—

**Statistically significant correlation.*

Figure 1: Scatter plot of 25OH VitD3 vs HbA1c among study participants (n=173).

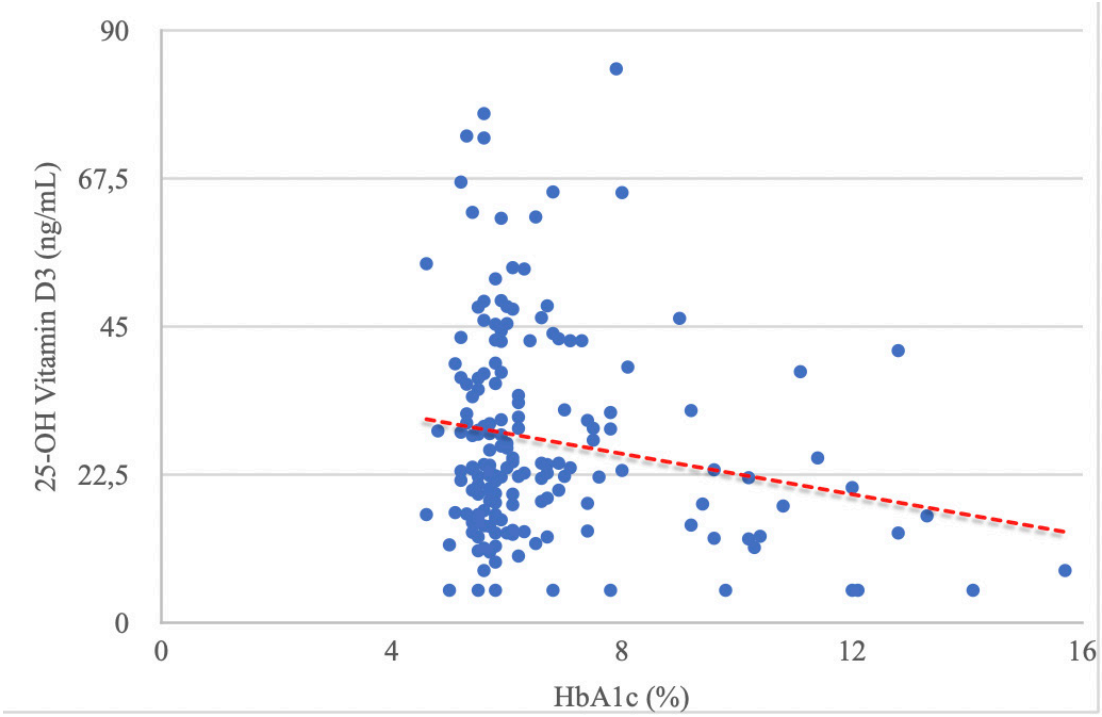

Table 6 to 9 show the statistics of linear regression model that was developed taking different predictors and outcome variables. Each model had a moderate positive relationship between the predictor variables and outcome variables as described by the correlation coefficient (R) and R-squared values. The mean Cook's Distance value for each model was quite low, suggesting that the influence of individual data points on the estimated regression coefficients was minimal. This indicates that there were no influential outliers that could significantly distort the results [14]. All the models were statistically significant ($p<0.05$).

Table 6: Linear Regression model statistics: Model 1.

Model	R	R^2	Adjusted R^2	Overall Model Test				Mean Cook's Distance
				F	df1	df2	p	
1	0.489	0.239	0.211	8.68	6	166	<0.001	0.00871

Note: *1. Model estimated using sample size of N=173*
2. Dependent / Outcome Variable: HbA1c
3. Independent / Predictor Variables: Age, Gender, TC, TG, HDL, 25OH VitD3

Table 7: Linear Regression model statistics: Model 2.

Model	R	R^2	Adjusted R^2	Overall Model Test				Mean Cook's Distance
				F	df1	df2	p	
2	0.511	0.262	0.235	9.8	6	166	<0.001	0.0112

Note: *1. Model estimated using sample size of N=173*
2. Dependent / Outcome Variable: TC
3. Independent / Predictor Variables: Age, Gender, HbA1c, TG, HDL, 25OH VitD3

Table 8: Linear Regression model statistics: Model 3.

Model	R	R^2	Adjusted R^2	Overall Model Test				Mean Cook's Distance
				F	df1	df2	p	
3	0.492	0.242	0.214	8.83	6	166	<0.001	0.00849

Note: *1. Model estimated using sample size of N=173*
2. Dependent / Outcome Variable: TG
3. Independent / Predictor Variables: Age, Gender, HbA1c, TC, HDL, 25OH VitD3

Table 9: Linear Regression model statistics: Model 4.

Model	R	R^2	Adjusted R^2	Overall Model Test				Mean Cook's Distance
				F	df1	df2	p	
4	0.533	0.284	0.258	11	6	166	<0.001	0.00658

Note: *1. Model estimated using sample size of N=173*
2. Dependent / Outcome Variable: HDL
3. Independent / Predictor Variables: Age, Gender, HbA1c, TC, TG, 25OH VitD3

Discussion

The present tertiary care hospital-based study provided a comprehensive evaluation of 25OH VitD3 levels in relation to glycemic status and cardiometabolic risk factors. Our finding will contribute to resolve ongoing debate regarding whether vitamin D deficiency is only a marker of poor metabolic health or it is an independent determinant of dysglycemia and dyslipidemia.

One of the important observations from the study stated that more than 35% study participant were vitamin D3 deficient and more than 30% were having insufficient levels of vitamin D3. Mean serum level of 25OH VitD3 were 27.8 ng/mL (n=173) which again falls within vitamin D3 insufficiency range that depicts the magnitude of the subnormal vitamin D status. Many other studies have also reported similar high prevalence of vitamin D deficiency even in apparently healthy populations [15–19]. Despite India being a sun-light rich country, such paradoxically low vitamin D levels may be due to adaptation to urban lifestyle, indoor occupational pattern, reduced outdoor physical activity, darker skin pigmentation, dietary insufficiency, and pollution-related UVB attenuation can be few of the major factors causing hypovitaminosis D [16,20,21]. Upon normality check with Shapiro-Wilk Test, we found many metabolic parameters did not follow a Gaussian distribution. This suggests heterogenous distribution of these cardiometabolic parameters in hospital-based population. To maintain appropriateness, strength and validity of the statistical inferences, non-parametric tests were utilized for the variables not following normal distribution [13].

Gender based differences in lipid metabolism exist due to difference in hormonal milieu between them. Oestrogen enhances hepatic LDL receptor expression, promotes reverse cholesterol transport and increases apolipoprotein A1 synthesis that increases HDL concentration. On the other side, greater visceral obesity along with androgens are associated increased flux of free fatty acids into portal circulation enhancing hepatic VLDL synthesis. Androgens also increase hepatic lipase activity which along high TG increases HDL catabolism promoting atherogenic lipid profile pattern [22]. In our study, male participants exhibited significantly lower HDL and higher TG/HDL, TC/HDL and LDL/HDL ratios compared to females. These findings are consistent with previously done studies [22–24]. However, 25OH VitD3 did not differ between both the genders, which suggests that gender-based difference in lipid indices may not be attributed to vitamin D status of the individuals.

A comparison of cardiometabolic indices was made in the study participants divided in three groups based on ADA defined glycemic categories. We found significant difference in age, HDL, TG, VLDL, TG/HDL ratio, TC/HDL ratio and non-HDL cholesterol. Diabetic individuals were relatively older in age and they exhibited atherogenic dyslipidemia. They had elevated TG, VLDL, TG/HDL and TC/HDL ratios and lower HDL levels compared with non-diabetic participants. These findings show characteristic pattern of diabetic dyslipidemia caused by insulin resistance [25,26]. Insulin inhibits hormone sensitive lipase and reduces free fatty acid flux to the liver and thereby reducing hepatic VLDL production. In the state of insulin resistance (IR), there is increased lipolysis in adipose tissue resulting increased free fatty delivery to hepatocyte and causing increased TG synthesis and VLDL secretion. IR also reduce lipoprotein lipase activity and impair peripheral TG clearance. Elevated TG increases cholesterol ester transfer protein (CETP) mediated exchange of TG and cholesterol ester between HDL and TG rich VLDL causing HDL to become TG rich and making them more susceptible to hepatic lipase mediated catabolism and leading to reduced serum HDL level [27]. Many studies have shown elevated TG/HDL ratio as a surrogate marker of insulin resistance and increased levels of small dense LDL particles which have shown to participate in

atherogenic plaque formation in blood vessels [27–29]. However, serum 25OH Vit D3 did not significantly differ across these groups divided as per glycemic status, which suggest that despite high prevalence of vitamin D deficiency, it may not be a primary determinant for glycemic dysregulation and dyslipidemia in the study participants. We also stratified the participants as per their vitamin D status as deficient, insufficient, and sufficient groups. No statistically significant differences were observed in glycemic indices, lipid parameters and atherogenic ratios. This finding further reinforces the fact that vitamin D deficiency alone is not the driving force for cardiometabolic derangements in clinical settings [30].

Analysis of correlation matrix revealed many significant relations between various cardiometabolic parameters. A strong positive correlation between age and HbA1c suggest age as a strong determinant for dysglycemic state. Such changes can be attributed to occurrence of gradual β-cell dysfunction, reduced incretin effect, mitochondrial functional decline, sarcopenia, reduced physical activity, increased occurrence of obesity and chronic low-grade inflammation as the age advances [31]. Correlation of HbA1c with lipid profile and ratios further reflects bidirectional relation between dyslipidemia and insulin resistance. Hepatic de-novo lipogenesis is activated by hyperglycemia through activation of carbohydrate-responsive element-binding protein (ChREBP) and sterol regulatory element-binding protein-1c (SREBP-1c) which increases TG synthesis. On the other side, lipid accumulation in skeletal muscle and liver impairs insulin signalling via diacylglycerol (DAG) mediated activation of protein kinase C (PKC) pathways. Both these mechanisms establish vicious cycle and enhance effects of each other [28,32,33].

We observed weak but a significant negative correlation ($\rho = -0.186$) of 25OH VitD3 with HbA1c. Vitamin D did not show any significant correlation with other lipid indices. Vitamin D have found to affect metabolism in several way. The pancreatic β-cells expresses vitamin D receptors (VDR). Vitamin D is found to enhance insulin gene transcription through vitamin D response elements. It is also associated with modulation of intracellular calcium flux that drives the insulin exocytosis. Thus, deficiency of vitamin D may impair insulin secretion and affect glucose homeostasis [2]. On the other side, vitamin D reduces pro-inflammatory cytokines (TNF-α, IL-6) that interfere with insulin signalling by inducing serine phosphorylation instead of tyrosine phosphorylation of signalling pathway intermediates. Chronic vitamin D deficiency may promote low-grade inflammation and insulin resistance [31,34]. Vitamin D also influences adipocyte differentiation and lipid storage that further affect adipose tissue homeostasis [35]. We could not find any direct significant correlation of vitamin D with lipid profile indices. However, strong correlations of HbA1c with lipid profile and negative correlation of Vitamin D with HbA1c can indirectly suggest effect of vitamin D on person's lipid profile by modulating the metabolism as mentioned above. Findings from our study aligns with the findings reported by Liu et al [8], Ge L et al [36], Alqahtani RM et al [37] and Abdo B et al [38]. Studies have also suggested that vitamin D supplementation in vitamin D deficient persons do not affect the dyslipidemia in them [36,39–41]. Many researchers have found a significant association of dyslipidemia with vitamin D deficiency [42–46]. Though similar pattern of lipid profile changes was observed, the changes are not statistically significant in our study. Mechanism for changes in lipid profile in vitamin D deficiency can be increased cholesterol synthesis via increased 3-hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase expression through insulin-induced gene-2 (Insig-2) expression down-regulation which is followed by inhibition of sterol regulatory element-binding protein 2 (SREBP-2) through reduced transcriptional activity of Vitamin D receptor (VDR) in vitamin D deficiency [47]. Vitamin D also modulate microsomal triglyceride transfer protein (MTP), and thus reduces the synthesis and secretion of triglycerides [48]. Vitamin D also affects insulin signalling and inflammatory state, thereby affects serum TG and HDL levels [49]. Thus, correlations of HbA1c with vitamin D and lipid profile parameters in our study suggests that vitamin D may act as a secondary modulator rather than a primary driver of hyperglycaemia by modestly influencing the β-cell responsiveness and insulin receptor signalling, thereby influencing lipid metabolism [38].

Four regression models were developed to explore independent determinants. Each model had a moderate R value and low mean Cook's distance that confirmed model's stability and absence of influential outliers. Collectively all regression models highlight that HbA1c and lipid indices accounted much for explaining variances in them along with age and gender while 25OH VitD3 contributed minimally. Analysis further stats that vitamin D though has an important role in metabolism, it is not the only and primary determinant for development of dysglycemia and dyslipidemia [30].

Cross-sectional observational studies have several limitations that should be considered when interpreting the results. We could not establish causal relationship between glycemic and cardiometabolic parameters with vitamin D deficiency. Longitudinal studies are needed to identify these associations. Certain unmeasured factors such as genetic predispositions, dietary habits, physical activity, body mass index, central obesity indices, addictions, seasonal variation in vitamin D synthesis, etc, can substantially influence the correlations. Being a single centre study with limited number of participants, the study results cannot be implemented to general population. This study provides a future direction for planning of a multicentric longitudinal study with participant of different ethnicity, geographical regions and socioeconomic groups that would strengthen the findings and would make them more reliable and applicable in different populations. A randomized controlled trials conducted with adequate dosing and specified

duration may help conclude whether correction of vitamin D deficiency confers metabolic benefit in specific subgroups.

Conclusion

Vitamin D deficiency and insufficiency is highly prevalent in the population. Screening and supplementation for them can improve overall skeletal health. Serum 25OH VitD3 had weak negative correlation with HbA1c and it was not a strong independent predictor in multivariate regression analysis. Classical metabolic markers remain stronger determinants of cardiometabolic risk. Thus, vitamin D may serve as a contributory metabolic modulator rather than a primary etiological factor in dysglycaemia and dyslipidemia. Vitamin D correction cannot be viewed as a standalone strategy for glycaemic and lipemic control.

Competing interests

The authors declare that they have no competing interests to disclose.

Declaration of conflict of interest

The authors affirm that this study is free from any conflicts of interest.

Ethical Approval

This investigation was conducted in accordance with the ethical guidelines of the Declaration of Helsinki on biomedical research on humans and was approved by the Institutional Ethics Committee of AIIMS Rajkot. Letter Number: AIIMS/RAJKOT/IEC/6th/ER/07.

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Data Availability Statement

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Credit Authors:

[1]AS: Conceptualization, Methodology, Review, Editing and validation, Data curation, supervision and editing.
[2]DP: Conceptualization, Methodology, Review, Editing and validation.
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[1]SD: Original Draft, Data curation, editing.
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Supplier name for reagents/apparatus

1. Reagents/consumables/column for HPLC based ArkRay ADAMS- HA 8180T for HbA1c: Authorized distributor - SPSS Medline; New Delhi (India)
2. Fully automatic integrated chemistry and Immunoassay analyzer: Vitros 5600; QuidelOrtho USA
3. Kits/reagents/consumables for Vitro 5600 integrated analyzer: Authorized distributor – Olympus, Rajkot (India)
4. ArkRay ADAMS- HA 8180T HPLC analyzer for HbA1c: Arkray Japan
5. Control: Biorad; Genetix Ahmedabad (India)

References:

1. Voltan G, Cannito M, Ferrarese M, Ceccato F, Camozzi V. Vitamin D: An Overview of Gene Regulation, Ranging from Metabolism to Genomic Effects. Genes (Basel). 2023;14(9). doi:10.3390/GENES14091691
2. Argano C, Mirarchi L, Amodeo S, Orlando V, Torres A, Corrao S. The Role of Vitamin D and Its Molecular Bases in Insulin Resistance, Diabetes, Metabolic Syndrome, and Cardiovascular Disease: State of the Art. Int J Mol Sci. 2023;24(20). doi:10.3390/IJMS242015485
3. Dong B, Zhou Y, Wang W, et al. Vitamin D Receptor Activation in Liver Macrophages Ameliorates Hepatic Inflammation, Steatosis, and Insulin Resistance in Mice. Hepatology. 2020;71(5):1559-1574. doi:10.1002/HEP.30937
4. Zhang Y, Ni P, Miao Y, et al. Vitamin D3 improves glucose metabolism and attenuates inflammation in prediabetic human and mice. J Nutr Biochem. 2024;130. doi:10.1016/J.JNUTBIO.2024.109659
5. Wong ND, Sattar N. Cardiovascular risk in diabetes mellitus: epidemiology, assessment and prevention. Nat Rev Cardiol. 2023;20(10):685-695. doi:10.1038/S41569-023-00877-Z
6. Pennells L, Kaptoge S, Østergaard HB, et al. SCORE2-Diabetes: 10-year cardiovascular risk estimation in type 2 diabetes in Europe. Eur Heart J. 2023;44(28):2544-2556. doi:10.1093/EURHEARTJ/EHAD260
7. Hariharan R, Odjidja EN, Scott D, et al. The dietary inflammatory index, obesity, type 2 diabetes, and cardiovascular risk factors and diseases. Obes Rev. 2022;23(1). doi:10.1111/OBR.13349
8. Liu YJ, Duan JW, Lu DH, Zhang F, Liu HL. Association between vitamin D status and cardiometabolic risk factors in adults with type 2 diabetes in Shenzhen, China. Front Endocrinol (Lausanne). 2024;15. doi:10.3389/FENDO.2024.1346605
9. Bhaduri G, Samajdar SS, Chakraborty S, Saboo B, Joshi

SR. Prevalence and risk factors of hypovitaminosis D among patients with diabetes mellitus from India: A systematic review and meta-analysis. Diabetes Metab Syndr Clin Res Rev. 2025;19(10). doi:10.1016/j.dsx.2025.103326
10. Kamboj P, Dwivedi S, Toteja GS. Prevalence of hypovitaminosis D in India & way forward. Indian J Med Res. 2018;148(5):548-556. doi:10.4103/IJMR.IJMR_1807_18
11. Shivane VK, Sarathi V, Bandgar T, Menon P, Shah NS. High prevalence of hypovitaminosis D in young healthy adults from the western part of India. Postgrad Med J. 2011;87(1030):514-518. doi:10.1136/PGMJ.2010.113092
12. Committee ADAPP. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2025. Diabetes Care. 2024;48(Suppl 1):S27. doi:10.2337/dc25-S002
13. Vrbin CM. Parametric or nonparametric statistical tests: Considerations when choosing the most appropriate option for your data. Cytopathology. 2022;33(6):663-667. doi:10.1111/cyt.13174
14. Zhu H, Ibrahim JG, Cho H. PERTURBATION AND SCALED COOK'S DISTANCE. Ann Stat. 2012;40(2):785-811. doi:10.1214/12-AOS978
15. Kumar GT, Chugh R, Eggersdorfer M. Poor Vitamin D Status in Healthy Populations in India: A Review of Current Evidence. Int J Vitam Nutr Res. 2015;85(3-4):185-201. doi:10.1024/0300-9831/a000228
16. Ghosh A, Monisha S, Sunny AS, Diwakar L, Issac TG. Prevalence and patterns of vitamin D deficiency and its role in cognitive functioning in a cohort from South India. Sci Rep. 2024;14(1). doi:10.1038/s41598-024-62010-5
17. Karibayeva I, Bilibayeva G, Yerzhanova A, et al. Prevalence of Vitamin D Deficiency Among Adults in Kazakhstan: A Systematic Review and Meta-Analysis. Medicina (Kaunas). 2024;60(12). doi:10.3390/medicina60122043
18. Mendes MM, Gomes APO, Araújo MM, Coelho ASG, Carvalho KMB, Botelho PB. Prevalence of vitamin D deficiency in South America: a systematic review and meta-analysis. Nutr Rev. 2023;81(10):1290-1309. doi:10.1093/nutrit/nuad010
19. Mogire RM, Mutua A, Kimita W, et al. Prevalence of vitamin D deficiency in Africa: a systematic review and meta-analysis. Lancet Glob Heal. 2020;8(1):e134-e142. doi:10.1016/S2214-109X(19)30457-7
20. P A, S M, B N, SK G. Vitamin D deficiency in India. J Fam Med Prim care. 2018;7(2):41-44+55. doi:10.4103/jfmpc.jfmpc_78_18
21. Praveen PA, Singh A, Lakshmy R, et al. Prevalence and Correlates of Vitamin D Deficiency among Adult Population in Urban and Rural Areas of the National Capital Region of Delhi, India. WHO South-East Asia J public Heal. 2023;12(2):104-109. doi:10.4103/WHO-SEAJPH.WHO-SEAJPH_113_22
22. Palmisano BT, Zhu L, Eckel RH, Stafford JM. Sex differences in lipid and lipoprotein metabolism. Mol Metab. 2018;15(19):45-55. doi:10.1016/j.molmet.2018.05.008
23. Kolovou GD, Anagnostopoulou KK, Damaskos DS, et al. Gender differences in the lipid profile of dyslipidemic subjects. Eur J Intern Med. 2009;20(2):145-151. doi:10.1016/j.ejim.2008.06.011
24. Victor BM, Teal V, Ahedor L, Karalis DG. Gender differences in achieving optimal lipid goals in patients with coronary artery disease. Am J Cardiol. 2014;113(10):1611-1615. doi:10.1016/j.amjcard.2014.02.018
25. Ndzie Noah ML, Adzika GK, Mprah R, Adekunle AO, Adu-Amankwaah J, Sun H. Sex-Gender Disparities in Cardiovascular Diseases: The Effects of Estrogen on eNOS, Lipid Profile, and NFATs During Catecholamine Stress. Front Cardiovasc Med. 2021;8. doi:10.3389/fcvm.2021.639946
26. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc Diabetol. 2018;17(1). doi:10.1186/s12933-018-0762-4
27. Alcover S, Ramos-Regalado L, Girón G, Muñoz-García N, Vilahur G. HDL-Cholesterol and Triglycerides Dynamics: Essential Players in Metabolic Syndrome. Antioxidants. 2025;14(4):434. doi:10.3390/antiox14040434
28. Duan M, Zhao X, Li S, et al. Metabolic score for insulin resistance (METS-IR) predicts all-cause and cardiovascular mortality in the general population: evidence from NHANES 2001-2018. Cardiovasc Diabetol. 2024;23(1). doi:10.1186/s12933-024-02334-8
29. Oliveri A, Rebernick RJ, Kuppa A, et al. Comprehensive genetic study of the insulin resistance marker TG:HDL-C in the UK Biobank. Nat Genet. 2024;56(2):212-221. doi:10.1038/s41588-023-01625-2
30. Che B, Zhong C, Zhang R, et al. Triglyceride-glucose index and triglyceride to high-density lipoprotein cholesterol ratio as potential cardiovascular disease risk factors: an analysis of UK biobank data. Cardiovasc Diabetol. 2023;22(1). doi:10.1186/s12933-023-01762-2
31. Manousaki D, Harroud A, Mitchell RE, et al. Vitamin D levels and risk of type 1 diabetes: A Mendelian randomization study. PLoS Med. 2021;18(2). doi:10.1371/JOURNAL.PMED.1003536
32. Uddin MF, Garapati A, Gyanendra KC, et al. Relationship Between Glycosylated Hemoglobin and Serum Lipid Profile in Patients With Type 2 Diabetes Mellitus: A Cross Sectional Analysis. Heal Sci Reports. 2025;8(7):e70965. doi:10.1002/hsr2.70965
33. Iizuka K, Takao K, Yabe D. ChREBP-Mediated Regulation of Lipid Metabolism: Involvement of the Gut Microbiota, Liver, and Adipose Tissue. Front Endocrinol (Lausanne). 2020;11:587189. doi:10.3389/fendo.2020.587189

34. Liu GT, Fenercioglu AK. The Anti-Inflammatory Roles of Vitamin D for Improving Human Health. Curr Issues Mol Biol 2024, Vol 46, Pages 13514-13525. 2024;46(12):13514-13525. doi:10.3390/cimb46120807
35. Lu S, Cao ZB. Interplay between Vitamin D and Adipose Tissue: Implications for Adipogenesis and Adipose Tissue Function. Nutr 2023, Vol 15, Page 4832. 2023;15(22):4832. doi:10.3390/nu15224832
36. Ge L, Gao S, Kia N, Wang Y, Hua L. Effect of vitamin D supplementation on body composition, lipid profile, and glycemic indices in patients with obesity-associated metabolic syndrome: a systematic review and meta-analysis. Diabetol Metab Syndr. 2025;17(1):287. doi:10.1186/S13098-025-01799-1
37. Alqahtani RM, Alsulami EF. The Association Between Glycated Hemoglobin (HbA1c) Level and Vitamin D Level in Diabetes Mellitus Patients: A Cross-Sectional Study. Cureus. 2023;15(10). doi:10.7759/CUREUS.47166
38. Abdo B, Abdullah M, AlShoaibi IA, et al. Relationship Between Glycated Hemoglobin (HbA1c) and Vitamin D Levels in Type 2 Diabetes Patients: A Retrospective Cross-Sectional Study. Cureus. 2024;16(6):e62468. doi:10.7759/CUREUS.62468
39. Lu Q, Liang Q, Xi Y. The effects of vitamin D supplementation on serum lipid profiles in people with type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Front Nutr. 2024;11:1419747. doi:10.3389/FNUT.2024.1419747/FULL
40. Bahrami LS, Ranjbar G, Norouzy A, Arabi SM. Vitamin D supplementation effects on the clinical outcomes of patients with coronary artery disease: a systematic review and meta-analysis. Sci Reports 2020 101. 2020;10(1):12923-. doi:10.1038/s41598-020-69762-w
41. Rezaei S, Tabrizi R, Nowrouzi-Sohrabi P, et al. The Effects of Vitamin D Supplementation on Anthropometric and Biochemical Indices in Patients With Non-alcoholic Fatty Liver Disease: A Systematic Review and Meta-analysis. Front Pharmacol. 2021;12:732496. doi:10.3389/FPHAR.2021.732496/TEXT
42. Frențușcă C, Babeș K. Association between vitamin D deficiency and serum lipid levels in a group of Romanian patients. Med Pharm reports. 2024;97(3):263-269. doi:10.15386/MPR-2714
43. Cheng YL, Lee TI, Chien YM, Lee TW, Chen YJ. Vitamin D level regulates serum lipids discrepantly in adults with and without dyslipidemia. Endocr Connect. 2023;12(9). doi:10.1530/EC-23-0013
44. Sharba ZF, Shareef RH, Abd BA, Hameed EN. Association between Dyslipidemia and Vitamin D Deficiency: a Cross-Sectional Study. Folia Med (Plovdiv). 2021;63(6):965-969. doi:10.3897/FOLMED.63.E62417
45. Frentusca CF, Babes K, Galusca DI. VITAMIN D DEFICIENCY AS AN INDEPENDENT PREDICTOR OF CARDIOVASCULAR DISEASE. Acta Endocrinol (Bucharest, Rom 2005). 2023;19(3):319-325. doi:10.4183/AEB.2023.319
46. Li B, Wang J, Xu J, et al. Association between dyslipidemia and vitamin D deficiency: a cross-sectional study in Chinese healthy population. Front Endocrinol (Lausanne). 2025;16. doi:10.3389/FENDO.2025.1450924
47. Li S, He Y, Lin S, et al. Increase of circulating cholesterol in vitamin D deficiency is linked to reduced vitamin D receptor activity via the Insig-2/SREBP-2 pathway. Mol Nutr Food Res. 2016;60(4):798-809. doi:10.1002/MNFR.201500425
48. Hussain MM, Nijstad N, Franceschini L. Regulation of microsomal triglyceride transfer protein. Clin Lipidol. 2011;6(3):293-303. doi:10.2217/CLP.11.21
49. Malekmohammad K, Bezsonov EE, Rafieian-Kopaei M. Role of Lipid Accumulation and Inflammation in Atherosclerosis: Focus on Molecular and Cellular Mechanisms. Front Cardiovasc Med. 2021;8. doi:10.3389/FCVM.2021.707529