Correlation of Vitamin D Status with Glycaemic Status of Individuals- A Cross Sectional Study in a Rural Tertiary Care Hospital of North Bengal, India

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ABSTRACT

BACKGROUND

Recent pandemic of vitamin D deficiency is co-existing with type II diabetes mellitus pandemic. Even in India, vitamin D insufficiency/deficiency is common among individuals with pre-diabetes. If correlation can be established between these two and risk of impaired glucose tolerance (IGT) or diabetes can be predicted based on serum vitamin D status, much early detection of pre-diabetes or diabetes will be possible and preventive measures can be taken. Not too many studies have been done in this context, especially in North Bengal region of West Bengal, India. We wanted to evaluate the correlation between vitamin D status and glycaemic status of individual and predict the risk of impaired glucose tolerance depending on vitamin D, independent of other factors.

METHODS

After ethical clearance and informed consent, 430 study subjects were interviewed, examined, blood sample collected and tested. Data was entered in Microsoft Excel 2007 and analysed using appropriate software. Correlation and multinomial regression analysis were done.

RESULTS

Mean ± SD of serum 25(OH) D level is found to be 21.53±7.06 ng/ml among a total of 430 study participants. 41.86% of participants were found to be with insufficient vitamin D status. Pearson's correlation between serum 25(OH) D level and post prandial blood sugar is found to be strongly negative while Spearman's correlation between vitamin D status and post prandial glycaemic status of individuals is found to be strongly positive. If vitamin D status changes from "Sufficient" to "Insufficient" or "Deficient", risk of IGT increases by 17 times and 16.3 times respectively.

CONCLUSIONS

Strong positive correlation exists between vitamin D status and glycaemic status of individuals. Estimation of 25(OH) D level may be used as a screening test for detection of risk of IGT.

KEY WORDS

Vitamin D, Diabetes Mellitus, Spearman's Rank Correlation Coefficient

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DOI: 10.14260/jemds/2020/57

Financial or Other Competing Interests: None.

How to Cite This Article:
Konar S, Banerjee R. Correlation of vitamin D status with glycaemic status of individuals- a cross sectional study in a rural tertiary care hospital of North Bengal, India. J. Evolution Med. Dent. Sci. 2020;9(05):252-255, DOI: 10.14260/jemds/2020/57

Submission 26-09-2019,
Peer Review 08-01-2020,
Acceptance 16-01-2020,
Published 03-02-2020.

BACKGROUND

'Sunshine vitamin' i.e. Vitamin D, a secosteroid hormone, is essential for life in all higher organisms and is found as cholecalciferol (Vitamin D3) in vertebrates[1]. 25- hydroxy vitamin D [25(OH) D], hydroxylated and predominant form of the vitamin, plays many biological roles in calcium absorption, regulation of bone and mineral metabolism, muscle strengthening, cellular proliferation and differentiation, immune system modulation, inhibition of renin synthesis, erythropoiesis etc[2]. It also down-regulate the transcription of various proinflammatory cytokine genes (hallmark of type II diabetes mellitus) like IL-2, IL-12, Tumor Necrosis Factor-α. And has a protective role on β cell. [3,4,5,6] Deficiency of the said vitamin, emerged as a pandemic in recent year, leads to apoptosis of β cell and production of cytokines (TNF-α, IL-6), glucotoxicity and lipotoxicity, which are the major features among the patients of another pandemic of 21st century i.e. T2DM.[6,7,8,9]

Co-existence of vitamin D deficiency and hyperglycemia are now well established as shown in studies from different parts of the world.[10,11,12] Even in India, vitamin D insufficiency/deficiency is common among individuals with pre-diabetes[13]. Moreover, changing lifestyle, urbanization and modernization has led to possible reduction of people being exposed to direct sunlight and inadequate intake of dietary vitamin D.[14] As a result, vitamin D deficiency or insufficiency prevails in all over the Indian subcontinent.[15,16,17]

As per available literatures not too many studies have been done in this context, especially in North Bengal region of West Bengal, India. So, this study was undertaken to find out the correlation between vitamin D status and glycaemic status of individual and determine the risk of impaired glucose tolerance depending on vitamin D status, independent of other factors.

METHODS

Selection of Participants

After obtaining ethical clearance from Institutional Ethics Committee, a cross sectional study was undertaken at North Bengal Medical College and Hospital from July 2016 to June 2017 amongst the Medicine OPD patients. Considering prevalence of impaired glucose tolerance to be 50%, sample size for the study was estimated to be 430 (p= 50%, d= 0.05, 10% non-response). Every alternate attendee in Medicine OPD, of either sex, were approached for being a study subject. Those having frank diabetes, autoimmune diseases, chronic kidney & liver disorders, morbidly obese, immune-compromised or taking drugs that can alter serum lipid profile, blood glucose and serum 25(OH) D levels, on hormone replacement therapy, substance abusers were excluded from the study.

Data & Blood Sample Collection

After getting written informed consent from eligible & willing subjects, they were interviewed using pre-structured, pretested questionnaire, anthropometric measurements were done for calculation of Body mass index (BMI) [Weight in Kg/ Height in m^2], and blood samples were collected in fluoride & clotted vials. Serum was separated within 30-45 minutes of collection by centrifuge machine.

Estimation of Blood Parameters

Plasma glucose and Serum Calcium was estimated using Glucose Oxidase-Peroxidase (GOD/POD) Method and OCPC (o-Cresolphthalein Complexone) Method respectively. According to American Diabetes Association (2014), normal glucose tolerance was considered as a) Fasting plasma glucose level <5.6 mmol/l (100 mg/dl) and b) 2-hour post-prandial plasma glucose level <7.8 mmol/l (140 mg/dl). Subjects having fasting plasma glucose level between 5.6 mmol/l & 6.9 mmol/l (100 mg/dl & 125 mg/dl) and 2-hour post-prandial plasma glucose level between 7.8 mmol/l & 11 mmol/l (140 mg/dl & 199 mg/dl) were diagnosed as Impaired Fasting Glucose and Impaired Glucose Tolerance respectively[18]. Serum 25(OH) D levels were estimated by ELISA method and reference value is depicted in the below table.

Level of Serum [25(OH)D] in ng/ml	Status of Vitamin D
<20	Deficient
20-29	Insufficient
30-70	Sufficient
>70	Potential Toxicity
Reference Values[19,20]	

Statistical Analysis

Data so obtained by interview and laboratory investigations, are checked for completeness and entered in Microsoft Excel version 2007. Again, checked for consistency, were cleaned, copied in SPSS version 22.0 and codified. Pearson's, Spearman's rank correlation and multinomial logistic regression was done for analysis of data and results are depicted in tables and graphs. p value <0.05 is considered as statistically significant.

RESULTS

It is found that mean ± SD of age of study participants are 37.47 ±12.63 years with majority (36%) belonging to 30-39 years age group. Most of the participants are male (54.7%) (Table 1). Mean ± SD of serum 25(OH) D level is found to be 21.53±7.06 ng/ml. sufficient vitamin D status is the lowest found (11.63%) while Deficient status is the most (46.51%) among the subjects. 41.86% participants are found to be with insufficient vitamin D status (Table 2). Regarding blood sugar parameters, mean ± SD of PPBS level is found to be 160±29.4 md/dl while mean ± SD of FBS level of subjects is 106.4±12.7 mg/dl. Most of them (61.6%) are found to be impaired glucose tolerant followed by normoglycemic (19.8%) and diabetic (18.6%) (Table 2). Pearson's correlation between serum 25 (OH) D level and fasting blood sugar level is found to be (-ve) 0.524 while with that of post prandial blood sugar is (-ve) 0.492. Both are statistically significant (Table 3).

Analysis between vitamin D status and post prandial glycaemic status shows IGT in 69.5% of the subjects with insufficient vitamin D status and in 65% with deficient vitamin D status. Prevalence of diabetes mellitus is much more (30%) in vitamin D deficient subjects. Spearman's rank correlation coefficient between vitamin D status and glycaemic status of individual is found to be (+ve) 0.445 which is statistically significant (Table 4).

	Frequency	Percentage
Age Group		
20-29	120	27.9
30-39	155	36.0
40-49	100	23.3
50-59	25	5.8
60-69	10	2.3
70-79	20	4.7
Total	430	100
Sex		
Female	195	45.3
Male	235	54.7
Total	430	100

Table 1. Distribution of Study Population According to Their Age & Sex (n=430)

Vit D Status	Frequency	Percentage
Deficient	200	46.51
Insufficient	180	41.86
Sufficient	50	11.63
Total	430	100.00
Glycaemic status of the individuals as per post prandial blood glucose	**Frequency**	**Percentage**
DM	80	18.6
IGT	265	61.6
Normoglycemic	85	19.8
Total	430	100

Table 2. Distribution of Study Population According to Their Vitamin D Status and Post Prandial Glycaemic Status (n=430)

	Pearson Correlation	Significance Level
FBS	-0.524	p<0.05
PPBS	-0.492	p<0.05

Table 3. Correlation of Serum 25(OH) D Level with Blood Sugar Parameters (n=430)

Glycaemic Status / Vitamin D Status	DM	IGT	Normoglycemic	Total	Chi square	Correlation (Spearman's rho)
Deficient	60(30)	130(65)	10(5)	200(100)	p<0.05, df=4	0.445, p<0.05
Insufficient	15(8.3)	125(69.5)	40(22.3)	180(100)		
Sufficient	5(10)	10(20)	35(70)	50(100)		
Total	**80 (18.6)**	**265(61.6)**	**85(19.8)**	**430(100)**		

Table 4. Distribution of Study Population According to Their Vitamin D Status and Post Prandial Glycaemic Status (n=430)

Multinomial Regression Analysis					
Glycaemic Status[a]	**Predictor Variables**	**Adjusted Odds Ratio**	**Sig.**	**95% Confidence Interval for AOR**	
				Lower bound	**Upper bound**
DM	Age	1.8	0.000	1.404	1.906
	Male	9.0	0.002	2.073	12.342
	Female[b]	0			
	Vit D Deficient	7.8	0.067	4.987	22.016
	Vit D Insufficient	5.1	0.079	0.778	12.577
	Vit D Sufficient[b]	0			
IGT	Age	1.7	0.000	1.354	1.893
	Male	27.4	0.000	15.698	41.267
	Female[b]	0			
	Vit D Deficient	16.3	0.005	7.956	19.073
	Vit D Insufficient	17.0	0.000	4.085	32.984
	Vit D Sufficient[b]	0			
a. The reference category for dependent variable is: Normoglycemic.					
b. This parameter is set to zero because it is redundant.					

Table 5. Multinomial Regression Analysis Showing Risk of DM & IGT (n=430)

In multinomial regression analysis, taking 'normoglycemic' as reference category for dependent variable and adjusted for other independent variables, it is found that, with change in vitamin D status from "Sufficient" to "Insufficient" and "Deficient", risk of IGT increases by 17 times and 16.3 times respectively and both of the findings are statistically significant. Change in vitamin D status in the same manner, as previously mentioned, increases the risk of Diabetes mellitus by 5.1 times and 7.8 times respectively but the findings are not statistically significant. Statistically significant finding of males being at 27.4 times higher risk of developing IGT than females are also found. With one-year increase in age risk of IGT increases by 1.7 times (Table 5).

DISCUSSION

In this observational study at North Bengal Medical College and Hospital from July 2016 to June 2017 amongst the Medicine OPD patients, it is found that majority of the study population belonged to age group 30-39 years (36%) followed by 20-29 years age group (27.9%). Most of them were male (54.7%). 46.51% study participants are found to be vitamin D deficient while 41.86% are vitamin D insufficient. A study on Asian subjects done by Soo Lim et al[21]. showed that 51.6% had vitamin D insufficiency. Another study in North Indian community had showed that 75.8% participants were vitamin D deficient.[19] Differences in ethnicity, varying degree of exposure to sunlight may play a role behind such diverse findings. Most of the present study population (61.6%) are found to be impaired glucose tolerant followed by normoglycemic (19.8%). In a study conducted at D. Y. Patil University, School of Medicine Bajaj AH et al had found 51.38% subjects were diabetic and 48.61% were non-diabetic. However, they had considered DM based on fasting blood sugar while the present study relies on post prandial blood sugar level. Statistically significant, strong negative correlation is found between serum 25(OH) D levels and both fasting and post prandial blood sugar levels. That means that with decrease in serum 25 (OH) D level, both FBS & PPBS levels will increase. Similar findings were showed in a study done by Kirubhakaran Kanakaraju et al in Tamilnadu

69.5% of the study population having insufficient vitamin D status has IGT while 30% with vitamin D deficiency has DM. Association between vitamin D status and glycaemic status is found to be statistically significant by chi-square test. The study of Bajaj AH had found that 33.3% of vitamin D deficient subjects were diabetic.[22] The finding lies in close proximity of the present study. Again, statistically significant, strong positive correlation is found between vitamin D status and glycaemic status of individual which means that with deterioration in vitamin D status, glycaemic status will also deteriorate from normoglycemic to DM through IGT. Study finding of Kant et al. indirectly supports this where they showed that vitamin D deficiency is inversely related to glycaemic control (HbA1c) of individual.[23]

In multinomial regression analysis, taking 'normoglycemic' as reference category for dependent variable it is found that, with deteriorating vitamin D status, risk of IGT increases many times and that is independent of all other predictor variables. Robert Scragg et al had concluded in their study that IGT is associated with low serum concentrations of [25 (OH) D].[24] Males are at higher risk of developing IGT than females.

CONCLUSIONS

Vitamin D status is one of the determining factors of glycaemic status of individuals. With increasing burden of diabetes, it will always be better if it can be detected much early or even in pre-diabetes period so that corrective measures can be taken. Serum 25(OH) D level estimation may be used as a screening for the risk of IGT. However, to establish a causal association between vitamin D status and glycaemic status of individual, large scale prospective, multi-centric studies should be conducted.

ACKNOWLEDGEMENT

Authors thank the study participants, health staff, laboratory technicians and college authorities for their support.

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