Ref: Ro Med J. 2023;70(3)
DOI: 10.37897/RMJ.2023.3.5

Observational study between level of vitamin D, anthropometric status and metabolic profiles in patients with type 2 diabetes mellitus

Rucsandra Elena Danciulescu Miulescu[1,2], Diana Loreta Paun[1,3], Iuliana Gherlan[1,3], Radu Ilinca[1]

[1]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[2]"NC Paulescu" National Institute of Diabetes, Nutrition and Metabolic Diseases Bucharest, Romania
[3]"CI Parhon" National Institute of Endocrinology, Bucharest, Romania

ABSTRACT

Introduction. Type 2 diabetes mellitus (T2DM) is currently an important global health disease. At the same time vitamin D deficiency is considered the other public health problem around the world. Some studies suggest involving insufficient or deficiency of vitamin Din the etiopathogenesis of T2DM.

Materials and methods. 58 patients, 33 women (56.89%) and 25 men (43.10%) were included in the observational study. Demographics (age, gender), personal anamnestic data (duration of diabetes, micro-and macrovascular complications, therapy with vitamin D supplements), anthropometric and biochemical parameters were assessed. The anthropometric measurement included height (meters), weight (kg) and body mass index (BMI) defined as a ratio of weight to the square of height (kg/m2). Biochemical parameters included the fasting blood glucose, glycated hemoglobin (HbA1c), serum total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, very-low density lipoprotein (VLDL) cholesterol, triglycerides (TG), as well the level 25(OH)D. We followed the correlation between vitamin D levels and the duration of diabetes, BMI, blood glucose levels, HbA1c, TC, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, TG.

Results. The average values recorded were 11.72 years for the duration of T2DM, 31.77 kg/m^2 for BMI, 169.00 mg/dL for blood glucose levels, 8.01% for HbA1c, 200.40 mg/dL for TC, 129.04 mg/dL for LDL-cholesterol, 47.67 mg/dL for HDL-cholesterol, 26.69 mg/dL for VLDL-cholesterol and 160.34 mg/dL for TG.

Conclusion. Following statistical analysis, the observational study highlight statistically negative correlation recorded between the level of vitamin D and BMI, glycemic balance (highlighted by the level of fasting blood glucose and HbA1c). The results found nonsignificant correlation between the levels of vitamin D: duration of diabetes and lipid profile.

Keywords: type 2 diabetes mellitus, insufficient or deficiency of vitamin D, metabolic consequences

INTRODUCTION

T2DM is a disease with an important global health impact. Every 2 years the International Diabetes Federation (IDF) elaborates an atlas on global estimates levels diabetes and projections for the next few years. According to IDF, 537 million adults are living with diabetes in 2021 worldwide. The number of patients diagnosed with diabetes will grow to 643 million by 2030, and 783 million by 2045 [1]. At the same time vitamin D deficiency is considered another public health with a worldwide impact [2]. In 2008 it has been estimated that vitamin D deficiency or insufficiency affects one billion people worldwide [3]. The principal measure of vitamin D status is represented by total 25-hydroxyvitamin D (25 (OH)D) [4,5]. Optimal serum concentrations of 25(OH)D begin of 30 ng/mL [3]. Vitamin D insufficiency is defined as a 25(OH)D of 21-29 ng/mL and vitamin D deficiency is defined as a value of 25(OH) D < 20 ng/mL [5,6].

Corresponding author:
Diana Loreta Paun
E-mail: dianaloreta_paun@yahoo.com

Article History:
Received: 21 September 2023
Accepted: 28 September 2023

Some studies suggest involving insufficient or deficiency of vitamin D in pathogenesis of T2DM. The following mechanism is proposed:

1. Impaired pancreatic β cell function,
2. Insulin resistance,
3. Inflammation [7,8].

The purpose of this study was to evaluate the correlation between level of vitamin D and anthropometric and metabolic parameters in patients with T2DM.

MATERIALS AND METHODS

We conducted an observational study between 2020 and 2022. The research was carried out by analyzing the observation sheets of 2896 patients with T2DM who addressed during the mentioned period to the National Institute of Diabetes and Metabolic Diseases "N Paulescu" and Nicodiab Private Practice. Of the 2896 patients, only 86 respectively 2.96% showed dosing serum levels of 25(OH)D. The reduced number of patients was due to the fact that the determination of the level of 25(OH)Dis not routinely sustained as settlement in some national health programs. Demographics (age, gender), personal anamnestic data (duration of diabetes, micro-and macrovascular complications, therapy with vitamin D supplements), anthropometric and biochemical parameters were assessed. The anthropometric measurement included height (meters), weight (kg) and BMI defined as a ratio of weight to the square of height (kg/m^2). Biochemical parameters included the fasting blood glucose, HbA1c, serum total TC, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, TG, as well the level 25(OH)D. The plasma glucose, TC, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, TG were measured by spectrophotometry, HbA1c was assayed with a high-performance liquid chromatographic (HPLC) and the level 25(OH)D by a chemiluminescent method. Of the 86 patients with T2DM who had the determination of 25(OH)D, 28 patients were undergoing therapy with vitamin D supplements and were excluded from the research. We followed the correlation between vitamin D levels and the duration of diabetes, BMI, blood glucose levels, HbA1c, TC, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, TG. All the tests were run in an SR EN ISO 15189:2013 accredited laboratory which ensures quality of results. Moreover, proficiency testing participation for these parameters of the laboratory was successful throughout the study.

STATISTICAL ANALYSES

The statistical analyses were carried out using the R Studio software (R Core Team 2022). Thus, descriptive statistics analyses and correlation analyses were performed with the psych package (Revelle W, 2022), and the graphs were made with the ggplot2 package (Wickham H, 2016).

The comparison between the study and the control group was performed using the t-student test for independent samples. To analyze the associations between vitamin D level, duration of diabetes, BMI, blood glucose levels, HbA1c and lipid profile (TC, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, TG) person correlation analyzes (r) were performed. For all analyses, a statistical significance threshold $p < 0.05$ was taken into account.

RESULTS

58 patients, 33 women (56.89%) and 25 men (43.10%) were included in the observational study. The average values recorded were 11.72 years for the duration of T2DM, 31.77 kg/m2 for BMI, 169.00 mg/dL for blood glucose levels, 8.01% for HbA1c values, 200.40 mg/dL for TC, 129.04 mg/dL for LDL-cholesterol, 47.67 mg/dL for HDL-cholesterol, 26.69 mg/dLfor VLDL-cholesterol and 160.34 mg/dL for TG.

Microvascular complications were present in 9 patients (15.51%) the most common complication being represented by non-proliferative diabetic retinopathy. Macrovascular complications were much more frequent, they were highlighted in 32 patients (55.17%), the most common complication being hypertension.

The averages, standard deviations and correlations between the measured variables are given in Table 1.

A statistically insignificant negative correlation was recorded between the level of vitamin D and duration of diabetes ($r=-0.10$; $p>0.05$, highlighted in Figure 1).

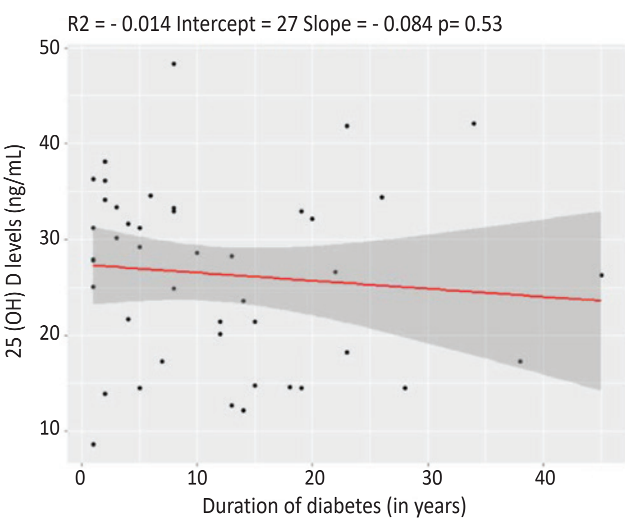

FIGURE 1. Correlation between the level of vitamin D and the duration of diabetes

TABLE 1. The averages, standard deviations and correlations between the measured variables

	Averages	SD	1	2	3	4	5	6	7	8	9	10
1. Age (years)	63.37	9.44	—									
2. Duration of diabetes (years)	11.72	10.52	0.48***	—								
3. BMI (kg/m²)	31.77	5.07	0.29	0.38**	—							
4. Blood glucose levels (mg/dL)	169	61.52	0.15	0.37*	0.15	—						
5. HbA1c (%)	8.01	1.97	0.21	0.53***	0.40**	0.67***	—					
6. TC (mg/dL)	200.4	48.56	-0.07	-0.08	-0.21	0.20	-0.03	—				
7. LDL cholesterol (mg/dL)	129.04	43.97	-0.18	-0.07	-0.17	0.29	0.07	0.86***	—			
8. HDL cholesterol (mg/dL)	47.67	10.63	-0.04	-0.29	-0.12	-0.44**	-0.35*	-0.10	-0.16	—		
9. VLDL cholesterol (mg/dL)	26.69	11.34	-0.21	0.09	-0.22	0.39	0.55	0.11	0.03	-0.67	—	
10. TG (mg/dL)	160.34	60.21	0.04	0.22	-0.07	0.48**	0.38*	0.46**	0.40*	-0.39*	0.91*	—
11. 25(OH)D levels (ng/mL)	26.38	9.31	-0.18	-0.10	-0.49***	-0.42**	-0.33*	0.02	0.01	0.28	-0.15	-0.24

*Abbreviation and specifications *p<0.05; **p<0.01; ***p<0.001; SD–standard deviations*

Between the level of vitamin D and BMI, a statistically significant moderate negative correlation was recorded, r=-0.49 (p<0.001). Regression analysis indicates that 22% of the variation in vitamin D levels can be explained by the BMI variation (Figure 2).

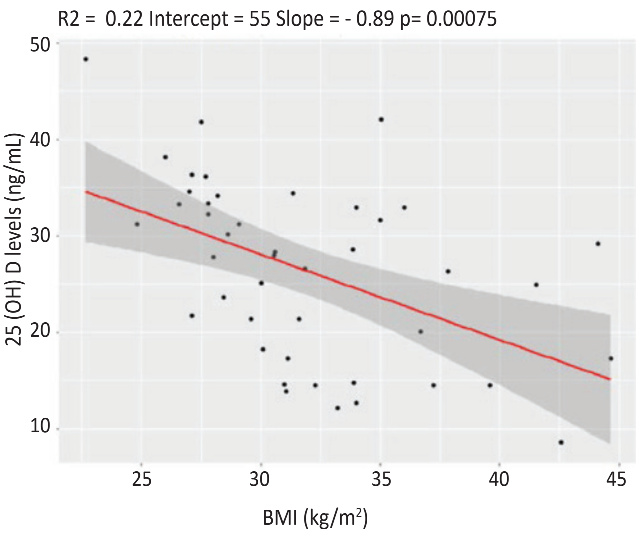

FIGURE 2. Correlation between the level of vitamin D and BMI

Between the level of vitamin D and the fasting blood glucose, a statistically significant moderate negative correlation was recorded, r=-0.42 (p<0.01) highlighted in vitamin D levels can be explained 16% by the variation in blood glucose levels.

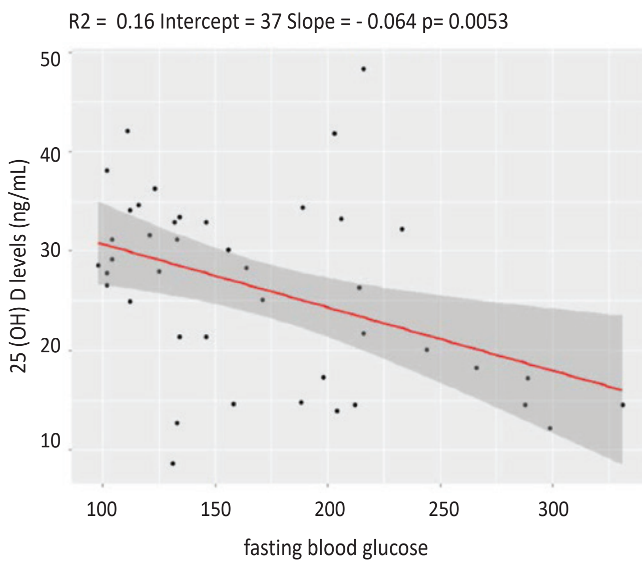

FIGURE 3. Correlation between the level of vitamin D and fasting blood glucose

The moderate negative correlation between the level of vitamin D and HbA1c was statistically significant with r=-0.33, p<0.05. The variation in vitamin D levels can be explained at a rate of 8.4% by the variation in HbA1c (Figure 4).

The correlation between the level of vitamin D and the lipid profile was statistically insignificant and is presented in Figure 5.

In relation to the serum values of 25(OH)D, the patients were divided into two groups, respectively: study group-patients with vitamin D deficiency or in-

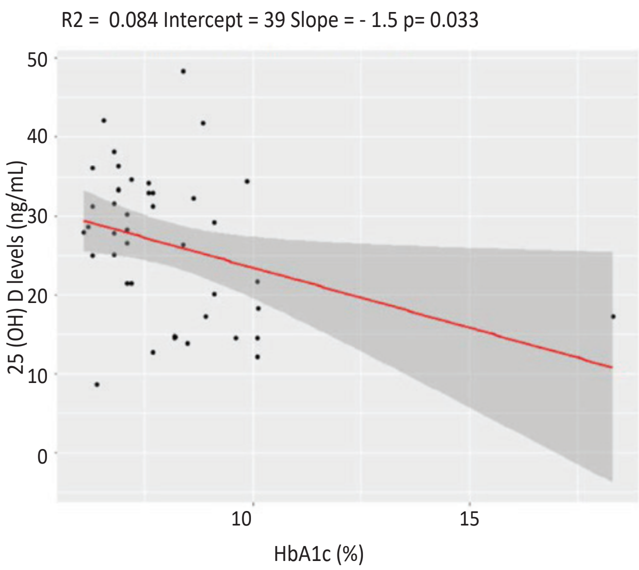

FIGURE 4. Correlation between the level of vitamin D and HbA1c

vitamin D include stimulating the expression of insulin receptors, improving the transport of insulin-dependent glucose [11,12]. Chronic inflammation is involved in the development of insulin resistance, which increases the risk of T2DM. The receptor for vitamin D is expressed by macrophages and dendritic cells, suggesting that vitamin D plays an important role in modulating inflammatory responses [7,8].

A statistically significant moderate negative correlation was recorded between vitamin D levels and BMI. The relation between low vitamin D and excess weight can be partially explained by storage of vitamin D in adipose tissue. Other possible mechanisms involved are represented by lower dietary intake, less skin exposure in obese patients, bariatric procedures, altered metabolism or reduced activation or increased catabolism [13].

The relationship between the level of vitamin D and the glycemic balance (level of fasting blood glu-

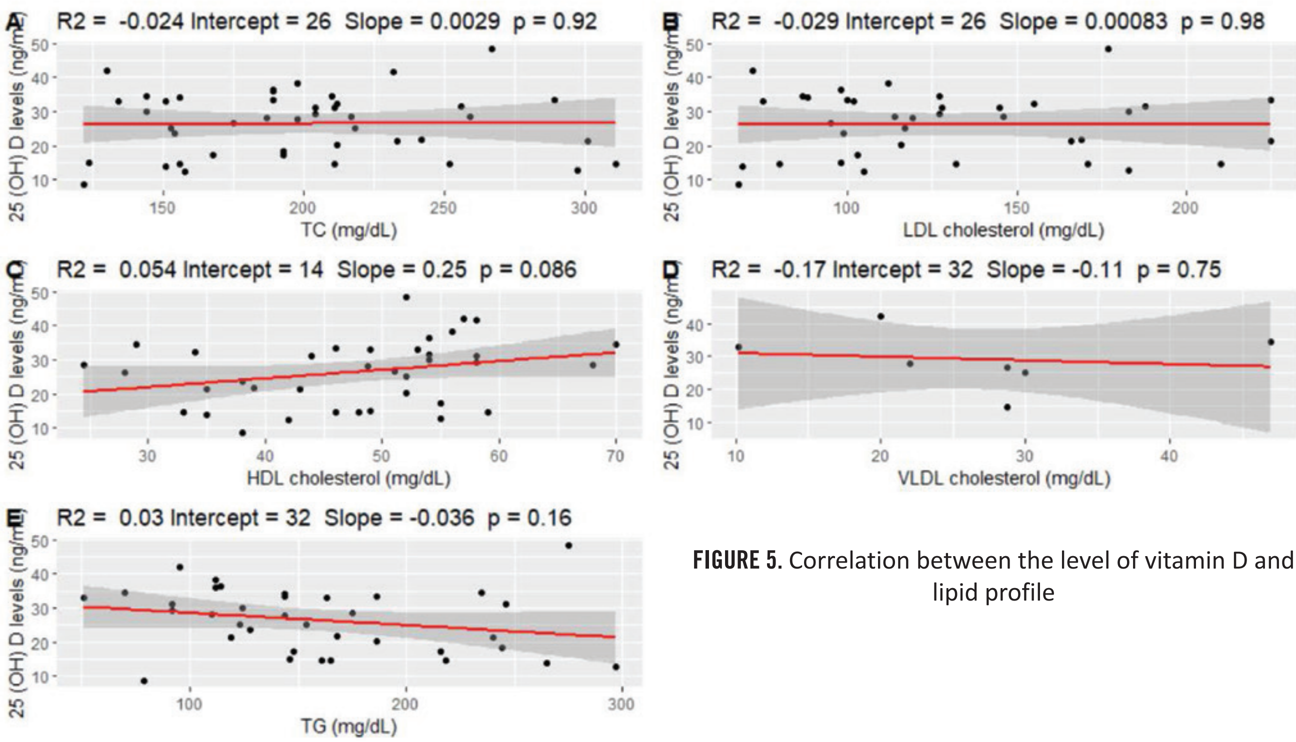

FIGURE 5. Correlation between the level of vitamin D and lipid profile

sufficiency and control group-patients without vitamin D deficiency the main characteristics of the lots are presented in Table 2.

DISCUSSION

Some studies support the hypothesis of the involvement of vitamin D deficiency in the etiopathogenesis of diabetes mellitus based on the observation of the existence of receptors for vitamin D and 1-α hydroxylase in ß-pancreatic cells. Vitamin D stimulates the secretion of insulin mechanism indirectly mediated by the normalization of extracellular calcium concentration [9,10]. Other signaling pathways of

cose and HbA1c), highlight a statistically significant negative correlation. Zoppini G and coworkers evaluated the association between HbA1c and 25(OH)D in 715 patients with T2DM. The authors concluded than high HbA1c levels are associated with low concentration of serum vitamin D, independently of duration of diabetes [14]. The Tromsø study highlighted that serum 25(OH)D levels are inversely associated with HbA1c [15].

The relationship between serum concentration of 25(OH)D and lipid profile in patients with T2DM are uncertain. Possible mechanisms involved in relation between vitamin D and lipid levels are: vitamin D affect negatively parathyroid hormone and the high

TABLE 2. The main characteristics of the lots

The main characteristics of the lots	Study Group		Control Group		Difference in Means (Student's t test)	Statistical significance
	Mean	SD	Mean	SD		
1. Age (years)	64,00	9,57	62,55	9,44	1,45	SI
2. Duration of diabetes (years)	13,31	11,14	9,65	9,53	3,66	SI
3. BMI (kg/m^2)	33,94	5,05	28,96	3,56	4,98	p<0.001
4. Fasting blood glucose(mg/dL)	185,16	69,76	147,74	41,38	37,42	0,044
5. HbA1c (%)	8,47	2,44	7,43	0,91	1,04	SI
6. TC (mg/dL)	203,56	52,34	196,45	44,40	7,11	SI
7. LDL cholesterol (mg/dL)	129,16	43,79	128,89	45,64	0,27	SI
8. HDL cholesterol (mg/dL)	45,33	10,84	50,88	9,76	5,55	SI
9. VLDL cholesterol (mg/dL)	27,40	3,64	25,73	19,06	1,67	SI
10. TG (mg/dL)	9,88	7,10	6,85	4,57	3,03	SI
Vitamin D levels (ng/mL)	20,23	6,16	35,26	4,68	15,03	p<0.001

Abbreviation and specifications: the comparison is significant at the level p< 0.05; SI-Statistically Insignificant

level of this hormone may grow calcium influx in adipocytes what drives the increasing lipase expressionand secondary generates increasing various lipid factors [16,17], vitamin D can generate the excretion of TG by promoting calcium absorption in the intestine and cause an increase in HDL levels [18]. Currently not exist extensive observational studies that explored the correlation between the level of vitamin D and lipid profile. In a cross-sectional study published in 2017, Ge H and coworkers evaluated the association between serum 25(OH)D concentration and lipid profile in the rural population of China. In this study low serum 25(OH)D levels were associated with higher prevalence of dyslipidemia [19]. Bashir NA and collaborators evaluated lipid profile in 127 patients with vitamin D deficiency. The study revealed that "A significant effect of vitamin D insufficiency or deficiency on serum level of cholesterol, triglycerides, and LDL and increases the levels more than the double and decreases the level of HDL" [20]. Saedisomeolia A and coworkers have evaluated in a cross-sectional study the association between serum 25(OH)D levels and lipid profile in 108 patients with T2DM. The results of the study highlighted that serum concentrations of 25(OH)D were inversely associated with levels of TG [21]. In an observational study, Jorde R and Grimnes E exploring the association between serum 25(OH)D levels and lipid profile. The results highlighted that from serum 25(OH)D there were positive and strong associations with TC, HDL-cholesterol, LDL-cholesterol and a negative association with TG [22]. However, taking vitamin D supplements has no improve lipid profile in experimental and epidemiology studies [23]. We found nonsignificant correlation between the level of vitamin D and lipid profile, but the correlation between serum 25(OH)D levels and lipid profile requires carrying out large interventional studies.

CONCLUSION

Between the level of vitamin D and BMI in this observational study it was observed statistically significant moderate negative correlation. Glycemic balance and the level of vitamin D show a statistically significant negative correlation. However, it is necessary to confirm these data in prospective studies. The correlation between vitamin D level and lipid profile was statistically insignificant.

Research is limited by the small number of patients investigated. Dosing of the level of 25(OH)D is not routinely performed in diabetic patients. Under the National Diabetes Program, the determination is not settled.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. Pract IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract.* 2021;183:109119. doi: 10.1016/j.diabres.
2. Holick MF. The vitamin D deficiency pandemic and consequences for nonskeletal health: mechanisms of action. *Mol Aspects Med.* 2008 Dec;29(6):361-8. doi: 10.1016/j.mam.2008.08.008.
3. James WP. 22nd Marabou Symposium: the changing faces of vitamin D. *Nutr Rev.* 2008 May;66(5):286-90. doi: 10.1111/ j.1753-4887.2008.00034.x.
4. IOM (Institute of Medicine). Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: The National Academies Press, 2011.
5. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al; Endocrine Society. Evaluation, treatment, and

prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011 Jul;96(7):1911-30. doi: 10.1210/jc.2011-0385.
6. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, Tmava Berisha A, et al. Vitamin D deficiency 2.0: an update on the current status worldwide. *Eur J Clin Nutr.* 2020 Nov;74(11):1498-513. doi: 10.1038/s41430-020-0558-y.
7. Palomer X, González-Clemente JM, Blanco-Vaca F, Mauricio D. Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. *Diabetes Obes Metab.* 2008 Mar;10(3):185-97. doi: 10.1111/j.1463-1326.2007.00710.x.
8. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. *Am J Clin Nutr*. 2004 May;79(5):820-5. doi: 10.1093/ajcn/79.5.820.
9. Mathieu C, Gysemans C, Giulietti A, Bouillon R. Vitamin D and diabetes. *Diabetologia*. 2005 Jul;48(7):1247-57. doi: 10.1007/s00125-005-1802-7.
10. Mathieu C. Vitamin D and diabetes: Where do we stand? *Diabetes Res Clin Pract.* 2015 May;108(2):201-9. doi: 10.1016/j.diabres.2015.01.036.
11. Seshadri KG, Tamilselvan B, Rajendran A. Role of Vitamin D in Diabetes. *J Endocrinol Metab.* 2011;1(2):47–56. doi: 10.4021/jem23w.
12. Tamilselvan B, Seshadri KG, Venkatraman G. Role of vitamin D on the expression of glucose transporters in L6 myotubes. *Indian J Endocrinol Metab.* 2013 Oct;17(Suppl 1):S326-8. doi: 10.4103/2230-8210.119642.
13. Vanlint S. Vitamin D and obesity. *Nutrients*. 2013 Mar 20;5(3):949-56. doi: 10.3390/nu5030949.
14. Zoppini G, Galletti A, Targher G, Brangani C, Pichiri I, Negri C, et al. Glycated haemoglobin is inversely related to serum vitamin D levels in type 2 diabetic patients. *PLoS One*. 2013 Dec 16;8(12):e82733. doi: 10.1371/journal.pone.0082733.
15. Hutchinson MS, Figenschau Y, Njølstad I, Schirmer H, Jorde R. Serum 25-hydroxyvitamin D levels are inversely associated with glycated haemoglobin (HbA(1c)). The Tromsø Study. *Scand J Clin Lab Invest*. 2011 Sep;71(5):399-406. doi: 10.3109/00365513.2011.575235.
16. Wang JM, Ye SD, Li SM, Hu W. Correlations of 25(OH)D level with blood lipid, inflammatory factors and vascular endothelial function in diabetic patients. *Eur Rev Med Pharmacol Sci.* 2018 Feb;22(3):731-735. doi: 10.26355/eurrev_201802_14303.
17. Young KA, Rasouli N. Serum lipid profile as a tool to predict incident diabetes: Is it a wishful thinking? *J Diabetes Complications.* 2020 Dec;34(12):107755. doi: 10.1016/j.jdiacomp.2020.107755.
18. Kazlauskaite R, Powell LH, Mandapakala C, Cursio JF, Avery EF, Calvin J. Vitamin D is associated with atheroprotective high-density lipoprotein profile in postmenopausal women. *J Clin Lipidol.* 2010 Mar-Apr;4(2):113-9. doi: 10.1016/j.jacl.2010.01.006.
19. Ge H, Sun H, Wang T, Liu X, Li X, Yu F, et al. The association between serum 25-hydroxyvitamin D3 concentration and serum lipids in the rural population of China. *Lipids Health Dis.* 2017 Nov 14;16(1):215. doi: 10.1186/s12944-017-0603-6.
20. Bashir NA, Bashir AAM, Bashir HA. Effect of Vitamin D deficiency on Lipid Profile. *Am J Lab Med.* 2019;24(1):11–18. doi: 10.11648/j.ajlm.20190401.12.
21. Saedisomeolia A, Taheri E, Djalali M, Moghadam AM, Qorbani M. Association between serum level of vitamin D and lipid profiles in type 2 diabetic patients in Iran. *J Diabetes Metab Disord.* 2014 Jan 7;13(1):7. doi: 10.1186/2251-6581-13-7.
22. Jorde R, Grimnes G. Exploring the association between serum 25-hydroxyvitamin D and serum lipids-more than confounding? *Eur J Clin Nutr.* 2018 Apr;72(4):526-533. doi: 10.1038/s41430-018-0088-z.
23. Bouillon R, Manousaki D, Rosen C, Trajanoska K, Rivadeneira F, Richards JB. The health effects of vitamin D supplementation: evidence from human studies. *Nat Rev Endocrinol.* 2022 Feb;18(2):96-110. doi: 10.1038/s41574-021-00593-z.