Int J Nutr Sci 2025;10(4):622-629

International Journal of Nutrition Sciences

Journal Home Page: ijns.sums.ac.ir

ORIGINAL ARTICLE

Long Term Association of Ramadan Fasting and Renal Function in Patients with Chronic Kidney Disease

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ARTICLE INFO

Keywords:
Fasting
Ramadan
Renal function
Glomerular filtration rate
Blood urea nitrogen

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Received: April 10, 2025
Revised: July 2, 2025
Accepted: July 11, 2025

ABSTRACT

Background: Throughout Ramadan fasting (RF), muslims strictly avoid eating, drinking, and sexual intercourse together with other actions. This study aimed to determine the long-term association of RF with renal function and blood urea nitrogen (BUN) in patients with chronic kidney disease (CKD).

Methods: In a cross-sectional study, 8725 individuals from Mashad Cohort Study were enrolled during a period of 10 years and followed through 3-year intervals to moderate the risk of losing contact. To asses renal function, glomerular filtration rate (GFR), BUN and creatinine were measured. RF was evaluated by a 16-item questionnaire. CKD was defined by National Kidney Foundation guideline as GFR<60 ml/min/1.73 m^2. Patients were categorized in three groups based on GFR of eGFR≥60, 60-89, and <15 mL/min per 1.73 m^2.

Results: The mean age was 57.4 years and 48.1% were female. There was no significant relationship between RF and GFR, but a significant relationship was observed between fasting in other months and GFR. Loss of consciousness and severe hypoglycemia were higher among those with a GFR<45. Fasting during life, RF and in months other than Ramadan was accompanied by an increase in creatinine. Age was also associated with a significant rise in creatinine and BUN levels.

Conclusion: This study suggests that patients with stable mild/moderate CKD may be allowed to fast if they are carefully monitored for their health status.

Please cite this article as: Alinezhad-Namaghi M, Esmaily H, Abdollahpour N, Darroudi S, Latifi MR, Ghazizadeh Z, Kiyani F, Ferns GA, Saberi-Karimian M, Ghayour-Mobarhan M. Long Term Association of Ramadan Fasting and Renal Function in Patients with Chronic Kidney Disease. Int J Nutr Sci. 2025;10(4):622-629. doi: 10.30476/ijns.2025.105096.1383.

Introduction

Fasting in the month of Ramadan, the ninth month of the lunar calendar consisting of 354 days, is one of the main principles of the Islamic faith (1). Throughout this month, muslims are required to strictly avoid eating, drinking, and sexual intercourse together with other actions during the day which begins with dawn and ends with the setting of the sun (2). The number of the days in this calendar differs from that of the Gregorian calendar, which consists of 365 days. In accordance with the disparity between the number of the days in each year, Ramadan can fall on any season in the respective year. The length of the day during the holy month ranges from 12 to 18 hours based on geographical regions (1). Certain groups of people such as pregnant women, those breastfeeding babies, travelers, or unhealthy adults suffering from some diseases such as chronic kidney disease (CKD) are exceptions to the rule. However, some religiously devoted individuals with critical diseases insist on fasting despite their serious medical conditions, which could result in un-repairable consequences (3-6).

CKD is a progressive condition that affects 9.1%, a population of approximately 700 million people internationally. The disease has a higher prevalence among women 9.5% in comparison with men who comprise 7.8% of the affected population (7-10). In Iran, it covers approximately 15.14% of the population (11). CKD is defined as kidney damage or an approximate glomerular filtration rate (eGFR) under 60 mL/min/1.73 m^2 which lasts for at least 3 months regardless of the cause (12). CKD is connected to a variety of adverse outcomes including cardiovascular disease, serious kidney damage, and for those who survive, a downturn in the quality of life, as well as mortal effects in the worst cases (13-15). In Muslim countries such as Iran, patients with CKD who intend to fast need to be assessed for the risks involved (3).

Creatinine and blood urea nitrogen (BUN) are often used in the assessment of renal function. However, for clinical use, creatinine-based estimated GFR (eGFR) or serum creatinine is mainly utilized. Creatinine is directly associated with muscle mass, and reduces under the effect of aging or a decrease in muscular mass (16). GFR equations use serum creatinine and a number of corrective factors for gender, age, and body mass as substitutes for the non-GFR influences on serum creatinine. These equations are more precise than creatinine alone (17, 18). BUN is linked to liver perfusion, and dietary protein intake in healthy individuals. BUN may be increased due to gastrointestinal bleeding as well as fever, and drops with low protein diets, abnormal liver function and fasting (18).

A significant amount of research has shown that fasting during Ramadan has no adverse effects on healthy individuals (19-22). It does not result in abnormalities in urine volume, pH, osmolality, urinary excretion of electrolytes and solutes, creatinine, serum urea, potassium and sodium (23). While fasting during Ramadan may also be safe for diabetic patients, renal transplant recipients and patients with urinary stones (3), some studies have shown inconsistencies on the effect of fasting in patients with CKD (2, 24-26). A previous study has evaluated the effect of fasting during Ramadan on patients with CKD (24), including those undergoing hemodialysis (24) and those receiving peritoneal dialysis (26). These studies demonstrated that long-term Ramadan fasting (RF) can be tolerated with no considerable complications. However, severe dehydration, renal damage as a result of hyperviscosity and electrolyte imbalance are likely to occur in patients suffering from CKD over long summer days (3). As a result, we decided to study the long -term association of RF and renal function in individuals with CKD.

Materials and Methods

This cross-sectional study during the last 10 years was carried out on individuals recruited from Mashad Cohort Study, who had no known history of infectious diseases or major systemic inflammation and were without a family history of stroke, myocardial infarction, and diabetes mellitus (27). For the current study, individuals with incomplete data about Ramadan fasting questionnaire or laboratory data were excluded and the final analysis was done on 8725 subjects. CKD was defined using the National Kidney Foundation guideline as a GFR<60 mL/min/1.73 m^2 (3). GFR was calculated from abbreviated prediction equation provided by the Modification of Diet in Renal Disease (MDRD) study as follows: $GFR=186\times(\text{serum creatinine})^{-1.154}\times(\text{Age})^{-0.203}\times(0.742 \text{ if female})\times(1.210 \text{ if African-American})$. In this equation, GFR is expressed as mL/min per 1.73 m^2, and serum creatinine is expressed as mg/dL (18, 28). Participants were categorized in three different groups based on GFR level namely eGFR≥60, eGFR=60-89, and eGFR<15 mL/min per 1.73 m^2.

Creatinine and BUN were measured in all samples using a standard procedure by autoanalyzer Model BT3000 (28). The telephone interview was used to address the short- and long-term RF effects in the past 5 years. A 16-item questionnaire was divided into two categories of (i) RF basic information with

13 questions and (ii) Ramadan nutritional habits with 3 questions. The tool's overall relevance, clarity and comprehensiveness were rated at 0.95, 0.97 and 0.95, respectively. The Pearson correlation coefficient was 0.85 (29). The study population characteristics were previously described (30).

Informed consent was obtained using protocols approved by the Ethics Committee of the university (ID= 951214; IR.MUMS.fm.REC.1396.293). Data were analyzed using SPSS software (Version 20, SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to evaluate the normality of distribution. Descriptive statistics including mean±standard deviation (SD) was utilized for normally distributed variables or median±interquartile range (IQR) for not normally distributed variables. A student's t-test was applied for normally distributed variables. The Mann-Whitney U test was employed for not normally distributed variables, while Chi-square or Fisher exact tests were used for categorical variables. All the analyses were two-sided and statistical significance was set at p value<0.05.

Results

A total of 8725 subjects (mean age=58.12±8.17 years; 30.6% male and 48.1% female) were recruited from Mashad Cohort Study population. Table 1 shows the baseline characteristics of patients who were included in this analysis. As shown in Figure 1, a total of 3831 subjects had GFR≥60 (43.9%), 4113 participants had GFR=45-59 (47.1%), and 781 individuals had GFR<45 (9%), (Table 1). Based on Chi-square test, there was no significant relationship between fasting in general or fasting in Ramadan and GFR, but a meaningful relationship was observed between fasting in other months and GFR and the frequency of GFR<45 was higher among the participants who had not fasted in other months (p<0.032). Moreover, a significant positive relationship was noticed between the age at which the participants had started to fast and GFR, (p<0.001) (Table 2).

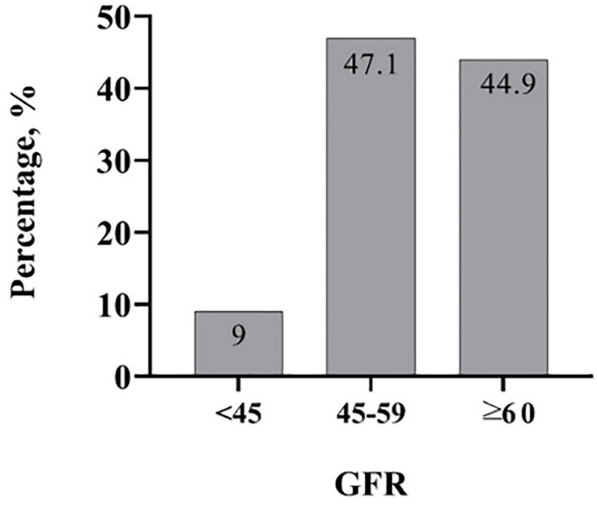

Figure 1: Prevalence of CKD stages.

Participants who were categorized based on their GFR were also investigated regarding the complications associated with RF. Loss of consciousness and severe hypoglycemia were higher among those with a GFR lower than 45 mL/min/1.73 m^2 (p<0.001) (Table 3). In the multivariate regression, following adjustment for age, sex, marriage and job, fasting during life, RF and fasting in months other than Ramadan was accompanied by an increase in creatinine. A rise in the initiation age of RF was associated with a relatively modest rise in creatinine level and an elevated BUN level (p<0.001) (Figure 2).

Table 1: Baseline characteristics of the participants.

Variable	Frequency
Sex, N (%)	
Male	3450 (30.6)
Female	5416 (48.1)
Job, N (%)	
Employed	6375 (56.6)
Unemployed	461 (4.1)
Retired	1599 (14.2)
Marital status, N (%)	
Single	77 (0.7)
Married	7752 (68.8)
Divorce	144 (1.3)
Widow	813 (7.2)
Age (years), mean±SD	58.12±8.17
BUN (mg/dL), mean±SD	59.761±13.626
Creatinine (mg/dL), mean±SD	1.109±0.2378
GFR (mL/min/1.73 m^2), mean±SD	57.460±9.026

GFR: Glomerular Filtration Rate; BUN: Blood Urea Nitrogen; SD: Standard deviation.

Table 2: Fasting parameters and the categorized GFR.

Variable		GFR (ml/min/1.73 m²)			*P* value
		<45	45-60	>60	
Fasting during life	Yes	725 (93.5%)	3855 (94.4%)	3586 (94.4%)	0.61
	No	50 (6.5%)	227 (5.6%)	214 (5.6%)	
Fasting in Ramadan	Yes	719 (92.8%)	3798 (93.1%)	3538 (93.2%)	0.92
	No	56 (7.2%)	280 (6.9%)	260 (6.8%)	
Fasting in other months	Yes	223 (28.9%)	1370 (33.7%)	1269 (33.5%)	0.032
	No	548 (71.1%)*	2700 (66.3%)	2521 (66.5%)	
Start of Ramadan fasting age		11.40±4.27	11.77±3.94	12.53±3.96	<0.001
Ramadan meals	Iftar, Sehri	47 (6.5%)	266 (6.9%)	298 (8.3%)	0.18
	Iftar, Sehri, Dinner	13 (1.8%)	94 (2.4%)	74 (2.1%)	
	Iftar, Dinner	11 (1.5%)	54 (1.4%)	44 (1.2%)	
	Iftar	656 (90.2%)	3443 (89.3%)	3172 (88.4%)	
Parent's Ramadan fasting record	Yes	770 (98.6%)	4072 (99%)	3790 (98.9%)	0.59
	No	11 (1.4%)	41 (1%)	41 (1.1%)	
Mother's Ramadan fasting record	Yes	774 (99.1%)	4078 (99.1%)	3792 (99%)	0.73
	No	7 (0.9%)	35 (0.9%)	39 (1%)	

GFR: Glomerular Filtration Rate. *p value<0.05.

Table 3: Severe problems in fasting subjects in categorized GFR.

Variable		GFR (mL/min/1.73 m²)			*P* value
		<45	45-59	≥60	
Heart attack	No	775 (99.2%)	4098 (99.6%)	3820 (99.2%)	0.12
	Yes	6 (0.8%)	15 (0.4%)	11 (0.3%)	
Stroke	No	777 (99.4%)	4106 (99.8%)	3823 (99.8%)	0.16
	Yes	4 (0.6%)	7 (0.2%)	8 (0.2%)	
Coma	No	781 (100%)	4111 (99.9%)	3829 (99.9%)	0.82
	Yes	0	2 (0.1%)	2 (0.1%)	
Loss of consciousness	No	759 (97.2%)	4061 (98.7%)	3787 (98.9%)	<0.001
	Yes	22 (2.8%)*	52 (1.3%)	44 (1.1%)	
Severe hypoglycemia	No	760 (97.3%)	4053 (98.5%)	3751 (97.9%)	0.021
	Yes	21 (2.7%)*	60 (1.5%)	80 (2.1%)	

GFR: Glomerular Filtration Rate. *p value <0.05.

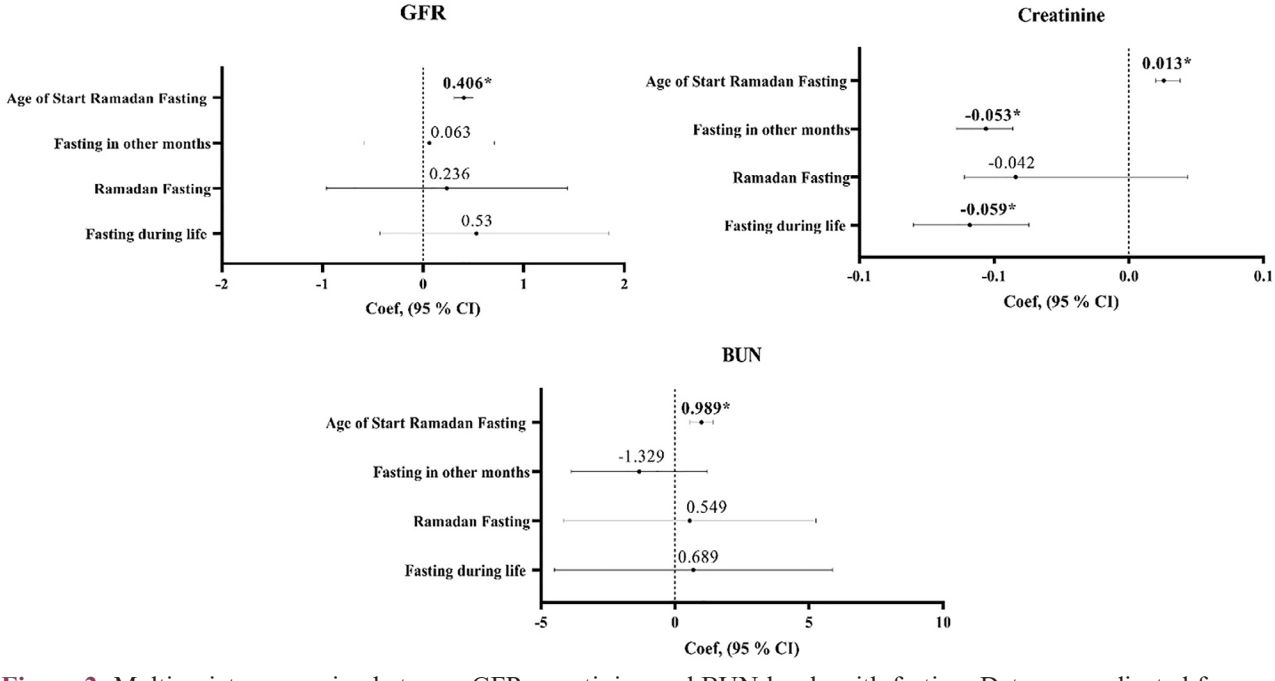

Figure 2: Multivariate regression between GFR, creatinine and BUN levels with fasting. Data were adjusted for age, sex, marriage, and job. GFR: glomerular filtration rate; BUN: blood urea nitrogen. *p value<0.05.

Discussion

It was shown that RF was not associated with a significant change in renal function in individuals with CKD. Generally, there was no significant difference in GFR, creatinine and BUN concentrations in the fasting group when compared to the non-fasting group. Fasting at older ages, however, was associated with increased GFR, BUN, and creatinine levels. Moreover, loss of consciousness risk and severe hypoglycemia were found to be higher in patients with a GFR less than 45. In the present study, we used the MDRD to calculate renal function. The true prevalence of CKD within a community is difficult to ascertain because early to moderate stages of CKD are often asymptomatic. The approximate rate of CKD in the general population was 10-14%. At stages 3-5 of the disease, the most important cause of mortality was demonstrated to be cardiovascular diseases. Additionally, the most important complications for the patients were illustrated to be inclusive for metabolic acidosis, anemia, hyperphosphatemia, hyperkalemia, increased infection risk and mineral bone disease (12). Though, in some studies, it was shown that RF was safe for healthy people (20, 21), other studies pointed to contradictory results in patients with CKD (2).

El-Wakil *et al.* reported that RF could lead to renal tubular damage (2). Dogan *et al.* found that urinary N-acetyl-β D glucosaminidase was higher in CKD patients. Although, compensatory mechanisms after fasting may occur, no significant difference in GFR changes was noted between patients with CKD and healthy people (3). Another study involving stages 2-4 of CKD did not observe any notable disruption in renal function during Ramadan (31). Some studies suggest that RF does not have a significant detrimental effect on renal function. However, it is important to note that these studies typically involve a relatively small number of patients with mild to moderate renal impairment. In our study, adult patients aged 35-65 years (mean age of 57.4 years) with CKD were followed for 10 years to monitor their renal function. Over the course of this 10-year follow-up, any decline in renal function may have been occurred due to factors other than RF, such as the natural progression of CKD with age, the use of diuretics, sun exposure, sweating, and dehydration from physical activity or heat exposure (32, 33).

Some studies of patients with stage 3-5 of CKD found significant improvement in eGFR during Ramadan and the following month (25, 34). In a study conducted on stage 3-5 of CKD, a significant increase in serum creatinine and a notable decrease in GFR were observed at the end of the first week of Ramadan, possibly due to the use of diuretics and renin-angiotensin-aldosterone system antagonists. Additionally, an increase in the frequency of critical cardiovascular events was observed following the first week, which may be linked to creatinine level (35). Tarabeih *et al.* displayed that for groups with high fluid intake, serum creatinine and urea were significantly lower than in controls. Therefore, it is suggested that RF is not associated with a permanent increase in serum creatinine or urea in healthy individuals (36). However, in the present study, an increase in creatinine concentration was observed in the fasting group. Another study by NasrAllah *et al.* revealed that fasting groups exhibited a 30% increase in creatinine level and a decline in renal function (35). Similarly, a study by Bakhit *et al.* showed that 33% of 65 patients with stage 3 of CKD experienced an increase in creatinine level and deterioration of renal function after fasting (1). Conversely, another study concluded that fasting did not negatively affect creatinine levels (37). A study by Karatas *et al.* confirmed a significant decrease in creatinine level indicating an improved renal function in fasting CKD patients (34).

Emami-Naini *et al.* claimed an increase in BUN value after fasting even not to be significant. They highlighted the essential importance of hydration (38). In a study conducted by Kara *et al.* indicated no significant difference in urea value in stage 3-5 in CKD patients regardless of fasting (32). Karatas *et al.* verified a significant decrease in BUN value in stage 3-5 of CKD after fasting. However, they did not mention any difference in BUN/creatinine ratio before or after fasting. Based on these findings, they concluded that fasting did not lead to dehydration (23).

A recent study conducted on patients suffering from diabetes in CKD stage 3 compared with a fasting group with those who did not fast. They did not describe any difference in clinical or biochemical factors or any adverse events (39). In a meta-analysis including five studies, fasting during Ramadan was deemed safe for patients with stable early-stage of CKD (37). In our study, a significant correlation was found between GFR and both loss of consciousness and severe hypoglycemia. Recommended precautions included ensuring proper hydration, daily weight assessment, and monitoring electrolytes and creatinine concentrations after 2 weeks of fasting. Patients were advised to discontinue fasting if serum creatinine level increased by ≥30% from the baseline, or if there was any concern about electrolyte imbalances. Patients were also monitored once or twice weekly and instructed to watch for symptoms such as significant weight gain (>2 kg from baseline), shortness of breath, swelling, dizziness, weakness

or at times, and loss of appetite (40).

This study had several limitations. The cross-sectional design does not allow for the establishment of a cause-and-effect relationship between RF and renal function. Moreover, the data were collected retrospectively, relying on self-reported information which may introduce recall bias. The precision of renal function assessment may also be influenced by hydration status, diuretic use, and measurement variability in biochemical markers like creatinine and BUN. Additionally, the results may not be entirely applicable to populations outside of the studied region or to those with significantly different cultural, dietary, or healthcare practices.

Conclusion

This study suggests that patients with stable mild/moderate CKD could fast if they are carefully monitored during fasting.

Acknowledgement

The support provided by Mashhad University of Medical Sciences (MUMS) to conduct this study is highly acknowledged.

Funding

This study was supported by Mashhad University of Medical Sciences (Grant number: 951214). The funders had no involvement in study design; collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Authors' Contribution

Conception or design: M.An, H.E, M.SK, M.GM; Acquisition, analysis, or interpretation of data: N.A, S.D, MR.L, Z.G, F.K; Drafting the work: N.A, S.D, MR.L; Revising the work: M.AN, H.E, M.SK, M.GM, G.AF; Final approval of the version to be published: M.AN, H.E, M.SK, M.GM, G.AF; Agreement to be accountable for all aspects of the work: M.AN, H.E, N.A, S.D, MR.L, Z.G, F.K, G.AF, M.SK. M.GM; Funds Collection: M.GM

Conflict of Interest

The authors confirm no conflicts of interest.

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