Vitamin D3 level and Liver Enzymes Among a sample of Type 2 Diabetes patients in Hilla city, Iraq

Ahmed Mahdi Habeeb
Middle Technical University / Iraq

Atta Ah Mousa Al-Sarray
Middle Technical University / Iraq, attaahalsarray@gmail.com

Ali Hussein Al Hafidh
Middle Technical University / Iraq

Abstract

Background: The synthesis of vitamin D, a modified steroid required for the metabolism of calcium and phosphorus, occurs in the epidermis when exposed to sunlight.

Objective: Assessment of Vitamin D3 and Liver Enzyme Levels in Type 2 Diabetic Hilla Patients.

Patients and Methods: A total of 300 individuals among them 150 people suffering with type 2 DM were chosen as case and 150 age and sex matched healthy subjects were served as control of both genders whose ages ranged between 30 and 79 years were enrolled. The period of data collection lasted 5 months, it began on 1 November 2022 ending on 30 March 2023. Fasting blood sugar (FBS), Vitamin D3, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total serum bilirubin (TSB) were measured in patients' serum. The association of both Vitamin D3 and liver enzyme levels with T2DM and control was evaluated by Chi-square analyses.

Results the Mean±SD of the age was 55.4±10.1were T2DM and the Mean±SD of the age was 55.3±10.0 were control. the highest percentage of T2DM and control (33.3%) was in the age group 50–59 years, and the lowest percentage of T2DM and control (6.7%) was in the age group 30–39 years. The percentage of females represented (56.7%) and males (43.3%) in T2DM and control, and related to educational qualification, showed that the highest percentage (24.7%) could read and write, whereas the lowest percentage (13.3%) graduated from college or higher in T2DM. As for the educational qualifications of the control group, the highest percentage of them (38.0%) were in college or higher, whereas the lowest percentage of them (7.3%) were illiterate. The marital status showed that the highest percentage of them (93.3%) was married to T2DM and 98.7% was married to control, whereas the lowest percentage of them (6.7%) was single or widowed of T2DM and (1.3%) was single or widowed of control. A high percentage (55.3%) of T2DM were residents of urban areas, while the lowest percentage of them (44.7%) were residents of rural areas. the vitamin D3 level (deficient, insufficient, and normal) is 38.7%, 33.3%, and 28.0%, respectively, of T2DM, whereas the vitamin D3 level (deficient, insufficient, and normal) is 28.7%, 30.0%, and 41.3%, respectively, of control. The mean ALT, AST, TSB were 25.83±14.52, 22.29±10.46, and 12.91±4.30 respectively of T2DM, whereas The mean ALT, AST, TSB were 21.07±10.20, 20.67±8.02, and 10.88±3.02 respectively of control.

Conclusions: Vitamin D3 plays a crucial role in type 2 diabetes (T2D), and there is a significant difference between low vitamin D status and a higher risk of developing the disease. There were no statistically significant differences in some liver enzymes between individuals with T2DM and the control groups.

Recommendations: Vitamin D3, liver enzymes, and T2D need specially designed clinical studies carried out in well-defined populations.

Keywords: *Vitamin D3, Diabetes, Hilla City, Enzymes, Iraq.*

INTRODUCTION

A persistent metabolic disease called diabetes causes high glucose levels, which can seriously harm the heart, blood vessels, eyes, nerves, and kidneys. Type 2 diabetes (T2D), which usually affects adults, is the most prevalent and results from the body becoming resistant to insulin. The majority of the world's 422 million diabetics live in low- and middle-income countries, and the disease is directly responsible for 1.6 million yearly deaths, according to the WHO in 2021(1). Over the past four decades, Iraq has experienced a sharp rise in the frequency of diabetes, which now stands at 20%. Additionally, DM is regarded as a major source of death in the majority of developing nations, particularly in Iraq. Uncontrolled glucose may be to blame for this (2) .Key to the start and development of type 2 diabetes is pancreatic beta cell failure, which results from the interaction of genetic and acquired factors. (T2D). Beta cells are distinct endocrine cells that produce, store, and secrete insulin in response to a variety of integrated signals, closely regulating blood glucose levels. They have a 20 pg insulin content and an average circumference of 10 m. In the adult pancreatic islets, beta cells make up between 50 and 80 percent of the islet cells. (3). Over the past ten years, low blood levels of 25-hydroxyvitamin D have been identified as a potential risk factor for type 2 diabetes, and vitamin D supplementation has been suggested as a potential strategy to reduce diabetes risk. Given that both impaired pancreatic beta-cell function and insulin resistance have been associated with low blood levels of 25-hydroxyvitamin D, the theory that vitamin D status may affect the risk of type 2 diabetes is biologically feasible. (4).Bone mineralization is vitamin D3's most crucial activity. But it's becoming clear that vitamin D3 also serves a number of other, non-skeletal purposes. Its lack increases the chance of both skeletal and non-skeletal conditions, such as T2DM, immune problems, and cardiovascular diseases. A deficiency in vitamin D3 is said to have an inverse association with pre-diabetes and T2DM. Vitamin D3's function in glucose regulation is well established. Additionally, a higher plasma vitamin D3 concentration is linked to a lower chance of developing diabetes (5).But according to earlier research, T2D is a well-known cause of aberrant liver function tests. (LFTs). However, it has been demonstrated that the biomarkers for liver dysfunction, such as aspartate aminotransferase (AST), total serum bilirubin test (TSB), and alanine aminotransferase (ALT), are reliable measures of liver health and associated with insulin resistance (IR) and the risk of type 2 diabetes (T2D). Studies were carried out all over the globe to assess the connection between liver enzymes and T2D, and their results were different from diabetes (6).

Patients and Methods

The study is a case-control study that was conducted at the Diabetes and Endocrinology Center in Hilla, Iraq. The period of data collection lasted 5 months; it began on November 1, 2022, and ended on March 30, 2023. Inclusion criteria: Cases: all the patients who were diagnosed with Type 2 diabetes and

attended the Diabetes and Endocrinology Center in Hilla City; The controls were selected from Murjan Hospital and the Diabetes and Endocrinology Center in Babylon Governorate. who didn't have Type 2 diabetes. The controls were age- and sex-matched by a ratio of one to one. Exclusion criteria: Type 2 diabetics outside Babylon City; Type 2 diabetics who refuse to participate; Type 2 diabetics in out-of-place sample groups; Type 2 diabetics taking hypothyroidism or gestational diabetes.

Statistical data analysis

The analysis of the data was carried out using the available statistical package SPSS-28 (Statistical Packages for Social Sciences, version 28). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

The significance of the difference between different means (quantitative data) was tested using the Student t-test for the difference between two independent means or the ANOVA test for the difference among more than two independent means. The significance of the difference between different percentages (qualitative data) was tested using the Pearson chi-square test with the application of Yate's correction or the Fisher exact test whenever applicable. Statistical significance was considered whenever the P value was equal to or less than 0.05.

Results and Discussions

Out of 300 patients, 150 were T2D (85 females and 65 males), and 150 were control patients, age and sex matched. The demographic characteristics of T2DM and the control group of participants are displayed in Table 1.

The mean age for T2DM was 55.4±10.1 years and 55.3±10.0 years for controls. (33.3%) of the T2DM group were within the age range of 50–59 years; (93.3 %) of T2DM patients were married. A statistically significant association was detected in the variables of age groups, education level (P = 0.0001), and marital status (P = 0.008). No significant difference (P = 0.05) was observed in the variables of age, gender, residence, family members, and smoking cigarettes.

Table (1) Demographic characteristics of T2DM and control

Demographic characteristics		**T2DM**		**Control**		**P value**
		No	%	No	%	
Age (years)	30---39	10	6.7	10	6.7	-
	40---49	28	18.7	28	18.7	
	50---59	50	33.3	50	33.3	
	60---69	47	31.3	47	31.3	
	70---79	15	10.0	15	10.0	
	Mean ± SD(Range)	55.4±10.1(30-77)		55.3±10.0(30-77)		0.986
Gender	Male	65	43.3	65	43.3	-
	Female	85	56.7	85	56.7	
Educational level	Illiterate	34	22.7	11	7.3	0.0001*
	Read & Write	37	24.7	19	12.7	
	Primary	30	20.0	21	14.0	
	Secondary	29	19.3	42	28.0	
	College & Higher	20	13.3	57	38.0	
Marital status	Married	140	93.3	148	98.7	0.008*
	Single/Widow	10	6.7	2	1.3	
Residence	Rural	67	44.7	64	42.7	0.727
	Urban	83	55.3	86	57.3	
Smoking	Yes	21	14.0	20	13.3	0.985

cigarettes	No	129	86.0	130	86.7	
*Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05 level.						
#Significant difference between two independent means using Students-t-test at 0.05 level.						

The mean glucose level was 9.53±3.85 (mmol/L) for T2DM and 5.00±0.58 (mmol/L) for Control, the mean HbA1C level was 8.49±1.74 (%) for T2DM and 5.08±0.85 (%) for Control, the mean B. urea level was 4.28±1.23 (mmol/L) for T2DM and 3.96±0.99 (mmol/L) for Control, the mean GPT level was 25.83±14.52 (IU/L) for T2DM and 21.07±10.20 (IU/L) for Control and the mean TSB level was 12.91±4.30 (µmol/L) for T2DM and 20.67±8.02 (µmol/L) for Control.

Shown this Table2. A significant relation was detected between glucose, HbA1C, Blood urea, GPT and TSB at levels (P < 0.05).

Table 2 Association between and T2DM and Control according to Biochemical Tests

	T2DM	**Control**	**P value**
FBS (mmol/L)	9.53±3.85(4.0-19.3)	5.00±0.58(3.5-5.8)	0.0001#
HbA1C (%)	8.49±1.74(6.2-13.7)	5.08±0.85(4.0-13.6)	0.0001#
S Calcium (mmol/L)	2.16±0.22(1.8-2.6)	2.16±0.18(1.8-2.6)	0.794
B urea (mmol/L)	4.28±1.23(2.5-8.6)	3.96±0.99(2.5-7.5)	0.014#
S creatinine (mmol/L)	75.75±20.37(40-154)	76.42±14.61(45-105)	0.742
GPT (IU/L)	25.83±14.52(4-81)	21.07±10.20(5-52)	0.001#
GOT (IU/L)	22.29±10.46(6-86)	20.67±8.02(6-49)	0.132
TSB (µmol/L)	12.91±4.30(5.0-27.0)	10.88±3.02(5.0-25.0)	0.0001#
-Data were presented as Mean±SD (Range)			
#Significant difference between two independent means using Students-t-test at 0.05 level.			

Table3. Shown A significant difference was detected between glucose and vitamin D at these levels (P = 0.042).

Table 3 Association between and T2DM and Control according to Vitamin D3

		T2DM		**Control**		**P value**
		No	%	No	%	
Vitamin D3 (ng/mL)	Deficient (=<20)	58	38.7	43	28.7	0.042*
	Insufficient (20-29)	50	33.3	45	30.0	
	Normal (=>30)	42	28.0	62	41.3	
***Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05 level.**						

While there were Significant differences in the levels of liver enzymes between control and T2DM patients, with the exception of GOT, there were obvious deficiencies in vitamin D in T2DM patients. The amount of research describing how vitamin D affects calcium metabolism, bone integrity, and other processes is growing. Epidemiologic research has shown that vitamin D deficiency is linked to the emergence of metabolic syndromes,

such as T2D, because it participates in a number of crucial physiological pathways (6). The following is how vitamin D and type 2 diabetes are related: Gluconeogenesis in pancreatic alpha cells is triggered by central insulin resistance in pancreatic beta cells, increasing hepatic glucose synthesis in the initial state and impairing peripheral organ glucose utilization. This process affects insulin receptors in muscle, brain, and fatty tissues, resulting in decreased glucose absorption for energy requirements in peripheral tissue, increased adipose tissue lipolysis, increased gastrointestinal deficiency, and increased glucose adsorption in the kidney in impaired glucose tolerance. Since pancreatic cells produce VDRs and 1a-hydroxylase is detected in pancreatic tissue, which is comparable to the expression of insulin, numerous studies have examined the relationship between vitamin D and the physiological function of pancreatic cells. Calcium levels affect insulin release, and vitamin D deficiency has been linked to a reduction in glucose-induced insulin secretion.(7).Regarding liver enzymes, it was discovered that T2D individuals from Bangladesh and China had a significant prevalence of abnormal serum AST and ALT. Both investigations came to the same conclusion: T2D has been linked to abnormal LFTs and hepatic diseases(8) . Uncertainty surrounds the process by which T2 diabetes mellitus (T2DM) leads to abnormalities in liver enzymes. Noting that vitamin D deficiency inhibits glucose-facilitated insulin secretion, the potential theory is that elevated enzyme levels indicate an excess of fat deposition in the liver, a condition known as nonalcoholic fatty liver disease (NAFLD). This NAFLD is thought to be connected to the metabolic syndrome, which has a number of cardiovascular risk factors connected to IR and T2D. The primary marker for additional liver injury diagnostics used by clinicians on a regular basis is liver transaminases. As a result, the majority of people who have transaminase values above the normal range and are already developing chronic metabolic liver disease may be missed by the current normal values (6).Our findings were in line with those of the Iranian research by Rahmanian et al., which found no connection between gender differences and T2D (9). and rejects the claim made in Finnish research by Aregbesola et al. that there is a gender difference in T2D risk, with males having a higher T2D risk (10).According to a Nigerian study, living in an urban area increases the chance of older people developing new cases of diabetes,(11) Apart from a Polish study, which found that the degree of metabolic control of diabetes was not significantly influenced by the sociodemographic variations between groups according to place of residence, there is research that contradicts the findings of our study (12).Numerous empirical studies show that adequate vitamin D can reduce the risk of T2D, obesity, and metabolic syndrome. However, it is advantageous to confirm the theory that these diseases are made worse by hypovitaminosis D (13) .

Conclusions:

Vitamin D plays a crucial role in type 2 diabetes (T2D), and there is a significant difference between low vitamin D status and a higher risk of developing the disease. There were no statistically significant differences in some liver enzymes between individuals with T2DM and controls.

Recommendations:

Vitamin D, liver enzymes, and T2D need specially designed clinical studies carried out in well-defined populations.

Reference

1. World Health Organization. Diabetes [Internet]. 2021 [cited 2023 Mar 16]. Available from: https://www.who.int/health-topics/diabetes#tab=tab_1

2. Mikhael EM, Hassali MA, Hussain SA, Shawky N. Self-management knowledge and practice of type 2 diabetes mellitus patients in Baghdad, Iraq: A qualitative study. Diabetes, Metab Syndr Obes Targets Ther. 2019;12:1–17.

3. Mara Suleiman 1 LM 1, , Miriam Cnop 2, 3, Decio L. Eizirik 2 , Carmela De Luca 1, Francesca R. Femia 4, Marta Tesi 1, Silvia Del Guerra 1 and Piero Marchetti 1 4. The Role of Beta Cell Recovery in Type 2 Diabetes Remission. 2022; Available from: https://doi.org/10.3390/ijms23137435

4. Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR, et al. Vitamin D Supplementation and Prevention of Type 2 Diabetes. N Engl J Med [Internet]. 2019;381(6):520–30. Available from: https://d2dstudy.org/sites

5. Ata N, Rahman Z, Gilani M, Ishaq N, Khan MW, Haider QUA. Response of blood sugar fasting to vitamin D3 in individuals with pre-diabetes. Rawal Med J. 2022;47(1):18–21.

6. ElJilani M, Alemam H, Bashein A. Vitamin D and liver enzymes' levels in Libyans with type 2 diabetes. Libyan J Med Sci. 2021;5(3):116.

7. Ogail SF, Muhsin SN, Abbas WI. Evaluation of vitamin D level among patients with type 2 diabetes in Nineveh Governorate-Iraq. 2022;140(04):2279–85. Available from: https://www.healthsciencesbulletin.com/volume/BNIHS/140/04/evaluation-of-vitamin-d-level-among-patients-with-type-2-diabetes-in-nineveh-governorate-iraq-62c6642445cde.pdf

8. Islam S, Rahman S, Haque T, Sumon AH, Ahmed AM, Ali N. Prevalence of elevated liver enzymes and its association with type 2 diabetes: A cross-sectional study in Bangladeshi adults. Endocrinol Diabetes Metab. 2020;3(2):1–8.

9. Shojaei M, Rahmanian K, Jahromi AS. Relation of type 2 diabetes mellitus with gender, education, and marital status in an Iranian urban population. Reports Biochem Mol Biol [Internet]. 2013;1(2). Available from: www.RBMB.net

10. Aregbesola A, Voutilainen S, Virtanen JK, Mursu J, Tuomainen TP. Gender difference in type 2 diabetes and the role of body iron stores. Ann Clin Biochem. 2017;54(1):113–20.

11. Balogun WO, Gureje O. Self-reported incident type 2 diabetes in the ibadan study of ageing: Relationship with urban residence and socioeconomic status. Gerontology. 2012;59(1):3–7.

12. Dudzińska M, Tarach JS, Zwolak A, Kurowska M, Malicka J, Smoleń A, et al. Type 2 diabetes mellitus in relation to place of residence: Evaluation of selected aspects of socio-demographic status, course of diabetes and quality of life - a cross-sectional study. Ann Agric Environ Med. 2013;20(4):869–74.

13. Atta alsarray R haider shareef. Awareness of Healthcare Providers About COVID-19 Vaccinations in Karbala City. J Tech. 2022;4(2708–8383):91–6.