Annals of Short Reports

Research Article
Published: 11 Apr, 2019

Vitamin D Deficiency in Saudi Men with Type 2 Diabetes Mellitus

*Khalid S Aljabri**

Department of Endocrinology, King Fahad Armed Forces Hospital, Saudi Arabia

Abstract

Introduction: Vitamin D deficiency and Type 2 Diabetes Mellitus (T2DM) remain major health problems. Few published researches have been found that surveyed the prevalence of VDD in patients with T2DM in Saudi Arabia. We conducted a cross sectional study to investigate the prevalence vitamin D deficiency in male patients with T2DM.

Method: A cross-sectional single centre study was conducted in 1145 patients with T2DM. Patients with T2DM attending the Diabetes centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia between January 2018 and December 2018. The serum concentration of 25(OH)D and HbA1c were measured.

Results: There were 1145 male patients with T2DM. The mean age was 54.4 ± 16.5 years. The mean and median 25(OH)D concentrations were 52.7 ± 27.2 and 46.6 respectively.

The prevalence of different vitamin D status were; 55.6% deficient, 27.3% insufficient and 17.0% sufficient. VDD patients were statistically significant younger than patients with vitamin insufficiency or sufficiency (52.5 ± 16.4 *vs.* 56.3 ± 17.0 *vs.* 57.2 ± 15.2 respectively, p<0.0001). Vitamin D deficient patients have statistically significant higher HbA1c than patients with vitamin insufficiency or sufficiency (8.3 ± 2.0 *vs.* 7.7 ± 1.7 *vs.* 7.4 ± 1.7 respectively, p<0.0001). Moreover, vitamin D deficient patients have statistically significant lower 25(OH)D than patients with vitamin insufficiency or sufficiency (34.3 ± 8.9 *vs.* 60.6 ± 7.2 *vs.* 100.3 ± 23.0 respectively, p<0.0001).

The mean 25(OH)D was upward as age advanced with highest frequency of VDD was found in the sixth decades. In addition, 25(OH)D concentration was significantly positively correlated with age (r=0.128, p<0.0001) and significantly negatively correlated with HbA1c (r= -0.179, p<0.0001). HbA1c ≥7 was significantly associated with higher VDD.

Regression analysis of odd ratio of risk factors for patients with VDD showed that age and HbA1c were statistically significant associated with VDD, (OR=0.979; 95% CI=0.979-0.988), p<0.0001) and (OR=1.263; 95% CI=1.167-1.367, p<0.0001) respectively.

Conclusion: The prevalence of VDD in male patients with T2DM is high.

Keywords: Type 2 diabetes mellitus; Vitamin D deficiency; 25(OH)D

OPEN ACCESS

Correspondence:

Khalid S Aljabri, Department of Endocrinology, King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia, E-mail: khalidsaljabri@yahoo.com

Received Date: *08 Apr 2019*
Accepted Date: *06 May 2019*
Published Date: *11 May 2019*

Citation:

Aljabri KS. Vitamin D Deficiency in Saudi Men with Type 2 Diabetes Mellitus. Ann Short Reports. 2019; 2: 1037.

Introduction

There are growing data from studies of young adults, elderly persons, and youth in other countries that Vitamin D Deficiency (VDD) is an unrecognized and prevalent health problem [1-7]. VDD remains a major health problem in many parts of the world. Vitamin D deficiency is defined as serum 25(OH)D concentration <50 nmol/L [8,9]. Current studies confirm that the prevalence of VDD in the general world population is as high as 50% to 80%, even occurring in countries located in geographical areas which receive sunshine year-round [10]. The Middle East and the North African region in general including Saudi Arabia have very high prevalence of VDD even in the normal asymptomatic population [11-13].

The prevalence of Type 2 Diabetes Mellitus (T2DM) in Saudi Arabia is one of the highest reported in the world, reaching up to 30% in a recent study [14]. The prevalence of VDD in patients with T2DM varies from 70% to 90%, depending on the threshold used to define VDD [15-22]. Few published researches have been found that surveyed the prevalence of VDD in patients with T2DM in Saudi Arabia [23]. It has been reported that insulin secretion is dependent upon vitamin D and there is a positive correlation of vitamin D concentration with insulin sensitivity [24-29].

In areas such as Saudi Arabia where there is plentiful sunlight and many food products are fortified with vitamin D, it would be expected that the vitamin D level would be adequate in the majority of the population. Despite some cultural factors that may negatively affect serum vitamin D levels of Saudi women, these factors do not apply to males and hence vitamin D ranges may be expected to be different between males and females. Few data are available regarding the prevalence of VDD among Saudi men with T2DM. We conducted a cross sectional study to investigate the prevalence VDD in Saudi men with T2DM.

Methods

A cross-sectional single centre study was conducted in 1145 patients with T2DM. Patients with T2DM attending the Diabetes centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia between January 2018 and December 2018. Eligible patients were 20 years or older. Exclusion criteria were known hepatic or renal disease, metabolic bone disease, malabsorption, hypercortisolism, malignancy, immobility for more than one-week and medications influencing bone metabolism. The serum concentration of 25(OH) D was measured by competitive protein binding assay using kits (Immunodiagnostic, Bensheim, Germany). Plasma levels from 75.1 to 250 nmol/l considered sufficient, from 50 to 75 nmol/l insufficient and <50 nmol/l as deficient [30]. Glycosylated hemoglobin (HbA1c) was measured by the high performance liquid chromatography method (Bio-Rad Laboratories, Waters, MA, USA). The total number of cohort were separated on basis of age values into seven groups: 20-29 years, 30-40 years, 40-49 years, 50-59 year 60-70 years, 70-79 year and ≥ 80. The study was approved by the ethical committee board of King Fahad Armed Forces Hospital.

Statistical analysis

Data are presented as means ± Standard Deviation (SD) or numbers (%). Quantitative variables were compared between two groups by using the Student's test. Differences in categorical variables were analyzed using the chi-square test. Differences in mean serum 25(OH)D levels were tested with ANOVA. The relationship between continuous variables was assessed using coefficients of correlation. Logistic regression analysis was carried out to identify the independent predictors of vitamin D deficiency considering age and HbA1c as risk factors and to estimate Odds Ratio (OR) and 95% Confidence Interval (95%CI). P value <0.05 indicates significance. The statistical analysis was conducted with SPSS version 23.0 for Windows.

Results

There were 1145 male patients with T2DM (Table 1). The mean age was 54.4 ± 16.5 years. The mean and median 25(OH)D concentrations were 52.7 ± 27.2 and 46.6 respectively.

The prevalence of different vitamin D status was; 55.6% deficient, 27.3% insufficient and 17.0% sufficient (Table 2). VDD patients were statistically significant younger than patients with vitamin insufficiency or sufficiency (52.5 ± 16.4 *vs.* 56.3 ± 17.0 *vs.* 57.2 ± 15.2 respectively, p<0.0001). Vitamin D deficient patients have statistically significant higher HbA1c than patients with vitamin insufficiency or sufficiency (8.3 ± 2.0 *vs.* 7.7 ± 1.7 *vs.* 7.4 ± 1.7 respectively, p<0.0001). Moreover, vitamin D deficient patients have statistically significant lower 25(OH)D than patients with vitamin insufficiency or sufficiency (34.3 ± 8.9 *vs.* 60.6 ± 7.2 *vs.* 100.3 ± 23.0 respectively, p<0.0001).

The mean 25(OH)D was upward as age advanced with highest frequency of VDD was found in the sixth decades (Figures 1A,B). In addition, 25(OH)D concentration was significantly positively correlated with age (r=0.128, p<0.0001) and significantly negatively

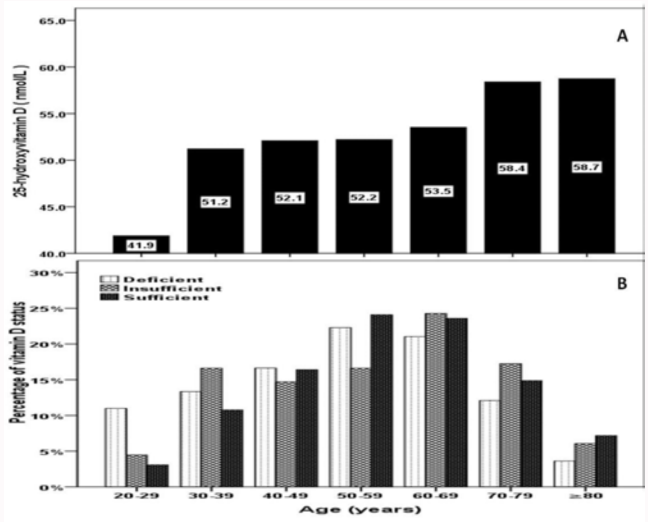

Figure 1: The mean of vitamin D concentration (nmol/l) A) and the percentage of vitamin D status B) in correlation to age groups.

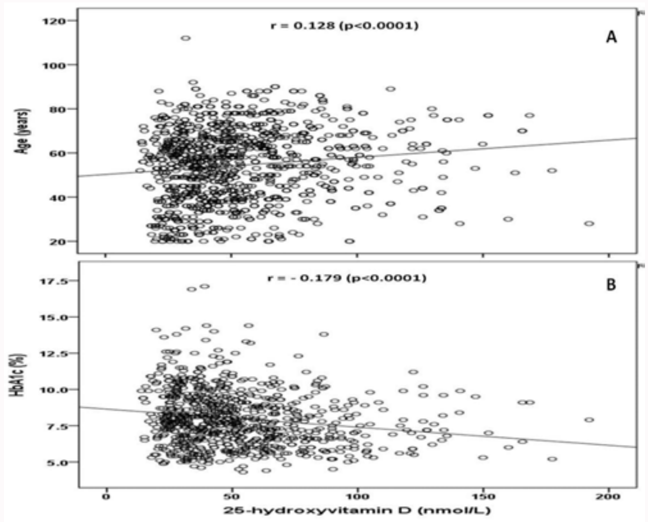

Figure 2: Correlation of 25-hydroxyvitamin D concentration and age A) and HbA1c B) in the study population.

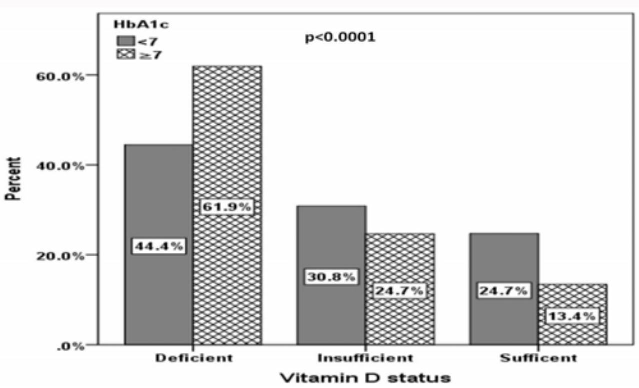

Figure 3: Vitamin D status in correlation to HbA1c groups.

Table 1: Patient characteristics [mean ± standard deviation or number (%)].

Variable	Values
Total	1145
Age (years)	54.4 ± 16.5
HbA1c (%)	8.0 ± 1.9
25-hydroxyvitamin D (nmol/L)	52.7 ± 27.2

correlated with HbA1c (r= -0.179, p<0.0001) (Figures 2A,B). HbA1c ≥ 7 was significantly associated with higher VDD (Figure 3).

Regression analysis of odd ratio of risk factors for patients with VDD showed that age and HbA1c were statistically significant associated with VDD, (OR=0.979; 95% CI=0.979-0.988), p<0.0001) and (OR=1.263; 95% CI=1.167-1.367, p<0.0001) respectively (Table 3).

Discussion

The results of the study in Jeddah, a sunny city located in the west part of Saudi Arabia, confirms the high prevalence of VDD and insufficiency among the Saudi males with T2DM and an even higher prevalence among middle age males. Approximately half had a 25(OH)D level below that commonly considered to represent frank deficiency (<50 nmol/l), and the majority had levels considered insufficient (<75 nmo/l). Further, we observed that age and HbA1c were independent [23] predictors of VDD. This finding is lower than other study (83%) conducted in Saudi Arabia. This finding is also corroborated by other studies in the region [31-35]. The causes of VDD could be due to changing life style with people adopting a more sedentary life, little exposure to sunlight, reduced outdoor activity, and changes in dietary habits. These factors also contribute to both development of T2DM and poor control of diabetes. It is of importance to state that our sample size is representative for a number of subjects suffering from T2DM in the area and study population of one institution does not represent the entire city of Jeddah, in addition the study sample confined to patients with T2DM but without comparable groups.

VDD is one of the most common medical conditions worldwide. An estimated one billion people in the world have VDD or insufficiency [36]. The prevalence of VDD among adult population was reported to be 14% to 59% with a higher prevalence in Asian countries [37-39]. Moreover, VDD is a worldwide epidemic. According to World Health Organization statistics, around one billion people are suffering from VDD throughout the world even in the sunniest areas; VDD is common when most of the skin is shielded from the sun. Studies in Saudi Arabia, the United Arab Emirates, Australia, Turkey, India, and Lebanon, 30% to 50% of children and adults had 25(OH)D levels under 50 nmol/L [5,12,40-42]. Sadat-Ali et al. [43] also demonstrated 10% prevalence of 25(OH)D levels <50 nmol/L in healthy Saudi men with a mean age of 28.5 [43]. In a study from Qatar, the mean overall 25(OH)D level was 29.2 nmol/L among healthcare professionals.

Table 3: Regression analysis for odd ratio of risk factors for patients with vitamin D deficiency.

Parameters	Odd Ratio (95% CI)	P value
Age (years)	0.979 (0.971-0.988)	<0.0001
HbA1c	1.263 (1.167-1.367)	<0.0001

It was lower in females (25.7 nmol/L) than in males (34.2 nmol/L) [44]. These results suggest that VDD is common even in very sunny areas emphasizing the importance of screening for VDD in these populations. Despite the fact that direct comparisons of results of different studies are difficult due to the use of different methods for the measurement of 25-OHD concentrations and that different definitions for vitamin D deficiency have been used, the findings of our study indicate that the rate of VDD status has an increasing trend.

Diabetes mellitus is currently the most prevalent chronic illness in the world having a prevalence of around 9% in the adult population and 30% of Saudi adults [14]. Vitamin D deficiency has received special attention lately because of its high incidence and its implication in the genesis of multiple chronic illnesses.

VDD was observed in a half proportion (55.6%) of our study population with a mean 25-OHD level of 34 nmol/l. This finding is lower than other study (83%) conducted in Saudi Arabia [23]. This finding is also corroborated by other studies in the region [31-35]. The causes of VDD could be due to changing life style with people adopting a more sedentary life, little exposure to sunlight, reduced outdoor activity, and changes in dietary habits. These factors also contribute to both development of T2DM and poor control of diabetes.

VDD was reported as quite common in young, normal Saudi adults in 1981 [12]. Back then however, VDD was more common among the elderly in discordance to the findings in our study, in which serum 25(OH)D was positively correlated with age, that is similar to the findings of Hashemipour et al. [45] in a cohort of 1210 Iranians adult [45]. The positive correlation of 25(OH)D to age is also in agreement with a study carried out in the US, where severe VDD was found to be more common among the young, and less common among the elderly [46].

VDD has received special attention lately because of its high incidence and its implication in the genesis of multiple chronic illnesses. The high prevalence of VDD in our study population underlines the fact that VDD is more common in chronic diseases like diabetes mellitus. Our study showed that 25(OH)D was inadequate in a large population of patients with T2DM. Lower 25(OH)D levels were associated with a poor glycemic control. This was more strongly associated with HbA1c (R= -0.179, p-value <0.0001). The study indicates a poor glycemic control in a majority of patients compared to patients with good glycemic control (68 *vs.* 32% respectively). In patients having HbA1c ≥ 7.0, VDD was significantly greater compared to 44% patients with good glycemic control (HbA1c <7) (62

Table 2: Vitamin D status among male patients with Type 2 diabetes mellitus patients [mean ± standard deviation or number (%)].

Variable	Vitamin D status			P values
	Deficient	Insufficient	sufficient	
Numbers	637 (55.6)	313 (27.3)	195 (17.0)	
Age (years)	52.5 ± 16.4	56.3 ± 17.0	57.2 ± 15.2	<0.0001
HbA1c (%)	8.3 ± 2.0	7.7 ± 1.7	7.4 ± 1.7	<0.0001
25-hydroxyvitamin D (nmol/L)	34.3 ± 8.9	60.6 ± 7.2	100.3 ± 23.0	<0.0001

vs. 44% respectively, p-value <0.0001). These findings are supported by a number of international studies [47-49]. Some studies show no association of a low 25(OH)D with HbA1c levels [47]. But inverse correlation between the level of 25(OH)D and glucose level is well known [48,49]. In many studies 25(OH)D levels were low in subjects having higher HbA1c values both in patients with or without diabetes mellitus indicating that they are inversely related [18,21,50,51]. Thus a poor glycemic control was associated with low 25(OH)D levels, showing an flipped relationship between serum 25(OH)D levels and T2DM as well as markers of adverse glucose hemostasis in many studies [51,52]. Vitamin D has various effects on glucose homeostasis. Besides its role in insulin secretion, it also has an influence on insulin resistance directly or via Ca indirectly [53]. Changes in Ca in primary insulin target tissues may contribute to peripheral insulin resistance via impaired insulin signal transduction, leading to decreased glucose transporter-4 activity [29]. The association between low 25(OH)D level and insulin sensitivity have been reported in cross-sectional and observational studies. The results from the trials on the effect of 25(OH)D and/or Ca supplementation on insulin resistance have showed improvement on insulin action [54].

These findings must be interpreted in light of acknowledged limitations. The study was done at only one centre. The study sample confined to patients with T2DM but without comparable groups.

In conclusion, the prevalence of VDD in male patients with T2DM is high. We recommend larger scale studies for detecting VDD in our population with T2DM and suggest planning strategies to supplement our population with vitamin D.

References

1. Tangpricha V, Pearce EN, Chen TC, Holick MF. Vitamin D insufficiency among free-living healthy young adults. Am J Med. 2002;112(8):659-62.
2. Gloth FM, Gundberg CM, Hollis BW, Haddad JG, Tobin JD. Vitamin deficiency in homebound elderly persons. JAMA. 1995;274(21):1683-6.
3. Kinyamu HK, Gallagher JC, Rafferty KA, Balhorn KE. Dietary calcium and vitamin D intake in elderly women: effect on serum parathyroid hormone and vitamin D metabolites. Am J Clin Nutr. 1998;67(2):342-8.
4. LeBoff MS, Kohlmeier L, Hurwitz S, Franklin J, Wright J, Glowacki J. Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. JAMA. 1999;281(16):1505-11.
5. El-Hajj Fuleihan G, Nabulsi M, Choucair M, Salamoun M, Hajj Shahine C, Kizirian A, et al. Hypovitaminosis D in healthy School children. Pediatrics. 2001;107(4):E53.
6. Docio S, Riancho JA, Perez A, Olmos JM, Amado JA, Gonzalez-Macias J. Seasonal deficiency of vitamin D in children: a potential target for osteoporosis preventing strategies. J Bone Miner Res. 1998;13(4):544-8.
7. Guillemant J, Taupin P, Le HT, Taright N, Allemandou A, Pérès G, et al. Vitamin D status during puberty in French healthy male adolescents. Osteoporos Int. 1999;10(3):222-5.
8. Chiu KC, Chu A, Go VI, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. Am J Clin Nutr. 2004;79(5);820-5.
9. Holick MF. Vitamin D deficiency. N Eng J Med. 2007;357(3):266-81.
10. Gind AA, Liu MC, Camargo CA Jr. Demographic differences and trends of vitamin D insufficiency in the US population, 1988-2004. Arch Intern Med. 2009;169(6):626-32.
11. Maalouf G, Gannage-Yared MH, Ezzedine J, Larijani B, Badawi S, Rached A, et al. Middle East and North Africa consensus on osteoporosis. J Muskuloskelet Neuronal Interact. 2007;7(2):131-43.
12. Sedrani SH, Elidrissy AW, El Arabi KM. Sunlight and vitamin D status in normal Saudi subjects. Am J Clin Nutr. 1983;38(1):129-32.
13. Al-Turki HA, Sadat-Ali M, Al-Elq AH, Al-Mulhim FA, Al-Ali AK. 25-Hydroxyvitamin D levels among healthy Saudi Arabian women. Saudi Med J. 2008;29(12):1765-8.
14. Alqurashi KA, Aljabri KS, Bokhari SA. Prevalence of diabetes mellitus in a Saudi community. Ann Saudi Med. 2011;31(1):19-23.
15. Mattila C, Knekt P, Männistö S, Rissanen H, Laaksonen MA, Montonen J, et al. Serum 25-hydroxyvitamin D concentration and subsequent risk of type 2 diabetes. Diabetes Care. 2007;30(10):2569-70.
16. Pittas AG, Dawson-Hughes B, Li T, Van Dam RM, Willett WC, Manson JE, et al. Vitamin D and calcium intake in relation to type 2 diabetes in women. Diabetes Care. 2006;29(3):650-6.
17. Thorand B, Zierer A, Huth C, Linseisen J, Meisinger C, Roden M, et al. Effect of serum 25-hydroxyvitamin D on risk for type 2 diabetes may be partially mediated by subclinical inflammation: results from the MONICA/KORA Augsburg study. Diabetes Care. 2011;34(10):2320-2.
18. 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.
19. Scragg R, Holdaway I, Singh V, Metcalf P, Baker J, Dryson E. Serum 25-hydroxyvitamin D3 levels decreased in impaired glucose tolerance and diabetes mellitus. Diabetes Res Clin Pract. 1995;27(3):181-8.
20. Mori H, Okada Y, Tanaka Y. Incidence of vitamin D deficiency and its relevance to bone metabolism in Japanese postmenopausal women with type 2 diabetes mellitus. Intern Med. 2015;54(13):1599-604.
21. Tahrani AA, Ball A, Shepherd L, Rahim A, Jones AF, Bates A. The prevalence of vitamin D abnormalities in South Asians with type 2 diabetes mellitus in the UK. Int J Clin Pract. 2010;64(3):351-5.
22. Miñambres I, Sánchez-Quesada JL, Vinagre I, Sánchez- Hernández J, Urgell E, de Leiva A, et al. Hypovitaminosis D in type 2 diabetes: relation with features of the metabolic syndrome and glycemic control. Endocr Res. 2014;40(3):160-5.
23. Al-Zaharani M. The prevalence of Vitamin D deficiency in Type 2 Diabetic patients. Majmaah J. 2013;1(1):18-22.
24. Zeitz U, Weber K, Soegiarto DW, Wolf E, Balling R, Erben RG. Impaired insulin secretory capacity in mice lacking a functional vitamin D receptor. FASEB J. 2003;17(3):509-11.
25. Clark SA, Stumpf WE, Sar M. Effect of 1,25 dihydroxyvitamin D3 on insulin secretion. Diabetes. 1981;30(5):382-6.
26. Johnson JA, Grande JP, Roche PC, Kumar R. Immunohistochemical localization of the 1,25(OH)2D3 receptor and calbindin D28k in human and rat pancreas. Am J Physiol. 1994;267(3 pt 1):356-60.
27. Maestro B, Campion J, Davila N, Calle C. Stimulation by 1, 25 dihydroxy vitamin D3 of insulin receptor expression and insulin responsiveness for glucose transport in U-937 human promonocytic cells. Endocr J. 2000;47(4):383-91.
28. Williams PF, Caterson ID, Cooney GJ, Zilkens RR, Turtle JR. High affinity insulin binding and insulin receptor effector coupling: modulation by Ca2+. Cell Calcium. 1990;11(8):547-56.
29. Zemel MB. Nutritional and endocrine modulation of intracellular calcium: implications in obesity, insulin resistance and hypertension. Mol Cell Biochem. 1998;188(1-2):129-36.
30. Hilger J, Friedel A, Herr R, Rausch T, Roos F, Wahl DA, et al. A systematic review of vitamin D status in populations worldwide. Br J Nutr. 2014;111(1):23-45.
31. Khan H, Ansari MA, Waheed U, Farooq N. Prevalence of Vitamin D

Deficiency in General Population of Islamabad, Pakistan. Ann Pak Inst Med Sci. 2013;9(1):45-7.

32. Masud F. Vitamin D levels for optimum bone health. Singapore Med J. 2007;48(3):207-12.

33. Zuberi LM, Habib A, Haque N, Jabbar A. Vitamin D deficiency in ambulatory patients. J Pak Med Assoc. 2008;58(9):482-4.

34. Mansoor S, Habib A, Ghani F, Fatmi Z, Badruddin S, Siddiqui I, et al. Prevalence and significance of vitamin D deficiency and insufficiency among apparently healthy adults. Clin Biochem. 2010;43(18):1431-5.

35. Ghauri B, Lodhi A, Mansha M. Development of baseline (air quality) data in Pakistan. Environ Monit Assess. 2007;127(1-3):237-52.

36. Scharla SH, Scheidt Nave C. Reference range of 25-hydroxy vitamin D serum concentrations in Germany. Clin Lab. 1996;42:475-7.

37. Vander Wielen RP, Lowik MR, Vanden Berg H, de Groot LC, Haller J, Moreiras O, et al. Serum vitamin D concentrations among elderly people in Europe. Lancet. 1995;346(8969):207-10.

38. Souberbielle JC, Cormier C, Kindermans C, Gao P, Cantor F, Baulia EE, et al. Vitamin D status and redefining serum parathyroid hormone reference range in the elderly. J Clin Endocrinol Metab. 2001;86(7):3086-90.

39. Holick MF. High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc. 2006;81(3):353-73.

40. Thuesen B, Husemoen L, FengerM, Jakobsen J, Schwarz P, Toft U, et al. Determinants of vitamin D status in a general population of Danish adults. Bone. 2012;50(3):605-10.

41. Marwaha RK, Tandon N, Reddy DR, Aggarwal R, Singh R, Sawhney RC, et al. Vitamin D and bone mineral density status of health schoolchildren in northern India. Am J Ckin Nut. 2005;82(2):477-82.

42. Sadat-Ali M, AlElq A, Al-Turki H, Al-Mulhim F, Al-Ali A. Vitamin D levels in healthy men in eastern Saudi Arabia. Ann Saudi Med. 2009;29(5):378-82.

43. Mahdy S, Al-Emadi SA, Khanjar IA, Hammoudeh MM, Sarakbi HA, Siam AM, et al. Vitamin D status in health care professionals in Qatar. Saudi Med J. 2010;31(1):74-7.

44. Hashemipour S, Larijani B, Adibi H, Javadi E, Sedaghat M, Pajouhi M, et al. Vitamin D deficiency and causative factors in the population of Tehran. BMC Public Health. 2004;4:38.

45. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. Mayo Clin Proc. 2003;78(12):1463-70.

46. Husemoen LLN, Thuesen BH, Fenger M, Jorgensen T, Glumer C, Svensson J, et al. Serum 25(OH)D and Type 2 Diabetes Association in a General Population: A prospective study. Diabetes Care. 2012;35(8):1695-700.

47. Palomer X, Gonzalez-Clemente J, Blanco-Vaca F, Mauricio D. Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. Diabetes Obes Metab. 2008;10(3):185-97.

48. Boucher BJ, Mannan N, Noonan K, Hales CN, Evans SJ. Glucose intolerance and impairment of insulin secretion in relation to vitamin D deficiency in east London Asians. Diabetologia. 1995;38(10):1239-45.

49. Hutchinson MS, Figenshau Y, NjølstadI, Schirmer H, Jorde R. Serum 25-hydroxyvitamin D levels are inversely associated with glycated haemoglobin (HbA(1c)).The TromsøStudy. Scand J Clin Lab Invest. 2011;71(5):399-406.

50. Kositsawat J, Freeman VL, Gerber BS, Geraci S. Association of A1Clevels with vitamin D status in U.S. adults: data from the National Health and Nutrition Examination Survey. Diabetes Care. 2010;33(6):1236-8.

51. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review andmeta-analysis. J Clin Endocrinol Metab. 2007;92(6):2017-29.

52. Borissova AM, Tankova T, Kirilov G, Dakovska L, Kovacheva R. The effect of vitamin D3 on insulin secretion and peripheral insulin sensitivity in type 2 diabetic patients. Int J Clin Pract. 2003;57(4):258-61.

53. Nazarian S, St Peter JV, Boston RC, Jones SA, Mariash CN. Vitamin D3 supplementation improves insulin sensitisity in subjects with impaired fasting glucose. Transl Res. 2011;158(5):276-81.