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# Evaluation of Long-Term Thirst due to Ramadan Fasting in Terms of Acute Kidney Injury

İsmail Baloğlu, Fatih Pektaş, Halil Zeki Tonbul, Nedim Yılmaz Selçuk, Kültigin Türkmen

Division of Nephrology, Necmettin Erbakan University School of Medicine, Konya, Turkey



## Abstract

**Objective:** Acute kidney injury (AKI) is characterized by a rapid decline (i.e., within hours and days) of renal function. Long-term thirst due to fasting may cause a decrease in both the intravascular volume and kidney perfusion. The aim of this study was to investigate the relationship between long-term thirst due to fasting and AKI.

**Materials and Methods:** Forty-five individuals (24 females, 21 males; mean age, 75±12 years) whose kidney function was normal and who were fasting during the month of Ramadan in 2014 participated in the study. The participants were divided into three groups: the first group was aged >60 years and using angiotensin-converting enzyme inhibitors for hypertension, the second group was aged >60 years and did not use drugs, and the third group was aged <40 years. The thirst period was 18 hours. The Acute Kidney Injury Network (AKIN) criteria were used for AKI diagnosis.

**Results:** When all groups were evaluated according to the AKIN-urinary output criteria, the first 6-hour period was the AKI stage1, and the final 12-hour period was the AKI stage 2. There was a small (0.06 mg/dL) but significant increase in the mean serum creatinine level in all groups (p=0.001). Cases could not be evaluated in terms of the AKIN creatinine criteria because the thirst period was not 48 hours long and the increase in creatinine levels was not >0.3 mg/dL.

**Conclusion:** The thirst due to fasting did not increase the risk of AKI in the population with a normal kidney function, and the AKIN-urinary output criteria alone were not adequate to evaluate AKI in patients who were fasting during the month of Ramadan.

**Keywords:** Acute kidney injury, Ramadan fasting, thirst

**Corresponding Author:** İsmail Baloğlu ✉ i_baloglu@hotmail.com

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## INTRODUCTION

Acute kidney injury is a clinical syndrome characterized by a rapid loss of kidney function as a result of decreased glomerular filtration rate (GFR), which develops within hours, days, or weeks (1). Risk factors for acute renal failure include advanced age, gender, concomitant diseases, sepsis, history of major surgery, cardiogenic shock, use of nephrotoxic drugs, and substance abuse (2). The diagnosis of acute kidney injury (AKI) is still based on an increase in serum creatinine levels and a decrease in the urine volume. Acute renal failure is defined as anincrease in serum creatinine levels by >0.3 mg/dL within 48 hours or a urine volume <0.5 mL/kg/h for 6 hours (3).

A long life spanleads to an increase in the number of elderly patients. Although the proportion of elderly population is determined to be 12% at present, the estimated elderly population expected after 25 years is 21%. In addition, life expectancy is increasing rapidly among elderly individuals aged >65 years in developed countries. Acute renal failure in elderly individuals is associated with a decreased metabolic capacity of the kidneys, certain aging-related anatomic or physiological changes in the kidneys, and more frequent occurrence of systemic diseases such as diabetes or hypertension (4).

Prolonged thirst due to fasting may result in a decreased intravascular volume and renal perfusion. Acute renal

failure is more common in elderly patients with a decreased renal reserve because they are more susceptible to ischemia (5-7). The use of a renin-angiotensin system (RAS) blocker is one of the important causes of prerenal AKI. The use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers in patients with hypotension or reduced blood volume (especially in those with heart failure) may contribute to the development of AKI (8). In this study, we aimed to determine whether long-term thirst due to Ramadan fasting leads to acute renal failure according to the AKIN criteria in patients who are elderly and/or are using RAS blockers.

## MATERIALS AND METHODS

The study protocol was approved by the Ethics Committee of the Necmettin Erbakan University School of Medicine. Written informed consent was obtained from study participants.

In this study, 45 (F/M:24/21) individuals who had applied to internal medicine clinics and were fasting were evaluated. The month of Ramadan coincided with July, a hot summer month, and the fasting period was too long (approximately 18 hours). The study was conducted on the 3rd and 4th weeks of Ramadan.

In the first group of patients, 15 patients aged >60 years who used an ACE inhibitor as an antihypertensive agent were evaluated. In the second group, 15 patients aged >60 years who received no medication were evaluated. In the last group, 15 healthy people aged <40 years were included. The fasting period was 18 hours. The AKIN criteria were used in the diagnosis and staging of AKI.

The body weight and blood pressure values measured in the morning and before the fasting break were recorded. Blood and urine samples were analyzed at 09.00 am and in the evening before the fasting break. Urea, creatinine, and urine densities were measured. Urine secreted during the 18-hour period of thirst/fasting was collected separately every 6 hours.

### Statistical Analysis

Clinical data were analyzed using The Statistical Package for the Social Sciences (SPSS) for Windows version 21.0 (IBM Corp.; Armonk, NY, USA). Descriptive statistics for each variable were presented. Continuous data were expressed as the mean±standard deviation. Categorical data were expressed as frequencies and percentages. Mixed analysis of variance (ANOVA) models were used to assess between-group differences in terms of continuous variables. Group and time main effects and their interaction were examined in these mixed ANOVA models. Tests of simple effects were performed when a significant main effect was reached. Baseline eGFR values were compared using ANOVA. A difference was considered significant when p-value was <0.05.



## RESULTS

The mean age of the patients was 75±12 (25-78) years, and the mean body weight was 75±12 kilograms GFR of the groups was calculated according to the modification of diet in the renal diseases study. On examining the group averages, GFR was higher in younger patients as expected (p<0.001) (Table 1).

The average volume of urine collected during the thirst period was 900±166 mL. It was observed that 70% of the total urine output occurred in the first 6-hour period. The average volume of urine collected during the second 6-hour period was 174±61 mL and during the third 6-hour period was 78±29 mL. When urine output was calculated in terms of mL/kg/h according to the AKIN-urinary output criteria, all the groups were found to have AKI stage 1 in the second 6-hour period and AKI stage 2 in the last 12-hour period (Table 2).

**Table 1.** Mean GFR values in patient groups according to MDRD

| | GFR (min-max) | p |
|---|---|---|
| Age <40 | 114.17+19.24 (85-150.6) | <0.001 |
| Age >60 | 81.94+11.62 (55.2-98.1) | |
| Age >60+ACE-I | 87.34+19.58 (61-129) | |

**Table 2.** Hourly mean urine volumes duringthe period of thirst

| | Second 6 Hours | Third 6 Hours | Last 12 Hours |
|---|---|---|---|
| Age <40 | 0.42±0.14 mL/kg/h | 0.17±0.07 mL/kg/h | 0.29±0.1 mL/kg/h |
| Age >60 | 0.40±0.12 mL/kg/h | 0.18±0.07 mL/kg/h | 0.28±0.08 mL/kg/h |
| Age >60+ACE-I | 0.35±0.11 mL/kg/h | 0.16±0.06 mL/kg/h | 0.25±0.09 mL/kg/h |

**Table 3.** Systolic and diastolic blood pressure

| | Systolic Blood Pressure (mmHg) | | Diastolic Blood Pressure (mmHg) | |
|---|---|---|---|---|
| | Morning | Before Fasting Break | Morning | Before Fasting Break |
| Age <40 | 115.00±12.00 | 113.00±13.00 | 76.00±5.00 | 78.00±4.00 |
| Age >60 | 126.00±9.00 | 124.00±10.00 | 88.00±3.00 | 85.00±6.00 |
| Age >60+ACE-I | 138.00±10.00 | 135.00±8.00 | 110.6±6.00 | 108.00±7.00 |

**Table 4.** Differences between groups (mixed analysis of variance models)

| | Group | Time | Group/Time Interaction |
|---|---|---|---|
| eGFR | <0.001 | <0.001 | 0.285 |
| Urine densities | 0.98 | <0.001 | 0.98 |
| Systolic blood pressure | <0.001 | 0.09 | 0.31 |
| Diastolic blood pressure | 0.08 | 0.80 | 0.91 |
| Weight | 0.019 | <0.001 | 0.98 |

**Table 5.** Serum creatinine level during the period of thirst

| | Morning | Evening (before fasting break) | p |
|---|---|---|---|
| Age <40 | 0.78±0.15 mg/dL | 0.85±0.13 mg/dL | p=0.001 |
| Age >60 | 0.88±0.12 mg/dL | 0.94±0.13 mg/dL | p=0.001 |
| Age >60+ACE-I | 0.77±0.14 mg/dL | 0.82±0.13 mg/dL | p=0.001 |

**Table 6.** Results of between-subjects effects according to mixed analysis of variance

| Source | df | Mean Square | F | p |
|---|---|---|---|---|
| Weight | | | | |
| Group | 2 | 1084.837 | 4.381 | 0.019 |
| Error | 42 | 247.605 | | |
| Systolic blood pressure | | | | |
| Group | 2 | 6915.833 | 25.328 | <0.001 |
| Error | 42 | 273.056 | | |
| Diastolic blood pressure | | | | |
| Group | 2 | 1123.333 | 5.962 | 0.005 |
| Error | 42 | 188.413 | | |
| eGFR | | | | |
| Group | 2 | 7537.408 | 16.210 | <0.001 |
| Error | 42 | 464.980 | | |
| Urine densities | | | | |
| Group | 2 | 138.100 | 3.481 | 0.040 |
| Error | 42 | 39.671 | | |
| Urine volume | | | | |
| Group | 2 | 573.889 | 0.020 | 0.980 |
| Error | 42 | 28036.032 | | |
| Hourly mean urine volume | | | | |
| Group | 2 | 0.017 | 1.070 | 0.352 |
| Error | 42 | 0.016 | | |

The patients' body weight was examined in the morning and before the fasting break. The average body weight of the group that did not use drugs and was aged >60 years was the highest among the three groups. There was a significant decrease in body weight due to 18 hours of hunger and thirst. While the average body weight of the three groups was 75±12 kg, the body weight decreased by 1.2 kg to 73.8±12 kg before the fasting break

**Table 7. Results of within-subjects effects according to mixed analysis of variance**

| Source | df | Mean Square | F | p |
|---|---|---|---|---|
| **Weight** | | | | |
| Time | 1 | 35.469 | 928.751 | <0.001 |
| Group x Time | 2 | 0.001 | 0.020 | 0.980 |
| Error | 42 | 0.038 | | |
| **Systolic blood pressure** | | | | |
| Time | 1 | 146.944 | 2.946 | 0.093 |
| Group x Time | 2 | 60.278 | 1.208 | 0.309 |
| Error | 42 | 49.881 | | |
| **Diastolic blood pressure** | | | | |
| Time | 1 | 17.778 | .439 | 0.511 |
| Group x Time | 2 | 41.111 | 1.016 | 0.371 |
| Error | 42 | 40.476 | | |
| **eGFR** | | | | |
| Time | 1 | 1373.193 | 29.780 | <0.001 |
| Group x Time | 2 | 59.639 | 1.293 | 0.285 |
| Error | 42 | 46.112 | | |
| **Urine densities** | | | | |
| Time | 1 | 3385.600 | 332.077 | <0.001 |
| Group x Time | 2 | 93.100 | 9.132 | 0.001 |
| Error | 42 | 10.195 | | |
| **Urine volume** | | | | |
| Time | 3 | 6808872.037 | 865.011 | <0.001 |
| Group x Time | 6 | 426.481 | 0.054 | 0.999 |
| Error | 126 | 7871.429 | | |
| **Hourly mean urine volume** | | | | |
| Time | 1 | 1.100 | 229.963 | <0.001 |
| Group x Time | 2 | 0.006 | 1.319 | 0.278 |
| Error | 42 | 0.005 | | |

(p<0.001).In addition, urinalysis was performed in the morning and before the fasting break. It was observed that urine densities were increased in all three groups (p<0.001). Systolic and diastolic blood pressures were measured in the morning and before the fasting break. The systolic blood pressure was the highest among the patients who were aged >60 years and used ACE inhibitors (Tables 3, 4). There were no significant changes in blood pressure. There was a small (0.06 mg/dL) but significant increase in the mean serum creatinine level in all the groups (p<0.001) (Table 5). Cases could not be evaluated in terms of the AKIN creatinine criteria because the thirst period was not 48 hours long and the increase in creatinine levels was not >0.3 mg/dL. Between-group differences in terms of continuous variables were examined using mixed ANOVA models (Tables 6, 7).

## DISCUSSION

Our study results showed numerous findings. First, although fasting caused a small but significant increase in creatinine levels, it did not cause an increase in AKI. Second, when there is limited fluid intake (such as the month of Ramadan), the kidneys may produce less urine. Therefore, it may be misleading to consider AKI on the basis of urine volume only. These findings have been presented in a less detailed form as a poster at the 54th ERA-EDTA Congress (9).

Various studies have shown that fasting during the month of Ramadan does not cause any adverse effects on healthy adults (10). However, in patients aged >60 years and in those taking ACE inhibitors, the effect of fasting on renal damage has not been studied. Elderly patients with a decreased renal reserve are more susceptible to ischemia, and therefore, AKI develops more frequently in them. In case of hypovolemia, angiotensin II plays an important role in maintaining intraglomerular pressure and GFR within the normal limits. The use of ACE inhibitors may impair this autoregulation and lead to a reduction in GFR in hypovolemia, especially in patients undergoing coronary bypass grafting (11). In our study, serum creatinine levels increased in all three groups but did not exceed the 0.3 mg/dL limit set by AKIN. In addition, because the thirst period was not 48 hours, no evaluation was made in this respect. In terms of increase in creatinine levels, there was no significant difference between the groups of patients aged <40 years and those aged >60 years as well as between the groups that did and did not use ACE inhibitors (p>0.05).

Cheah et al. (12) showed that during the month of Ramadan, the body is well adapted to hunger/thirst, and the renal function is not adversely affected. While the daytime urine output was significantly decreased, the night time urine output was increased, and the total urine volume remain unchanged. Under normal conditions, even a 2% decrease in the extracellular fluid volume increases osmolarity, stimulates antidiuretic hormone secretion, and prevents diuresis. In our study, the participants' body weight in the evening decreased by an average of 1.2 kg compared with that in the morning. The average urine output in the last 12 hours of the fasting period was approximately 250 mL, indicating the oliguria level. There was no difference between the groups in terms of urine volume (p>0.05).

The number of cases in studies on kidney function among patients with advanced-stage chronic kidney disease (CKD) are generally insufficient and have reported contradictory results. Especially in patients with sodium-losing nephropathy, fasting can lead to dehydration and impaired renal function (13). In 2014, Al Wakeel et al. (14) examined the effect of fasting during 14 hours in Ramadan on blood levels of certain parameters in 39 patients with stage 3-4 CKD and 32 patients on hemodialysis (HD). They showed that blood urea, creatinine, uric acid, and phosphorus levels were increased after the fasting period in patients on HD, and 25% of these patients developed hyperkalemia, although there was no significant effect on patients with stage 3-4 CKD (14).

It has been shown in various studies that there is no harmful effect of fasting on renal function in transplant patients with normal graft function. Similarly, Boobes et al. (15) found that there was no significant change in eGFR before and after the month of Ramadan. Our study has some limitations. First, all the patients enrolled in the study were Turkish. Second, our study had a single-center design, and the sample size was relatively small. Third, the patients were not evaluated in terms of the AKIN creatinine criteria.



## CONCLUSION

We found that long-term thirst due to Ramadan fasting caused a small but significant increase in creatinine levels in all the three groups, but this increase was not sufficient enough to be evaluated as per the AKIN creatinine criteria. When evaluating urinary output according to the AKIN criteria, it was observed that AKI stage 2 developed in all the three groups. After the fasting break, the urine volume returned to normal in a couple of hours. Therefore, the thirst caused by fasting did not increase the risk of AKI in the population with a normal renal function, and the AKIN-urinary output criteria alone were not enough to assess renal damage in patients who were fasting.

**Ethics Committee Approval:** Ethics Committee approval was received for this study from the Ethics Committee of the Necmettin Erbakan University (School of Medicine, Konya, Turkey).

**Informed Consent:** Written informed consent was obtained from the patients who participated in this study.

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