



VITAMIN D STATUS AND DIABETES MELLITUS

Dr. Mohammad Anwar Magsi¹, Dr. Aamir Ijaz², Dr. Aaizah Maryam³, Dr. Shagufta Yousaf⁴,
Dr. Fawaad Sana⁵, Dr. Najamuddin⁶

1. Trainee FCPSII Chemical Pathology
PNS SHIFA Hospital, Karachi
2. Professor Chemical Pathology
PNS SHIFA Hospital, Karachi
- 3,4,5,6.
PNS SHIFA Hospital, Karachi

Correspondence Address:
Dr. Mohammad Anwar Magsi,
Baloch Colony, Near Siddiq Masjid
Jan Muhammad Road, Quetta
mohammadanwar20000@gmail.com

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ABSTRACT... Introduction: Diabetes mellitus is a worldwide epidemic, similarly low Vitamin D levels constitutes a largely unrecognized epidemic in many populations. There is no study in our country to document the association between these two common metabolic disorders. **Objective:** To assess the degree of correlation between vitamin D status and various categories of hyperglycaemia in a Pakistani population. **Study Design:** Descriptive cross sectional study. **Place & Period of Study:** Department of Pathology, PNS SHIFA Hospital, Karachi; Jan 2013 to Aug 2013. Glucose levels were measured in eight six patients divided on the basis of their 25-hydroxyvitamin D3 (25OHD) levels in three groups, normal (>31 ng/ml), insufficient (20-31ng/ml) and deficient (<20ng/ml). 25OHD was measured by electrochemiluminescence using Roche Elecsys® Systems while glucose was estimated by routine methods on Roche Hitachi® Autoanalyser. **Results:** Vitamin D levels were inversely correlated with plasma glucose levels ($r=0.38$; $p<0.01$) with an Odd Ratio of 3.59 (95%confidence interval 1.29 to 8.70). Fasting plasma glucose was significantly higher in vitamin D deficient patients as compared to patients with normal vitamin D status ($p<0.05$). **Conclusions:** Vitamin D deficiency is negatively associated with plasma glucose levels.

Key words: Vitamin D3; Diabetes mellitus.

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INTRODUCTION

Vitamin D deficiency (VDD) is a world-wide epidemic with recent estimates indicating more than 50% global population at risk¹. This pandemic of inadequate vitamin D {VDD and vitamin D insufficiency (VDI)} has been found in all age groups even in those who are otherwise healthy and are not prone to deficiency². In Pakistan, prevalence of VDD has been reported upto 92% in ambulatory patients in various situations^{3,4}. The discovery of vitamin D receptors (VDR) in almost all the tissues has led to the identification of role of vitamin D in many organ systems of the body, instead of merely associated with bone disorders⁵. Vitamin D has also been found to play an important role in the disorders of glucose and insulin metabolism⁶. Inverse correlation between serum vitamin D levels and glycaemic levels has been shown in many studies⁵⁻⁷. Most of this data,

however, pertains to Caucasian population while studies in African American have not confirmed these findings and the association between VDD and diabetes mellitus (DM) is quite blurred⁸. Asians have a high prevalence of both DM and VDD and the association of these two disorders has been described in studies carried out in Asian living in the West⁹. Vitamin D replacement therapy in South Asian patients with diabetes has also been shown to decrease in HbA1c and weight¹⁰. Tehrani et al (2010) has shown that abnormal vitamin D concentrations were more common in South Asians with type 2 DM (T2DM) and diabetic control was inversely related to vitamin D status in South Asian women with T2DM¹¹. Conversely, Taylor and Wise (1997) have reported that vitamin D replacement may increase the insulin resistance and worsen the glycaemic control in Asians¹². Pakistan is one of the countries with a very high

burden of diabetic patients and a very high prevalence of hypovitaminosis D. So present study has been planned to find an association between these two metabolic diseases.

METHODS AND MATERIAL

In this cross sectional study 86 subjects were selected by non-probability convenience sampling out of the patients referred for vitamin D estimation. The sample population consisted of patients with normoglycaemia (NG), impaired fasting glucose (IFG), and DM. NG was defined as Fasting Plasma Glucose (FPG) < 5.6 mmol/L, IFG: 5.6 – 7.0 mmol/L and DM > 7.0 mmol/L (Position Statement-American Diabetic Association-2009)¹³. Similarly, on the basis of their 25OHD levels in blood the subjects were clustered in three groups, normal (>31 ng/ml), insufficient (20-31ng/ml) and deficient (<20ng/ml)¹⁴. 25OHD was measured by electrochemiluminescence using Roche Elecsys® Systems while glucose were estimated by routine methods on Roche Hitachi®.

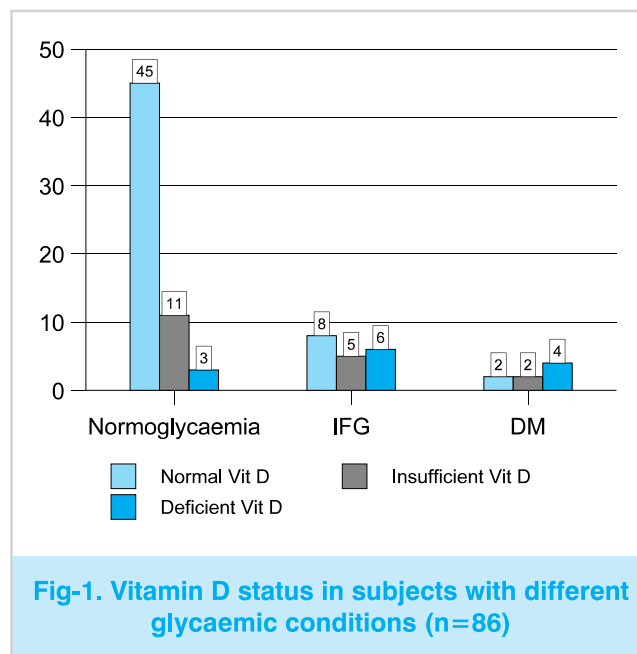
STATISTICAL ANALYSES

The data was recorded in SPSS version 17 and frequencies of various groups of subjects according to Vitamin D status were determined. Comparison of frequencies was carried out using Chi Square test and continuous data was compared by students` t test i.e. comparison of FPG in various groups of Vitamin D status. Then correlation studies were carried out between FPG and 25OHD levels using Pearson's Correlation Coefficient. VDD and VDI of vitamin D status groups were combined and IFG and DM of glucose categories were combined and then 2x2 table was constructed for comparison and calculation of Odds Ratio (OR) using chi-square test.

RESULTS

The sample population had a slight female preponderance (53%), while median age was 34 years (range: 19- 65 years). DM was more frequent in subjects with VDD (50% i.e. half of the patients with VDD were also having DM) and VDI (31.6%) as compared to subjects with normal vitamin D status (6.1%) (Table-I). Similarly, more patients with IFG

were found in VDD (25%) and VDI (26.3%) groups as compared to subjects with normal Vitamin D status (18.6%) (Table-I). This difference was found statistically significant ($p < 0.001$). A gradual worsening of glycaemic condition was found on progressing from normal vitamin D status to insufficiency and deficiency (Figure 1).



DISCUSSION

The association of Vitamin D and DM has been described for more than twenty five years now¹⁵. Many workers have shown evidence that vitamin D is related to various aspects of glucose metabolism e.g. improving beta-cell function of pancreas, insulin secretion and insulin sensitivity and is one of the most important environmental factors causing T2DM¹⁶⁻²⁰. Our data has shown two significant findings i.e. higher prevalence of IFG and frank DM in patients with VDI and VDD, and a significance correlation of FPG and vitamin D levels. Many cross-sectional studies carried out in Western populations have generally reported an inverse association between vitamin D status and prevalent hyperglycemia²¹. Similar associations between higher fasting plasma glucose levels and vitamin D status were observed in a community-based study of older adults without known diabetes²². Expressing this association in another manner, Tahrani et al (2010) has shown that a low

Vitamin D Status	No . of subjects (n=86)	Normoglycaemia (FPG <5.6 mmol/L)	IFG (FPG 5.6 - 7.0 mmol/L)	DM (FPG > 7.0 mmol/L)	Significance levels (Chi square test)
Normal (>30 ng/ml)	n=59	45 (76%)	11 (18.6%)	3 (5.1%)	Normal and insufficiency group (p=<0.001)
Insufficiency (20-30 ng/ml)	n=19	8 (42.1%)	5 (26.3%)	6 (31.6%)	Insufficiency and deficiency group (p=<0.001)
Deficiency (<20 ng/ml)	n=8	2 (25%)	2 (25%)	4 (50%)	Normal and deficiency group (p=<0.001)

Table-I. Distribution of various glycaemic groups in subjects with different Vitamin D Status
FPG: Fasting Plasma Glucose IFG: Impaired Fasting Glycaemia DM: Diabetes Mellitus

Vitamin D Status	No . of subjects (n=86)	(FPG mmol/L) (mean±SD)	Significance levels (independent t-test)	Pearson's correlation (r-value)	Significance levels (P value)
Normal (>30 ng/ml)	n=59	5.4±2.2	Normal and insufficiency Group (p=NS)	r = -0.38	P <0.001
Insufficiency (20-30 ng/ml)	n=19	6.3±2.3	Insufficiency and Deficiency Group (p=NS)		
Deficiency (<20 ng/ml)	n=8	8.1±3.8*	Normal and Deficiency Group (p<0.05)		

Table-II. Comparison of Fasting Plasma Glucose Levels in various groups of Vitamin D Status and Correlation Studies between FPG and Vitamin D Levels

	OR	95% Confidence Interval	
		Lower	Upper
Odds ratio for glucose level (Normal / abnormal)	3.359	1.297	8.701
N of Valid Cases	86		

Table-III. Risk Estimate of Vitamin D adequacy in Normal and abnormal glucose levels

serum 25OHD (<20 ng/ml) was more common in diabetics as compared to controls (83% vs. 70%; p < 0.07)¹¹. In another study from US, mean 25OHD levels among T2DM patients were found

significantly lower than in individuals without T2DM (OR 1.85; 95% CI 1.03 – 3.32; P = 0.038)²³. Conversely, in an Indonesian study 81% diabetic were found to be having VDD as compared to 75% non-diabetic (OR: 0.8; 95% CI 0.42 – 1.21; P = 0.46)²⁴ whereas our study showed an OR of 3.35 (95% CI: 1.29-8.70). This discrepancy is difficult to explain but is probably due to difference in age of the selected population.

The close association between vitamin status and DM has been further emphasized by the finding that inadequate vitamin D level is an important risk factor for the development of type 2 DM²⁵⁻²⁸. The intervention studies to improve glycaemic control with certain doses of vitamin D, however, have

shown variable results²⁹⁻³⁰. Beneficial effect of vitamin D on T2DM is needed to be confirmed in large trials specifically designed to test the hypothesis that vitamin D status is a direct contributor to the pathogenesis of T2DM. If such an intervention is clearly shown to be effective this could have substantial public health implications²¹.

This was the first study in our country in which an association of vitamin D status was studied with various categories of glucose abnormalities but with some limitations e.g. impaired glucose tolerance which is a category of hyperglycaemia based on oral glucose tolerance test could not be studied. Similarly data regarding glycosylated hemoglobin could not be recorded.

CONCLUSIONS

A significant association between diabetes mellitus and vitamin D inadequacy exists which implies that vitamin D deficiency or insufficiency is undesirable in patients with any form of hyperglycaemia.

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REFERENCES

- Prentice A. **Vitamin D deficiency: a global perspective:** Nutrition Reviews 2008; 66(2):S153-154.
- Holick MF. **High Prevalence of Vitamin D Inadequacy and Implications for Health.** Mayo Clin Proc. 2006;81(3):353-373.
- Zuberi LM, Habib A, Haque N, Jabbar A. **Vitamin D Deficiency in Ambulatory patients.** J Pak Med Assoc 2008;58(9):482-484.
- Iqbal R, Khan AH. **Possible causes of vitamin D deficiency in Pakistani population residing in Pakistan:** J Pak Med Assoc 2010;60(1):1-2.
- Danescu LG, Levy S, Levy J. **Vitamin D and diabetes mellitus:** Endocr 2009; 35(1):11-17.
- Mathieu C, Gysemans C, Giulietti A, Bouillon R. **Vitamin D and diabetes.** Diabetologia 2005;48:1247-1257.
- Forouhi NG, Luan J, Cooper A, Boucher BJ, Wareham NJ. **Baseline serum 25-hydroxy vitamin D is predictive of future glycemic status and insulin resistance.** The Medical Research Council Ely Prospective Study 1990 –2000. Diabetes 2008;57:2619-2625.
- Scragg R, Sowers MF, Bell C. **Serum 25-Hydroxyvitamin D, Diabetes, and Ethnicity in the Third National Health and Nutrition Examination Survey.** Diabetes Care 2004; 27:2813-2818.
- Goswami, R, Mishra SK, Kochupillai N. **Prevalence and potential significance of vitamin D deficiency in Asian Indians.** Indian J Med Res 2008; 127:229-238.
- Sabherwal S, V. Bravis V, Devendra D. **Effect of oral vitamin D and calcium replacement on glycaemic control in South Asian patients with type 2 diabetes.** Int J Clin Pract 2010; 64(8): 1084-1089
- 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):351-355.
- Taylor AV, Wise PH. **Vitamin D replacement in Asians with diabetes may increase insulin resistance.** Postgrad Med J. 1998;74(872):365-366.
- Position Statement, American Diabetic Association. **Diagnosis and Classification of Diabetes Mellitus.** Diabetes Care 2009;32(S1):562-567.
- Holick MF. **Vitamin D Deficiency.** N Engl J Med 2007; 357:266-268.
- Gedik O, Akalin S. **Effects of vitamin D deficiency and repletion on insulin and glucagon secretion in man.** Diabetologia 1986; 29:142-145.
- Allard P, Delvin EE, Paradis G, Hanley JA, O'Loughlin J, Lavalley C, et al. **Distribution of fasting plasma insulin, free fatty acids, and glucose concentrations, and of homeostasis model assessment of insulin resistance in a representative sample of Quebec children and adolescents.** Clin Chem 2003; 49: 644-649.
- Pittas AG, Lau J, Hu FB, Dawson-Hughes B. **The role of vitamin D and calcium in type 2 diabetes. A systematic review and metaanalysis s.** J Clin Endocrinol Metab 2007; 92:2017-2029.
- Ashraf A, Alvarez J, Saenz K, Gower B, McCormick K, Franklin F. **Threshold for effects of vitamin D deficiency on glucose metabolism in obese female African-American adolescents:** J Clin Endocrinol Metab 2009; 94(9):3200-06.

19. Grimnes G, Figenschau Y, Almas B, Jorde R. **Vitamin D, insulin secretion, sensitivity, and lipids results from a case-control study and a randomized controlled trial using hyperglycemic clamp technique.** *Diabetes* 2011; 60(11):2748–2757.
20. Rajkumar KL, Holick MF, Heras JDL, Arsalani SA, Lee SJ. **25-Hydroxyvitamin D concentrations and in vivo insulin sensitivity and beta-Cell function relative to insulin sensitivity in black and white youth.** *Diabetes* 2012;35(3):627–633.
21. Mitri J, Pittas AG. **Vitamin D and type 2 diabetes: a systematic review.** *European Journal of Clinical Nutrition* 2011; 65(9): 1005–1015.
22. Oh JY, Barrett-Connor E. **Association between vitamin D receptor polymorphism and type 2 diabetes or metabolic syndrome in community-dwelling older adults: the Rancho Bernardo Study.** *Metabolism* 2002; 51:356–359.
23. Szep Z, Guaraldi G, Shah SS, Lo Re V 3rd, Ratcliffe SJ, Orlando G, et al. **Vitamin D deficiency is associated with type 2 diabetes mellitus in HIV infection.** *AIDS.* 2011;25(4):525–529.
24. Hidayat R, Setiati S, Soewondo P, **The Association Between Vitamin D Deficiency and Type 2 Diabetes Mellitus in Elderly Patients.** *Acta Med Indones* 2010;42(3):123–129.
25. de Boer IH, Tinker LF, Connelly S, Curb JD, Howard BV, Kestenbaum B et al. **Calcium plus vitamin D supplementation and the risk of incident diabetes in the Women's Health Initiative.** *Diabetes Care* 2008;31:701–707.
26. Liu E, Meigs JB, Pittas AG, Economos CD, McKeown NM, Booth SL et al. **Predicted 25-hydroxyvitamin D score and incident of type 2 diabetes in the Framingham Offspring Study.** *Am J Clin Nutr* 2010;91:1627–1633.
27. Liu S, Song Y, Ford ES, Manson JE, Buring JE, Ridker PM. **Dietary calcium, vitamin D, and the prevalence of metabolic syndrome in middle-aged and older US women.** *Diabetes Care* 2005; 28:2926–2932.
28. 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;9:650–656.
29. von Hurst PR, Stonehouse W, Coad J. **Vitamin D supplementation reduces insulin resistance in South Asian women living in New Zealand who are insulin resistant and vitamin D deficient - a randomised, placebo-controlled trial.** *Br J Nutr* 2010;103, 549–555.
30. Jorde R, Figenschau Y. **Supplementation with cholecalciferol does not improve glycaemic control in diabetic subjects with normal serum 25-hydroxyvitamin D levels.** *Eur J Nutr* 2009;48:349–354.



To fight against one's
desires
 is the greatest of all fights.

Hazrat Ali (R.A)

