Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 1769–1771

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Review

Study of relationship between total vitamin D level and NAFLD in a sample of Egyptian patients with and without T2DM

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ARTICLE INFO

Article history:
Received 31 March 2019
Accepted 1 April 2019

Keywords:
Total vitamin D
T2DM and NAFLD

ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is increasing recently due to increasing the prevalence of obesity. Insulin resistance (IR) is the mutual pathological cause for both T2DM and NAFLD. Vitamin D acts against IR by its anti-inflammatory and regulation of insulin secretion as pancreatic beta cells express vitamin D receptor (VDR).

Aim: Assessment of relationship between Total vitamin D level and NAFLD a sample of Egyptian patients with and without T2DM.

Methods: The current study included 110 Egyptian subjects. They divided into 4 groups: Group 1: 30 diabetic patients with NAFLD Group 2: 30 diabetic patients without NAFLD Group 3: 30 NAFLD patients without diabetes Group 4: 20 healthy controls.

Vitamin D level assessment, AST, ALT, GGT, total cholesterol, LDL, triglycerides, fasting and 2 h post prandial plasma glucose, glycosylated hemoglobin, albumin and creatinine calculation of FLI were assessed.

Result: There was a statistical significant decrease in total vitamin D level in T2DM patients with NAFLD than either T2DM or NAFLD only patients.(15.5 ± 7.46 vs 24.4 ± 8.19 and 22.86 ± 9.58 ng/ml respectively) also Total vitamin D level is negatively correlated with age, weight, BMI, WC, total cholesterol, LDL, TG, FPG, HbA1c and FLI.

Conclusion: There is a decrease in total vitamin D in T2DM patients with NAFLD.

1. Introduction

Vitamin D is proven to have pleiotropic functions besides it role in calcium homeostasis, as it has an immune-modulator function and effect on insulin secretion and insulin sensitivity. Vitamin D deficiency is found to be associated with many diseases as autoimmune diseases, diabetes mellitus and cancers as colorectal cancer [1].

Type 2 diabetes mellitus (T2DM) is a worldwide burden as it affects quality of life by it chronic complications as vision impairment up to blindness due to retinopathy and end stage renal disease due to nephropathy [2].

Non-alcoholic fatty liver disease (NAFLD) is increasing recently due to increasing the prevalence of obesity [3].

Insulin resistance (IR) is the mutual pathological cause for both T2DM and NAFLD. [4], Vitamin D acts against IR by its anti-inflammatory and regulation of insulin secretion as pancreatic beta cells express vitamin D receptor (VDR) [5].

Vitamin D has an important role in insulin secretion by direct and indirect ways. Direct way is through VDR expression by β cells in the pancreas and activation of the transcription of insulin gene and thus is essential for insulin secretion. [5], the indirect way by Ca+2 influx through β cell membrane and mobilization of Ca+2 from intracellular organelles. [6], The available Ca+2 doesn't only have a role in activation of β cell calcium dependent endopeptidase -which produces insulin from proinsulin 19-but also, it has a role in β cell glycolysis which occur according glucose level in blood. [7]

Vitamin D expresses its receptor on many organs other than pancreas like liver and skeletal muscle. VDR mediates vitamin D action in insulin sensitivity as it affects the activities of insulin genes and receptors. Secondary hyperparathyroidism due to vitamin D deficiency promotes insulin resistance and lipogenesis through increased Ca+2 influx into the adipose tissue. Also, it decreases insulin secretion due to its effect on β cells. [7]

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https://doi.org/10.1016/j.dsx.2019.04.002
1871-4021/

Vitamin D inhibits activation and expression of tumor necrosis factor alpha (TNF-α) and IL-1 which are inflammatory markers of NAFLD - related liver injury. [8], Vitamin D hasn't only anti-inflammatory function but also it has anti-proliferative and anti-fibrotic activities in the liver by decreasing hepatic stellate cell activation, so it protects the liver against fibrosis. [9]

1.1. Aim of work

This study aimed to assess the relationship between Total vitamin D level and NAFLD in patients with and without T2DM.

2. Patients and methods

This case control study was conducted with 110 Egyptian subjects between 25 and 55 years from the endocrine outpatient clinic of Ain shams hospitals and El-Matarya teaching hospital. They divided into 4 groups: **Group 1**: 30 diabetic patients with NAFLD, **Group 2**: 30 diabetic patients without NAFLD, **Group 3**: 30 NAFLD patients without diabetes, **Group 4**: 20 healthy controls. Written consent was obtained from all subjects. Exclusion criteria: patients with chronic liver or kidney disease, Alcoholics, Any patients on drugs cause secondary steatosis or affecting vitamin D absorption or metabolism. All patients subjected to full history taking and full clinical examination-including body mass index and waist circumference and blood pressure (systolic and diastolic).

2.1. Laboratory studies

All subjects was conducted to AST, ALT, GGT, total cholesterol, LDL, triglycerides, fasting and 2 h post prandial plasma glucose, glycosylated hemoglobin, albumin and creatinine.

2.2. Assessment of NAFLD

All subjects was evaluated by abdominal ultrasonography and fatty liver index (FLI) calculation FLI = {e 0.953 × loge (TG mg/dl) + 0.139 × (BMI kg/m2) + 0.718 × loge (γ GT u/l) + 0.053 × (WC cm) - 15.745} divided by {1 + e0.953 × loge (TG mg/dl) + 0.139 × (BMI kg/m2) + 0.718 × loge (γ GT u/l) + 0.053 × (WC cm) - 15.745} × 100 Interpretation:

* ≤ 30: no steatosis
* 30–60: not conclusive
* ≥60 NALFD is present.

Total Vitamin D level assessment: Serum was separated and stored under - 25 °C and total vitamin D is assessed using The Cal biotech 25-hyroxy (25-OH) vitamin D ELISA kits.

2.3. Statistics

Statistics were done using SPSS version 18. Mean, range and standard deviation were used for description of quantitative data and numbers and percentage for qualitative data. Comparing between all groups was done using Analysis of variance (ANOVA) test and tukey's test was used to detect the significance between them. Chi-square test is used to compare between qualitative data and T test was used to compare between 2 groups. Pearson correlation co-efficient test was used to rank variables versus each other positively or inversely.

3. Result

The current study conducted with 110 adult Egyptians participants aged between 25 and 55 years.

They were divided into 4 groups as the following:

Group 1: Type 2 diabetic patients with NAFLD (n = 30)
Group 2: Type 2 diabetic patients without NAFLD (n = 30)
Group 3: NAFLD patients without T2DM (n = 30)
Group 4: Healthy controls (n = 20)

As regard total vitamin D level: All patient groups (1, 2 and 3) were lower than control (15.5 ± 7.46, 24.4 ± 8.19 and 22.86 ± 9.58 vs 55.8 ± 11.98 ng/ml respectively) and group 1 (T2DM + NAFLD) was lower than group 2 (T2DM) and 3 (NAFLD) (15.5 ± 7.46 vs 24.4 ± 8.19 and 22.86 ± 9.58 ng/ml respectively) Table (1).

As regard FLI: All patient groups (1, 2 and 3) were higher than control (68.11 ± 6.89, 51.76 ± 8.73 and 68.15 ± 6.354 vs and 37.53 ± 7.63 respectively). NAFLD groups (Group 1 and Group 3) were higher than group 2 (T2DM) (68.11 ± 6.89 and 68.15 ± 6.354 vs 51.76 ± 8.73 respectively) Table (1).

On correlating total vitamin D level with age: There's a negative correlation (r = −0.517) with highly significant difference (p value < 0.001), as total vitamin D level decreases with older patient than younger. Table (2).

There's a negative correlation with total vitamin D level and weight (r = −0.216), BMI (r = −0.279) and WC (r = −0.422) with highly significant difference (p value < 0.001) with weight and WC and significant difference (p value 0.008) with BMI, as total vitamin D level is lower in obese patients than lean one. Table (2).

Total vitamin D level is negatively correlated with cholesterol (r = −0.396). LDL (r = −0.365) and TG (r = - 0.333) with significant difference (p value 0.001) with TG and high statistically significance (p value < 0.001) with total cholesterol and LDL, as total vitamin D level decreases with high total cholesterol, LDL and TG. Table (2).

Total vitamin D level is negatively correlated with FPG (r = 0.216) and HbA1c (r = −0.233) with significant difference with FPG and HbA1c (p value 0.041 and 0.027 respectively). As total vitamin D decreases in patients with uncontrolled DM. Table (2).

Total vitamin D level is negatively correlated with FLI and ultrasound finding of fatty liver in this study (r = −0.470 and 0.268) with statistically significance (p value < 0.001 and 0.011), as total vitamin D level decreases in people with high FLI. FLI show a negative correlation with total vitamin D level more than ultrasound finding. Table (2).

4. Discussion

This current study shows that the vitamin D level in diabetic patients with NAFLD was lower than other groups either diabetic only, NAFLD only or healthy control which in agreement with **Dasarathy et al.,** who found that vitamin D level was lower in NAFLD patients with diabetes mellitus than patients with NAFLD only, NAFLD and healthy control [10].

The present study showed that the level of vitamin D is low in T2DM patients in comparing to healthy controls which in agreement **Wang et al**., who found that vitamin D level in T2DM patients is lower than controls [11].

The previous result is in disagreement with **Fondjo et al**., on their study in Ghana which conducted one hundred and eighteen T2DM patients and one hundred non diabetic individuals for vitamin D level assessment. They found low vitamin D level in both groups without any difference between them [12]. This may be attributed to many factors: dark color of population in Ghana which affect absorption of vitamin D through sun exposure in both groups plus poor nutritional and socioeconomic conditions in their country.

In the current study, the level of vitamin D was found to be

Table 1
Comparison between all studied groups as regard: Total vitamin D level and fatty liver index (FLI).

	Group 1 (N = 30) mean ± SD	Group 2 (N = 30) mean ± SD	Group 3 (N = 30) mean ± SD	Group 4 (N = 30) mean ± SD	Anova	
					F	P value
Total vitamin D (ng/ml)	15.5 ± 7.46	24.4 ± 8.19	22.86 ± 9.58	55.8 ± 11.98	83.934	<0.001*
FLI	68.11 ± 6.89	51.76 ± 8.73	68.15 ± 6.354	37.53 ± 7.63	94.54	<0.001*

Table 2
Correlation between total vitamin D level and (age, WC, weight, BMI, FBS, HbA1C, Total cholesterol, LDL, Triglyceride, FLI, bright fatty liver by ultrasonography).

All Patient groups	Total vitamin D ng/ml	
	R	P value
Age (Years)	−0.517	<0.001*
WC (cm)	−0.422	<0.001*
Weight (kg)	−0.216	0.041*
BMI (kg/m2)	−0.279	0.008*
FPG (mg/dl)	−0.216	0.041*
HbA1C (%)	−0.233	0.027*
Total cholesterol (mg/dl)	−0.396	<0.001*
LDL (mg/dl)	−0.365	<0.001*
Triglyceride (mg/dl)	−0.333	0.001*
FLI	−0.470	<0.001*
Bright fatty liver by ultrasonography	−0.268	0.011*

lower in older patients than younger one which in agreement with **Alfawaz et al**., who found that vitamin D deficiency with increasing age**.** [13], Vitamin D decreases in older population due to decreased skin integrity, lack of mobility which decreasing outdoors hours, decrease appetite, progressive decline of kidney function with aging and multiple comorbidities which may affect vitamin D level [14].

We found that the level of vitamin D level is low in obese patients in comparing to lean patients as vitamin D as it decreased in high BMI patients which in agreement with **Shamaila Rafiq et al.,** who found the inverse relationship between vitamin D level and BMI [15].

The present study showed that vitamin D level was low in patients with high cholesterol, low density lipoprotein (LDL) and triglycerides which in agreement with **López-Bautista et al.,** who observed that vitamin D level was low in individuals with high cholesterol, LDL and triglycerides [16].

The current study showed that vitamin D level was low in subjects with high FPG and glycosylated hemoglobin (HbA1c) which in agreement with **Daniel Mauss et al.,** They found that vitamin D deficiency was evident in subjects with high FPG and HbA1c [17].

The present study showed that there's a negative correlation between vitamin D level and fatty liver index (FLI) as high FLI patients had low vitamin D level which in agreement with **He et al.,** who found that vitamin D level had a negative correlation with FLI**.** [18]

5. Conclusion

Total vitamin D level in type 2 diabetic patients with NAFLD is lower than healthy controls and either diabetic or NAFLD only groups.

Total vitamin D level is negatively correlated with body mass index, waist circumference, total cholesterol, LDL, triglycerides, Fasting plasma glucose, glycosylated hemoglobin and degree of fatty liver index.

NAFLD should be treated with life style modification and encourage use novel drugs to prevent its complications.

List of abbreviation

NAFLD	non-alcoholic fatty liver diseases
LDL	low density lipoprotein
TG	triglycerides
WC	waist circumference
FLI	fatty liver index
BMI	body mass index
VDR	vitamin D receptor
IR	insulin resistance

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.04.002.

References

[1] Nair R, Maseeh A. Vitamin D: the "sunshine" vitamin. J Pharmacol Pharmacother 2012;3(2):118–26.
[2] Papatheodorou K, Papanas N, Banach M, et al. Complications of diabetes 2016. J Diabetes Res 2016;2016:6989453.
[3] Benedict M, Zhang X. Non-alcoholic fatty liver disease: an expanded review. World J Hepatol 2017;9(16):715–32.
[4] Kitade H, Chen G, Ni Y, et al. Nonalcoholic fatty liver disease and insulin resistance: new insights and potential new treatments. Nutrients 2017;9(4): E387.
[5] Al-Shoumer KA, Al-Essa TM. Is there a relationship between vitamin D with insulin resistance and diabetes mellitus? World J Diabetes 2015;6(8): 1057–64.
[6] Mitri J, Pittas AG. Vitamin D and diabetes. Endocrinol Metab Clin N Am 2014;43(1):205–32.
[7] Das Gautam. Vitamin D and type 2 diabetes. Practical Diabetes 2017;34(1): 19–24.
[8] Li J, Cordero P, Nguyen V, et al. The role of vitamins in the pathogenesis of non-alcoholic fatty liver disease. Integr Med Insights 2016;11:19–25.
[9] Cimini Flavia A, Barchetta Ilaria, Carotti Simone, et al. Relationship between adipose tissue dysfunction, vitamin D deficiency and the pathogenesis of non-alcoholic fatty liver disease World. J Gastroenterol 2017;23(19):3407–17.
[10] Dasarathy J, Periyalwar P, Allampati S, et al. Hypovitaminosis D is associated with increased whole body fat mass and greater severity of nonalcoholic fatty liver disease. Liver Int 2014;34(6):e118–127.
[11] Wang JM, Ye SD, Li SM, et al. Correlations of 25(OH)D level with blood lipid, inflammatory factors and vascular endothelial function in diabetic patients. Eur Rev Med Pharmacol Sci 2018;22(3):731–5.
[12] Fondjo LA, Sakyi SA, Owiredu WKBA, et al. Evaluating vitamin D status in pre- and postmenopausal type 2 diabetics and its association with glucose homeostasis. BioMed Res Int 2018;2018:9369282.
[13] Alfawaz H, Tamim H, Alharbi S, et al. Vitamin D status among patients visiting a tertiary care center in Riyadh, Saudi Arabia: a retrospective review of 3475 cases. BMC Public Health 2014;14(1):159.
[14] Meehan M, Penckofer S. The role of vitamin D in the aging adult. J Aging Gerontol 2014;2(2):60–71.
[15] Rafiq Shamaila, Jeppesen Per Bendix. Body mass index, vitamin D, and type 2 diabetes: a systematic review and meta-analysis. Nutrients 2018;10(9):1182.
[16] López-Bautista F, Posadas-Romero C, Ruiz-Vargas LY, et al. Vitamin D deficiency is not associated with fatty liver in a Mexican population. Ann Hepatol 2018;17(3):419–25.
[17] Mauss Daniel, Jarczok1 Marc N, Hoffmann1 Kristina, et al. Association of vitamin D levels with type 2 diabetes in older working adults. Int J Med Sci 2015;12(5):362–8.
[18] He X, Shen Y, Ma X, et al. The association of serum FGF23 and non-alcoholic fatty liver disease is independent of vitamin D in type 2 diabetes patients. Clin Exp Pharmacol Physiol 2018;45:668–74.