

Original Article

Fasting in Ramadan is Not Associated with Deterioration of Chronic Kidney Disease: A Prospective Observational Study

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ABSTRACT. Although not mandatory for patients, many Muslims fast in Ramadan. We aimed to investigate the effects of long hours (17.5) fasting on renal functions in patients with chronic kidney disease (CKD). Stage 3–5 CKD patients with stable renal function were recruited to this prospective observational study three months ahead of Ramadan in 2015. All patients were instructed regarding possible deleterious effects of dehydration caused by fasting. Forty-five patients (mean age 66.8 ± 10.3 years, 68.8% male) chose to fast and 49 (mean, age: 64.1 ± 12.6 years, 51% male) chose not to fast. Clinical and laboratory data were recorded before and after Ramadan. Baseline clinical and laboratory parameters were similar in the two groups, except for higher serum creatinine and lower estimated glomerular filtration rate (eGFR) in the nonfasting group (2.22 ± 0.99 vs. 1.64 ± 0.41 mg/dL, $P < 0.001$ and 31.9 ± 12.4 vs. 42.6 ± 9.8 mL/min, $P < 0.001$, respectively). More than 30% elevation in serum creatinine after Ramadan occurred in 8.8% and 8.1% of fasting and nonfasting patients, respectively ($P = 0.9$). More than 25% drop eGFR after Ramadan was noted in seven (15.5%) and six (12.2%) fasting and nonfasting patients, respectively ($P = 0.642$). Patients with 25% drop in eGFR (13 vs. 81) were older (72.3 ± 8.3 years vs. 64.3 ± 11.7 years, $P = 0.020$) and more frequently using diuretics (69.2% vs. 35.8%, $P = 0.023$). In multiple linear regression analysis, only advanced age was found to be associated with 25% drop in eGFR after Ramadan in the fasting group. Fasting during Ramadan was not associated with increased risk of declining in renal functions in patients with Stage 3–5 CKD. However, elderly patients may still be under a higher risk.

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Introduction

Fasting from sunrise to sunset during the Islamic holy month of Ramadan is one of the five pillars of the Islamic faith.¹⁻³ It does not only involve refraining from eating and drinking but also from smoking and taking

medications. Duration of the fasting ranges from 10 to 18 h per day and varies according to the geographic location and the season.^{4,5} Although people with chronic illnesses are exempted from fasting according to Islamic beliefs,⁶ many patients insist on fasting against medical advice as suggested.^{7,8} Prolonged fasting, changes in lifestyle and eating habits during Ramadan may cause complications such as dehydration, decreased blood pressure, and hyperviscosity predisposing to further kidney injury and thrombosis in patients with chronic kidney disease (CKD).⁹ A few studies have been performed on the impact of fasting in patients with CKD. In addition, there are no guidelines or standardized protocols about this topic. For this reason, prohibiting or discouraging a patient with CKD from fasting during Ramadan is always controversial.¹⁰ Every year, nephrologists have to deal with the dilemma of giving advice to the CKD patients who wish to fulfill their religious obligation of fasting during the month of Ramadan. In this study, our aim was to assess the impact of fasting during Ramadan on the renal functions in patients with CKD.

Methods

Patients who have been followed up for at least six months at Outpatient Clinic of Nephrology (Rize, Turkey) were included in this prospective observational study. Inclusion criteria were age 18 years or older, stable CKD (<10% fluctuations in serum creatinine in at least 3 readings within the last 3 months) at stages of 3, 4, or 5. Exclusion criteria were evidence of acute cardiovascular disease, infection, Stage 1 or 2 CKD [estimated glomerular filtration rate (eGFR) >60 mL/min/1.73 m²], patients on dialysis, and kidney transplant recipients. Selection of the patients was started three months ahead of beginning of the Ramadan 2015 (June 18th).

All patients were counseled regarding the possible health- and kidney-related hazards of fasting, and the importance of drinking water for at least 2 L/day. All patients who decided to fast did so throughout the Ramadan (appro-

ximately 17.5 h of fasting/day) and were designated as the study group. Patients who preferred not to fast were included as the control group. Fasting group took their medications during the evening and basically reversed the pattern of eating and treatment from day to night. The diet, especially protein intake, remained the same throughout the study in both groups.

All the patients were seen twice during the study, one month before and after Ramadan. Clinical, demographic, and laboratory data were collected from all patients using a standardized form. eGFR was calculated by a 4-variable modification of diet in renal disease equation.¹¹ Change in eGFR (mL/min) was calculated by subtracting the values before and after Ramadan. Deterioration of renal functions was defined as 30% rise in serum creatinine and/or 25% drop in eGFR levels from baseline after Ramadan.¹²

The study was approved by the Local Ethics Committee.

Statistical analysis

Statistical Package for the Social Sciences (SPSS) software version 20.0 (SPSS Inc, Chicago, IL, USA) was used for the statistical analysis. Data were presented as a mean \pm standard deviation. Yates correction Chi-square test was used for comparison of nonparametric variables. Mann-Whitney U-test was used for comparison of parametric variables between groups. Spearman's test was used for correlation analysis. Paired *t*-tests were used to assess the significance of changes between parameters before (baseline) and after Ramadan. Multiple linear regression analysis was used to assess the factors that predict deterioration of renal functions (30% rise of baseline serum creatinine) in the fasting group after Ramadan.

Results

A total of 94 patients (mean age 65.4 \pm 11.6 years, 56 males, 45 fasting and 49 nonfasting) with stable kidney function at Stage 3, 4, or 5 CKD were included in this prospective obser-

vational study. Baseline clinical and demographic characteristics were similar in the groups, except for higher baseline serum creatinine (1.64 ± 0.41 mg/dL vs. 2.22 ± 0.99 mg/dL, respectively, $P < 0.001$) and lower eGFR (42.6 ± 9.8 mL/min vs. 31.9 ± 12.4 mL/min, respectively, $P < 0.001$) in the non-fasting group (Tables 1 and 2). Likewise, CKD stages at baseline were significantly different between the fasting and nonfasting groups (Table 1).

Weight, BMI, systolic and diastolic blood pressure levels, and most of the biochemical parameters remained unchanged in both groups (Table 2). Decrease in levels of hemoglobin and serum calcium was seen after Ramadan in the fasting group only (13.3 ± 1.5 to 12.9 ± 1.6 g/dL, $P = 0.015$ and 9.4 ± 0.6 to 9.2 ± 0.4 mg/dL, $P = 0.012$, respectively) (Table 2).

Serum urea and creatinine levels did not change significantly between before and after Ramadan in either of the groups (Figure 1). Accordingly, deterioration in renal functions (30% increase in serum creatinine or 25% decrease in eGFR) was seen in a minority of

patients from each group, and the differences were not significant (Table 3). Mean changes in eGFR and proteinuria showed an insignificant trend toward improvement in the fasting group ($+1.82 \pm 15.81$ vs. -2.03 ± 8.23 mL/min, $P = 0.311$ and $P = -0.257 \pm 1.480$ vs. $+0.201 \pm 1.373$ mg/g, $P = 0.164$, respectively) (Table 3).

The only significant differences between patients in whom the renal function deteriorated and those with stable renal functions were the former group were older and use diuretics (72.3 ± 8.3 vs. 64.3 ± 11.7 , $P = 0.020$, and 9 (69.2%) vs. 29 (35.8%), $P = 0.023$, respectively) (Table 4).

Advanced age was found to be the only independent factor which predicted the deterioration of renal functions (25% drop in eGFR) [beta: 0.403, 95% confidence interval (0.003–0.020), $P = 0.010$] (Table 5 and Figure 2).

Discussion

The major concern for CKD patients regarding fasting is the possibility of dehydration and its deleterious consequences on the kidney function.¹³ If we have a closer look at the daily

Table 1. Baseline characteristics of study participants.

Patient characteristics	Fasting (n=45)	Nonfasting (n=49)	P
Age (years)	66.8±10.3	64.1±12.6	0.258
Gender (male, %)	31 (68.8)	25 (51)	0.078
Weight (kg)	78.5±15.6	79.2±16.2	0.623
BMI (kg/m ²)	24.2±0.6	24.6±0.4	0.536
Systolic BP (mm Hg)	147.5±27.5	156.7±32.4	0.239
Diastolic BP (mm Hg)	87.0±14.5	90.7±17.6	0.427
DM (n, %)	11 (24.4)	19 (38.7)	0.136
Antihypertensive medication (n, %)			
Diuretics	15 (33.3)	23 (46.9)	0.179
CCB	20 (44.4)	30 (61.2)	0.103
RAS blockers	19 (42.2)	22 (44.8)	0.794
Beta blockers	14 (31.1)	19 (38.7)	0.484
Alpha blockers	10 (22.2)	10 (20.4)	0.830
Baseline creatinine (mg/dL)	1.64±0.41	2.22±0.99	<0.001
Baseline eGFR (mL/min)	42.6±9.8	31.9±12.4	<0.001
CKD stages at baseline (n, %)			
Stage 3	37 (82.2)	24 (48.9)	
Stage 4	8 (17.8)	19 (38.7)	0.001
Stage 5	0 (0)	6 (12.4)	

BMI: Body mass index, BP: Blood pressure, DM: Diabetes mellitus, CCB: Calcium channel blockers, RAS: Renin-angiotensin system, eGFR: Estimated glomerular filtration rate, CKD: Chronic kidney disease.

Table 2. Changes in clinical and laboratory parameters after Ramadan according to fasting status.

Parameters	Fasting (n=45)		P	Nonfasting (n=49)		P
	Before Ramadan	After Ramadan		Before Ramadan	After Ramadan	
Weight (kg)	78.5±15.6	78.8±16.1	0.368	79.2±16.2	79.6±17.1	0.390
BMI (kg/m ²)	24.2±0.6	24.3±0.5	0.472	24.6±0.4	24.8±0.5	0.475
Systolic BP (mm Hg)	147.5±27.5	146.8±28.1	0.523	156.7±32.4	159.5±32.1	0.586
Diastolic BP (mm Hg)	87.0±14.5	86.4±14.4	0.684	90.7±17.6	90.2±17.4	0.691
FPG (mg/dL)	116.9±39.1	120.3±32.2	0.515	124.7±50.2	136.5±69.9	0.147
Urea (mg/dL)	66.5±25.4	68.8±25.1	0.630	90.0±41.4	84.4±35.7	0.163
Creatinine (mg/dL)	1.64±0.41	1.64±0.48	0.962	2.22±0.99	2.33±1.11	0.125
eGFR (mL/min)	42.6±9.8	44.4±15.5	0.444	31.9±12.4	29.8±13.7	0.090
Uric acid (mmol/L)	7.9±2.0	7.8±1.8	0.960	7.8±2.5	7.6±1.5	0.087
Sodium (mmol/L)	140.0±2.8	139.9±2.8	0.966	140.4±2.4	140.4±2.6	0.976
Potassium (meq/L)	4.7±0.6	5.4±0.7	0.397	4.7±0.5	4.9±0.5	0.094
Hemoglobin (g/dL)	13.3±1.5	12.9±1.6	0.015	12.1±1.9	12.0±1.0	0.481
Albumin (g/L)	4.2±0.5	4.1±0.3	0.074	4.0±0.2	4.0±0.4	0.082
Calcium (mg/dL)	9.4±0.6	9.2±0.4	0.012	9.2±0.6	9.3±0.5	0.307
Phosphorus (mg/dL)	3.6±0.6	3.7±0.7	0.316	3.7±0.7	3.8±1.0	0.849
intact PTH (pg/mL)	196.4±66.5	201.5±66.0	0.609	183.9±17.6	186.3±17.0	0.867
Total cholesterol (mmol/L)	210.1±56.9	203.3±44.2	0.256	220.9±53.5	215.2±49.6	0.306
TG (mmol/L)	167.5±91.5	179.5±102.3	0.479	190.2±97.1	188.2±100.2	0.869
LDL (mg/dl)	127.2±32.1	123.5±32.8	0.395	142.6±44.4	134.7±34.6	0.146
TIBC (g/L)	253.7±65.6	265.7±61.6	0.403	219.7±69.7	212.8±75.3	0.483
Ferritin (ng/mL)	83.2±13.2	92.4±14.1	0.365	150.3±24.5	163.0±27.2	0.255
Spot urine PCR (mg/g)	0.97±1.93	0.71±1.33	0.341	1.30±1.57	1.50±2.14	0.315

BMI: Body mass index, BP: blood pressure, FPG: Fasting plasma glucose, eGFR: Estimated glomerular filtration rate, TG: Triglyceride LDL: Low density lipoprotein, PCR: Protein creatinine ratio.

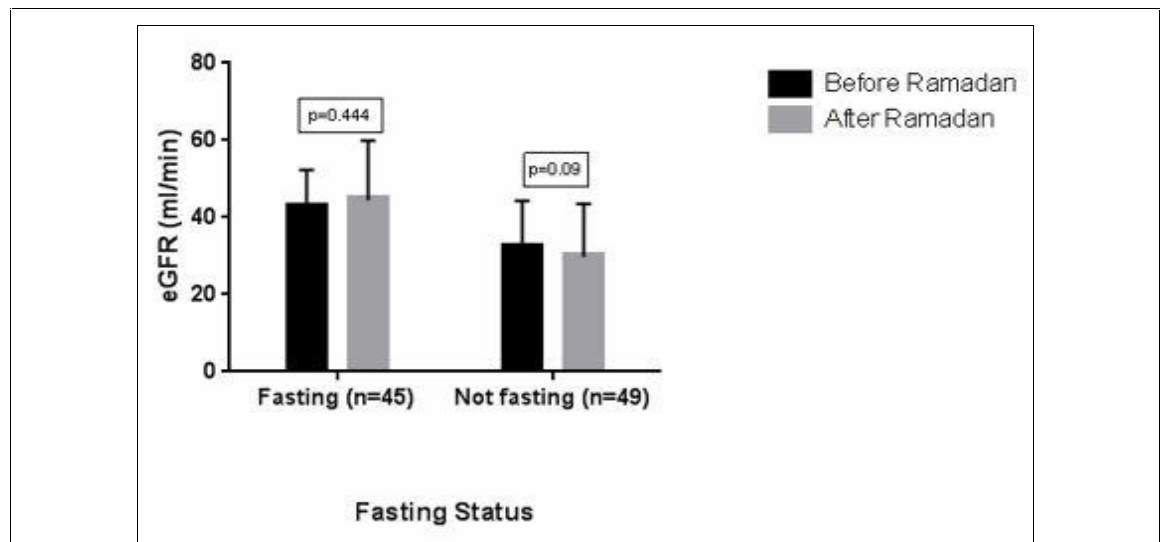


Figure 1. eGFR changes after Ramadan according to fasting status.

Table 3. Differences in renal functions after Ramadan according to fasting status.

Variable	Fasting (n=45)	Nonfasting (n=49)	P
30% rise of serum creatinine (n, %)	4 (8.8)	4 (8.1)	0.900
Change in eGFR (mL/min)	+1.82±15.81	-2.03±8.23	0.311
25% drop of eGFR (n, %)	7 (15.5%)	6 (12.2%)	0.642
Change in proteinuria (mg/g)	-0.257±1.480	+0.201±1.373	0.164

eGFR: Estimated glomerular filtration rate.

Table 4. Comparisons of demographic, clinical data and baseline renal functions between the groups with or without 25% drop of eGFR after Ramadan.

Patient characteristics	25% eGFR drop (+) (n=13)	25% eGFR drop (-) (n=81)	P
Age (years)	72.3±8.3	64.3±11.7	0.020
Gender (male, %)	6 (46.1)	50 (61.7)	0.288
Fasting (n, %)	7 (53.8)	38 (46.9)	0.642
DM (n, %)	4 (30.7)	26 (32.1)	0.924
Antihypertensive medication (n, %)			
Diuretics	9 (69.2)	29 (35.8)	0.023
RAS blockers	6 (46.1)	35 (43.2)	0.843
Baseline renal functions			
Serum creatinine (mg/dL)	1.77±0.83	1.97±0.82	0.402
eGFR (mL/min)	39.1±12.6	36.7±12.4	0.549
Spot urine PCR (mg/g)	1.24±1.63	1.13±1.70	0.840
CKD stages at baseline (n, %)			
Stage 3	10 (76.9)	51 (63)	
Stage 4	2 (15.4)	25 (30.8)	0.519
Stage 5	1 (7.7)	5 (6.2)	

DM: Diabetes mellitus, RAS: Renin-angiotensin system, eGFR: Estimated glomerular filtration rate, CKD: Chronic kidney disease.

Table 5. Multiple linear regression analysis of the factors that may predict 25% drop in eGFR in fasting group after Ramadan.

Variable	Beta	95% Confidence interval		P
		Lower	Upper	
Advanced age	0.403	0.003	0.020	0.010
Gender, male	-0.243	-0.336	0.037	0.114
Presence of DM	0.004	-0.189	0.195	0.978
RAS blockers	-0.084	-0.251	0.154	0.629
Diuretics	0.117	-0.138	0.279	0.496
Baseline eGFR	0.232	-0.002	0.015	0.110

DM: Diabetes mellitus, RAS: Renin-angiotensin system, eGFR: Estimated glomerular filtration rate.

fluid balance, under normal circumstances, insensible water loss occurs at about 500 mL per day.¹⁴ The daily average load of waste solutes that needs to be excreted is about 800 mOsm.¹⁵ A person with a normal urine concentration capacity is able to produce urine as dilute as 50 mOsm/L and as concentrated as 1200 mOsm/L; therefore, a minimum of 670 mL of urine would be required to excrete all

wastes. For kidney patients with a 50% reduction in urine concentrating ability, the minimum required urine volume would be 2 times more (1340 mL).¹⁵ Without the inclusion of water contained in food and generated by metabolism, a daily free water intake of 1340 + 500 mL (1840 mL) appears to be more than the minimum fluid requirement. In this study, all patients were instructed to drink at least 2 L of

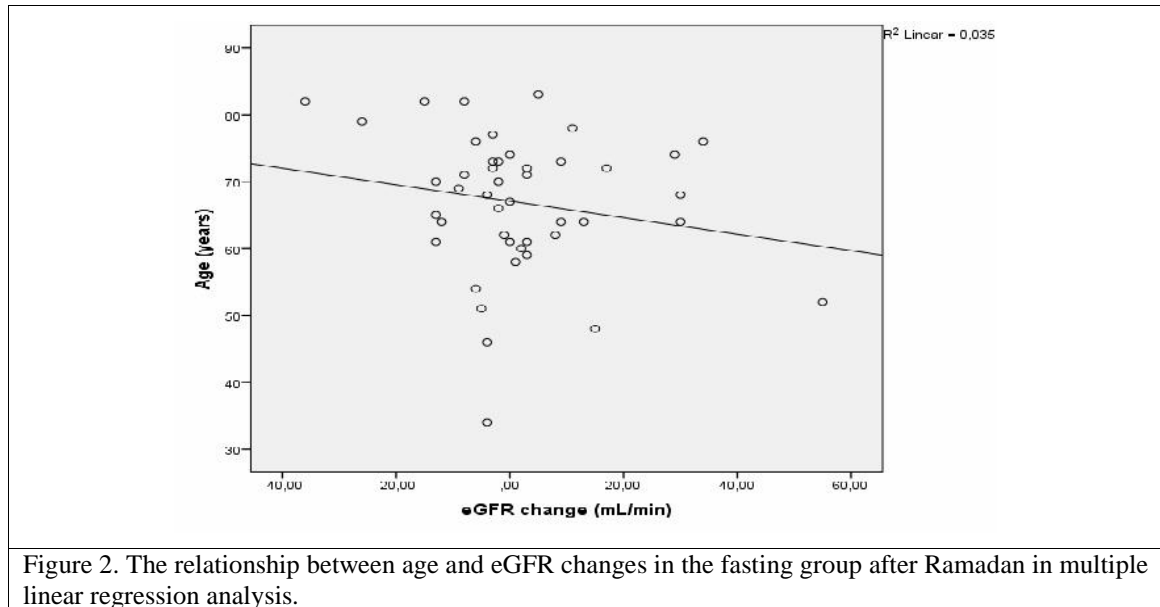


Figure 2. The relationship between age and eGFR changes in the fasting group after Ramadan in multiple linear regression analysis.

water or equivalents, which can be considered that all patients were having sufficient amount of daily water.

The results of this observational study suggest that fasting for 17.5 h for 30 days is not associated with progression or worsening in CKD within a short time of follow-up. These findings were in line with several other observational studies.¹⁶⁻¹⁹ In an observational study that compared fasting and nonfasting Stage 3–5 CKD patients from Egypt, authors reported that fasting patients had significantly more decline in eGFR and 30% rise in serum creatinine occurred 17% (9 patients) at the first week fasting.²⁰ However, by the end of Ramadan and three months after, differences in deviation of eGFR from baseline between fasting and nonfasting patients became insignificant although 13.2% (7) of fasting patients had 30% elevation from baseline creatinine at the end of Ramadan.²⁰ Renin–angiotensin–aldosterone system (RAAS) antagonists and diuretics were associated with increased risk of decline in renal functions at the 1st week.²⁰ Interestingly, osmolality, Na, K, and proteinuria were not different between pre-, during-, and post-Ramadan in fasting (12 h) 31 CKD patients, suggesting that 12 h of fasting may not have a significant effect on renal physiology.¹⁶

Studies that evaluated the effects of fasting in Ramadan on renal functions in post-transplant patients found no deterioration in renal function provided that at least one year had passed since transplantation and that eGFR values were >60 mL/min/1.73 m².²¹⁻²³ Another study assessed the changes in eGFR of renal transplant patients between baseline and after the third Ramadan fasting and found no significant differences between baseline and after the third Ramadan fasting (55.4 mL/min vs. 56.4 mL/min, $P = 0.8$, respectively).²⁴ Fasting before the completion of the first 12 months after kidney transplantation was investigated in 14 patients, and no adverse renal effects were seen.²⁵

Age and diuretic use were the only predictive factors of 25% drop in eGFR. NasrAllah and Osman found that RAAS antagonists and diuretics were associated with a decline in eGFR at the 1st week of Ramadan.²⁰ These can be interpreted as that although there appear to be no significant overall hemodynamic alterations during fasting in Ramadan in healthy participants, a subgroup of patients who were more susceptible to fluid alterations (such as elderly) may have worsened renal functions with additional insults such as diuretics and RAAS antagonists.²⁶

Finally, the hemodynamic effects of fasting

during Ramadan may not be the same across studies.^{27,28} None of the studies, including ours, report the amount of perspiration, the time that study participants stayed outdoor under sun exposure, the amount of exercise, or the type of work that they undertook. All these factors are important and can result in decreased renal functions.^{29,30} In addition, the duration of fasting in Ramadan changes from one year to another, and according to the geographic location, therefore the results from ours and other studies may not be generalized.

Conclusions

Fasting for one month in Ramadan (June–July 2015, Rize, Turkey) for approximately 17.5 hours each day was not associated with worsening of renal functions in patients with Stage 3–5 CKD. These findings were similar to the results from other observational studies both in patients with CKD and renal transplantation.

Conflict of interest: None declared.

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