

RETRACTED

East African Medical Journal Vol. 95 No. 10 October 2018

CASE CONTROL STUDY TO INVESTIGATE CORRELATION BETWEEN VITAMIN D DEFICIENCY AND PRE-DIABETES IN ARAR, SAUDI ARABIA

Jamal Alruwaili, Ph. Assistant Professor of Biochemistry, Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, Northern Border University, Arar-91431, Saudi Arabia.

Corresponding author: Jamal Alruwaili, Northern Border University, Arar-91431, Saudi Arabia. Email: malkh1195@hotmail.com

CASE CONTROL STUDY TO INVESTIGATE CORRELATION BETWEEN VITAMIN D DEFICIENCY AND PRE-DIABETES IN ARAR, SAUDI ARABIA

J. Alruwaili

ABSTRACT

Introduction: Pre-diabetes is associated with abdominal obesity, insulin resistance, non-alcoholic fatty liver disease and metabolic syndrome, and such individuals are at an increased risk for developing type-2 diabetes mellitus.

Methods: A total of 60 research subjects, all of them at least thirty years or older, were divided into two groups of 30 pre-diabetics and 30 normoglycemics. The subjects exhibiting diabetes, kidney, liver and heart diseases and pregnancy were excluded from the study. The fasting plasma glucose level and vitamin D level were measured.

Results: Pre-diabetic subjects were found to have significantly lower levels of vitamin D than compared to normoglycemic subjects with median levels of 17.68 and 31.72 mmol/l respectively ($P=0.000$).

Conclusions: It was found that vitamin D deficiency plays a significant role in the development of pathogenicity of type 2 diabetes mellitus.

INTRODUCTION

The relationship between vitamin D deficiency and diabetes mellitus has previously been established. Several previous studies have found a correlation between low vitamin D levels and prevalence of diabetes [1,2,3,4]. The evidence for linkage between vitamin D deficiency and diabetes mellitus is contradictory, and further well controlled studies are still needed. Only limited studies using the human model have been conducted so far [5,6]. Hence, the therapeutic role of vitamin D supplements and their effect on diabetic patients is being debated.

Pre-diabetes is a transition stage between normoglycemia and type 2 diabetes mellitus. A person is considered pre-diabetic when his/her blood glucose level is higher than normal but it is still not high enough to be

considered diabetes. Usually, pre-diabetes is diagnosed by a blood test. A fasting blood sugar (glucose) level of 110 to 125 mg/dL (by WHO criteria) or 100 to 125 mg/dL (by ADA criteria) is characteristic of pre-diabetes [7]. The onset of pre-diabetes occurs when the body becomes insulin resistant or unable to use insulin. Some risk factors for pre-diabetes are family history of diabetes, cardiovascular disease, increased triglyceride levels, low levels of HDL, obesity, high blood pressure, elevated fasting plasma glucose level, females who have had gestational diabetes, and have polycystic ovarian syndrome (PCOS).

A correlation between fasting plasma glucose (FPG) level and vitamin D deficiency has been reported by Pittas *et al.* as Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) for subjects exhibiting

RETRACTED

pre-diabetes [8]. A separate study of subjects having both vitamin D deficiency and pre-diabetes and using vitamin D supplements has reported no significant change in either insulin sensitivity or progression of diabetes, although HbA_{1c} was found to be significantly decreased [9]. Another study in India, reported a decrease in both insulin resistance and fasting plasma glucose level along with inflammatory markers among those taking vitamin D supplements [10]. This study investigated a possible correlation between low vitamin D levels and pre-diabetes in Arar, Saudi Arabia.

fasting plasma glucose (FPG) and vitamin D levels (Figure 2).

MATERIALS & METHODS

The procedures followed in this case control study are in accordance with the ethical standards laid down by the Arar Central Hospital (Arar, Saudi Arabia). The study was conducted in the time period between January, 2017 and March, 2017. It involved recruitment of 60 research subjects from both genders who were at least 30 years or older at the Arar Central Hospital (Arar, Saudi Arabia). The inclusion criteria were the classic symptoms of pre-diabetes such as increased thirst, polyuria, fatigue and blurred vision. Based on the measured FPG level, the patients were divided into two groups of 30 pre-diabetics (research subjects) and 30 normoglycemics (controls) (Figures 1 and 2). The patients exhibiting diabetes mellitus, renal, liver and heart diseases were excluded. In addition, pregnant female subjects and those using vitamin D supplements were excluded. All subjects exhibiting a vitamin D level less than 25 ng/mL were considered deficient in vitamin D while subjects with FPG of 100 – 126 mg/dL (5.6 – 6.9 mmol/L) were considered pre-diabetic. After a 12 hour overnight fast, 3 mL of venous blood samples were collected from the research subjects. The blood samples were then analyzed for

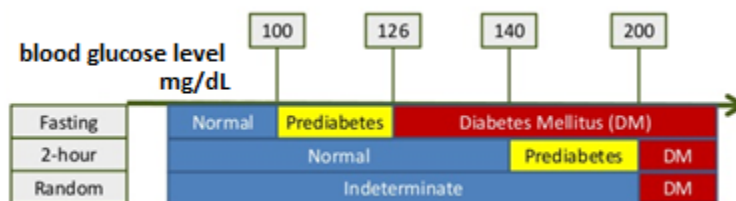


Figure 1: Schematic showing how pre-diabetes was defined by the study.

Figure 2: study

Screening of 60 patients at Arar Central Hospital using the inclusion criteria



30 patients classified as Pre-diabetic (research subjects) and 30 as Normoglycemic (controls)



Fasting Plasma Glucose (FPG) and Vitamin D levels of subjects and controls measured



Clinical data analysis by Biostatistics

Measurement of Fasting Plasma Glucose (FPG) Level: Fasting plasma glucose (FPG) level measurements are used for the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia and pancreatic islet cell carcinoma. FPG was analyzed in this study, using enzymatic photometric test by Mindray BS-400® chemistry analyzer (Mindray Medical Int. Ltd, China).

Measurement of Vitamin D Level: Physiologically, both vitamins D₂ and D₃ are bound to the vitamin D-binding protein (VDBP) in the plasma. Vitamin D₃ is transported to the liver to become calcifediol or 25-hydroxycholecalciferol (25-OH). Since calcifediol (25-OH) represents the major storage form of vitamin D in the body, its blood concentration is used to assess the

Schematic showing the design.

overall vitamin D status. In this study, calcifediol (25-OH) levels were determined using Elecsys Vitamin D Total Assay. This assay was used for the quantitative determination of total calcifediol (25-OH) in human serum and plasma, as an aid in the assessment of vitamin D sufficiency.

Statistical Analysis: The statistical analysis was conducted using SPSS

version 23 (Chicago, USA). The mean vitamin D levels were compared for pre-diabetic and normoglycemic subjects. The frequency for different age groups was expressed as a percentage. The odds ratio (OR) that was calculated, quantified the strength of the association between vitamin D deficiency and pre-diabetes. OR is the ratio of the odds of development of pre-diabetes in the presence of vitamin D deficiency and the odds of development of pre-diabetes in the absence of vitamin D deficiency.

RESULTS

Sixty subjects and controls were recruited from Arar Central Hospital (Arar, Saudi Arabia) based on their FPG levels (Figure 2). The research subjects were divided into two groups of pre-diabetics and normoglyemics

RETRACTED

after careful selection to meet all the inclusion criteria as shown in Table 1.

Table 1

Different characteristics of the normoglycemic (control) and pre-diabetic research subjects

Parameter	Pre-diabetics	Normoglycemics	P-value
Number (n)	30	30	
Gender (n) %	Male: (7) 23.3% Female: (23) 76.7%	Male: (3) 10% Female: (27) 90%	
Age years (median)	45	43.8	0.000
FPG mmol/L Median	5.96	4.91	0.000
Serum Vit D nmol/L			
Minimum	15.81	29.46	0.000
Maximum	19.55	33.98	
Mean	17.68	31.72	

The sex breakdown of the subjects was 76.7% females and 23.3% males. There was no significant age difference between both pre-diabetics and controls. The median age of research subjects was 45 and 43.8 years for males and females, respectively. Pre-diabetic subjects were found to have significantly low levels of vitamin D as compared to normoglycemics with median levels of 17.68 and 31.72 mmol/l respectively (P=0.000). A significant inverse correlation was also found between serum vitamin D and FPG levels (Pearson Correlation = -0.649, P = 0.000) which is shown in Table 2. The calculated value of -0.649 suggests a negative correlation between the vitamin D level and pre-diabetes. The odds ratio (OR) for vitamin D deficiency in normoglycemic and pre-diabetic groups was found to be 4.078 (P< 0.0001) which suggests a strong possibility for a link between low vitamin D levels and pre-diabetes (Table 2).

Table 2

Pearson correlation between Vitamin D and FPG levels for the two groups

Correlations		Fasting plasma glucose	Vitamin D	Odds Ratio (OR)	95% Confidence Level
Fasting plasma glucose	Pearson Correlation	1	-0.649**	4.078	CI (3.330, 4.312)
	Sig. (2-tailed)		0.000		
	N	60	60		
Vitamin D	Pearson Correlation	-0.649**	1		
	Sig. (2-tailed)	0.000			
	N	60	60		

DISCUSSION

Pre-diabetes is an early stage of glucose metabolism disorder and considered to be a significant risk factor in microvascular and cardiovascular disorders along with complications associated with type 2 diabetes such as nephropathy, neuropathy and retinopathy [11]. In this study, vitamin D levels of a sample of the population of the Northern Region of Saudi Arabia were measured and a possible correlation between the level of vitamin D and pre-diabetes was investigated. The study found that pre-diabetic subjects have significantly low levels of vitamin D compared to those of normoglycemics. A significant inverse correlation was also seen between serum vitamin D and FPG levels as shown in Table 2. The odds ratio (OR) of 4.078 for vitamin D deficiency in normoglycemic and pre-diabetic groups suggests a strong possibility for a link between low vitamin D levels and pre-diabetes (Table 2).

The findings of this study are completely in agreement with the studies by Qurrat-ul-Ain *et al.* [12] who reported that low vitamin D levels in adults correlated with glucose intolerance. Another study by Pinelli, comprising Arab Americans, reported that males with glucose intolerance tend to have lower levels of vitamin D [13]. Some studies have reported very different types of correlation between vitamin D level and prediabetes. According to the data reported by NHANES III, non-Hispanic blacks show no correlation between the two parameters. Furthermore, one study in Finland involving 7503 subjects has shown that higher levels of vitamin D lowered the incidence of diabetes by 72% among males. However, it showed no significant change among females after adjustment for type 2 diabetes risk factors [14].

Any discrepancy between the findings of this study from any previously published studies

can be explained by taking into consideration the differences between the participants in terms of race, body mass index (BMI) and other factors that contribute to low vitamin D levels and high blood glucose levels [11]. The negative correlation between vitamin D deficiency and pre-diabetes found by this study shows a high involvement of vitamin D for glucose regulation in blood. Although, the effect of vitamin d level on glucose metabolism may also depend on other factors such as ethnic and genetic background, gender, obesity and co-morbidities [15].

CONCLUSION

The comparison of mean vitamin D levels between pre-diabetic and normoglycemic subjects revealed significant differences between the two groups. This goes to prove that individuals with vitamin D deficiency are at a higher risk of developing type 2 diabetes mellitus and it points to a need for use of vitamin D supplements by the pre-diabetics.

REFERENCES

1. Pittas AG, Nelson J, Mitri J, Hillmann W, Garganta C, et al. Plasma 25-Hydroxyvitamin D and Progression to Diabetes in Patients at Risk for Diabetes. *Diabetes Care*. 2012;**35**(3):565-573.
2. Gagnon C, Lu ZX, Magliano DJ, Dunstan DW, Shaw JE, Zimmet PZ, et al. Serum 25-hydroxyvitamin D, calcium intake, and risk of type 2 diabetes after 5 years. *Diabetes Care*. 2011;**34**(5):1133-1138.
3. Deleskog A, Hilding A, Brismar K, Hamsten A, Efendic S, Å–stenson CG. Low serum 25-hydroxyvitamin D level predicts progression to type 2 diabetes in individuals with prediabetes but not with normal glucose tolerance. *Diabetologia*. 2012;**55**(6):1668-1678.
4. Scragg R, 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

RETRACTED

- Medical Research Council Ely Prospective Study. *Diabetes*. 2008;**57**(10).
5. Kotsa K, Yavropoulou MP, Anastasiou O, Yovos JG. Role of vitamin D treatment in glucose metabolism in polycystic ovary syndrome. *Fertility and sterility*. 2009;92(3):1053-8.
 6. 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. *British Journal of Nutrition*. 2010;103(04):549-55.
 7. Jellinger, Paul S. "What You Need to Know about Prediabetes." *Power of Prevention*, American College of Endocrinology. Vol. 1, issue 2, May 2009.
 8. Pittas AG, Harris SS, Stark PC, Dawson-Hughes B. The effects of calcium and vitamin D supplementation on blood glucose and markers of inflammation in nondiabetic adults. *Diabetes care*. 2007;30(4):980-6.
 9. Davidson MB, Duran P, Lee ML, Friedman TC. High-dose vitamin D supplementation in people with prediabetes and hypovitaminosis D. *Diabetes care*. 2013;36(2):260-6.
 10. Dutta D, Mondal SA, Choudhuri S, Maisnam I, Reza AHH, Bhattacharya B, et al. Vitamin-D supplementation in prediabetes reduced progression to type 2 diabetes and was associated with decreased insulin resistance and systemic inflammation: an open label randomized prospective study from Eastern India. *Diabetes research and clinical practice*. 2014;103(3):e18-e23.
 11. American Diabetes A. Impact of intensive lifestyle and metformin therapy on cardiovascular disease risk factors in the diabetes prevention program. *Diabetes care*. 2005;28(4):888-94.
 12. Qurrat-ul-Ain DAK, Ijaz A, Khan FA, Latif A. Decreased Serum 25-Hydroxycalciferol Levels in Pre-diabetic Adults. *Journal of the College of Physicians and Surgeons Pakistan*. 2016;26(2):87-90.
 13. Pinelli NR, Jaber LA, Brown MB, Herman WH. Serum 25-hydroxy vitamin d and insulin resistance, metabolic syndrome, and glucose intolerance among Arab Americans. *Diabetes care*. 2010;33(6):1373-5.
 14. Knekt P, Laaksonen M, Mattila C, Härkänen T, Marniemi J, Heliövaara M, et al. Serum vitamin D and subsequent occurrence of type 2 diabetes. *Epidemiology*. 2008;19(5):666-71.
 15. Pittas AG, Nelson J, Mitri J, Hillmann W, Garganta C, Nathan DM, et al. Plasma 25-hydroxyvitamin D and progression to diabetes in patients at risk for diabetes. *Diabetes care*. 2012: DC_111795.