Havilah Polur et al /J. Pharm. Sci. & Res. Vol.5(1), 2013, 5 - 7

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Study of Vitamin D: A Risk Factor of Type2 Diabetes Mellitus

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Abstract

Introduction: Vitamin D is known for its calcium absorption and bone metabolism; but now been recognized as an accessible predictor, risk factor and bio marker of type 2 diabetes mellitus.

Objective: Epidemiological evidence suggests Hypovitaminosis D may be associated with type – 2 diabetes and thought to be a risk factor for development of type- 2 diabetes. So, this study is done to find the association of vitamin D and type2 diabetes mellitus.

Research Design and Methods: A case control study was done by randomly selecting 120 diabetic subjects aged 35 to 70 years attending O.P of Santhiram general hospital Nandyal. All subjects were investigated for their vitamin D levels. We classified them in to two groups one with insufficient vitamin - D levels as cases (n=80) and sufficient vitamin D levels as controls (n=40). We determined all the baseline diabetic profile like BMI, Fasting blood glucose, fasting Insulin, HbA1C, HomaIR, Homa β levels and blood pressure.

Results: The prevalence of diabetes in females (62.5%) is higher than males (37.5%). The prevalence of mean levels of Vitamin D is less in females (36.5%) compared to males (48.2%). All the baseline metabolic risk factors of diabetes are increased in vitamin D deficient group. Vitamin D shows a significant negative correlation with Homa IR (r = -0.917, P= <0.0001) and HbA1c (r= -0.993 P= <0.0001). The crude odds ratio of vitamin D with HomaIR shows a strong association of vitamin D with diabetes 7.3457 95% CI (2.6193 -20.6007) p=<0.002. The relative risk of vitamin D with insulin and HomaIR is also significantly increased. 2.1613 95% CI (1.2491-3.7396) p<0.0059, 2.7663 95% CI (1.3752 – 5.5648) p<0.0043 respectively.

Conclusion: This study reports an inverse association between vitamin D, future glycemia and insulin resistance. This is potentially important in understanding the etiology of abnormal glucose metabolism and could be used to prevent the development of type 2 diabetes.

INTRODUCTION

Vitamin – D "Mystifying Vitamin" is well known for its regulation of calcium absorption and bone metabolism, but now this hormone has got a pleiotropic effects with possible roles in the pathogenesis of cancer [1,2-4], Cardiovascular disease, multiplesclerosis and type 1,2 diabetes. Vitamin – D deficiency is now emerging as a major health problem with an estimation of about 1 billion people. In India, vitamin – D deficiency is found to be an epidemic despite plenty of sunshine In North India 96% of neonates, 91% of healthy school girls, 84% of pregnant women and 78% of healthy hospital staff were found to have vitamin- D deficiency [5]..

Vitamin-D3 is thought to be one among the risk factors; and play a role in the etiology of Type 2 D.M. Hence it is considered as a potential modifier of diabetes risk [6,7]. Current definitions suggested [1,8,9] vitamin – D as sufficiency if its concentration is >75 nmol/L or 30 µg/L, Hypovitaminosis – D <75 nmol/L or <30 µg/L, insufficiency < 50 nmol/L or < 20 µg/L, deficiency<25nmol/L or 0 to 20 µg/L. In view of increasing prevalence of diabetes and its micro and macro vascular complications globally, it is imperative to discover modifiable risk factors and implement effective preventive measures to address this growing epidemic. The aim of our study is to investigate the association between serum 25(OH)-D3 concentration and markers of metabolic risk including glucose, insulin resistance and β-cell dysfunction.

MATERIALS AND METHODS

The present study was done among 120 diabetic patients of age between35-70 yrs attending Outpatient department of Santhiram general hospital. All patients were undergone vitamin D level estimation. Patients with vitamin -D levels >75 nmol/L were taken as controls (n=40) and with <75 nmol/L were taken as cases (n=80). All subjects were investigated for their baseline diabetic profile which includes body mass index (BMI) ,blood pressure (B.P). fasting blood sugar (FBS), fasting insulin, glycosylated hemoglobin (HbA1C), insulin resistance (HomaIR), Homa β levels. Blood glucose was estimated by glucose- peroxidase (GOD-POD)method, HbA1C by ion exchange resin method, insulin by electro Chemiluminiscence immunoassay and vitamin D by direct ELISAKIT(Immunodiagnostic) [8,10,11].

STATISTICAL ANALYSIS

Basal fasting glucose, Insulin, HbA1c and two derived Homa indices were estimated. Their mean (S.D) were calculated and P- values were done. HomaIR was computed as follows. Fasting Insulin (µIu/ml) x Fasting glucose (mmol/ml) ÷ 22.5 [1, 8, 12] or FPI X FBG ÷ 405 (FBG in mg/dL). Homa β was calculated as 20 x fasting Insulin (µIu/ml) ÷ Fasting Glucose (mmol/ml) – 3.5. Pearson's correlation coefficients were calculated to find the type of association between vitamin - D and other variables. The strength of association of vitamin - D and other diabetic risk factors is done by odds ratio and relative risk of vitamin - D was also done to assess the risk of vitamin - D in diabetes.

RESULTS

The current study included 120 diabetic patients aged between 35 – 70 yrs. All individuals were undergone biochemical investigations for their vitamin D status. Sufficient vitamin D individuals (> 75 nmol/L) were taken as controls and vitamin D (<75 nmol/L) were taken as cases. So, (n=80) cases and controls (n=40) were investigated for diabetic profile which includes BMI, B.P, FBS, HbA1C, fasting Insulin, HomaIR and Homa β levels.

Table 1 Displays the comparison between vitamin D groups of controls and cases. The vitamin D insufficient groups were found to be significantly younger than control group. The mean BMI (31.142±3.824) was significantly higher in vitamin D insufficient group (P<0.0001). Cases show significant higher levels of base line fasting Insulin, glucose, HomaIR and lower Homa β than their matched controls (p<0.0001). Females made up 66.6% of the sample. The mean age was 52.5 ± 10 years. The mean vitamin D levels were found to be higher in men (48.2 ± 3.56) than in women (36.5 ± 6.23) P<0.0001. The prevalence of vitamin D deficiency in females is 80% and it is 52.5% in males, showing a higher vitamin D deficiency in females. The prevalence of diabetes in vitamin D deficiency individuals is 66.6%, in males it is 37.5% and in females 62.5%. showing that females are more prone for acquiring diabetes with associated vitamin D deficiency.

Table 2 Shows the correlation coefficients of vitamin D with BMI, HbA1C, Insulin, HomaIR and HomaIR vs. Homa β. All bivariate correlations are strongly associated and statistically significant. Vitamin D has a negative correlation with HomaIR, Insulin, BMI and HbA1C. Table shows that there is a decrease in vitamin D levels with increasing diabetic profile.

Table 3 Shows the crude odds ratio of vitamin D with other metabolic risk factors. Vitamin D shows strong association with HomaIR, BMI, and Insulin in order, which are all statistically significant.

Table 4 Shows the relative risk of entire diabetic population of the study. Vitamin D is an independent risk factor for diabetes. The increased fasting insulin, HomaIR is significantly associated with diabetes risk, while Homa β with a lower risk of diabetes.

Table 1

S.no	*Parameters*	*Controls (n=40) (Patients with vitamin D (> 75 nmol/L)*	*Cases (n=80) (with vitamin D<75 nmol/L))*	*P value*
1	Age	41.62±9.34	48.67±20.4	<0.0001
2	BMI	26.004±2.27	31.142±3.824	<0.0001
3	FBS (mmol/ml)	6.334±2.053	9.786±2.041	<0.0001
4	HbA1C	5.72±1.102	7.315± 0.924	<0.0001
5	Fasting Insulin (uIu/L)	13.167 ±8.637	24.795±8.174	<0.0001
6	Homa IR	4.352±4.170	11.123±5.281	<0.0001
7	Homa β	103.591± 45.93	84.416±31.87	<0.0001
8	Vitamin D (nmol/L)	71.757± 15.42	41.71±7.269	<0.0001

Table 2

	BMI	*HbA1C*	*INSULIN*	*HOMAIR*	*HOMAβ*	*IR VS B*
CORRELATION	- 0.413	- 0.993	- 0.9443	- 0.917	0.638	0.515
P-VALUE	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Table 3

	BMI	*INSULIN*	*HOMAIR*	*HOMAB*	*FBS*
VITD O.R	5.3953	5.1538	7.3457	0.6488	5.1538
95%CI	(2.26-12.88)	(2.05-12.92)	(2.62-20.80)	(0.30-1.37)	(2.05-12.92)
P-VALUE	<0.0001	0.0005	0.0002	0.2568	0.0005

Table 4

	BMI	*INSULIN*	*HOMAIR*	*HOMAB*	*FBS*
VITD RR	2.14	2.1613	2.7663	0.8537	2.1613
95%CI	(1.310-3.52)	(1.249-3.73)	(1.37-5.564)	(0.65-1.123)	(1.25-3.74)
P-VALUE	0.0024	0.0059	0.0043	0.2587	0.0059

DISCUSSION

India is a tropical country and is sunny all around the year. Vitamin D deficiency is found to be an epidemic inspite of plenty of sunlight [5, 8,9]. This is mainly due to darker skin pigmentation, reduced physical activity, pollution, inadequate sun exposure (purdah system), low consumption of vitamin D rich foods, absence of fortification, old age, female sex, higher latitudes and winter season. Ford et al. in third NHANES [1,13,14] reported an inverse association between vitamin D and metabolic risk factors.

The pathophysiolgy of vitamin D deficiency in diabetes is thought to be because of polymorphism of vitamin D receptor VDR gene(Taql, BSml, Apal and Fokl), influence glucose homeostasis ,insulin secretion and sensitivity. Signs of inflammation in β-cells and release of excess levels of interleukin (IL-1,6,8), intracellular adhesion molecules and cyclooxygenase-2 were also foud in implicating diabetes. [1, 5,15].

Low levels of vitamin D brings about an elevation of intracellular calcium which influence insulin secretion and sensitivity by augmenting calmodulin binding to IRS-1. This intefers with insulin stimulated tyrosine phosphorylation and PI3-kinase activation. Protection of insulin secreting capacity of β-cells and suppression of peripheral inflammation was found to be the major role of vitamin D in insulin resistant condition.[5]

The present study found that female participants had significantly lower mean vitamin D levels than males [14,16,17]. All the baseline risk parameters of diabetes like IR, glucose status, HbA1c were significantly higher in vitamin D deficiency individuals than without vitamin D deficiency. Current study also found a negative association of vitamin D with Insulin resistance and HbA1C, and a positive correlation between vitamin D and Homa β levels. These findings are in perfect accordance with the PROMISE STUDY and Ely population based prospective studies. Forouhi et al. reported [1, 10,18] a significant inverse association of baseline serum 25(OH) D with HomaIR in white subjects from UK. Gagnon et al. found a significant positive association of vitamin D with Homa β sensitivity in Australian diabetes, obesity and lifestyle study.

Our study also included the relative risk, which shows fasting glucose, insulin and HomaIR are strongly associated with diabetes risk while Homa β with lower risk of diabetes. This study is in accordance with the women's health initiative observational study done by Song et al [11]. BMI was significantly associated with vitamin D status. This may be because of sequestration of vitamin into adipose tissue resulting in low serum levels [7, 8, 19]. On the other hand, insufficient vitamin D participants had higher odds for HomaIR, insulin and fasting glucose and BMI. These findings show increased risk of metabolic syndrome [2-4,8,19,20] and associated cardiovascular risk with Hypovitaminosis D. This study also gives an impression over vitamin D status of the population and its adverse effect on health particularly females.

CONCLUSION

We have demonstrated an inverse association of vitamin D and insulin resistance; and also there exists a strong association of vitamin D and diabetes [3]. It is also found to be one of the risk factors and potentially important in understanding the etiology of type 2 diabetes. Demonstration of causal role of Hypovitaminosis D in these disorders would lead to new targets for efforts to prevent type 2 D.M and possibly its treatment.

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