RESEARCH
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DETECTING THE EFFECT OF VITAMIN K2 DEFICIENCY IN PATIENTS WITH DIABETES MELLITUS AND CARDIOVASCULAR DISEASE

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Abstract
Object: The current study aimed to find the correlation between vitamin K2 and chronic diseases such as diabetes and cardiovascular disease by studying a number of physiological and biochemical variables represented by RBS, HbA1c, lipid profile, liver enzymes, as well as antioxidants in men with diabetes and cardiovascular disease in Baghdad.
Subject: The study included 80 people whose ages ranged between (15-75) years. Samples were collected from people visiting Al-Imam Al-Kazemin Medical City in Baghdad - Iraq. The experiment was designed into four groups. The first group included 20 healthy people representing the control group. The second group included 20 people with type 1 diabetes (completely dependent on insulin), the third group included 20 people with type 2 diabetes (non-insulin dependent), and the fourth group included 20 people suffering from cardiovascular disease (CVD).
Result: The results indicated that there is a relationship between the concentration of vitamin K2 level and the variables that were found in the study, as there was a significant decrease in the concentration of vitamin K2 in all groups of patients compared to the control group, While the levels of only HDL in the lipid profile, as well as GSH, decreased for all groups of patients compared to the control group.
Conclusion: conclude from all the results that there is a significant effect of vitamin K2 in improving insulin sensitivity in people with diabetes, thus reducing the risk of diabetes and also important in the prevention and treatment of arterial calcifications and cardiovascular disease.
Keywords: vitamin K2 - diabetes – RBS – HbA1c - cardiovascular - antioxidants - liver enzymes.

1. Introduction

Vitamin K is among the group of fat-soluble vitamins and can be obtained from plants, bacteria, and animals, and is necessary for blood clotting [1]. It plays a It plays a major role as a cofactor in the synthesis of blood clotting proteins in the liver [2]. Recently, interest in its functions in extrahepatic tissues has increased. Vitamin K deficiency is usually caused by abnormal absorption and not by a lack of the vitamin in food. Regardless of its effect on clotting, chronic deficiency below the normal limit of vitamin K may be a risk factor for many diseases such as osteoporosis, atherosclerosis, cancer, insulin resistance, neurological diseases, etc. There are three types of vitamin K: vitamin K1, K2, natural forms and (K3) is the synthetic form. Our study targeted the second type of this vitamin (K2). It is known that vitamin K2 reduces the risk of diabetes through its ability to improve insulin sensitivity and glucose metabolism. Vitamin K2 also reduces the risk of cardiovascular disease because of its It has an effect on activating Matrix Gla Protein (MGP), one of the vitamin K-dependent proteins that works to prevent the calcification of Ca++ on the lining of blood vessels, as it binds with Ca++ and is transported to its correct places in the bones and teeth and works to strengthen them.[3].

The aim of the study was to evaluate vitamin K2 and its relationship to diabetes and cardiovascular disease based on:

- Evaluation of vitamin K2 concentration.
- Measuring the concentration of biochemical variables represented by random blood sugar (RBS) and cumulative blood sugar (HbA1c).
- Measuring the concentration of the antioxidant represented by glutathione (GSH) and the oxidative stress represented by malonialdehyde (MDA).
- Measuring the concentration of liver enzymes ALT and AST.
- Measurement of total lipid profile (TC, TG, HDL, LDL, vLDL)

This study assumed that the level of vitamin K2 is low in vitamin K2 for patients suffering from type 1 and type 2 diabetes and cardiovascular disease.

2. Materials and methods:

The current study was conducted in the period between August 15, 2023, and November 15 of the same year on patients attending the Imam al-Kazemin Medical City. Before starting the study and collecting samples, the approval of the Ministry of Health - Baghdad Al-Karkh Health Directorate was obtained, after contacting the Iraqi University, College of Education, to facilitate our mission to collect samples for our study.

The study included collecting 80 samples from males, whose ages ranged between (15-75) years. They were divided into four groups. The first group consisted of 20 samples from healthy people, which included a control group. The second group consisted of 20 samples from patients with type 1 diabetes (who depended on taking Insulin) as well as the third group included 20 samples from patients with type 2 diabetes (not dependent on taking insulin), while the fourth group included 20 samples for cardiovascular diseases (blood pressure, atherosclerosis, and myocardial infarction). While the study excluded many cases of

diseases associated with diabetes and cardiovascular diseases, including cancer, intestine and liver diseases, after conducting clinical and laboratory examinations of all samples.

A complete medical history was taken for all patients, focusing on age, duration of diabetes and its treatment, family history of the disease, and nature of living. Clinical examinations were conducted, including measuring the body mass index (BMI) and obesity classification according to World Health Organization standards.

Laboratory tests include evaluating vitamin K2 concentrations, random blood sugar levels (RBS), and HbA1c levels, in addition to measuring the lipid profile, liver enzymes ALT and AST, and the antioxidants GSH and MDA.

Samples were taken as follows: 5 ml of fasting venous blood (12-16 hours) was collected and divided into two parts: the first part consisted of 2 ml of blood added to EDTA tubes (to determine the RBS-HbA1c-CBC ratio) and the second part was 3 ml of blood was placed in gel tubes and stored at a temperature of (-80) degrees Celsius to evaluate (vitamin K2 - lipid profile - liver enzymes ALP-AST antioxidants MDA, GSH) using the diagnostic kit for each test.

Statistical work was conducted on the data using the statistical package program (SPSS-20) by applying the mean and standard deviation for quantitative variables and categorical factors when comparing groups.

3. Results and discussion:

3.1 Concentrations of HbA1c, RBS, and vitamin K2 compared to the control group:

The results shown in Figure (1) and Table (1) showed that there were significant differences between the study groups in the level of vitamin K2 compared to the concentration of HbA1c in the blood serum when the groups were compared. The results showed that the group of patients with type 2 diabetes (not dependent on taking insulin) The group had the most low levels of vitamin K2, followed by the group of type 1 diabetics (who depend on taking insulin) with a slight significant difference, which were respectively (324.43±12.45) and (331.13±10.03) ng/ml, and then came the cardiovascular disease group. There was a smaller decrease in blood sugar levels, which was (503.28±20.59) ng/ml compared to the healthy control group, which was (692.97±11.26) ng/ml at the probability level (P≤0.001).

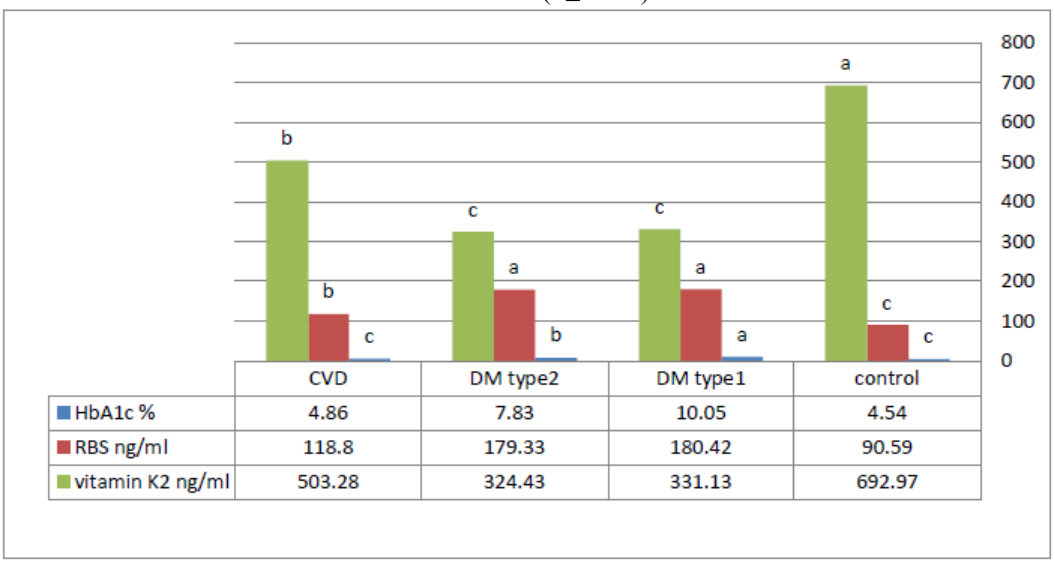

Figure 1: shows an estimate of the vitamin K2 concentration level, HbA1c and RBS in blood serum study groups compared to the control group at the probability level P≤0.001.

Table 1: shows an estimate of the vitamin K2 concentration level, HbA1c and RBS

Parameters	Mean±SD				P-value
	Control	DM type1	DM type2	CVD	
HbA1c%	4.54±0.61	10.05±2.66	7.83±2.58	4.86±0.47	0.001*
RBS ng/ml	90.59±4063	180.42±48.62	179.33±34.51	118.8±19.57	
Vitamin K2 ng/ml	692.97±11.26	331.13±10.03	324.43±12.45	503.28±25.30	
*(P≤0.001)					

Many studies have shown that diabetes and its relationship to vitamins are based on some variables. A study was reported on type 2 diabetes metabolism and its relationship to vitamin K2 levels, the results of which agreed with the current study [4]. The results of the study also agreed[5]. also agreed. Through their study of changes in Obestatin levels, lipid profiles, and some heart function indicators in patients with type 2 diabetes. The reason for the increase in blood sugar levels in this type of diabetic patient is lipid peroxidation, complications affecting blood vessels, and oxidative stress [6]. Likewise, many studies have shown the existence of a relationship between vitamin K2 and diabetes, as the results of the study conducted by [7]. showed that the relationship of vitamin K2 to diabetes is summarized in three ways: The first way is the regulation of osteocalcin OC, which is a protein that depends on VK and has appeared in many Animal studies have shown that it enhances

beta cell proliferation and insulin secretion, in addition to increasing insulin sensitivity [8, 9]. Many studies have also confirmed that osteocalcin plays an important role in enhancing glucose metabolism by increasing insulin secretion and adiponectin expression [10, 11]. The second way is through the anti-inflammatory effect. It has been proven that inflammation may cause insulin resistance[12]. The third method is the lipid-lowering effect [13].

3.2 Lipid profile:

The results of the study shown in Figure (2) and Table (2) showed a significant increase in all disease groups compared to the control group, which recorded the highest values for lipid profile concentrations at a significant level P≤0.001.

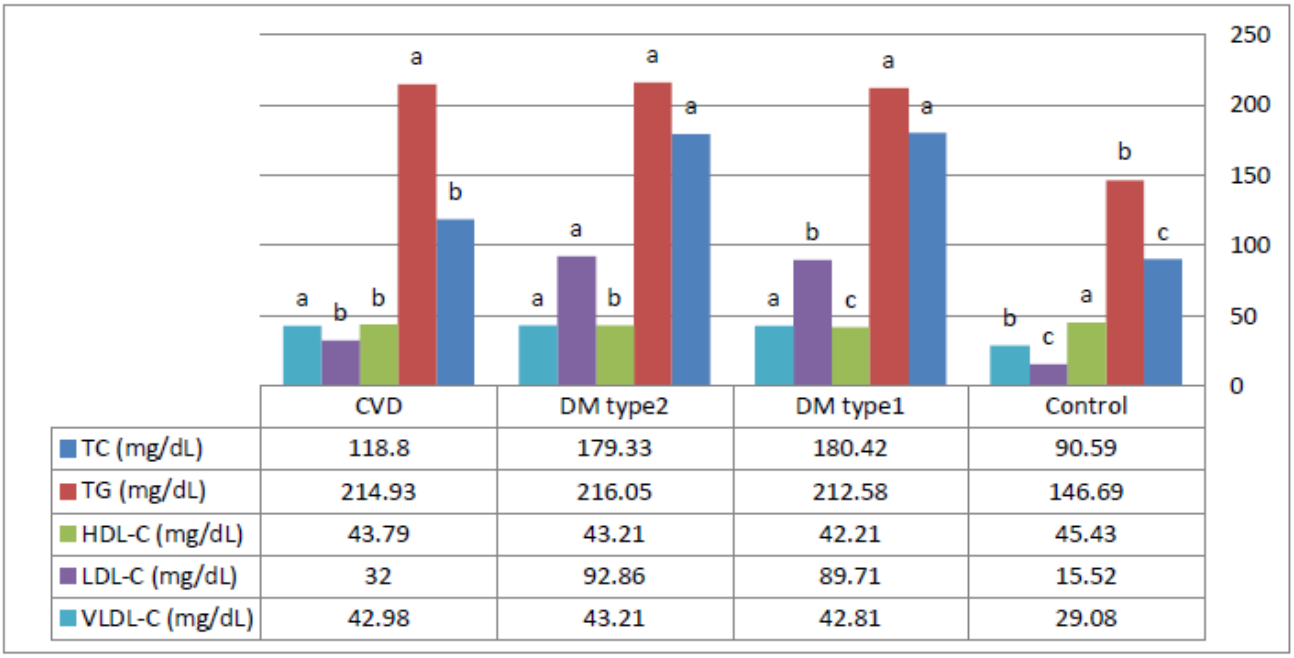

Figure 2: shows an estimate of the level of lipid profile concentrations in the blood serum for the study groups Compared to the control group at probability level P≤0.001.

Table 2: shows an estimate of the level of lipid profile concentrations

Parameters	Mean±SD				P-value
	Control	DM type1	DM type2	CVD	
TC(mg/dL)	90.59±1.03	180.42±10.87	179.33±7.71	118.8±4.37	0.001*
TG(mg/dL)	146.69±5.26	212.58±3.91	216.05±22.68	214.93±1.93	
HDL-C (mg/dL)	45.43±1.61	42.21±0.79	43.21±0.84	43.79±1.74	
LDL-C (mg/dL)	15.52±1.11	89.71±9.26	92.86±7.62	32±4.51	
VLDL-C (mg/dL)	29.08±4.80	42.81±3.96	43.21±4.53	42.98±1.72	
*(P≤0.001)					

This study agrees with the researcher's findings[14]. As well as the researcher's findings[15] , During their study of biochemical variables in the blood serum of cardiovascular patients, they found that high blood sugar harms the eyes, kidneys, legs, and blood vessel walls. The level of cholesterol increases in patients with diabetes. In the case of severe and chronic diabetes, cholesterol production in tissues decreases, while its level in the blood increases as a result of high concentration. LDL-C and VLDL-C contain high levels of cholesterol, as well as the disorder Diabetes is caused by high lipid profile, which is one of the causes of heart disease.[14]Concentration results also appeared TG increased significantly in all groups of patients compared to the control group, and the results of this study agreed with other studies[16]Through their study, they evaluated the effect of cumulative glucose on the body mass and lipid profile of patients with type 2 diabetes in Iraq. The increase in the concentration of triglycerides is due to excessive consumption of foods rich in fats, which leads to an increase in the production of chylomicrons in the intestines, which when they break down cause the release of fatty acids[17]. As for concentration HDL-C The results of the current study showed a slight significant decrease for all groups of patients compared to the control group. I agreed Results of this study With what the researcher found[5] This is due to the decrease in levels HDL-C leads to a decrease in the activity of the enzyme lipoprotein lipase (LPL), which leads to the breakdown of triglycerides (TG) into fatty acids and glycerol [18]. While the results of the current study showed an increase in levels LDL-C in patient groups compared with the control group. The results of this study are consistent with his.

4.2. Oxidative stress and antioxidants:

The results of the current study, shown in Figure (3) and Table (3), showed a significant decrease in the level of the antioxidant represented by glutathione (GSH) and a significant increase in the level of malondialdehyde (MDA) in the patient group compared to the control group at a probability level of P≤0.001.

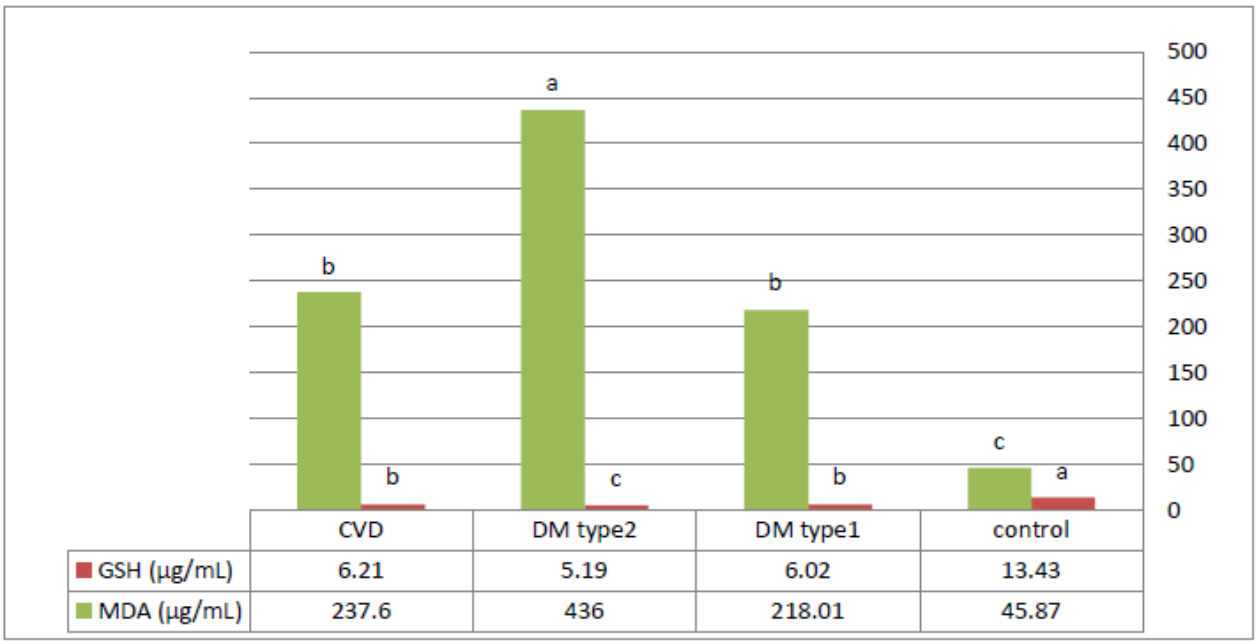

Figure 3: shows an estimate of the level of vitamin K2 concentrations, GSH, MDA In Serum for groups the study compared to the control group at probability level P≤0.001.

Table 3 : Shows the estimation estimate of the level of vitamin K2 concentrations, GSH, MDA.

Parameters	Mean±SD				P-value
	Control	DM type1	DM type2	CVD	
GSH (µg/mL)	13.43±1.77	6.02±0.93	5.19±0.97	6.21±0.65	0.001*
MDA (µg/mL)	45.87±2.10	218.01±23.24	436±17.58	237.6±43.03	
*(P≤0.001)					

The results agreed with this study on the total status of antioxidants in relation to oxidant stress in type 2 diabetes [19]. The type 2 diabetes group was the group with the lowest concentration level GSH and the highest levels of MDA concentration level, high blood sugar works to generate free radicals[20]. Diabetic patients with other chronic disorders such as high blood pressure and ischemic heart disease, as well as any chronic disease, can induce increased oxidative stress[21, 22]. High oxidative stress is a good explanation for the development and progression of complications in diabetes, which is a significant increase in concentration MDA among diabetics and cardiovascular patients, but the highest increase in the group of patients with type 2 diabetes[23]. This may be a noticeable increase in firing MDA is attributed to peroxidative damage to lipids from oxidative stress that develops during diabetes. There are many studies that support the theory of increased oxidative stress in diabetes by estimating MDA by reactive substances of Thio Barbituric Acid [24]. The study also found a significant increase in levels MDA in diabetes and cardiovascular disease compared to healthy controls[24].

In addition, in our study, we found a decrease in antioxidants represented by: GSH in patient groups compared to healthy people. This increase in oxidative stress is attributed to the decrease in antioxidants to combat oxidative stress to reduce oxidative damage. When the total antioxidant status is high and sufficient to combat oxidative stress, MDA levels are within normal limits and vice versa[25].

Conclusion:

We conclude, from what the results of the current study showed, that there is a correlation between levels of vitamin K2 concentration and type 1 and type 2 diabetes and cardiovascular disease, based on biochemical variables, and the relationship was negative inverse, as the higher the concentrations of the variables (HbA1c, RBS) for diabetics, the lower the concentration. Vitamin K2, and according to the results built by the study and interpreted in this research, there are several effects of vitamin K2, including its sensitivity to insulin, as well as its protection against arterial calcification and cardiovascular disease. Therefore, we recommend studying the effect of using vitamin K2 as a nutritional supplement in patients with diabetes and cardiovascular disease. As well as finding the health benefits of this vitamin in these cases of patients.

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