ORIGINAL ARTICLE

Association Of Vitamin D Status And Diabetes Mellitus

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ABSTRACT

Objective: To evaluate the association of 25-hydroxyvitamin D_3 (25OHD)inadequacyand hyperglycaemia in a Pakistani adult population.
Study Design: Case control study
Place & Period of Study: Department of Pathology, PNS SHIFA Hospital, Karachi; Aug 2011 to Nov 2011.
Method and Material: Plasma Glucose levels were measured in 86 patients divided on the basis of their 25-hydroxyvitamin D_3 (25OHD)levels in three groups, normal (>31 ng/ml), insufficient (20-31ng/ml) and deficient (<20ng/ml). Vitamin D insufficiency (VDI) and Vitamin D Deficiency (VDD) are collectively called Vitamin D inadequacy. 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 VDD patientsas compared to patients with normal vitamin D status ($p<0.05$).
Conclusion: Higher glucose levels were found more frequent in patients with Vitamin D deficiency.
Keywords: Vitamin D_3, Diabetes mellitus; Association; risk factor

Introduction: Vitamin D deficiency (VDD) is a world-wide epidemic with recent estimates indicating more than 50% global population at risk[1]. This pandemic of inadequate vitamin D (VDD and vitamin D insufficiency) has been found in all age groups even in those who are otherwise healthy and are not prone to deficiency[2].In Pakistan, prevalence of VDD has been reported up-to 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 disorders[5]. Vitamin D has also been found to play an important role in the disorders of glucose and insulin metabolism[6]. Inversecorrelation between serum vitamin D levels and glycaemic levels has been shown in many studies[5-7].Most of this data, however, pertains to Caucasian populationwhilestudies in African American have not confirmed these findings and the association between VDD and diabetes mellitus (DM) is quite blurred[8]. 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 West[9]. Vitamin D replacement therapy in South Asian patients with diabetes has also been shown to decrease HbA1c and weight[10]. Tehraniet 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 T2DM[11]. Conversely, Taylor and Wise (1997) have reported that vitamin D replacement may increase the insulin resistance and worsen the glycaemic control in Asians[12]. Pakistan is one of the countries with a very high burden of diabetic patients and a very high prevalence of hypovitaminosis D[3,4]. So present study has been planned to evaluate an association between these two metabolic diseases.

Methods and Material: In this case control study 86subjectswere selected by non-probability convenience sampling out of the patients (mostly Armed Forces Persons and their families) referred for vitamin D estimation. Sample size wascalculated by WHO calculator taking hyperglycaemia (12%) as the least proportion outcome variable, 5% margin of error and 95% confidence interval. The subjects on vitamin D replacement therapy, patients of type1diabetes and patients with normoglycaemia as a result of anti-diabetic treatment were excluded from study. 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[13]. Similarly, on the basis of their 25OHDlevels 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 usingChi Square test, while continuous data i.e. Plasma glucose and 25OHDwas compared by students` t test. Then correlation studies were carried out between FPG and

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25OHD levels using Pearson`s Correlation Coefficient. VDD and vitamin D insufficiency (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 Odd 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). Vitamin D inadequacy was found in 27 (31%) subjects. 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 1).Similarly, more patients with IFG were found in VDD (25%) and VDI (26.3%) groups as compared to subjects with normal Vitamin D status. Gradual worsening of glycaemic condition was found on progressing from normal vitamin D status to insufficiency and deficiency (Figure1).Plasma glucose was significantly higher in VDD patientsas compared to those subjects with normal vitamin D status ($p < 0.05$) (Table 2). Vitamin D levels were inversely correlated with plasma glucose levels ($r=-0.38$;$p< 0.01$) (Table 2). Table 3 shows that Vitamin D inadequacy in normal and abnormal glucose groups (OR: 3.59; 95% confidence interval 1.29-8.70

Discussion: The association of Vitamin D and DM has been described for more than twenty five years now[15]. 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 sensitivityand is one of the most important environmental factors causing T2DM[16-20]. Our data has shownttwo 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 havegenerally reported an inverse association between vitamin Dstatus and prevalent hyperglycemia[21].Similar associations between higher fasting plasma glucose levels and vitamin D status were observed in a community-based study of older adults without known diabetes[22]. Expressing this association in another manner, Tahrani et al (2010) has shown that a low 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, mean25OHDlevels among T2DMpatients 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 Indonasian 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.

Theclose 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 DM[25-28]. The intervention studies to improve glycaemic control with certain doses of vitamin D, however, have shown variable results[29-30].Beneficial effectof vitamin D on T2DMis needed to be confirmed in large trialsspecifically designed to test the hypothesis that vitamin Dstatus 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 implications[21].

This was among the initial studies in our countryto examine the association of vitamin D status 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.

Conclusion:A significant associationbetween diabetes mellitus and vitamin D inadequacy exists which imply that vitamin D deficiency or insufficiency is undesirable in patients with any form of hyperglycaemia.

Table 1: Distribution of various glycaemic groups in subjects with different Vitamin D Status

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 (>30ng/ml)	n=59	45 (76%)	11(18.6%)	3 (5.1%)	Normal and Insufficiency Group (p= <0.001)
Insufficiency (20-30ng/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)

FPG: Fasting Plasma Glucose, **IFG:** Impaired Fasting Glycaemia, **DM:** Diabetes Mellitus

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