Association of vitamin D and insulin resistance among the adults with newly detected prediabetes attending in a tertiary care hospital of Bangladesh

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Abstract

Several studies have found an inverse association between vitamin D level and insulin resistance (IR) causing prediabetes and diabetes. So the current study was done to find out the association between serum vitamin D level and IR among adults with prediabetes. This cross-sectional study was carried out in 140 newly detected adults with prediabetes according to ADA 2018 criteria. The 25(OH) D cutoffs to define deficiency and insufficiency were used according to Endocrine Society (USA) criteria, measurement of vitamin D & insulin (fasting) was done by chemiluminescent microparticle immunoassay (CMIA). Data were analyzed using SPSS (version 22.0) and presented as table and figure. P-value ≤0.05 was considered significant. In this study, most of the population was 30 years and above (73%). The Male-female ratio was 1:7, the majority of participants came from urban areas (81%) and it was observed that there was an increasing trend of insulin resistance across increasing severity of vitamin D deficiency though it was not statistically significant (p= 0.74). In conclusion, vitamin-D deficiency/insufficiency is common among individuals with prediabetes in our country, but there were no association had been found between vitamin D and insulin resistance in individuals with prediabetes.

Introduction

Prediabetes is an important metabolic state that predisposes an individual to a high probability of future progression to diabetes and vitamin D deficiency is thought to influence the pathogenesis of type 2 DM (T2DM) by affecting either insulin sensitivity, β-cell function or both.[1,2] Activation of adipocytes modulates intracellular calcium concentrations and can affect changes in lipogenesis and lipolysis. It is therefore assumed that vitamin D is involved in modulating the tissue response to insulin.[3] One of the hallmarks of T2DM is low-grade inflammation which can be a result of an increase in circulating cytokines such as tumor necrosis factor α (TNF-α) and interleukin (IL)-6 which contribute significantly to insulin resistance in muscle and adipose tissue.[4] Vitamin D tends to down-regulate the transcription of various proinflammatory cytokine genes like IL-2, IL-12, and TNF-α.[5,6]

In insulin resistance, there is reduced glucose clearance in skeletal muscles, impaired suppression of glucose production by the liver and decreased rates of lipolysis in adipose tissue or their combination. The longitudinal Whitehall II study described by Tabak et al.[7] found 29% lower insulin sensitivity at 13 years before the onset of T2DM. Thus, IR represents an early abnormality, which is compensated by augmented β-cell function for a long time before the insulin-glucose feedback loop fails.[8] So, this study was done to find out the association between vitamin D and IR among adults with prediabetes, which may be of good help for the clinician to address the situation more appropriately.

Methods

This cross-sectional study was conducted in the department of Endocrinology of Bangabandhu Sheikh Mujib Medical University (BSMMU) from March 2019 to February 2020.Total 140 adult (age group of 18yrs and above) with prediabetes according to ADA 2018 criteria, were enrolled in this study after getting ethical approval from the institutional review board (IRB) BSMMU. Patients currently on vitamin D and calcium or who had received any one of them within the last 120 days and patients receiving any medications that may alter vitamin D level and glucose tolerance (anticonvulsant, ketoconazole, glucocorticoids, rifampicin, isoniazid, oral contraceptive) and patient having endocrine disorders (hyperthyroidism, hypothyroidism, hyperparathyroidism, Cushing syndrome) or chronic

disease like CKD, CLD were excluded from this study. Informed written consents were obtained from all subjects. Measurement of vitamin D & insulin (fasting) was done by chemiluminescent microparticle immunoassay (CMIA) in the Department of Biochemistry and Molecular Biology, BSMMU. IR was determined by the homeostasis model assessment of insulin resistance (HOMA-IR). The 25(OH) D cutoffs to define deficiency and insufficiency were used according to Endocrine Society (USA) criteria.[9] Data were analyzed using SPSS (version 22.0) and presented as table and figure. P-value ≤0.05 was considered significant.

Results

In this study, most of the population was 30 years and above (73%). Male female ratio was 1:7, majority of the participants came from urban areas (81.4%) most of them have an occupation that belonged to manual, unskilled, and unemployed, middle class was the predominant socio-economic category in the study population (Table-I).

Table-I	
Socio-demographic characteristics of the study population (N = 140)	
Parameters	Frequency (%)
Age of the respondent	
Less than 30 years	38 (27.1)
30 years and above	102 (72.9)
Region*	
Urban	114 (81.4)
Rural	26 (18.6)
Gender	
Male	52 (37.1)
Female	88 (62.9)
Occupation**	
Managerial and professional	24 (17.1)
Nonmanual	4 (2.9)
Manual	26 (18.6)
Manual unskilled	6 (4.3)
Institutionalized, retired, unemployed	80 (57.1)
Socio- economic status†	
Lower	56(40)
Middle	65(46.4)
Higher	19(13.6)
Physical Activity*†	
Low	12 (9.1)
Moderate	116 (87.9)
High	4 (3.0)

  * : According to Bangladesh national conservation strategy [10]
 ** : According to registrar general occupational classification [11]
  † : According to monthly household income [12]
 *† : According to international physical activity questionnaire [13]

Table-II	
Clinical and biochemical characteristics of the study population	
Parameters	Frequency (%)
BMI	
Underweight & Normal	20 (14.3)
Overweight & Obese	120 (85.7)
Acanthosis nigricans	
Present	6 (4.4)
Absent	132 (95.7)
Vitamin D	
Deficiency (< 20 ng/ml)	110 (78.6)
Insufficiency (20-29.9)	28 (20.0)
Sufficiency (≥ 30 ng/ml)	2 (1.4)
Insulin Resistance	
IR absent (HOMA-IR < 2.6)	30 (21.4)
IR present (HOMA-IR ≥ 2.6)	110 (78.6)

Overweight and obese were (86%) according to the WHO criteria for Asians, most of the participants (79%) were in vitamin D deficient group and insulin resistance present about 79% of participants (Table - II)

It was observed that there was an increasing trend of insulin resistance across increasing severity of vitamin D deficiency though statistically significant association had not been found (p = 0.74). There was a significant association between physical activity and insulin resistance (P < 0.001) and those who were highly physically

Table-III			
Association between HOMA-IR & other cofactors			
Parameters	HOMA IR status		p-value
	(HOMA-IR < 2.6)	(HOMA-IR ≥2 .6)	
Vitamin D status			
Deficiency (< 20 ng/ml)	24 (21.8%)	86 (78.2%)	0.74
Insufficiency (20-29.9)	6 (21.8%)	22 (78.2%)	
Sufficiency (≥ 30 ng/ml)	0	2 (100%)	
Age of respondent			
Less than 30 years	12(31.6%)	26(68.4%)	0.074
30 years and above	18(17.7%)	84(82.4%)	
Region			
Urban	26(22.8%)	88(77.2%)	0.41
Rural	4(15.4%)	22(84.6%)	
Gender			
Male	20(38.5%)	32(61.5%)	<0.001
Female	10(11.4%)	78(88.6%)	
Physical activity			
Low	4(33.3%)	8(66.7%)	<0.001
Moderate	22(19.0%)	94(81.0%)	
High	4(100.0%)	0(0.0%)	
BMI			
Underweight & Normal	10 (50.0%)	10 (50.0%)	0.001
Overweight & Obese	20 (16.7%)	100 (83.3%)	

active had low insulin resistance. A significant association was also found between BMI and insulin resistance (p=0.001), about 83% of participant with overweight and obese had insulin resistance. In this study, it was also found that gender has a significant association with insulin resistance (p<0.001) (Table - III).
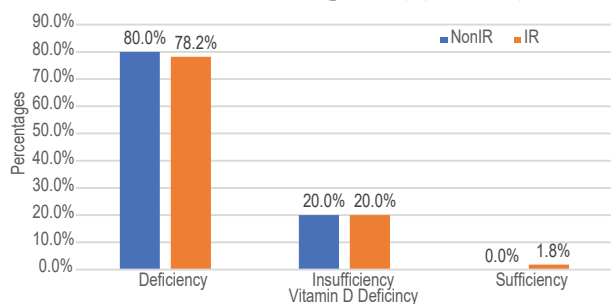
Figure - 1: Distributions of vitamin D status and HOMA - IR

Figure-1 described the distributions of vitamin D status and insulin resistance among the participants. This figure depicts that there is no association between these two variables (p-value 0.74). Almost similar percentages of participants were found in each group of vitamin-D status.

Here the unadjusted model showed that, the female participants, BMI, overweight & obese group were positively correlated with insulin resistance. On the other hand, the vitamin D status of the participant had no role in insulin resistance. In the adjusted model we found that females were more likely to develop insulin resistance than males [OR 6.05, 95% CI (2.03 – 17.97)]. A similar kind of findings was also found in overweight and obese group where they were 2.36 times more prominent for developing insulin resistance than other counterparts (Table - IV).

Table-IV						
Factors associated with insulin resistance, results from univariate and multivariate logistic regression						
Parameters	Unadjusted OR	p-value	95% CI	Adjusted OR	p-value	95% CI
Vitamin D status						
Deficiency	ref		-	ref		-
Insufficiency	1.02	0.96	0.37 - 2.81	1.14	0.84	0.33 - 4.00
Sufficiency						
Age of the respondent						
Less than 30 years	ref		-	ref		-
30 years and above	2.15	0.078	0.91 - 5.505	1.28	0.67	0.39 - 4.22
Gender						
Male	ref		-	ref		-
Female	4.87	<0.001	2.05 - 11.56	6.05	0.001	2.03 - 17.97
Physical activity						
Low	ref		-	ref		-
Moderate	2.13	0.24	0.58 - 7.73	0.63	0.56	0.13 - 2.99
High						
BMI						
Underweight & Normal	ref		-	ref		-
Overweight & Obese	5.0	0.002	1.84 - 13.58	2.36	0.018	1.29 - 15.81

Discussion

In this study it was found that substantial percentage of the participants was vitamin D deficient according to Endocrine Society criteria and a significant percentage had insulin resistance although there was no association between vitamin D and insulin resistance among the adults with prediabetes. Similar findings were also observed in other studies done in people with prediabetes.[14-16]

Different mechanisms have been suggested for the effects of vitamin D on pancreas: presence of vitamin D receptors on pancreatic □ cells, expression of vitamin D activating 1□ hydroxylase in pancreatic □ cells, the insulin gene having vitamin D response element and the transcription of insulin receptor genes being increased by vitamin D. Protective effects of vitamin D on glucose prediabetes and diabetes, maybe due to well-known effects of vitamin D, such as its anti-inflammatory properties, its effects on calcium and phosphorus metabolism and regulation of the insulin receptor gene.[17-20]

It has been observed that vitamin D increases in calcium content of the cells, in turn leading to increased transport of glucose into the muscle.[21] Vitamin D also regulates nuclear PPAR (Peroxisome proliferative activated receptor) that has an important role in the insulin sensitivity.[22] Vitamin D deficiency is associated with increases in inflammation. Vitamin D attenuates the expression of proinflammatory cytokines involved in insulin resistance such as interleukins, IL-1, IL-6, TNF-□, also down regulates NF-K□ (Nuclear factor) activity.[23]

A review by Mitri et al, found that people with higher vitamin D blood levels (>25ng/ml) had a decreased chance of getting glucose intolerance later in life compared to those with the lowest levels. After conducting a meta-analysis and review of the impact of vitamin D and calcium on glycemic control in patients with type 2 diabetes, Pittas et al concluded that insufficient vitamin D and calcium appears to hinder glycemic control and that supplementing both nutrients may be necessary to optimize glucose metabolism.[24]

In this study it was also found that the female gender has an association with insulin resistance and similar findings were also observed in another study by Bhatt et al.[25] Particularly, one of the clinical characteristics commonly associated with insulin resistance is obesity. It has been proposed that vitamin D deficiency directly promotes IR and obesity.[26] Findings of our study support this theory.

The data from various studies were discordant, while a study on 7904 individuals by Ford FS et al[27] showed a negative correlation of vitamin D levels with metabolic syndrome. One study on Bangladeshi adult individuals by Hossain HT et al also found an inverse association of vitamin D level with metabolic syndrome but some other studies did not find such association.[29,30] This difference can be explained based on sample size and difference in ethnicity.

Limitation

The present study had certain limitations. Firstly, the number of study subjects, if higher, would have made the findings more significant. Secondly, the patients were from OPD of our hospital which was not a true representative of the normal population. Thirdly, presences of confounding effect of unforeseen variables (dietary habit, solar exposure, etc.) that influence the variable parameters were not included in the present study). Fourthly, the cross-sectional nature of our study was one of the major limitations and Liquid Chromatography-Tandem Mass Spectrometry (LC/MS) method was not available to measure vitamin D levels.

Recommendation

Longitudinal prospective studies are warranted to assess whether insulin resistance in prediabetes individuals with lower vitamin D actually results in increased progression to diabetes in Bangladeshi adults.

Conclusion

Vitamin D deficiency was common in adults with prediabetes but these findings seem to suggest that there was no association between vitamin D and insulin resistance among adults with prediabetes.

Conflict of interest

The author(s) declared no potential conflicts of interest concerning the research, authorship and/or publication of this article.

Acknowledgements

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