Increasing Overnight Fluid Intake and Kidney Function During Ramadan Fasting: A Randomized Controlled Trial

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ABSTRACT

Background. All healthy Arab individuals are obligated to abstain from eating, drinking, and sexual relations from dawn to sunset during Ramadan, which is one of the 5 pillars of Islam. Fasting effects various body systems, apart from the renal system. Fasting can also increase serum creatinine levels because of dehydration. Our aim was to examine the effects of increased fluid intake during the night on serum creatinine and urea levels.

Methods. This randomized controlled trial included 58 healthy subjects who were randomly divided into 2 groups of 29. The hydrated group drank 2 to 3 L of fluid from sunset to the dawn of the next day. Kidney function was measured before, during, and 1 month after Ramadan.

Results. After adjustment for sociodemographic variables, the control group exhibited higher means of serum concentrations of creatinine and urea and lower estimated glomerular filtration rate than the hydrated group. The Ramadan group exhibited highest means of serum levels of creatinine and urea and the lowest estimated glomerular filtration rate compared with the pre- and post-Ramadan periods. All results were statistically significant at $P < .05$.

Conclusions. We found that Ramadan fasting was not associated with a permanent increase in serum creatinine or urea. For those groups with a high fluid intake, serum creatinine and urea were significantly lower than the controls suggesting a favorable effect of hydration during the nonfasting hours. This compensated with the dehydration occurring during daylight, as dehydration is responsible for increased concentrations of urea and creatinine. This study adds further evidence that Ramadan fasting does not affect the renal system of healthy subjects; however, fluids should be increased at night, during nonfasting hours.

World-wide, all religions recommend a period of fasting during the year. Distinctive to the Islamic religion is the Ramadan fast, occurring during the ninth month of the Islamic calendar for an entire month each year. Muslims partake of 2 meals, one immediately after sunset and the other just before dawn, thus, fasting for a period ranging from 11 to 18 hours. We hypothesize that physiological changes that occur during Ramadan will differ from those occurring during other types of fasting. According to Islam, ill individuals are exempt from fasting, especially, those afflicted with chronic diseases (ie, diabetes, hypertension, liver and kidney disease), even though a significant number insist on following this religious practice because of their faith and personal satisfaction [1−3]. In such cases, physicians are faced with a dilemma as to what clinical advice can be offered to their fasting patient.

In this study, research was conducted on the effect of Ramadan fasting on kidney physiology in both ill and healthy individuals, assisting the physician in rendering the right decision. This study was performed on healthy individuals with normal kidney function. The month of Ramadan is a 30-day period each year when Muslims abstain from eating, drinking, and sexual intercourse during the daylight hours. During this period,

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unhealthy adults, pregnant or menstruating women, and travelers are not required to fast. Protracted fasting can lead to changes in lifestyle, sleep patterns, and meal intake time, resulting in endocrine process disturbances and increased dehydration risk [4].

Ramadan fast occurs during the ninth month of the Islamic calendar [5,6]. Fasting on Ramadan is considered amongst the 5 pillars of Islam. The observance of Ramadan requires healthy Muslim men and women to abstain from eating, drinking, and sexual relations from dawn to sunset. After sunset, one may eat and drink without any restrictions until the dawn of the next day [7]. People who are ill, women who are menstruating, prepubertal children, and travelers are exempt from fasting [8].

In 2011, Grim and Hsu estimated the world's Muslim population at 1.57 billion, 23% of the world's population [9]. For this reason, it is crucial for health personnel practicing either in Muslim countries or other parts of the world to be aware of the effects of fasting on the various body systems and the physiological alterations related to fasting [10]. The effect of fasting has been extensively studied in the literature, and has been proved safe in healthy individuals [10,11]. Fasting has been shown to generate beneficial effects on the lipid profile by decreasing blood cholesterol, triglycerides, low density lipoprotein cholesterol, and very low density lipoprotein cholesterol [12], increasing high density lipoprotein cholesterol and decreasing body weight and fasting blood glucose [6,11,13]. Furthermore, Meo and Hassan found that fasting was not associated with adverse effects on the different body systems (ie, heart, liver, kidney, metabolic, eye, and cognitive functions) [11]. As for the renal system, studies have showed no adverse effects of fasting on kidney transplant patients after 1 year of transplantation [14,15] or an increased risk of calculus formation [16]. Some studies have provided evidence of no adverse effects related to fasting even in patients on regular hemodialysis [6,17,18].

Despite the safety of fasting on the kidneys, some studies have shown increased urea and creatinine levels above baseline amongst healthy individuals, without clinical significance [5], which has been attributed to decreased fluid intake, thus, resulting in a decreased glomerular filtration rate [11]. However, these changes are transitory and reach baseline again as soon as Ramadan concludes [19]. In this study, we will focus on the effect of Ramadan fasting on the renal system and the relationship between serum biomarkers and hydration status amongst the fasting healthy subjects. We hypothesize that increased fluid intake from sunset to the dawn of the next day is associated with beneficial effects on kidney function tests.

SUBJECTS AND METHODS

Study Design

Setting and population. This randomized controlled study was conducted in 2018. The study lasted for 12 weeks from May 2018 to August 2018. The Institutional Review Board of the College of Medicine and Health Sciences, An-Najah National University, granted ethical approval (#13 May). The festival of Ramadan in 2018 occurred between May 16, 2018 and June 14, 2018. The average fasting time was ~16 hours with an average temperature outside of 32°C. All participants signed an informed consent form.

Inclusion criteria. Inclusion criteria included age ≥18 years old, free of any medical history of diabetes, hypertension, and heart or kidney disease, and willingness to voluntarily participate in the study.

Study groups. The random number generation function in the Statistical Package for Social Sciences (SPSS, version 23.0, IBM Corp., Armonk, New York) randomized patients into 2 groups. The sample size, according to the GPower, was 52 subjects; however, we decided to include 58 healthy subjects who were not afflicted with kidney disease. Pregnant women were not included in the study. The controls comprised subjects who were asked to continue their normal overnight fluid intake without intervention by the investigators. On average, the controls drank 620 mL of water. The hydrated group was asked to drink 2 to 3 liters of fluid overnight. Fluid intake was determined according to the American Dietary Guidelines, based on the average consumption of a healthy population aged 19 to 30.The requisite amount of drinking according to the American Dietary Guidelines was ~9 cups (~2.2 L) for women and ~13 cups (~3 L) for men [20]. Both groups were asked to precisely record their intake of water and fluid. Both groups fasted the entire month of Ramadan, an average of 16 hours per day.

Data Collection

Demographic and clinical characteristics were obtained from the participants including age, sex, medical history, weight, height, averaged overnight fluid intake, and baseline blood pressure reading. The estimated glomerular filtration rate (eGFR) was calculated by the Cockrofft-Gault equation using serum levels of creatinine, sex, age, and weight. The biochemical markers as well as the blood pressure readings were collected on the first, 10th, 20th, and 30th days of Ramadan, before fasting (at dawn) and before breaking the fast (at sunset), and 30 days post Ramadan. All blood samples were sent to the laboratory for analysis immediately after collection and were analyzed on the same day.

Statistical Analysis

Descriptive statistics summarized the demographic and biomedical characteristics of the subjects. Percentage frequencies summarized the categorical variables; mean standard deviation (SD) determined the continuous variables. We used the t and $\chi 2$ test to examine any statistically significant differences between the groups as to the demographic and clinical characteristics. To account for individual variations in outcome measures, a repeated measure analysis using linear mixed-models examined any significant differences between the biochemical parameters during and after Ramadan in both groups. All outcome variables were normally distributed and no data transformation was needed. Any P value <.05 was considered to be statistically significant. All analyses were conducted using the SPSS computer software version 23.0 (IBM Corp).

RESULTS

Baseline Characteristics of the Subjects

Fifty-eight subjects were enrolled in the study: 29 controls and 29 in the hydrated group. No statistically significant differences between the controls and the hydrated groups were found in age, height, systolic and diastolic blood pressures, hematocrit, baseline serum creatinine level, baseline urea level, and sex. The controls exhibited a higher weight average (72.3 kg) than

the hydrated group (70.5 kg). *P* value was .02, which was considered significant statistically. The baseline demographic and clinical characteristics of both groups are summarized in Table 1.

Effect of Ramadan Fasting on Biochemical Parameters During Ramadan

The linear mixed model function, which calculated the effects of Ramadan fasting on biochemical parameters, showed that the control group exhibited a higher change of 0.214 mg/dL in the mean serum creatinine level (95% confidence interval [CI] 0.191, 0.238, $P < .001$) compared with the hydrated group, and a higher change of 6.16 mg/dL in the mean urea (95% CI 5.29, 7.03, $P < .001$) compared with the hydrated group (Table 2, Fig 1).

Effect of Ramadan Fasting on Biochemical Parameters in Relation to Time Period: Pre, During and Post Ramadan

We studied the effects of the time period (before Ramadan, Ramadan, and 30 days after the end of Ramadan) in both groups relating to the biochemical parameters (urea and creatinine) and eGFR (Tables 2 and 3, Figs 1 and 2).

Creatinine. The mean serum creatinine of both groups was 0.96, 1.11, and 1.07 mg/dL before, during, and after Ramadan, respectively. This difference was statistically significant at $P < .001$. The increase in creatinine was on average 0.33 mg/dL in the controls vs the hydrated group (95% CI 0.313, 0.339, $P = .001$). Furthermore, the creatinine was on average 0.113 mg/dL lower and 0.036 mg/dL higher during the pre-Ramadan period and Ramadan period, respectively, compared with the post-Ramadan period. Both values were statistically significant ($P < .05$) (Table 3, Figs. 2, 3, and 4).

Urea. The controls exhibited a higher change of 12.84 mg/dL in the mean serum urea level (95% CI 11.99, 13.68, $P = .001$) compared with the hydrated group during all periods. The mean serum urea level was lower by 7.29 mg/dL during the pre-Ramadan period (95% CI −9.29, −5.28, p 0.001) compared with post Ramadan. On the other hand, during Ramadan, the mean serum urea level change was higher by 3.6 mg/dL compared with the post-Ramadan period, and also statistically significant (95% CI 2.03, 5.18, $P = .001$) (Table 3, Figs. 2 and 6).

Estimated glomerular filtration rate. The controls exhibited a mean eGFR of 108.9 mL/min/1.73 m^2, whereas, the hydrated group exhibited a mean eGFR of 150.1 mL/min/1.73 m^2 during all periods (pre, during, and post Ramadan). This difference was statistically significant with a P value $< .001$. During the pre-Ramadan period, the eGFR averaged 12.74 mL/min/1.73 m^2 higher than the post-Ramadan period, (95% CI 5.61, 19.86, $P = .001$). Conversely, during the Ramadan period, the eGFR was on average 5.54 mL/min/1.73 m^2 lower than the post-Ramadan period (95% CI −8.75, −2.34, $P = .001$) (Table 3, Figs. 2, 5, and 7).

Table 1. Baseline Characteristics of Both Groups (Control and Hydrated)

Variable	Control Group (n = 29)	Hydrated Group (n = 29)	*P* Value
Age (y)	23.4 (2.32)	22.7 (1.74)	.20
Height (m)	1.72 (3.68)	1.71 (2.21)	.39
Sex (male) n, (%)	19 (65.5)	19 (65.5)	.99
Weight (kg)	72.3 (3.52)	70.5 (1.99)	.021
BMI	24.0 (0.97)	23.2 (0.72)	.001
Systolic BP (mm Hg)	115 (3.99)	114 (3.77)	.36
Diastolic BP (mm Hg)	66.4 (7.64)	66.9 (3.23)	.77
MAP	82.8 (6.17)	82.8 (3.03)	.99
HCT	46.1 (2.70)	44.9 (3.21)	.12
Creatinine	0.78 (0.07)	0.80 (0.09)	.49
Urea	22.5 (3.35)	22.5 (3.35)	.99
eGFR= mL/min/1.73 m^2	142 (14.2)	137 (15.1)	.14

Data are mean (SD), unless otherwise stated.
BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; HCT, hematocrit; MAP, arterial pressure mean.

DISCUSSION

The aim of this randomized controlled study was to assess the effects of increased overnight fluid intake during Ramadan on the kidney function tests of healthy fasting subjects (hydrated group), specifically, their serum creatinine and serum urea level and their eGFR compared with other healthy fasting subjects who drank during the night. After controlling for within person variations, we found statistically significant differences between the controls and the hydrated group in the means of the serum creatinine and urea level and the estimated eGFR during the Ramadan period and the entire study period (pre, during, and post Ramadan). After adjusting for sociodemographic variables, the controls exhibited higher means of serum levels of creatinine and urea and a lower eGFR than the hydrated group. The Ramadan period subjects exhibited the highest means of creatinine serum levels and urea and the lowest eGFR compared with the pre- and post-Ramadan periods. We also found no clinically adverse effects on renal function tests in both groups. All of the variables returned to their baseline values 1 month after Ramadan.

Our findings that no adverse outcomes on the kidney functions were observed corresponds with the Cheah et al's results [21]. El-Wakil et al also concluded that Ramadan fasting could be injurious to only those with an underlying kidney disease or patients with chronic kidney disease [22]. Our results are consistent with Azizi [10], Sliman and Khatib [23], and El-Hazmi et al's findings [24], who concluded that Ramadan fasting does not affect renal functions despite the insignificant changes in the serum urea and creatinine levels, thus providing further support to their conclusions that Ramadan fasting is safe amongst healthy subjects. The increase in the serum level of urea could be attributed to the catabolism of body mass [5] or a direct result of the dehydration status of the body and decreased renal blood flow during fasting [25], which was partially prevented in the hydrated group, resulting in a much lower increase in the serum urea compared with the controls. Creatinine is a low-molecular weight, nonprotein-bound endogenous substance produced in the body through muscle breakdown and is freely filtered by the

Table 2. Adjusted Effects of Ramadan Fasting on the Study Variables During Ramadan

Biochemical Parameter	Predictor Variable	Effect Estimate (95% CI)	SE of Effect Estimate	Mean (95% CI)	SE of Mean	*P* Value
Serum creatinine level mg/dL	Intercept	0.91 (0.865, 0.955)	0.022	-	-	<.001
	Group					
	Hydrated	Ref	-	0.82	0.11	
	Control	0.21	0.01	1.03 (0.19, 0.24)	0.11	<.001
	Time (Ramadan)					
	Day 30	Ref	-	1.01 (0.97, 1.06)	0.022	
	Day 20	−0.088 (−0.126, −0.051)	0.018	0.929 (0.909, 0.949)	0.009	<.001
	Day 10	−0.116 (−0.157, −0.074)	0.020	0.902 (0.888, 0.916)	0.006	<.001
	Day 1	−0.144 (−0.191, −0.097)	0.023	0.874 (0.845, 0.902)	0.013	<.001
Serum urea mg/dL	Intercept	35.75	1.43	-	-	<.001
	Group					
	Hydrated	Ref	-	29.42 (28.41,30.43)	0.51	
	Control	6.16 (5.30, 7.03)	0.01	35.59 (34.58, 36.60)	0.51	<.001
	Time (Ramadan)					
	Day 30	Ref	-	38.84 (36.0, 41.68)	1.417	
	Day 20	−4.78 (−7.37, −2.20)	1.28	34.05 (33.44, 34.67)	0.309	<.001
	Day 10	−6.81 (−9.56, −4.05)	1.37	32.03 (31.56, 32.50)	0.234	<.001
	Day 1	−13.72 (−16.58, −10.87)	1.42	25.11 (24.23, 25.99)	0.44	<.001
eGFR mL/min/1.73 m^2	Intercept	129.97 (123.68, 136.26)	3.15	-	-	<.001
	Groups					
	Hydrated	Ref	-	135.5 (130.9, 140.1)	2.30	
	Control	−24.95 (−30.81, −19.08)	2.93	110.6 (106.0, 115.2)	2.30	<.001
	Time (Ramadan)					
	Day 30	Ref	-	117.5 (111.9, 123.1)	2.79	
	Day 20	5.11 (1.49, 8.73)	1.80	122.6 (118.9, 126.2)	1.82	.006
	Day 10	6.82 (2.33, 11.31)	2.25	124.3 (121.3, 127.3)	1.50	.003
	Day 1	10.48 (5.23, 15.73)	2.65	127.9 (123.5, 132.4)	2.21	<.001

CI, confidence interval; eGFR, estimated glomerular filtration rate; SE, standard error.

glomerulus. The increase in the serum level of creatinine can also be explained by the dehydration during fasting [19], reflecting the effects of increased fluid intake amongst the hydrated group on their minimal increase of serum urea and creatinine.

We also found that the Ramadan period was associated with the highest serum levels of creatinine and urea and the lowest levels of estimated eGFR when compared with the pre- and post-Ramadan period, implying that these changes are intermittent and reversible after the conclusion of Ramadan. Al Muhanna [26], who studied the effects of Ramadan on patients with chronic kidney disease, found a transient reduction in the calculated eGFR 2 weeks after Ramadan. Hassan et al [3] reported similar findings regarding the changes in urea levels amongst Ramadan fasters; however, in patients with chronic kidney disease the levels ranged from 62.6, 78.8, and 63.1 mg/dL in pre-, during, and post-Ramadan periods, respectively. This supports the results we obtained as to the serum urea levels during the 3 periods. The estimated GFR values were highest during the pre-Ramadan period, decreased during the Ramadan period, and increased again 1 month post Ramadan (Table 3). These changes were statistically significant as opposed to Hassan et al [3] who did not find any significant changes relating to the eGFR during the same periods of the study.

Despite the fact that the controls exhibited a higher mean serum creatinine (1.2 mg/dL) compared with 0.86 mg/dL in the hydrated group, it is still on the upper limit of normal given the fact that the eGFR was within normal limits in both groups (108.95 mL/min/1.73 m^2 in the controls and 150.10 mL/min/1.73 m^2 in the hydrated group). This study also highlights the

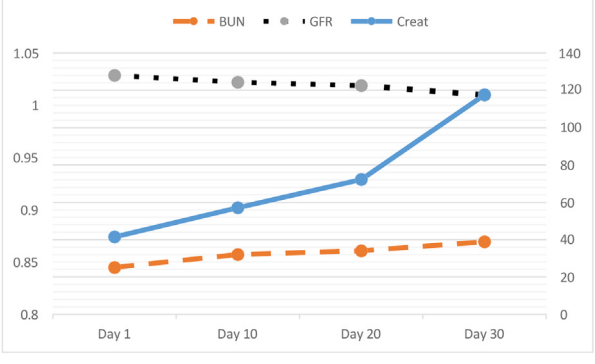

Fig 1. Effects of Ramadan fasting on creatinine, BUN, and eGFR during Ramadan. eGFR, estimated glomerular filtration rate. BUN, urea nitrogen blood; eGFR, estimated glomerular filtration rate.

Table 3. Adjusted Effects of Ramadan Fasting on the Study Variables, Pre, During, and Post Ramadan

Biochemical Parameter	Predictor Variable	Effect Estimate (95% CI)	SE of Effect Estimate	Mean (95% CI)	SE of Mean	*P* Value
Serum creatinine level mg/dL	Intercept	0.91	0.75	-	-	.001
	Group					
	Hydrated	Ref	-	0.86 (0.73, 1.04)	0.074	
	Control	0.33 (0.31, 0.34)	0.006	1.21 (1.05, 1.37)	0.077	.001
	Time					
	Post-R	Ref	-	1.074 (0.915, 1.233)	0.077	
	Ramadan	0.036	0.016	1.11 (0.954, 1.266)	0.075	.032
	Pre-R	−0.113	0.027	0.961 (0.799, 1.123)	0.079	.001
Serum urea mg/dL	Intercept	34.651	4.98	-	-	.001
	Group					
	Hydrated Control	Ref	−0.421	-	-	.001
		12.84 (11.99, 13.68)		-	-	
	Time Post-R Ramadan					
	Pre-R	Ref	−0.784	-	-	.001
		3.60 (2.032, 5.177)	1.011	-	-	.001
		−7.29 (−9.30, −5.29)		-	-	
eGFR mL/min/1.73 m2	Intercept	147.70	2.32	-	-	.001
	Group					
	Hydrated Control	Ref	−2.80	150.1(145.3, 154.8)	33.86	.001
		−41.14 (−46.7, −35.5)		108.96 (104.2, 113.7)	34.99	
	Time Post-R Ramadan					
	Pre-R	Ref	−1.60	127.13 (123.4, 130.8)	34.40	.001
		−5.54 (−8.75, −2.34)	3.58	121.59 (118.5, 124.5)	34.39	.001
		12.74 (5.61, 19.86)		139.88 (132.4, 147.3)	34.54	

CI, confidence interval; eGFR, estimated glomerular filtration rate; R, Ramadan; SE, standard error.

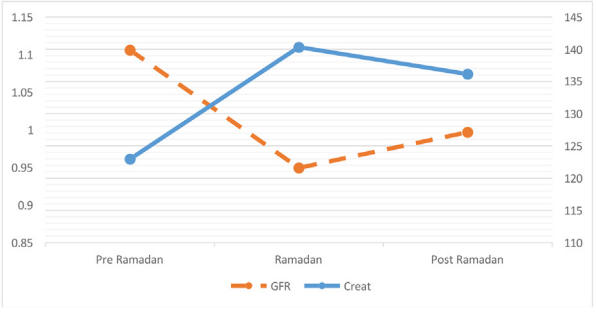

Fig 2. Effects of Ramadan fasting on creatinine and eGFR, pre, during, and post Ramadan. eGFR, estimated glomerular filtration rate.

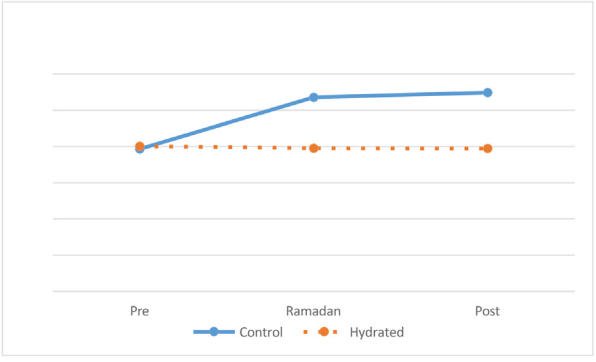

Fig 3. Comparison between hydrated and nonhydrated creatinine, pre, during, and post Ramadan.

importance of increased fluid intake overnight in order to overcome the possible, although temporary, slight increase in kidney biomarkers in the blood.

Strengths

This is the first study that enrolled healthy subjects divided into 2 groups, depending on the amount of fluid drunk overnight during the month of Ramadan. We also reported data regarding kidney function tests during 3 different points of time: before, during, and after completion of Ramadan.

Limitations

This study was conducted with a relatively small number of participants. We recommend further studies encompassing a larger number of participants in order to provide clearer guidelines for both clinicians and dieticians counselling the fasters. The participants were followed for only 1 month after Ramadan had concluded. However, the serum levels of urea and creatinine were close to but not identical to the pre-Ramadan levels. We recommend following the participants for a period of 3 months post Ramadan. Another limitation was the lack of urine analysis before the study to rule out the presence of proteinuria, glucosuria, osmolality, and sodium

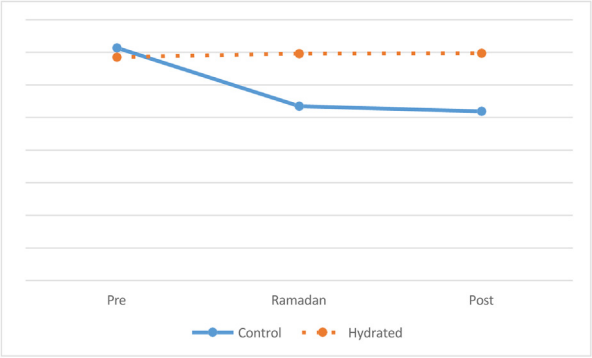

Fig 4. Comparison between hydrated and nonhydrated GFR, pre, during, and post Ramadan. GFR, glomerular filtration rate

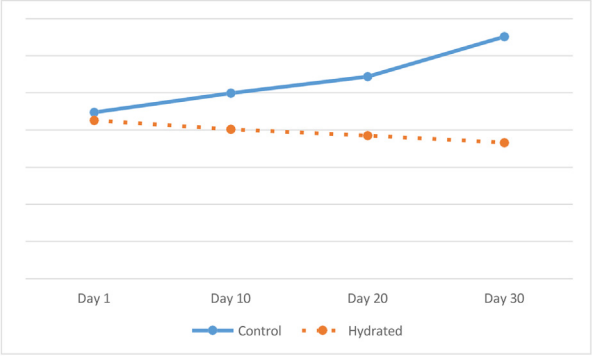

Fig 5. Comparison between hydrated and nonhydrated creatinine during Ramadan.

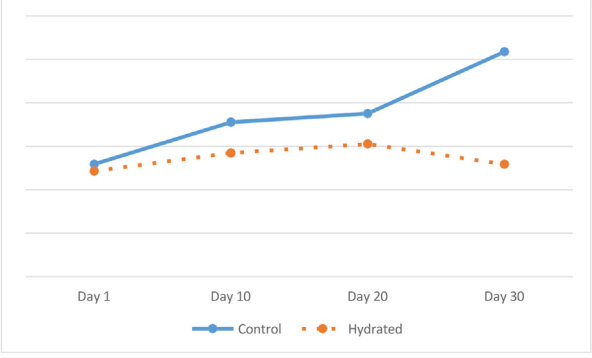

Fig 6. Comparison between hydrated and nonhydrated urea during Ramadan.

and to ensure the absence of underlying kidney disease amongst the participants. We focused only on the serum creatinine and the medical histories of the subjects.

Another limitation was the small sample size. We recommend that future studies include a larger sample. Tests should include kidney function, blood sodium, blood osmolarity, blood hematocrit, calculation of eGFR, urine sodium, urine osmolarity, and creatinine protein ratio.

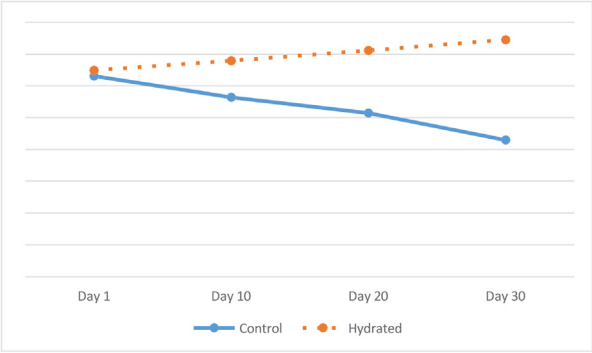

Fig 7. Comparison between hydrated and nonhydrated GFR during Ramadan. GFR, glomerular filtration rate.

CONCLUSIONS

This study adds further evidence that Ramadan fasting does not affect the renal system of healthy subjects. Fasting was found associated with increased kidney biomarkers in the blood, namely, creatinine and urea nitrogen, however, these changes were only temporary and disappeared when Ramadan was concluded. We also emphasized the importance of increased overnight fluid intake. In a group of healthy subjects with no evidence of preexisting kidney disease, we found that Ramadan fasting was not associated with a permanent increase in serum creatinine or urea. In the hydrated group, with a high water intake, the serum creatinine and urea were found significantly lower than in the controls, suggesting a favorable effect of hydration during nonfasting hours. Furthermore, larger, multicenter trials are warranted in order to obtain clearer evidence as to the beneficial effects of increased overnight fluid intake on Ramadan fasters.

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