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PLASMA COENZYME Q10 LEVELS OF INDIVIDUALS WITH NEWLY DIAGNOSED TYPE 2 DIABETES AND DIABETES INDIVIDUALS WITH ADVANCED MICROALBUMINURIA: A COMPARATIVE STUDY

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ABSTRACT

Objective: *Diabetes is a chronic disease that causes the development of microalbuminuria. CoQ10 deficiency is common in people with type 2 diabetes. This study aims to evaluate whether coenzyme Q10 (CoQ10) levels are a risk factor for diabetes and microalbuminuria in newly diagnosed diabetes and advanced microalbuminuria.*

Material and Method: *The study was conducted with patients who came to the internal medicine outpatient clinic. Plasma CoQ10 and malondialdehyde (MDA) values of 90 people in total, including 30 people in each group, newly diagnosed Type 2 diabetes (Group D), diabetes mellitus with microalbuminuria (Group M), and the control group (Group C) were examined.*

Results: *There was no difference between plasma CoQ10 and MDA levels of newly diagnosed type 2 diabetes patients and those with microalbuminuria ($p>0.05$). There was a negative correlation between CoQ10 and fasting glucose and HbA1c in all groups ($p<0.05$). A positive correlation was observed between CoQ10 and MDA ($p<0.05$). CoQ10 level of the control group was found to be higher than Group D and M ($p<0.05$); the difference between Group M and Group D was not significant ($p>0.05$). As a result of regression analysis, increasing the CoQ10 value was found to have a protective effect on the risk of diabetes (95 %CI: $p=0.005$).*

Conclusion: *This study showed that individuals with low blood sugar and HbA1c had high CoQ10 levels. We think that CoQ10 can be considered a risk factor for diabetes, and further studies examining total CoQ10 and ubiquinol/ubiquinone ratio would be beneficial.*

Keywords: *Coenzyme Q10, malondialdehyde, microalbuminuria, oxidative stress, type 2 diabetes.*

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YENİ TEŞHİS EDİLEN TİP 2 DİYABETLİ BİREYLER İLE İLERİ MİKROALBÜMİNÜRİSİ OLAN DİYABETLİ BİREYLERİN PLAZMA KOENZİM Q10 DÜZEYLERİ: KARŞILAŞTIRMALI BİR ÇALIŞMA

ÖZET

Amaç: Diyabet, mikroalbuminüri gelişimine neden olan kronik bir hastalıktır. Tip 2 diyabetli kişilerde CoQ10 eksikliği yaygındır. Bu çalışmanın amacı, yeni tanı diyabetli ve ileri mikroalbüminürili diyabetlilerde koenzim Q10 (CoQ10) düzeylerinin diyabet ve mikroalbümüri için risk faktörü olma durumunun değerlendirilmesidir.

Materyal ve Metot: Çalışma dahiliye polikliniğine başvuran hastalar ile yapıldı. Her grupta 30'ar kişi olmak üzere, yeni tanı almış Tip 2 diyabet (Grup D), mikroalbüminürili diabetes mellitus (Grup M) ve kontrol grubu (Grup C) toplam 90 kişinin plazma CoQ10 ve MDA değerleri incelendi.

Bulgular: Yeni tanı almış tip 2 diyabet hastalarının plazma CoQ10 ve malondialdehit (MDA) düzeyleri ile mikroalbuminürisi olan hastalar arasında fark yoktu (p>0,05). Tüm gruplarda CoQ10 ile açlık glukoz ve HbA1c düzeyleri arasında negatif korelasyon vardı (p<0.05). CoQ10 ve MDA ortalamaları arasında pozitif korelasyon gözlendi (p<0,05). Kontrol grubunun CoQ10 düzeyi yeni tanı almış diyabetli grup ve mikroalbuminürisi olan gruptan yüksek bulundu (p<0,05); Grup M ve Grup D arasındaki fark anlamlı değildi (p>0,05). Regresyon analizi sonucunda CoQ10 değerinin artırılmasının diyabet riski üzerinde koruyucu etkisi olduğu tespit edildi (%95 GA; p=0,005).

Sonuç: Kan şekeri ve HbA1c'si düşük olan bireylerin CoQ10 düzeyinin yüksek olduğu belirlendi. CoQ10'un diyabet için bir risk faktörü olarak değerlendirilebileceğini ve toplam CoQ10 ve ubiquinol/ubiquinone oranının inceleneceği ileri çalışmaların faydalı olacağını düşünüyoruz.

Anahtar kelimeler: Koenzim Q10, malondialdehit, mikroalbüminüri, oksidatif stres, tip 2 diyabet.

INTRODUCTION

Diabetes mellitus (DM) is a common chronic disease that increases blood glucose levels due to the deficiency, insufficiency or use of insulin secreted by the pancreas due to genetic, inflammatory and metabolic stress.[1] High blood glucose level is a marker of uncontrolled DM. As the disease progresses, increased blood glucose can cause irreversible damage to the heart, blood vessels, eyes, kidneys and nerve tissue. In 2021, the global prevalence of diabetes between 20 and 79 was 10.5% (536.6 million people) and will rise to 12.2% (783.2 million) in 2045. In addition, global diabetes-related health expenditures are estimated to be US$ 966 billion by 2021 in Turkey and to reach US$ 1.054 billion by 2045.[2]

According to the estimation of the World Health Organization, in 2030, it has been reported that there will be 578 million diabetic patients worldwide, and the deaths due to complications arising from hyperglycemia in these patients will double.[3] The most common cause of diseases such as chronic kidney failure is diabetes. Kidney diseases develop in approximately one-third of type 1 diabetes patients and half of those with type 2 diabetes.[4] With the onset of diabetes, the glomerular filtration rate increases, causing the kidneys to increase in size by approximately 20%. After the hyperfiltration stage, microalbuminuria develops as the glomerular filtration rate declines to normal levels.[5] The increase in some oxygen agents, such as reactive oxygen species (ROS), formed when nutrients such as dietary fat and glucose are converted to ATP in the mitochondria, has been associated with increased insulin resistance.[6] CoQ10 deficiency is observed in the mitochondria of insulin-resistant adipose and muscle tissues. CoQ10 is a fat-soluble antioxidant molecule important in oxidative phosphorylation, fatty acid, pyrimidine and lysosomal metabolism in all cells, both mitochondrial and extramitochondrial.[7,8] The reduction of mitochondrial coenzyme causes insulin resistance in adipocytes due to increased superoxide/hydrogen peroxide production.[9]

CoQ10 deficiency, especially ubiquinol (reduced CoQ10 form), is frequently observed in patients with type 2 diabetes. It has been reported that blood CoQ10 levels are significantly reduced in type 2 diabetic patients, associated with increased plasma glucose, HbA1c and oxidative stress markers. In a study conducted with 28 patients with diabetes and 10 healthy individuals, Malondialdehyde (MDA), a marker of oxidative stress, was found to be significantly higher in diabetic patients than in healthy individuals, and CoQ10 level, an indicator of antioxidant capacity, was found to be significantly lower in diabetic patients compared to healthy individuals.[10] There is also evidence that CoQ10 may benefit clinical status in patients with type II diabetes, chronic kidney disease,

and liver disease.[11] Mohammadi *et al*. reported that CoQ10 supplementation (200 mg/day for three months) significantly reduced HbA1c levels in type II diabetics.[12]

Similarly, Zahedi *et al*. found that CoQ10 supplementation (150 mg/day for three months) significantly improved fasting plasma glucose and HbA1c levels.[13] The benefit of CoQ10 supplementation on glycemic control and blood lipid levels was confirmed in a recent meta-analysis by Zhang *et al*.[14]

This study aims to examine the plasma levels of malondialdehyde (MDA) and coenzyme Q10 (CoQ10), which are markers of oxidative stress, in newly diagnosed DM patients and DM patients with microalbuminuria and whether there is a difference between these parameters and healthy individuals. However, it is to investigate whether plasma CoQ10 levels of patients with diabetes mellitus are a predictor of diabetes and its complication, microalbuminuria.

MATERIAL AND METHOD

Study Design and Participants

This cross-sectional study was conducted with 90 volunteers aged between 20 and 55 who applied to the Internal Medicine outpatient clinic of Health Sciences University Istanbul Bağcılar Training and Research Hospital between April 2018 and April 2019.

After obtaining their informed consent, the study participants were divided into 3 groups, 30. The first group consists of individuals with newly diagnosed diabetes (Group D), the second group consists of diabetic individuals with severe microalbuminuria (≥300 mg/g) (mean age of diabetes 4.96±3.11 years) (Group M), and the third group is the control group (Group C), which consists of healthy individuals. Ethics committee approval for this study was obtained from the Ethics Committee of Health Sciences University Istanbul Bağcılar Training and Research Hospital (No:2018.03.3.05.036).

Individuals with newly diagnosed Type 2 diabetes mellitus, individuals with diabetes mellitus who developed microalbuminuria, and healthy individuals who volunteered to participate in the study were included in the study. Individuals with a history of type 1 diabetes mellitus, coronary heart failure, liver disease, cancer, kidney failure, cerebrovascular disease, pregnant, alcohol and cigarette users, and those taking antioxidant nutritional supplements were not included in this study.

Data Collection

A dietitian took the height and body weight of the individuals participating in the study under anthropometric measurement standards, and the body mass index (BMI) was calculated with the formula body weight (kg)/height (m^2) Fasting glucose, HbA1c, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride, microalbuminuria, AST, ALT, urea, creatinine, MDA and CoQ10 levels of individuals in the morning hours after fasting for at least 8 hours were measured by the nurse in straight tubes.[15] Blood samples were taken into biochemistry tubes with a gel clot activator and kept until coagulation occurred, and then their serums were separated by centrifugation at 4000 g for 10 minutes. The separated sera were portioned and taken into Eppendorf tubes without additives, stored at -80°C, and then analyzed in bulk.

Malondialdehyde and Coenzyme Q10 Analysis

MDA analysis Human Malondialdehyde ELISA Kit and Coenzyme Q10 analysis were performed with Human Coenzyme Q10 ELISA Kit.[16,17]

Statistical Analysis

This study performed statistical analyses with the NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program. In evaluating the data, besides descriptive statistical methods (mean, standard deviation, median, interquartile range), the distribution of variables was examined with the Shapiro-Wilk normality test. One-way analysis of variance was used for the comparisons of normally distributed variables, Tukey multiple comparison test was used for subgroup comparisons, Kruskal Wallis test was used for intergroup comparisons of non-normally distributed variables, Dunn's multiple comparison test was used for subgroup comparisons, chi-square test was used for qualitative data comparisons, Pearson correlation test was used to determine the relations of the variables with each other. Factors affecting the risk of diabetes were examined using Binary Logistic Regression Analysis and the Backward Wald method. The results were evaluated at the significance level of $p<0.05$.

RESULTS

Twenty-three (76.67%) of 30 newly diagnosed individuals with diabetes (Group D) were included in the study, individuals with diabetes (Group M) who developed microalbuminuria, and 17 (56.67%) of the control group (Group C) were male. The mean age of Group D was 45.83±6.55 years, the mean age of

Table 1. Age and anthropometric characteristics of the groups by gender

	Group D			Group M			Group C				
Variables	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	p^1	p^2
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**		
Gender	23 (%76.67)	7 (%23.33)	30 (%100)	17 (%56.67)	13 (%43.33)	30 (%100)	17 (%56.67)	13 (%43.33)	30 (%100)		
	Mean±SD	**Mean±SD**	**Mean±SD**	**Mean ±SD**	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Mean±SD**		
Age (years)	46±7.06	46±4.97	45.83±6.55	48.35±5.17	47.08±6.58	47.80±5.75	37.71±10.75	41.38±5.49	39.3±8.93	0.006	0.038
Body weight (kg)	86.09±16.17	68.43±12.57	81.97±16.99	84.35±14.43	85.62±23.02	84.9±18.29	75.29±10.2	67.38±9.06	71.87±10.36	0.017	0.062
Height (cm)	171.48±7.3	157±5.94	168.1±9.3	173.71±5.59	160.54±5.32	168±8.5	171.65±5.43	161.15±6.18	177.1±7.75	0.472	0.402
BMI (kg/m²)	29.2±4.29	27.8±5.39	28.86±4.5	27.85±3.77	33.18±8.49	30.16±6.7	25.5±2.87	25.84±2.09	25.66±2.5	0.004	0.089

SD: Standard deviation, ***:** Kruskal Wallis test (***p1*:** Between groups for male. ***p2*:** Between groups for female) **BMI:** Body Mass Index, Group **D:** Diabetes group, Group **M:** Microalbuminuria Group, **Group C:** Control Group

Group M was 47.80±5.75 years, and the mean age of Group C was 39.3±8.93 years ($p<0.05$). The mean BMI of the individuals participating in the study is 28.86±4.5 kg/m² in Group D, 30.16±6.7 kg/m² in Group M and 25.66±2.5 kg/m² in Group C. While the mean BMI between the groups was statistically significant in males ($p>0.05$), the difference was statistically insignificant in females ($p>0.05$) (Table 1).

The blood cholesterol level of Group C (179.97±40.36 mg/dL) was found to be statistically significantly lower than Group D (223.73±56.78 mg/dL) ($p<0.05$). A statistically significant difference was found between the Direct LDL mean of Group D, Group M and Group C ($p=0.001$). Blood triglyceride levels of Group D (244.53±154.3 mg/dL) and Group M (191.13±126.24 mg/dL) were statistically significant than Group C (97.17±44.43 mg/dL) ($p=0.001$). HbA1c, glucose, and ALT levels were lower in Group C than in other groups ($p=0.001$). No statistically significant difference was observed between the groups in HDL cholesterol, urea, creatinine, AST and CoQ10 levels ($p>0.05$). MDA level was statistically significantly higher in Group C (12.18 nmol/ml) compared to Group D (4.95 nmol/ml) and Group M (4.22 nmol/ml) ($p<0.005$) (Table 2). The microalbuminuria level of Group C was 0.93±0.63 mg/dL, compared to Group D (4.04±5.1 mg/dL) and Group M (43.07±28.55 mg/dL) and was statistically significantly lower ($p=0.001$). In addition, Group D's microalbuminuria level was statistically significantly lower than Group M's ($p=0.0001$) (Table 2). Group D's microalbumin/creatinine ratio was statistically significantly lower than Group M's ($p<0.05$). Although the CoQ10 level of Group C was higher than the other groups, the difference between the groups was not statistically significant ($p>0.05$). The MDA level of Group C was found to be statistically significantly higher than Group D and Group M ($p=0.023$, $p=0.002$). Mean MDA was insignificant between Group D and Group M ($p=0.333$) (Table 2).

Table 2. Biochemical parameters of the groups

Biochemical Parameter	**Group D**	**Group M**	**Group C**	***p***
	Mean±SD	**Mean±SD**	**Mean±SD**	
Cholesterol (mg/dL)	223.73±56.78	201.47±43.35	179.97±40.36	0.003*
Direct LDL (mg/dL)	148.59±39.47	132.77±29.59	114.47±28.8	0.001*
HDL Cholesterol (mg/dL)	51.4±36.09	47.46±8.9	48.1±12.37	0.770*
Triglyceride (mg/dL)	244.53±154.3	191.13±126.24	97.17±44.43	0.001*
Urea (mg/dL)	28.06±5.39	32.51±9.26	29.43±8.79	0.094*
Creatinine (mg/dL)	0.72±0.13	0.76±0.23	0.69±0.17	0.324*
AST (IU/L)	24.68±13.74	28.38±16.69	21.47±6.64	0.232‡
ALT (IU/L	36.06±30	36.51±27.4	21.43±16.47	0.001‡
HbA1c (%)	10.2±2.39	9.18±1.9	5.45±0.44	0.001*
Glucose (mg/dL)	239.94±72.3	208.3±70.69	88.4±8.38	0.001*
Microalbuminuria spot urine (mg/dL)	4.04±5.1	43.07±28.55	0.93±0.63	0.001‡
Microalbumin/creatinine (mg/g)	26.65±34.33	410.33±333.08	5.33±2.79	0.001‡
CoQ10 (ng/mL)	26.12±42.08	15.4±14.78	51.88±54.96	0.491‡
MDA (nmol/ml)	10.9±16.84	6.65±10.34	22.46±22.42	0.005‡

$\bar{x}$: Average value, **SD:** standart deviation, ***:** One-Way analysis of variance, **‡:** Kruskal Wallis test
Group D: Diabetes group, **Group M:** Microalbuminuria Group, **Group C:** Control Group, **LDL:** low-density lipoprotein, **HDL:** high-density lipoprotein. **AST:** Aspartate Aminotransferase, **ALT:** Alanine transaminase, **HbA1c:** glycated haemoglobin, **CoQ10:** Coenzyme Q10, **MDA:** malondialdehyde

The difference between microalbuminuria level and microalbumin/creatinine values between Group D and Group M was statistically significant ($p=0.001$). The difference between Group D and Group C glucose, HbA1c, cholesterol, direct LDL, triglyceride, ALT, MDA, microalbuminuria, microalbumin/creatinine levels and body weight, and BMI values was statistically significant ($p<0.05$). The difference in body weight, BMI and glucose, HbA1c, triglyceride, ALT, MDA, microalbuminuria, and microalbumin/creatinine ratio between Group M and Group C was statistically significant ($p<0.05$). When the CoQ10 level of Group C was compared with Group D and Group M, the difference was statistically significant ($p<0.05$). In contrast, the difference between Group D and Group M was not statistically significant ($p>0.05$) (Table 3).

No statistically significant negative correlation was observed between CoQ10 levels and glucose (r:-0.029, *p*:0.789) and HbA1c (r:-0.024, *p*:0.819) values of all individuals. A statistically significant negative correlation was found between MDA levels and glucose (r:-0.364, *p*:<0.001) and HbA1c (r:-0.354, *p*:<0.001) values. A statistically significant positive correlation was found between CoQ10 and MDA in all individuals (r=0.656, *p*<0.001). A statistically significant negative correlation was observed between CoQ10 values and glucose values of Group C (r=-0.402 *p*=0.028).

As a result of regression analysis, increasing the CoQ10 value was found to have a protective effect on the risk of diabetes (95% CI: *p*=0.005). It was determined that increasing the BMI value increased the likelihood of diabetes by 1.306 times (*p*=0.003) (Table 4).

DISCUSSION

In cases where blood glucose levels cannot be controlled in individuals with type 2 diabetes, neuropathy, nephropathy, visual impairment, lower extremity diseases, amputations, permanent damage to organs and cardiovascular diseases that cause significant morbidity and mortality may develop. However, diabetes; is a treatable disease that allows people to live a healthy and long life.[3] Diabetes mellitus is the most common cause of diabetic nephropathy, chronic renal failure and end-stage renal disease. Kidney diseases develop in approximately one-third of type 1 diabetes patients and half those with type 2 diabetes.[4] CoQ10, a vitamin-like substance, plays a decisive role in energy production and scavenging activity of free oxygen radicals in human cells. Most of the concentration of CoQ10 represents tissues and organs with high energy consumption needs. Decreased CoQ10 level is associated with antioxidative imbalance. It has been stated that CoQ10 is the antioxidant that has the most effect in the initial stages of lipid peroxidation, and oral supplementation has been recommended.[18] It has been reported that vascular complications increase, and lipid peroxidation occurs due to hyperglycemia in diabetic individuals. However, it has been reported that diabetic vascular complications occur with the increase of oxidative stress and peroxidation of lipid and LDL-cholesterol in the membranes.[19] In another study, positive correlations were found between the LDL-chole/CoQ10 ratio, considered a risk factor for atherosclerosis, and the total-arm/HDL-chole ratio. CoQ10 content in single lipoprotein classes has been reported to be closely related to CoQ10 plasma concentration.[20] In our study, the blood cholesterol level of Group C was statistically significantly lower than that of Group D, and the mean LDL was statistically significantly lower than both groups of individuals with diabetes. In our study, no statistically significant difference was found between HDL cholesterol levels of all groups.

Table 3. Comparison of anthropometric and biochemical parameters between groups

	Group D / Group M	Group D / Group C	Group M / Group C
Body weight (kg)*	0.748	0.037	0.005
BMI (kg/m²)*	0.559	0.034	0.002
Glucose (mg/dL)*	0.097	0.001	0.001
HbA1c (%)*	0.073	0.001	0.001
Cholesterol (mg/dL)**	0.169	0.002	0.19
Direct LDL(mg/dL)**	0.157	0.001	0.086
Triglyceride (mg/dL)**	0.191	0.001	0.008
AST (IU/L)*	0.518	0.608	0.106
ALT(IU/L)***	0.673	0.004	0.001
Microalbuminuria spot urine (mg/dL)**	0.001	0.001	0.001
Microalbumin/creatinine (mg/g)**	0.001	0.001	0.001
CoQ10 (ng/mL)*	0.569	0.043	0.002
MDA(nmol/ml)*	0.333	0.023	0.02

:** Tukey Multiple Comparison Test, *:** Dunn's Multiple Comparison Test, **Group D:** Diabetes group, **Group M:** Microalbuminuria Group, **Group C:** Control Group, **BMI:** Body mass index, **HbA1c:** glycated haemoglobin, **LDL:** low-density lipoprotein, **AST:** Aspartate Aminotransferase, **ALT:** Alanine transaminase, **CoQ10:** Coenzyme Q10, **MDA:** malondialdehyde

Table 4. Binary Logistic Regression Analysis Results

	Group		Univariate	
	Group C	**Group D+Group M**	**OR (95% CI)**	***p***
CoQ10 (ng/mL)	51.88±54.96	20.76±31.73	0.983 (0.971-0.995)	0.005
MDA (nmol/ml)	22.46±22.42	8.77±14.02	0.959 (0.933-0.986)	0.003
Age (years)	39.3±8.93	46.82±6.19	1.14 (1.066-1.22)	<0.001
Cholesterol (mg/dL)	179.97±40.36	212.6±51.33	1.016 (1.005-1.027)	0.006
Direct LDL(mg/dL)	114.47±28.8	140.68±35.49	1.025 (1.009-1.042)	0.002
HDL Cholesterol (mg/dL)	48.1±12.37	49.43±26.13	1.003 (0.982-1.025)	0.791
Triglyceride (mg/dL)	97.17±44.43	217.83±142.34	1.018 (1.009-1.028)	<0.001
Urea (mg/dL)	29.43±8.79	30.29±7.84	1.014 (0.958-1.073)	0.635
Creatinine (mg/dL)	0.69±0.17	0.74±0.18	5.43 (0.402-73.262)	0.203
AST (IU/L)	21.47±6.64	26.53±15.27	1.043 (0.991-1.098)	0.108
ALT(IU/L)	21.43±16.47	36.28±28.49	1.046 (1.006-1.087)	0.023
HbA1c (%)	5.45±0.44	9.69±2.2	272.452 (2.876-25809.745)	0.016
Glucose (mg/dL)	88.4±8.38	224.12±72.67	1.267 (1.051-1.526)	0.013
BMI (kg/m²)	25.66±2.54	29.51±5.7	1.306 (1.098-1.554)	0.003

Univariate regression analysis, Cox & Snell R^2= %69.2, Snell R^2= %96.2

Group D: Diabetes group, **Group M:** Microalbuminuria Group, **Group C:** Control Group, **CoQ10:** Coenzyme Q10; **MDA:** malondialdehyde, **LDL:** low-density lipoprotein, **HDL:** high-density lipoprotein, **AST:** Aspartate Aminotransferase, **ALT:** Alanine transaminase, **HbA1c:** glycated haemoglobin, **BMI:** body mass index

According to Abdollahzad *et al.*'s study on rats, serum ALP, ALT and AST activity as markers of liver function in diabetic rats who did not receive CoQ10 supplementation were significantly increased compared to the control group.[21] In our study, no statistically significant difference was observed in the AST averages of the liver function tests of our 3 groups. In contrast, the ALT average of Group C was

significantly lower than the other groups. In addition, no statistically significant difference was observed between the newly diagnosed diabetes group and the diabetes group with microalbuminuria.

When the CoQ10 level of Group C was compared with Group D and Group M, the difference was statistically significant. In contrast, the difference between Group D and Group M was insignificant. When the plasma MDA and CoQ10 levels of individuals with newly diagnosed diabetes and those with microalbuminuria were compared, no statistically significant difference was found. Plasma CoQ10 deficiency, particularly ubiquinol (reduced CoQ10 form), is frequently observed in individuals with type 2 diabetes. The ubiquinol/ubiquinone ratio is generally a good marker for oxidative stress. Ubiquinone levels generally increase at low ubiquinol levels, indicating an ineffective conversion between ubiquinone and ubiquinol. It also indicates that the body's ability to scavenge free radicals is reduced.[22] El-ghoroury *et al*. in their study with 28 diabetic patients and 10 healthy individuals, found that MDA, a marker of oxidative stress, was significantly higher in diabetic patients than in healthy individuals, and CoQ10, an indicator of antioxidant capacity, was significantly lower in diabetic patients than in healthy individuals.[10]

Our study observed a negative correlation between CoQ10 levels and fasting glucose values. In another study by Samimi *et al*. conducted on rats, CoQ10 supplementation caused a significant reduction in MDA levels and a significant improvement in lipid profiles.[23] According to an analysis by Huang *et al*. of the effect of CoQ10 on the cardiovascular and metabolic biomarkers in obese individuals with type 2 diabetes, CoQ10 supplementation has been reported to have beneficial effects on fasting blood glucose, HbA1c and triglyceride concentrations in obese type 2 diabetes patients.[24] Our study found a negative correlation between CoQ10 and fasting glucose and HbA1c.

It has been reported that CoQ10 supplementation has beneficial effects on glucose metabolism and malondialdehyde levels in patients with diabetic nephropathy.[25] Raygan *et al*., compared with the placebo, daily intake of 100 mg CoQ10 supplementation for 8 weeks in metabolic syndrome patients had beneficial effects on serum insulin levels and HOMA-IR. However, no effect was observed in fasting plasma glucose, lipid concentrations and inflammatory markers.[26] Our study observed a negative correlation between CoQ10 and fasting blood glucose and HbA1c. Other studies have not shown a significant effect on plasma CoQ10 levels and HbA1c, fasting blood sugar.[27,28]

Gholami *et al*. stated that the decrease in antioxidant defense in type 2 diabetes patients is due to CoQ10 deficiency, and CoQ10 deficiency leads to the pathogenesis and complications of Type 2 diabetes. In their study where they made 100 mg/day CoQ10 supplementation for 12 weeks in women with type 2 diabetes. They stated that CoQ10 supplementation caused a decrease in MDA levels, which could lead to a decrease in oxidative stress.[29] It is considered that antioxidants such as CoQ10 may be a promising therapeutic strategy in preventing or improving diabetic complications due to increased oxidative stress indicators and low antioxidant levels in individuals with diabetes.[30,31] Mewaza *et al*. reported that taking ubiquinol, the reduced form of CoQ10, in addition to routine drugs used in the treatment of type 2 diabetes, significantly improved glycemic control and improved insulin secretion in healthy volunteers, but they could not detect a significant difference in MDA and LDL levels.[32] Uncontrolled hyperglycemia in diabetic patients generates large amounts of free radicals due to the oxidation of glucose and glycosylation of proteins.[33] Lipid hydroperoxides can decompose into several aldehydes, such as malondialdehyde and 4-hydroxy-2-nonenal, which can disperse from their production sites and oxidize protein or DNA, causing further damage. The reduced form of ubiquinol, coenzyme Q10, functions as an electron donor, preventing the initiation and propagation of lipid peroxidation.[34] According to the study of Fatani *et al*., in the type 2 diabetes group with uncontrolled blood sugar, mean HbA1c increased significantly compared to the type 2 diabetes group with blood sugar under control, and MDA, which expresses lipid peroxidation; it was found in the type 2 diabetes group with blood sugar under control and higher than the type 2 diabetes group.[35] Our study found no statistical difference between the diabetic patient group and the diabetic patient group with microalbuminuria regarding MDA levels. It has been reported that MDA concentration is significantly higher in individuals with type 2 diabetes and impaired glucose tolerance.[36,37] Another study reported that patients with controlled blood glucose levels had lower serum MDA and HbA1c levels, and oxidative sensitivity decreased as glycemic control increased.[38] It was determined that there was no significant difference between the MDA levels of individuals with diabetes who developed diabetic nephropathy and those with diabetes who did not. However, the MDA level of the control group was lower when compared to the healthy control group.[39] In our study, CoQ10 and MDA levels were similar in newly diagnosed diabetes patients and diabetic patients with microalbuminuria.

CONCLUSION

Although there was no statistically significant difference in CoQ10 and MDA blood levels between newly diagnosed type 2 diabetic patients and type 2 diabetic patients with advanced microalbuminuria, a statistically significant negative correlation was found between CoQ10 and fasting glucose and HbA1c levels. In this study, total CoQ10 level was examined. In terms of the importance of future studies, it is recommended to examine the ubiquinol/ubiquinone ratio along with total CoQ10. Individuals with diabetes are exposed to intense oxidative stress, which affects blood sugar regulation and antioxidant defense mechanisms; Therefore, we think that low CoQ10 level may be a risk factor for possible complications of diabetes and further studies may be useful.

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Author Contribution

Osman Yıldırım, Birsen Demirel, and Erdal Gündoğan designed the research. Osman Yıldırım, Birsen Demirel, and Hande Seven Avuk performed the research, analyzed, and interpreted the data. Osman Yıldırım and Erdal Gündoğan contributed to sample collection in policlinics. Osman Yıldırım, Birsen Demirel, and Hande Seven Avuk wrote the manuscript. All the authors had primary responsibility for the final content, and all authors reviewed the manuscript rigorously and approved the final version submitted for publication.

*The authors declare that there are no conflicts of interest.

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