Research Article

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The effect of Ramadan fasting on renal functions in patients with chronic kidney disease

[Kronik Böbrek Yetmezlikli Hastalarda Oruç Açlığının Renal Fonksiyonlar Üzerine Etkisi]

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Abstract

Objective: We aimed to investigate the effects of Ramadan fasting on renal functions in patients with stage 3 and 4 chronic kidney disease.
Materials and methods: The study was conducted in Ramadan month which was between June and July. Patients were evaluated before Ramadan, the week immediately following the end of the Ramadan, and 3 and 6 months after Ramadan.
Results: Twenty-four fasting (mean age of 68 ± 13 years) and 55 non-fasting individuals (mean age of 69 ± 9 years) were included in this study. There was no statistically significant difference for creatinine levels in the first week after Ramadan in both groups compared to levels before Ramadan ($p = 0.070$, $p = 0.470$, respectively). The groups were compared according to the criteria of deterioration in renal function (reduction of 25% in GFR and 30% increase in serum creatinine levels). There were no statistically significant differences between the two groups according to these two criteria ($p = 0.452$, $p = 0.660$, respectively). In univariate and multivariate logistic regression analysis, the presence of diabetes mellitus and proteinuria were found to be independent risk determinants of renal dysfunction.
Conclusion: Patients with diabetes mellitus and prominent proteinuria may constitute critical patient groups for renal function deterioration during Ramadan fasting.

Keywords: Chronic kidney disease; diabetes mellitus; fasting; proteinuria; Ramadan.

Öz

Amaç: Evre 3 ve 4 kronik böbrek hastalarında Ramazan orucunun renal fonksiyonlar üzerindeki etkisini araştırmayı amaçladık.
Gereç ve yöntem: Çalışma haziran ve temmuz aylarına denk gelen Ramazan ayında yapıldı. Hastalar Ramazan öncesinde, Ramazan bitimini takip eden ilk haftada, 3. ay ve 6. ayda değerlendirildi.
Bulgular: Çalışmaya oruç tutan 24 kişi (ortalama yaşları 68 ± 13 yıl) ve oruç tutmayan 55 kişi (ortalama yaşları 69 ± 9 yıl) dahil edildi. Her iki grupta da Ramazan öncesindeki ve Ramazan ayını takip eden ilk haftadaki serum kreatinin düzeyleri arasında anlamlı farklılık yoktu (sırasıyla $p = 0.070$, $p = 0.470$). Gruplar renal fonksiyonlarda bozulma kriterlerine (GFH'da % 25'in üzerinde azalma ve serum kreatinin düzeylerinde % 30'dan fazla artış) göre karşılaştırıldı. Bu iki kritere göre gruplar arasında istatistiksel olarak anlamlı farklılıklar yoktu (sırasıyla $p = 0.452$, $p = 0.660$). Univariate ve multivariate lojistik regresyon analizlerinde diabetes mellitus ve proteinürinin varlığı renal fonksiyon bozukluğunun bağımsız risk belirleyicileri olarak saptandı.
Sonuç: Diabetes mellitusu ve belirgin proteinürisi olan hastalar Ramazan orucu açlığında böbrek fonksiyonlarında bozulma için riskli hasta gruplarını oluşturabilir.

Anahtar Kelimeler: Kronik böbrek hastalığı; diabetes mellitus; oruç; proteinüri; ramazan.

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Introduction

Ramadan month is a 30-day period in which Muslims abstain from eating, drinking and sexual contact during daylight hours each year. In this period, unhealthy adults, pregnant cases or women during menstrual period and travelers are not obliged to fast [1]. In Ramadan, people remain hungry and thirsty in summer for approximately 17 h during the fast. There are also serious nutritional differences during the day. However, many patients fast even though they have serious illnesses, such as chronic kidney disease (CKD), diabetes mellitus (DM) or hypertension (HT) [2]. Since the Arabic calendar employs a lunar cycle, the Arabic year contains 354 days. So, Ramadan moves 11 days every year and therefore can occur during any of the four seasons [3].

Studies of healthy people have shown that Ramadan fasting is safe [4, 5] and may be beneficial in terms of blood pressure, blood lipid levels, oxidative stress, insulin sensitivity, and chronic heart disease [5, 6]. In healthy individuals, Ramadan fasting does not cause abnormalities in urine volume, osmolality, pH, urinary excretion of solutes and electrolyte, serum urea, creatinine, sodium and potassium [7]. Ramadan fasting may also be safe in diabetic patients [2], renal transplant recipients [8] and patients with urinary stones [9].

CKD is defined as kidney damage or an estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m^2 persisting for 3 months or more irrespective of the cause. CKD is classified according to Kidney Disease: Improving Global Outcomes (KDIGO guidelines) into Stage 1/G1 (eGFR ≥90 mL/min per 1.73 m^2), Stage 2/G2 (eGFR = 60–89 mL/min per 1.73 m^2), Stage 3/G3a (eGFR = 45–59 mL/min per 1.73 m^2), Stage 3b/G3b (eGFR = 30–44 mL/min per 1.73 m^2), Stage 4/G4 (eGFR = 15–29 mL/min per 1.73 m^2), and Stage 5/G5 (eGFR <15 mL/min per 1.73 m^2). Proteinuria is classified into normal or mild increase/A1 (spot urine protein-creatinine ratio [PCR] <150 mg/g), moderate increase/A2 (spot urine PCR = 150–500 mg/g) and severe increase/A3 (spot urine PCR >500 mg/g) [10].

In previous studies, the effects of Ramadan fasting were investigated in patients with CKD [3], under hemodialysis [11] and peritoneal dialysis treatment [12]. These studies have shown that long-term Ramadan fasting is tolerable. But, severe dehydration, renal damage after hyperviscosity and electrolyte disturbances can occur in patients with CKD during long summer days [13]. Dehydration can cause bigger problems, especially in the elderly. In this patient population there are problems with overfeeding and adaptation to the CKD diet during the *Suhur* period *before dawn*. In Muslim countries like Turkey, risk assessments of patients with CKD who want to fast in Ramadan are needed. The possible complications are unknown according to the disease stage, and how to regulate the medication; moreover, there is no definite consensus on risk assessment and recommendations in this respect.

Therefore, we aimed to investigate the short and long-term effects of Ramadan fasting on renal functions in patients with stage 3 and 4 CKD.

Materials and methods

This prospective study was carried out at Hitit University, Erol Olçok Training and Research Hospital after obtaining written informed consent from all participants and approval of the local ethics committee.

This study was conducted in Ramadan, between June and July. The study included 24 fasting patients (11 females) and 55 non-fasting patients (29 females). Individuals over 18 years of age with at least 6 months of stage 3 and 4 CKD were included in this study. These patients were stable for the last 3 months in terms of renal progression. Patients with mild levels of renal damage defined as CKD stage 1 and 2 and patients with advanced renal damage of CKD stage 5 with high dehydration risk were not included in the study. Patients who were under 18 years of age, had active infection within the last month, had acute coronary and cerebrovascular events, had uncontrolled DM and HT, had acute renal damage in CKD, were receiving hemodialysis and peritoneal dialysis treatment, and had renal transplant were excluded from the study.

CKD etiology in patients were as follows: HT in 35, DM in 36, chronic glomerulonephritis in 1, polycystic kidney disease in 2, urological reasons in 4, and amyloidosis in 1 patient. The patients were evaluated for the presence of DM, HT, peripheral artery disease [PAD], coronary artery disease [CAD; angina, myocardial infarction], heart failure, lung disease [chronic obstructive pulmonary disease, bronchial asthma, asbestosis, occupational lung disease], and cerebrovascular disease [CVD; transient ischemic attack, stroke, etc.]. Concurrent medications that the patients had been receiving were recorded.

They were asked whether they would fast during the Ramadan month or not. Patients who would like to fast based on their own wishes were identified as the fasting group. Those who would not like to fast were identified as the non-fasting group. Patients were evaluated before Ramadan, the week immediately following the end of Ramadan, and 3 and 6 months later.

All patients were initially evaluated by the same nephrologist and dietician. Patients were warned not to spend a long time in the sun, as well as to get enough fluid after *Iftar at sunset* (1.5–2 L of fluid). Patients with signs of dehydration were advised to be hospitalized immediately. The medications and diets were re-arranged according to the time of *Iftar at sunset* and *Suhur before dawn*. Oral antidiabetic drugs and used insulin doses were reduced by one-third or one-half. Diabetic patients were advised to monitor their blood glucose levels four times daily in the following order; before fasting (*Suhur* time), in the middle of day, before eating dinner, and at midnight. These patients had a fasting period of approximately 17 h. Patients at risk for hyperkalemia and metabolic acidosis were recruited during the first week of the fast. Biochemical parameters were studied at specified times for the patients. Deterioration of renal functions was defined as ≥30% rise in serum creatinine and/or ≥25% decrease in glomerular filtration rate (GFR) levels from baseline after Ramadan [10]. No patient was excluded during the study duration.

Blood samples were collected after 12-h fasting in the morning. The serum samples were centrifuged at 1500 *g* for minutes to obtain serum and use it for the analysis of biochemical parameters [sodium (Na), potassium (K), calcium (Ca), phosphorus, blood urea nitrogen (BUN), serum creatinine (Cr), uric acid, albumin, parathormone (PTH), ferritin]. Hemoglobin and HCO_3 measurements were made using standard methods in the routine clinical laboratory. Serum creatinine levels were measured with the calorimetric Jaffe method. Proteinuria levels were calculated according to the ratio of protein/creatinine in the morning spot urine.

Biochemical blood parameters, spot urine protein and creatinine tests were measured photometrically with standard measurement methods using commercial kits with a Beckman Coulter AU5800 autoanalyzer. Full blood counts were measured with standard measurement method using commercial kits with a Mindray BC 5800 automated full blood count device. The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula [10]. Patients had arterial pressure (AP) values taken as the mean of three measurements taken on both arms.

Statistics

Statistical Package for the Social Sciences (SPSS) software version 23.0 (SPSS Inc, Chicago, IL, USA) was used for the statistical analysis. Data are presented as mean ± standard deviation or median (25^{th}–75^{th} Inter Quartile Range) as appropriate. Univariate and multivariate logistic regression analyses were used to assess the factors that predict the deterioration of renal functions in the fasting group after Ramadan. All reported p values were two-tailed, and those less than 0.05 were considered statistically significant.

Results

Twenty-four fasting (mean age of 68 ± 13 years) and 55 non-fasting individuals (mean age of 69 ± 9 years) were included in this study. Demographic characteristics, CKD etiologies, comorbidities and used medications are shown in Table 1. There was no statistically significant difference according to the age, gender, systolic and diastolic blood pressure values and CKD stages of fasting and non-fasting patients ($p = 0.890$, $p = 0.630$, $p = 0.522$, $p = 0.508$, $p = 0.256$, respectively).

There was no statistically significant difference between eGFRs of fasting and non-fasting groups before Ramadan ($p = 0.306$). There was also no statistically significant difference between the fasting and non-fasting groups in terms of proteinuria, albumin, HCO_3, PTH, Na, K, Ca, phosphorus, and uric acid values before Ramadan ($p = 0.218$, $p = 0.070$, $p = 0.741$, $p = 0.174$, $p = 0.07$, $p = 0.620$, $p = 0.885$, $p = 0.121$, $p = 0.898$, respectively) (Table 1).

There was no statistically significant difference among creatinine levels in both fasting and non-fasting groups during the sixth month of follow up (Tables 2 and 3). In the fasting group, the first- and third-month creatinine values remained increased compared to values before Ramadan, but it was not statistically significant. However, in the sixth month, creatinine levels were similar to levels before Ramadan ($p = 0.070$) (Table 2). In the non-fasting group, there was no increase in creatinine values compared to the values before Ramadan, and they remained close to these levels until the end of the sixth month ($p = 0.470$) (Table 3).

During the 6 months of follow-up, fluctuations in proteinuria levels were observed in the fasting group, but these fluctuations were not statistically significant ($p = 0.765$) (Table 2). In the non-fasting group, proteinuria decreased significantly at the end of the first month ($p = 0.035$), also there were statistically significant differences between the levels of proteinuria in the third and sixth months when compared to the values of the first month ($p = 0.034$, $p = 0.001$, respectively) (Table 3). Biochemical parameters of all groups for 6-months follow-up are presented in detail in Tables 2 and 3.

Table 1: The demographics, CKD etiology, co-morbid diseases, used drugs and comparison of initial laboratory parameters of groups.

	Fasting (n = 24)	Non-fasting (n = 55)	p-Value
Age (years)	68 ± 13	69 ± 9	0.890
Gender (M/F)	13/11	26/29	0.630
SBP (mmHg)	141 ± 22	138 ± 17	0.522
DBP (mmHg)	85 ± 13	83 ± 12	0.508
CKD etiology			
Diabetes mellitus, n (%)	12 (50)	24 (43.6)	0.631
Hypertension, n (%)	11 (45.8)	24 (43.6)	0.857
Chronic glomerulonephritis, n (%)	0	1 (1.8)	–
Polycystic kidney disease, n (%)	0	2 (3.6)	–
Urological Diseases, n (%)	1 (4.2)	3 (5.5)	0.810
Amyloidosis, n (%)	0	1 (1.8)	–
Co-morbid diseases			
Diabetes mellitus (Y/N)	10/14	27/28	0.543
Hypertension (Y/N)	23/1	52/3	0.810
CAD (Y/N)	14/10	22/33	0.132
HF (Y/N)	6/18	6/49	0.109
PAD (Y/N)	3/21	1/54	0.081
CVD (Y/N)	2/22	3/52	0.629
COPD (Y/N)	4/20	10/45	0.871
Used drugs			
ACEi/ARB (N/Y)	9/15	21/34	0.954
Beta blockers (N/Y)	12/12	29/26	0.823
CCB (N/Y)	13/11	24/31	0.388
Statine (N/Y)	16/8	41/14	0.472
Stage 4 n (%)	6 (25)	21 (38.2)	0.256
Stage 3 n (%)	18 (75)	34 (61.8)	
BUN (mg/dL)	27 (24–35)	33 (26–42)	0.119
Cr (mg/dL)	1.76 (1.47–2.05)	1.89 (1.63–2.20)	0.150
eGFR (mL/min/1.73 m^2)	35.2 (29.4–42.9)	34.1 (27.2–40.6)	0.306
Na (mEq/L)	141 (140–141)	140 (138–142)	0.073
K (mEq/L)	5.1 (4.8–5.5)	5.0 (4.5–5.6)	0.620
Ca (mg/dL)	9.3 ± 0.5	9.3 ± 0.5	0.885
Phosphorus (mg/dL)	3.3 (2.9–3.7)	3.5 (3.1–4.1)	0.121
Uric acid (mg/dL)	6.8 ± 1.2	6.8 ± 1.2	0.898
PTH (pg/mL)	88 (58–122)	100 (71–158)	0.174
Albumin (g/dL)	4.0 (3.7–4.3)	4.2 ± 0.3	0.070
HCO_3 (mmol/L)	22 (21–23)	21 (20–23)	0.741
Hb (g/dL)	12.4 ± 1.7	12.8 ± 1.6	0.351
Proteinuria (mg/g)	0.651 (0.276–2.420)	0.448 (0.142–0.980)	0.218

CKD, Chronic kidney disease; M, male; F, female; SBP, systolic blood pressure; DTA, diastolic blood pressure; CAD, coronary artery disease; HF, heart failure; PAD, peripheral artery disease; CVD, cerebrovasculary disease; COPD, chronic obstructive pulmonary disease; ACEi/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; CCB, calcium canal blockers; BUN, blood urea nitrogen; GFR, glomerular filtration rate; PTH, parathormone.

The groups were compared according to the criteria of deterioration in renal function (reduction of 25% in eGFR and/or 30% increase in serum creatinine levels). For the fasting group, 25% reduction in eGFR was observed in 12.5% of the patients and 30% increase in serum creatinine levels was seen in 12.5% of the patients; while in the non-fasting group, reduction of 25% in eGFR was observed in 7.3% of the patients and 30% increase in serum creatinine levels was seen in 16.4% of the patients. There was no statistically significant difference between groups for eGFR and creatinine levels ($p = 0.452$, $p = 0.660$, respectively). When the changes in eGFR were examined, no significant difference was found between the groups [–2.0 (–5.96 to 1.26) vs. –0.64 (–3.74 to 2.93)], in fasting and non-fasting groups, respectively, $p = 0.415$). There was also no significant difference between groups for change in proteinuria before and after Ramadan [–0.045 (–0.830 to 0.174)

Table 2: Biochemical parameters of fasting group before and after the 1st, 3rd and 6th month of Ramadan (n = 24).

	Before Ramadan	1st month	3rd month	6th month	p-Value
BUN (mg/dL)	27 (24–35)	32 (25–41)	35 (25–44)	33 (28–49)[a]	0.015
Cr (mg/dL)	1.76 (1.47–2.05)	1.84 (1.61–2.11)	2.08 (1.41–2.60)	1.78 (1.49–2.26)	0.070
GFR (mL/min/1.73 m^2)	35 (29–43)	34 (27–41)	33 (20–44)	35 (23–48)	0.183
Proteinuria (mg/g)	0.65 (0.28–2.42)	0.90 (0.25–1.62)	0.62 (0.25–1.84)	0.96 (0.23–2.99)	0.765
Na (mEq/L)	141 (140–141)	140 (138–141)	140 (138–141)	140 (139–141)	0.198
K (mEq/L)	5.1 (4.8–5.5)	5.1 (4.7–5.6)	5.2 (4.9–5.4)	5.0 (4.8–5.2)	0.651
Ca (mg/dL)	9.3 (9.0–9.7)	9.3 (8.9–9.8)	9.2 (8.9–9.5)	9.4 (8.9–9.7)	0.232
P (mg/dL)	3.3 (2.9–3.7)	3.3 (2.8–3.8)	3.2 (2.8–4.0)	3.4 (3.0–4.0)	0.567
Uric acid (mg/dL)	6.8 (5.9–7.7)	6.8 (5.8–7.9)	6.7 (5.9–8.0)	6.8 (5.7–8.4)	0.717
PTH (pg/mL)	88 (58–122)	89 (68–160)[b]	101 (64–149)	146 (88–178)[c]	0.014
HCO_3 (mmol/L)	22 (21–23)	22 (21–24)	22 (20–23)	22 (21–23)	0.444
Albumin (g/dL)	4.0 (3.7–4.3)	4.2 (3.8–4.3)	4.0 (3.8–4.4)	3.9 (3.7–4.4)	0.639
Ferritin (ng/mL)	55 (38–147)	79 (50–129)	86 (58–137)[d]	92 (95–163)[e]	0.002
Hb (g/dL)	12.4 ± 1.7	12.5 ± 2.1	12.6 ± 1.8	12.4 ± 1.8	0.828

[a]p = 0.004 vs. before Ramadan. [b]p = 0.041 vs. before Ramadan. [c]p = 0.014 vs. before Ramadan, p = 0.041 vs. 3rd month. [d]p = 0.004 vs. before Ramadan. [e]p = 0.014 vs. before Ramadan, p = 0.014 vs. 1st month.

Table 3: Biochemical parameters of non-fasting group before and after the 1st, 3rd and 6th month of Ramadan (n = 55).

	Before Ramadan	1st month	3rd month	6th month	p-Value
BUN (mg/dL)	33 (26–42)	32 (26–42)	33 (26–40)	32 (25–44)	0.937
Cr (mg/dL)	1.89 (1.63–2.20)	1.91 (1.67–2.30)	1.90 (1.56–2.21)	1.88 (1.59–2.18)	0.470
GFR (mL/min/1.73 m^2)	34.1 ± 9.0	33.3 ± 10.6	34.0 ± 10.6	35.5 ± 11.0	0.348
Proteinuria (mg/g)	0.45 (0.14–0.98)	0.37 (0.16–0.93)[a]	0.40 (0.18–1.03)	0.53 (0.21–0.97)	0.002
Na (mEq/L)	140 (138–142)	139 (137–141)	139 (138–141)	139 (138–141)	0.406
K (mEq/L)	5.0 (4.5–5.6)	5.0 (4.7–5.5)	5.0 (4.7–5.3)	4.8 (4.6–5.1)	0.059
Ca (mg/dL)	9.3 ± 0.5	9.3 ± 0.5	9.3 ± 0.5	9.2 ± 0.5	0.487
P (mg/dL)	3.5 (3.1–4.1)	3.5 (3.0–3.9)	3.5 (3.0–4.1)	3.5 (3.0–3.8)	0.800
Uric acid (mg/dL)	6.8 ± 1.2	7.2 ± 1.2	6.7 ± 1.2	6.6 ± 1.0	0.098
PTH (pg/mL)	100 (71–158)	94 (72–144)	96 (68–148)	99 (78–140)	0.198
HCO_3 (mmol/L)	21 (20–23)	23 (20–24)	23 (21–24)	23 (22–24)	0.226
Albumin (g/dL)	4.2 ± 0.3	4.2 ± 0.3	4.1 ± 0.3[b]	4.1 ± 0.4	0.043
Ferritin (ng/mL)	88 (45–140)	85 (50–149)	89 (59–166)	89 (51–154)	0.490
Hb (g/dL)	12.8 ± 1.6	12.8 ± 1.9	13 ± 1.8	12.7 ± 1.7	0.149

[a]p = 0.035 vs. before Ramadan, p = 0.034 vs. 3. month, p = 0.001 vs. 6. month. [b]p = 0.003 vs. 0. month, p = 0.009 vs. 6. month.

mg/g vs. −0.022 (−0.270 to 0.035) mg/g, in fasting and non-fasting groups, p = 0.890].

In univariate and multivariate logistic regression analyses, the presence of diabetes mellitus and proteinuria were found to be independent risk determinants of renal dysfunction (Table 4).

Discussion

In our study, it was observed that Ramadan fasting did not cause a significant change in renal function in stage 3–4 CKD patients. There was no statistically significant difference in proteinuria, GFR and creatinine levels of the fasting group compared to the non-fasting group. The presence of diabetes mellitus and proteinuria were found to be independent risk factors for renal dysfunction.

GFR is generally accepted as the best overall index of kidney function. GFR can be estimated from serum creatinine by equations that use age, gender, race, and body size as surrogates for creatinine generation [10]. For GFR measurement, the Cockcroft-Gault Formula, The Modification of Diet in Renal Disease (MDRD) study equation and the 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation methods are used [10]. The 2012 KDIGO guidelines recommend that clinical laboratories report eGFR in all adults using CKD-EPI creatinine equations. In our study, we used the

Table 4: Univariate and multivariate logistic regression analysis of the factors that may predict ≥25% drop in eGFR in fasting group after Ramadan.

	Univariate analysis				Multivariate analysis			
	B	Wald	OR (95%CI)	p-Value	B	Wald	OR (95%CI)	p-Value
Proteinuria	0.654	8.787	1.923 (1.248–2.963)	0.003	0.600	5.471	1.821 (1.102–3.010)	0.019
DM	−2.853	7.057	0.058 (0.007–0.473)	0.008	−2.525	5.189	0.080 (0.009–0.703)	0.023
Age	−0.031	1.112	0.969 (0.915–1.027)	0.292				
Gender	−0.366	0.333	0.693 (0.200–2.404)	0.564				
GFR	0.017	0.273	1.017 (0.954–1.084)	0.601				
HT	−19.545	0.000	0.995 (0.985–1.005)	0.999				
CAD	0.604	0.838	1.829 (0.502–6.659)	0.360				

DM, Diabetes mellitus; GFR, glomerular filtration rate; HT, hypertension, CAD, coronary artery disease.

CKD-EPI formula using serum creatinine levels as recommended by the KDIGO guidelines for calculating of renal functions. GFR is crucial for diagnosis, management, therapy and prognosis of CKD [10]. KDIGO refers to a GFR <60 mL/min/1.73 m^2 as decreased GFR. The true incidence and prevalence of CKD within a community are difficult to ascertain because early to moderate CKD is usually asymptomatic. The prevalence of CKD is approximately 10%–14% in the general population [10]. Among all CKD patients, the rate with stage 3–5 CKD is around 3–5% [10]. The incidence of CKD varies from country to country with no clear rate known. The most important cause of mortality among stage 3–5 CKD patients is cardiovascular disease. Cardiovascular diseases are responsible for more than 50% of deaths [10]. Additionally, the significant complications for these patients include anemia, metabolic acidosis, hyperkalemia, hyperphosphatemia, mineral bone disease and increased infection risk [10].

Though it was shown that Ramadan fasting is safe for healthy individuals [4, 5], there are contradictory results from studies researching the effect of fasting on renal functions in chronic kidney disease patients.

In hemodialysis patients, the Ramadan fast may be dangerous because of the increased risk of dehydration, long-term fasting or volume overload due to the excess fluid intake after *Iftar* [14]. Decreased insulin secretion may cause a tendency toward hyperkalemia in hemodialysis patients. Ramadan fasting is reliable in terms of electrolyte balance and blood pressure changes [15]. In our study, the Ramadan fasting did not cause significant potassium elevation.

In the study by El-Wakil et al., it was argued that Ramadan fasting could cause renal tubular injury [16]. In this study, urinary N-acetyl-β-D-glucosaminidase levels were significantly higher in patients with CKD, although there was no significant difference in GFR changes between CKD patients and healthy controls. This finding suggests that renal tubular cell damage may develop without change in GFR, due to the compensatory mechanisms after fasting. A study of stage 2–4 CKD patients did not observe any significant disruption in renal functions during the month of Ramadan [17].

Most studies suggest that Ramadan fasting does not have a significant effect on renal function, but these studies involve a relatively small number of patients with mild to moderate impaired renal function. Patients in our study were elderly patients with stage 3–4 renal failure and their renal function was followed for 6 months. A 6-month follow-up accounted for some handicaps, such as the possibility that patients may develop impairment in renal function due to various causes other than Ramadan fasting and the possibility of natural progression of CKD.

In a study conducted with stage 3–5 CKD patients, a significant increase in serum creatinine and a significant decrease in GFR were observed at the end of the first week of Ramadan, but no statistically significant difference was detected in GFR levels in the first and third months after Ramadan. The authors suggested that reduction in renal function during the first week may be associated with the use of renin-angiotensin-aldosterone system antagonists and diuretics. In addition, an increase in the frequency of major cardiovascular events was observed after the first week, and this increase may be related to creatinine levels [18]. In another study, evaluating the effects of Ramadan fasting on renal function in stage 3–5 CKD patients, it was emphasized that fasting does not have an effect on renal function, but advanced age and diuretic use may affect it [19]. However, in this study, heterogeneity of fasting and non-fasting groups regarding the distribution of the patients according to the CKD stages is prominent and therefore the results may be inaccurate. In our study, no association was found between concomitant diseases other than diabetes mellitus, medications and loss of renal function. However, sun exposure, sweating and fluid loss

due to physical exertion, and activity at work can affect renal function [20].

Proteinuria is an early finding of glomerular disease in diabetic nephropathy. Due to identification before the reduction in GFR, it is valuable as an early marker of injury. Proteinuria is a risk for all-cause and cardiovascular mortality, kidney failure, and CKD progression in the general population [21].

The 2012 KDIGO guidelines emphasize the diagnostic and prognostic importance of proteinuria levels in CKD classification. Numerous studies in patients with diabetic and nondiabetic renal diseases confirm that marked proteinuria is associated with a faster rate of CKD progression [22]. Therapies that decrease proteinuria generally slow GFR decline [23]. The presence of albuminuria likely reflects generalized endothelial cell dysfunction, thus increasing the risk of atherosclerosis [24]. Reduction of marked proteinuria is often associated with a better renal outcome [23]. In the literature, we did not find any study that found an increase in proteinuria levels after Ramadan fasting. On the contrary, some studies found a decrease in proteinuria levels. In a recent study, 24-h urinary protein was significantly decreased in the fasting group [25]. In addition, Bernieh et al. found better lipid profile, reduction in proteinuria and fractional extraction of sodium [14]. In our study, there was no increase in proteinuria levels after Ramadan fasting in accordance with the literature. However, proteinuria was found to be an independent risk factor for deterioration of renal function in multivariate logistic regression analysis.

Diabetes mellitus is the leading cause of CKD and end-stage renal disease (ESRD) [26]. Patients with ESRD either on dialysis or with renal transplant as a result of diabetes have the highest annual mortality compared with patients with ESRD secondary to any other cause [26]. Symptomatic uremia and fluid overload occur in diabetic patients at higher GFR than in ESRD from other causes. They also have a higher incidence of cardiovascular and atherosclerotic diseases. Diabetic CKD patients have more rapid progression to ESRD compared to patients with CKD linked to other causes [27].

The Epidemiology of Diabetes and Ramadan (EPIDIAR) study found that 42.8% and 78.7% of patients with Type 1 and Type 2 DM, respectively, fasted for at least 15 days during Ramadan [2]. The CREED study reported that 94.2% of Tip 2 DM patients fasted for at least 15 days, while 63.6% fasted every day [28]. Fasting causes significant changes in sleep patterns. Glucose intolerance and insulin resistance may develop linked to lack of sleep. Linked to changes in the circadian rhythm of cortisol, patients may develop feelings of lethargy [29]. Additionally, hyperglycemia may develop linked to overeating during *Iftar* due to hunger [30]. Fasting can result in excessive glycogenolysis and gluconeogenesis in individuals with Type 1 DM or Type 2 DM [30]. Individuals with diabetes are at increased risk of hypoglycemia, hyperglycemia, dehydration and diabetic ketoacidosis (DKA) [31, 32]. In 2017 Diabetes Research and Clinical Practice Guidelines, CKD stage 4–5 was considered a very high-risk group, while CKD stage 3 was considered a high risk group. The guide recommended that these patients should not fast [31]. In accordance with 2017 diabetes guidelines, we found that DM was an independent risk determinant of renal dysfunction like proteinuria in multivariate logistic regression analysis.

In conclusion, the findings of the present study indicate that the Ramadan fasting did not have any significantly negative effect on renal function in stage 3–4 CKD patients. However, patients with diabetes mellitus or prominent proteinuria may constitute critical patient groups for renal function deterioration.

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