Original Article

Relationship Between Vitamin D Status and Cardiovascular Risk Factors in Patients with Type 2 Diabetes Mellitus in Shaheed Benazir Abad

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ABSTRACT

Objective: To find out and identify hypovitaminosis D predictors for patients who have type 2 diabetes mellitus and vitamin D levels with glycemic control and cardiovascular risk variables.

Study Design: A cross-sectional study

Place and Duration of Study: This study was conducted at the Hospital Shaheed Benazir Abad from October 2018 and November 2019.

Materials and Methods: A cross-sectional study was conducted on 108 patients with consecutive patients treated at an outpatient department hospital Shaheed Benazir Abad.

Results: A total of 108 patients with T2-DM average period of 14.34 ± 8.05 and 9, 2 ± 2.1 percent with HbA1c were evaluated. Age was 58.29±10.34 years in average. Mostly, females (72.2%) with hypertension (75.9%) and dyslipidemia (76.8 percent). BMI was 28.01 ± 4.64 kg/m 2; overweight was 75.9%. Hypovitaminosis D was 62 percent prevalent. Independent hypovitaminosis D predictor was found to be women (OR 3.10, p =0.02), dyslipidemia (OR 6.50, p<0.01) and obesity OR 2.55, p =0.07) under the multiple logistic regression. Only the total cholesterol (β=−0,36, p<0,01) and BMI(β=−0.21, p=0.04) were still correlated with 25- hydroxyvitamin D in multiple linear regressions.

Conclusion: The prevalence of hypovitaminosis D in our T2DM participants has been as high. Hypovitaminosis D predictors were gender dyslipidemia and obesity. Low 25-hydroxyvitamin D levels were associated with high level of cholesterol of BMI.

Key Words: Vitamin D, Type 2 diabetes mellitus, Obesity, Dyslipidemia

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INTRODUCTION

Type 2 diabetes mellitus is a critical and rapidly increasing global health problem. Diabetes affected 382 million people in 2013, and the figure is expected to rise to 592 million by 2035. T2DM has the highest prevalence rates in developed countries.[1]

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Hypovitamin D is a global pandemic that affects one billion people[2], with estimates that its occurrence is rising rapidly.[2] Vitamin D has many pleiotropic effects out of the skeleton and the endocrine system as a major hormone for mineral homeostasis and bone integrity.[3] It is shown that hypovitaminosis D in patients with type 2 diabetes mellitus is normal in recent times.[4] In patients with type 2 diabetes, Hypovitaminosis D is likely to be neglected cardiovascular risk factor[5,6], since vitamin D appears to affect many pathways associated with the coronary artery, including inflammation, vascular calcification, smooth muscle cell proliferation in the vascular tissue, myocyte hypertrophy, arterial intimate thickness, renin-angiotensin system, blood-pressured blood.[7–9]

To further explore this question, we were working to determine the prevalence of hypovitaminosis D in patients with type 2 mellitus diabetes and to examine the connection between the vitamin D concentration and the glycemic control and risk factors for cardio-vascular disease.

MATERIALS AND METHODS

Between October 2018 and November 2019, a cross-sectional analysis was carried out with successive patients being treated in the Shaheed Benazir Abad ambulatory department. Type 2 diabetes mellitus in adult patients. We did not include any other form of diabetes or vitamin D or predecessors, pregnant wo men, chronic kidney disease, or post-bariatric mal-absorption or status patients, or cholestyramine or orlistat therapy.

In order to collect data on age, sex, self-reported ethnicity, time of diagnosis and drug use and comorbidités, we have carried out personalized interviews. Participants with lightweight clothes and no shoes weighed height to nearest 0.1cm and weight to the nearest 0.1 kg. The BMI participants were classified as overweight (25.0–29.9 kg/m2) and BMI participants (soon

30.0 kg/m2) were classified as obese. All patients were required to quit oral antidiabetic medicine and insulin.

For 3 days and for 10 hours at least before serum tests patients were asked to avoid stressful physical activity and alcohol consumption. For storage within 24 hours of collection, blood samples were processed. A chemiluminescence kit was used for serum 25-hydroglyvitamin D [25(OH)D] that recognizes both vitamin D2 and vitamin D3 equally. In each test the manufacturer carried out two levels of controls. On the basis of repeated study of a pooled control 15 and 13 percent were inter- and intra-assay coefficients of variance. The lower detection limits for the test were 2.8 ng/mL. In terms of deficiency (<20 ng/mL), insufficiency (20-29 ng/mL) and sufficiency (alternative to 30 ng/mL), 25-hydroxyvitamin D was stratifiably classified according to the 2011 endocrine society classifications. Using an HPLC test on the automated analyzer, serum glycated hemoglobin (HbA1c) has been measured.

Statistical analyses: Continuous data have been shown as median or median (±standard deviation) (inter-quartile range). A correlation analysis by Pearson's was used to determine the relationship between continuous parameters indicating glycemic regulation and cardiovascular risk factors with 25(OH)D levels. Then, variables associated with 25(OH)D were entered in a multiple linear regression model with $p < 0.10$. (with vitamin D level as the dependent variable). A similar strategy was used to determine logistic regression predictors for hypovitaminosis D (a binary event). A logistic regression model was entered into the variables associated with hypovitaminosis D ($p < 0.10$), in univariate analysis. In the final analysis, a two-side

p value <0.05 was considered significant. The IBM SP SS version 20.0 was used as a basis to perform all statistical analyses.

RESULTS

A total of 108 participants were recruited with mean age was 58.29 ± 10.34 years. The majority (72.2 percent). The period of diagnosed diabetes type 2 was 14,34± 8,05 years (Table 1). Of these, for 5 years or more 89,8% of the patients suffered from type 2 diabetes mellitus. The majority of patients were on medication with an average dose of insulin (72.2%). It was only used with NPH and normal insulin. Means: NPH 29.45 ± 14.20 IU (8.0-84.0) and insulin of daily 13.74 ± 7.37 IU (4.0-36.0) was used. Metformin was the most widely used oral antidiabetic drug (77.8 percent). Metformin, insulin and metformin plus sulphonylurea were the most popular combinations. Hypertension (74.1 percent) and dyslipidemia were key comorbidities associated with type 2 diabetes mellitus (76.8 percent).

Average of 25(OH)D was 28:10 ± 9.16 Ng/mL. The total prevalence was 62% (39.8%) inadequate and 22.2% deficient) of hypovitaminosis D (Fig. 1). Hypovitaminosis D was more common in men (70 vs. 40%), in women (77,1 vs. 54,2%, in overweight, p=0,02), in women (72,3 vs. 28%), in men (72.3 vs. 28%), in women (71% vs. non-users, p=0,01) and in women (71% vs. 46,1%, in men and women).We performed uniform logistic regression tests. Sex, history of dyslipidemia, statine use and obesity have been identified as independent forecasters of hypovitaminosis D, and only female gender have emerged in the model (OR 3.10, p=0.02), dyslipidemia (OR 6.50 p<0.01) and obesity (OR 2.55, p=0.07) (Table 2).

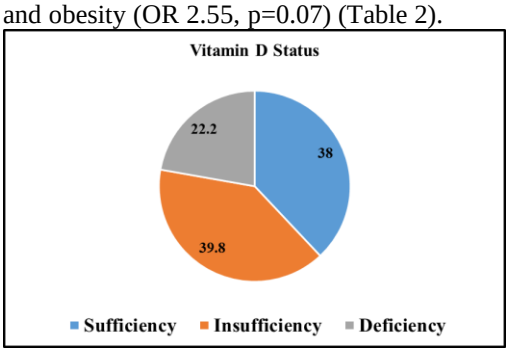

Figure No.1: Vitamin D status of 108 T2DM patients followed at an outpatient Endocrinology Clinic inShaheed Benazir Abad

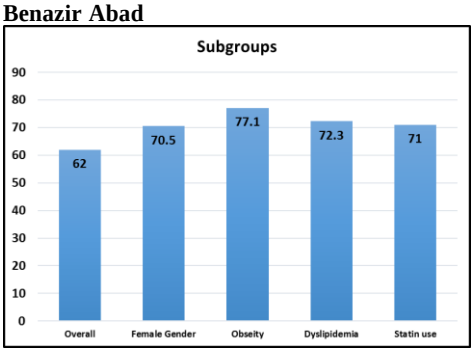

Figure No. 2: Prevalence of hypovitaminosis D: Overall and stratified into subgroups with significantlyhig herprevalence

Table No.1: Demographic and clinical characteristics of 108 T2DM patients followed at an outpatient Endocrinology Clinic

Variable		Overall	Hypovitaminosis D		P
		(n = 108)	No (n = 41)	Yes (n = 67)	
Age (years)		58.29 ± 10.34	58.24 ± 9.99	59.19 ± 10.33	0.48
Female gender		78 (72.2%)	23 (56.1%)	55 (82.2%)	*0.01*
Non-white skin color		97 (89.8%)	39 (95.1%)	58 (86.6%)	0.20
T2DM duration (years)		14.34 ± 8.05	15.38 ± 8.30	14.06 ± 8.30	0.59
BMI		28.01 ± 4.64	27.17 ± 3.87	28.65 ± 4.99	0.13
Obesity [a]		35 (32.4%)	8 (19.5%)	27 (40.1%)	*0.02*
Comorbidities	Hypertension	82 (74.1%)	30 (73.2%)	52 (77.6%)	0.60
	Dyslipidemia	83 (76.8%)	23 (56.1%)	60 (89.5%)	*<0.01*
Insulin use	Insulin use	78 (72.2%)	30 (73.2%)	48 (71.6%)	0.86
	NPH insulin	77 (71.3%)	29 (70.7%)	48 (71.6%)	0.92
	Regular insulin	42 (38.9%)	18 (43.9%)	24 (35.8%)	0.40
Oral antidiabetic agent	Sulfonylurea	26 (24.1%)	10 (24.4%)	16 (23.9%)	0.95
	Metformin	84 (77.8%)	34 (82.9%)	50 (74.6%)	0.31
	α-Glucosidase inhibitor	5 (4.6%)	1 (2.4%)	4 (6.0%)	0.40
Combination treatment	Insulin plus OAD	57 (52.8%)	24 (58.5%)	33 (49.2%)	0.35
	Insulin plus metformin	5 (4.6%)	2 (4.9%)	3 (4.5%)	1.00
	Insulin plus sulfonylurea	56 (51.8%)	24 (58.5%)	32 (47.8%)	0.28
	Metformin plus sulfonylurea	23 (21.3%)	9 (21.9%)	14 (20.9%)	0.90
Lipid lowering agents	Statins	69 (63.9%)	20 (48.8%)	49 (73.1%)	*0.01*
	Fibrates	4 (3.8%)	1 (2.4%)	3 (4.5%)	1.00
Antihypertensive agents		86 (79.6%)	33 (80.5%)	53 (79.1%)	0.86

Table No.2:Univariate and multivariate backward logistic regression analyses to identify independent predictors of hypovitaminosis D

Variable	Univariate	*p*	Multivariate	*p*
	OR (95% CI)		Adjusted OR (95% CI)	
Female gender	3.59 (1.49–8.63)	0.00	3.10 (1.16–8.29)	0.02
Dyslipidemia	6.71 (2.48–18.17)	0.00	6.50 (2.24–18.86)	<0.01
Statin use	2.86 (1.26–6.47)	0.01		
Obesity	2.86 (1.14–7.13)	0.02	2.55 (0.92–7.06)	0.07

All 4 variables were entered into the multivariate backward logistic regression model but statin use was removed by the system on the final step Dyslipidemia history of dyslipidemia, Obesity BMI ≥ 30 kg/m^2

Table No.3: Simple linear correlation and multiple linear regression with 25-hydroxyvitamin D levels as the dependent variable

Variables	Simple linear correlation	*p*	Multiple linear regression	*p*
	Pearson *r*		Unstandardized β coefficient	
BMI	−0.20 −0.22 −0.39	0.04	−0.41	0.04
HbA1c	−0.34	0.03	−0.09	<0.01
Total cholesterol	−0.23	0.00		
Triglycerides		0.00		
Microalbuminuria		0.02		

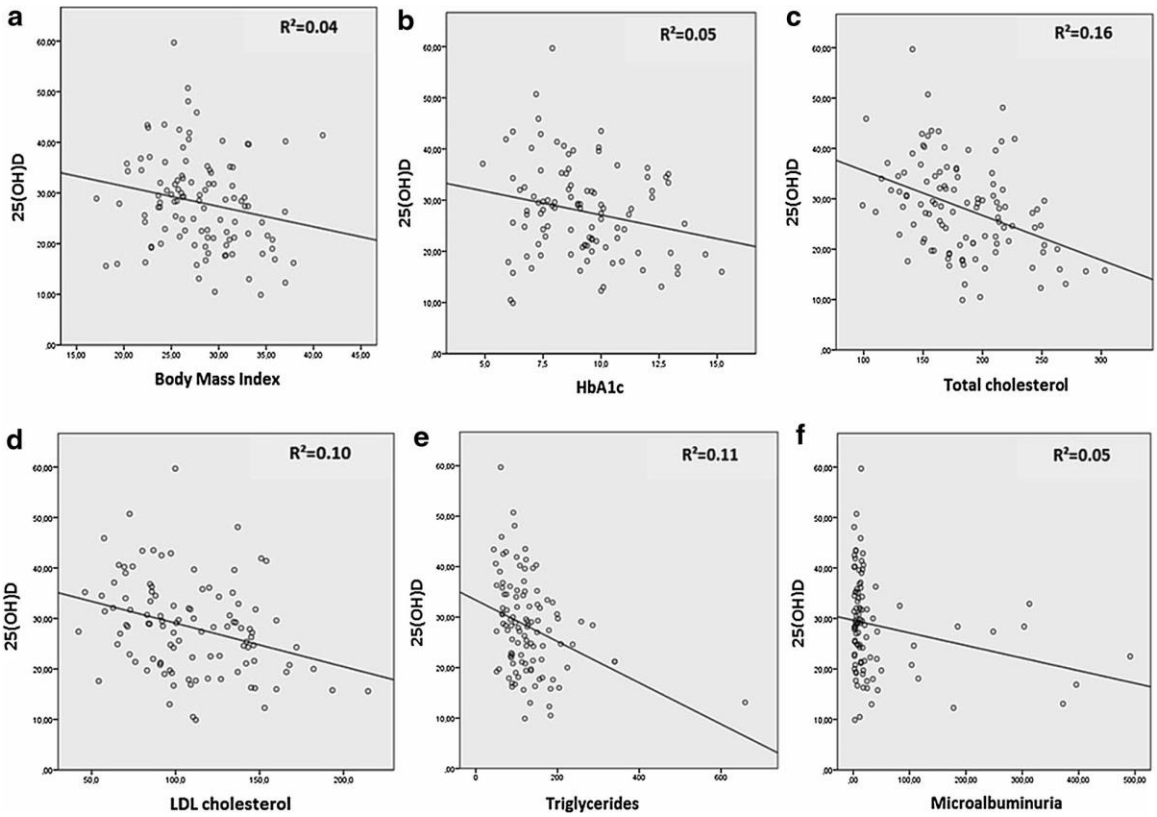

Figure No.3: Simple linear correlation between 25-hydroxyvitamin D and variables indicative of glycemic control and cardiovascular risk. 25(OH)D 25-hydroxyvitamin D, HbA1c glycated hemoglobin, LDL cholesterol low-density lipoprotein-cholesterol.

Correlation and multiple linear regression analyses have been performed to further study the relationship between the vitamin D levels, glycemic co ntrol and cardiovascular risk factors.

There were no links to blood concentrations of calcium phosphorus, alkaline phosphatase, PTH and vitamin D levels of diabetes, blood pressure, rapid glucose, HDL-c, ultralense CRP, uric acid, estimated glomerular filtration rates. Inverted, major variables with vitamin D levels have shown significantly reverse linear correlations: BMI (r=0,20, p=0,04), HbA1c (r=0,22), p=0,03) total cholesterol and micronuria (r=0,23, p=0,02); LDL-c (r=0,32, p<0,01), triglyceride (r= −0, 34, p<0,01) and microalbuminury (r=0.23, p= 0.02). (T able 3; Fig. 3). As total cholesterol and LDL-C are strongly associated (r = 0.932, p<0.01), we have opted to include in the last multiple linear regression model only one of those explanatory variables in order to prevent colinearity. The linear association with D-vitamin levels was greater than that of LDL-c and we selected total Cholesterol. These variables were then inserted into a multilinear backwards (vitamin D as the independent variable) regression model; the only total cholesterol (unstandardized coefficient $\beta = -0.09$, $p < 0.01$), and BMI (unstandardized coefficient $\beta = -0.41$, $p = 0.04$) were correlated with 25(OH) D levels independently of the standard (Table 3).

DISCUSSION

The high prevalence of hypovitaminosis D among individuals with type 2 diabetes found in this study may be considered surprising, given that Shaheed Benazir Abad. Our results arecomparable to thoseseen in non-tropical diabetic populations.[10–12] The high prevalence of hypovitaminosis D may be due to certain features of our study.[13]

Obesity was prevalent in our community, confirming the previously identified correlation between obesity and type 2 diabetes.[13] Obesity and hypovitaminosis D have been linked in many studies of diabetic patients.[12,14,15] Obese patients have lower serum vitamin D levels because vitamin D can be sequestered in body fat. Obesity is often attributed to a less healthy lifestyle, which includes less physical activity, less sun exposure, and, as a result, lowervitamin D levels and poorer clinical outcomes.[16]

Hoteit et al. and van der Meer et al.[17,18] proposed that female sex is a separate vitamin D deficiency indicator. Other findings of Type 2 diabetes confirm this result.[12,14,19]In our logistic regression model, female sex was an independent predictor of hypovitaminosis D.

Obesity is a known risk factor for vitamin D and type 2 diabetes. It ranges between the sexes and between races.[20–25] The women had higher BMIs

than men in our sample. The excessbody fat in women may have contributed to the observed gender-hypovitaminoid relationship. Dyslipidemia was independent predictor.

Our data are consistent with other literature studies that assessed risk of cardiovascular disease in patients with type 2 diabetes from sunny regions.[14,26]

It is controversial that HbA1c is linked to 25(OH)D. Similar to other previously published trials, we observed a strong poor adverse association between HbA1C and 25(OH)D.[10,15,21,26–28] However, when controlling for confounding variables is confirmed by Luo et al. and Al-Shoumer et al.[29,30] Considering that our mean 25(OH)D in Pakistan was very close to 30 ng/mL, further studies are required to assess the suitability of the current type 2 vitamin D cutoffs in Pakistan. In this analysis, a lower 25(OH)D normally reduced prevalence of hypovitamino D would have definitely resulted.[13]

CONCLUSION

We found that hypovitaminosis D is high in 62% of those participating in the treatment of Type 2 diabetes and that hypovitaminosis D is linked to female gender, obesityand dyslipidemia. The data show that adequate sunshine is not sufficient to prevent vitamin D deficiency alone and to sensitize the population, regardless of their geographical position, for hypovitaminosis D.

Author's Contribution:

Concept & Design of Study:	Masood Nabi Noor
Drafting:	Altaf Hussain Memon, Ahmed Hussain Suhag
Data Analysis:	Gunesh Kumar, Ghullam Mujtaba Shah, Ameer Abbas
Revisiting Critically:	Masood Nabi Noor, Altaf Hussain Memon
Final Approval of version:	Masood Nabi Noor

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract 2014;103(2):137–49.
2. Holick MF. Medical progress: Vitamin D deficiency. N Engl J Med 2007;357(3):266–81.
3. Verstuyf A, Carmeliet G, Bouillon R, Mathieu C. Vitamin D: a pleiotropic hormone. Kidney Int 2010;78(2):140–5.
4. Koshiyama H, Ikeda H, Honjo S, Nakamura Y, Tanaka K, Tsugawa N, et al. Hypovitaminosis D is frequent in Japanese subjects with type 2 diabetes. Diabetes Res Clin Pract 2007;76(3):470–1.
5. Cigolini M, Iagulli MP, Miconi V, Galiotto M, Lombardi S, Targher G. Serum 25-Hydroxyvitamin D3 Concentrations and Prevalence of Cardiovascular Disease Among Type 2 Diabetic Patients. Diabetes Care 2006;29(3):722–4.
6. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The Role of Vitamin D and Calcium in Type 2 Diabetes. A Systematic Review and Meta-Analysis. J Clin Endocrinol Metab 2007;92(6):2017–29.
7. Zittermann A, Schleithoff SS, Koerfer R. Putting cardiovascular disease and vitamin D insufficiency into perspective. Br J Nutr 2005;94(4):483–92.
8. Simpson RU, Hershey SH, Nibbelink KA. Characterization of heart size and blood pressure in the vitamin D receptor knockout mouse. J Steroid Biochem Mol Biol 2007;103(3–5):521–4.
9. Lee JI, Oh SJ, Ha WC, Kwon HS, Sohn TS, Son HS, et al. Serum 25-hydroxyvitamin D concentration and arterial stiffness among type 2 diabetes. Diabetes Res Clin Pract 2012;95(1):42–7.
10. Targher G, Bertolini L, Padovani R, Zenari L, Scala L, Cigolini M, et al. Serum 25-hydroxyvitamin D3 concentrations and carotid artery intima-media thickness among type 2 diabetic patients. Clin Endocrinol (Oxf) 2006;65(5):593–7.
11. Isaia G, Giorgino R, Adami S. High Prevalence of Hypovitaminosis D in Female Type 2 Diabetic Population. Diabetes Care 2001;24(8):1496–1496.
12. Jee D, Han K do, Kim EC. Inverse Association between High Blood 25-Hydroxyvitamin D Levels and Diabetic Retinopathy in a Representative Korean Population. Vavvas D, editor. PLoS One 2014;9(12):e115199.
13. Rolim MC, Santos BM, Conceição G, Rocha PN. Relationship between vitamin D status, glycemic control and cardiovascular risk factors in Brazilians with type 2 diabetes mellitus. Diabetol Metab Syndr 2016;8(1):77.
14. Foucan L, Vélayoudom-Céphise FL, Larifla L, Armand C, Deloumeaux J, Fagour C, et al. Polymorphisms in GC and NADSYN1 Genes are associated with vitamin D status and metabolic profile in Non-diabetic adults. BMC Endocr Disord 2013;13(1):36.
15. Bellan M, Guzzaloni G, Rinaldi M, Merlotti E, Ferrari C, Tagliaferri A, et al. Altered glucose metabolism rather than naive type 2 diabetes mellitus (T2DM) is related to vitamin D status in severe obesity. Cardiovasc Diabetol 2014;13(1):57.
16. Osei K. 25-OH vitamin D. Is it the universal panacea for metabolic syndrome and type 2 diabetes? J Clin Endocrinol Metab 2010;95(9):4220–2.

17. Hoteit M, Al-Shaar L, Yazbeck C, Bou Sleiman M, Ghalayini T, El-Hajj Fuleihan G. Hypovitaminosis D in a sunny country: Time trends, predictors, and implications for practice guidelines. Metabolism 2014;63(7):968–78.
18. van der Meer IM, Middelkoop BJC, Boeke AJP, Lips P. Prevalence of vitamin D deficiency among Turkish, Moroccan, Indian and sub-Sahara African populations in Europe and their countries of origin: an overview. Osteoporos Int 2011;22(4):1009–21.
19. Mitri J, Pittas AG. Vitamin D and Diabetes. Endocrinol Metab Clin North Am 2014;43(1): 205–32.
20. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2011;96(7):1911–30.
21. Kositsawat J, Freeman VL, Gerber BS, Geraci S. Association of A1C Levels With Vitamin D Status in U.S. Adults: Data from the National Health and Nutrition Examination Survey. Diabetes Care 2010;33(6):1236–8.
22. Zhao G, Ford ES, Li C. Associations of Serum Concentrations of 25-Hydroxyvitamin D and Parathyroid Hormone With Surrogate Markers of Insulin Resistance Among U.S. Adults Without Physician-Diagnosed Diabetes: NHANES, 2003-2006. Diabetes Care 2010;33(2):344–7.
23. Forouhi NG, Ye Z, Rickard AP, Khaw KT, Luben R, Langenberg C, et al. Circulating 25-hydroxyvitamin D concentration and the risk of type 2 diabetes: results from the European Prospective Investigation into Cancer (EPIC)-Norfolk cohort and updated meta-analysis of prospective studies. Diabetologia 2012;55(8): 2173–82.
24. McGill AT, Stewart JM, Lithander FE, Strik CM, Poppitt SD. Relationships of low serum vitamin D3with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. Nutr J 2008;7(1):4.
25. Benjamin A, Moriakova A, Akhter N, Rao D, Xie H, Kukreja S, et al. Determinants of 25-hydroxyvitamin D levels in African-American and Caucasian male veterans. Osteoporos Int 2009;20(10):1795–803.
26. Yu JR, Lee SA, Lee J-G, Seong GM, Ko SJ, Koh G, et al. Serum Vitamin D Status and Its Relationship to Metabolic Parameters in Patients with Type 2 Diabetes Mellitus. Chonnam Med J 2012;48(2):108.
27. Al-Timimi DJ, Ali AF. Serum 25(OH) D in diabetes mellitus type 2: Relation to glycaemic control. J Clin Diagnostic Res 2013;7(12):2686–8.
28. Manickam B, Neagu V, Kukreja SC, Barengolts E. Relationship Between Glycated Hemoglobin and Circulating 25-Hydroxyvitamin D Concentration In African American And Caucasian American Men. Endocr Pract 2013;19(1):73–80.
29. Luo C, Wong J, Brown M, Hooper M, Molyneaux L, Yue DK. Hypovitaminosis D in Chinese type 2 diabetes: Lack of impact on clinical metabolic status and biomarkers of cellular inflammation. Diabetes Vasc Dis Res 2009;6(3):194–9.
30. Al-Shoumer KA. Is there a relationship between vitamin D with insulin resistance and diabetes mellitus? World J Diabetes 2015;6(8):1057.