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Impact of Ramadan fasting on eGFR in patients with late stage chronic kidney disease

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ABSTRACT

Aims: Ramadan fasting is a significant religious practice observed annually by approximately 1.9 billion adult Muslims worldwide. However, its potential impact on kidney health in individuals with chronic kidney disease (CKD) remains a subject of concern. This study aimed to investigate the effects of Ramadan fasting on renal function in patients with stage 3-5 CKD and to identify any associated risk factors.

Methods: A single-center, self-controlled longitudinal observational study was conducted on 192 stable patients with stage 3-5 CKD who observed Ramadan fasting. The fasting period was about 14-15 hours per day for one month Various clinical parameters, including eGFR, blood urea nitrogen (BUN), sodium (Na^+), potassium (K^+), calcium (Ca^{++}), phosphorus, parathyroid hormone (PTH), albumin, uric acid, fasting glucose, total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and hemoglobin (Hgb), were measured before and after Ramadan fasting. $P<0.05$ was assumed significant.

Results: The study results demonstrated no significant deterioration in eGFR during Ramadan fasting (pre-Ramadan: 43.54±11.04 vs post-Ramadan: 44.28±11.51, $p=0.063$). Additionally, traditional risk factors for CKD progression, such as diabetes mellitus (DM), hypertension (HT), cardiovascular disease CVD, and age, did not show a significant association with eGFR changes during fasting ($p>0.05$). Furthermore, the use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARB) did not impact eGFR (0.084). Notably, Ramadan fasting led to improvements in metabolic parameters, such as fasting glucose and lipid profile, except for triglyceride levels ($p<0.001$).

Conclusion: The study results indicate that Ramadan fasting does not appear to have adverse effects on kidney function in individuals with CKD, although certain metabolic changes were observed.

Keywords: Ramadan fasting, chronic kidney disease, glomerular filtration rate, metabolic parameters, kidney function

INTRODUCTION

Ramadan fasting is a fundamental pillar of Islam and involves abstinence from food and drink from dawn to sunset for approximately 30 days. This annual period of fasting poses potential physiological challenges to the human body, including the renal system. Existing literature is controversial regarding the impact of Ramadan fasting on kidney function in individuals with chronic kidney disease. This controversy may vary depending on factors such as the study design, duration of fasting, presence of comorbidities, and guidance provided by healthcare providers.[1-4] Additionally, previous studies have primarily focused on acute renal hemodynamic alterations during the Ramadan period, and the long-term impact of Ramadan fasting on renal function remains unknown.[1,2]

Understanding the effects of Ramadan fasting on kidney health is of great importance for healthcare professionals to ensure appropriate guidance and management for individuals observing fasting during this holy month. It allows for the identification of potential risks and the implementation of preventive measures to safeguard renal function. Furthermore, it assists in addressing the concerns of individuals with pre-existing kidney diseases who wish to observe the fast.

The Muslim calendar follows a lunar cycle spanning 355 days per year. Consequently, the month of Ramadan can occur during any period of the Gregorian calendar, completing its full cycle approximately every 33 years. This leads to Ramadan fasting taking place across different seasons, resulting in varying durations of

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fasting. In equatorial regions, the average fasting period ranges from 12 to 14 hours, while in certain geographical locations, it can extend up to 22 hours.[5]

This study aimed to investigate renal function longitudinally for six months in patients with stage 3-5 chronic kidney disease (CKD) who underwent approximately 14-15 hours of Ramadan fasting for one month.

METHODS

The study was carried out with the permission of by Zonguldak Bülent Ecevit University Non-interventional Clinical Researches Ethics Committee (Date: 10.06.2022, Decision No: 2022/14). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This is a single-center, self-controlled longitudinal, and observational study conducted at our state hospital's nephrology outpatient clinic between March 2021 and July 2022. The study included 195 patients with stable stage 3-5 chronic kidney disease (CKD) who were regularly monitored in our nephrology outpatient clinic and observed fasting during the month of Ramadan (Figure 1). Participants were followed up for a duration of six months. Demographic and clinical characteristics of the participants were recorded, and informed consent was obtained. We relied on the measurements that were performed in our central laboratory.

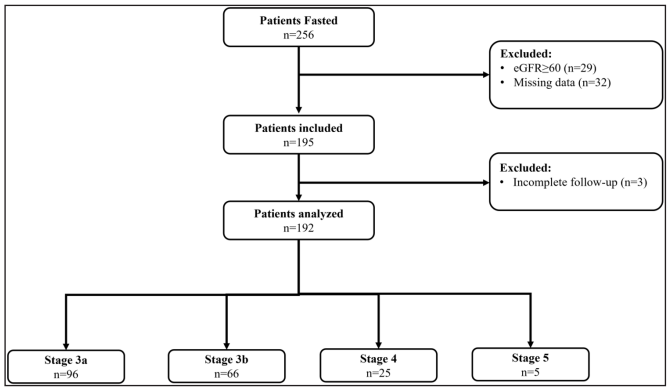

Figure 1. Flowchart of the study population, Abbreviations: eGFR: estimated glomerular filtration rate

Inclusion criteria consisted of participants aged above 18 years, those who observed fasting during Ramadan and had an estimated glomerular filtration rate (eGFR) of <60, as well as patients with a recent blood sample analysis before the study commencement.

Exclusion criteria encompassed patients under 18 years of age, those with active malignancy, acute kidney injury on CKD, a history of hospitalization or missing data.

Measurements: The study collected data on a range of variables, including age, diabetes mellitus (DM), body mass index (BMI), hypertension (HT), gender, cardiovascular disease (CVD), cerebrovascular event (CVE), lung disease, smoking, use of oral antidiabetic medication (OAD) and insulin, utilization of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARB), beta blockers, and alpha blockers, as well as parameters such as proteinuria, physician consultations, chronic kidney disease (CKD) etiology, CKD stages, estimated glomerular filtration rate (eGFR), blood urea nitrogen (BUN), sodium (Na^+), potassium (K^+), calcium (Ca^{++}), phosphorus, parathyroid hormone (PTH), albumin, uric acid, fasting glucose, total cholesterol (T. cholesterol), triglyceride, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and hemoglobin (Hgb). These measurements were taken before Ramadan (pre-Ramadan), after Ramadan (post-Ramadan month-6), and, in some cases, during the 6-month follow-up period. The study aimed to assess changes in these laboratory parameters during and after Ramadan fasting in patients with chronic kidney disease.

BMI calculation: BMI = weight (in kilograms) / (height [in meters])^2.

Physician consultations: A group of patients with CKD (but not patients with eGFR <30 ml/min/1.73 m²) applied to their physician for Ramadan fasting counseling and received advice relating to drug and diet adjustment during Ramadan fasting.

Data source: Data were collected from the hospital software and nephrology clinic documents.

Statistical Analysis

The data analysis was conducted using SPSS version 15.0 for Windows. Descriptive statistics, including mean (± standard deviation), median (range or interquartile range), and proportions (n, %), were employed to summarize and describe the demographic characteristics and baseline measurements of the study population. Paired t-tests or Wilcoxon signed-rank tests were utilized to compare paired measurements within the same group, such as pre-Ramadan versus post-Ramadan month-6 data. Chi-square tests and Fisher's exact tests were employed to assess the association between categorical variables, such as gender and comorbidities, and outcomes of interest, including cardiovascular disease, lung disease, and smoking status. Regression analysis was conducted to explore the impact of independent variables on dependent variables, potentially revealing any relationships between different factors. A significance level of $p < 0.05$ was considered statistically significant, indicating that results with a p-value below this threshold were considered noteworthy and unlikely to occur due to chance alone.

RESULTS

A total of 195 participants were initially evaluated for the study. However, three patients (two from stage 4 and 1 from stage 5) had to undergo hemodialysis treatment due to worsening kidney functions during the follow-up and were subsequently excluded from the analysis. These individuals had an eGFR of less than 20 ml/min/1.73 m² and had participated in Ramadan fasting without prior counseling. The vast majority of the remaining patients (nearly all) successfully completed a full month of Ramadan fasting, adhering to a fasting duration of 14-15 hours.

For an additional subset of the study population, 30 CKD patients with an eGFR below 30 ml/min/1.73 m² observed Ramadan fasting without receiving any prior counseling. Their experiences were recorded retrospectively based on their statements. Table 1 presents a comprehensive analysis of the demographic characteristics, comorbidities, and clinical parameters of the study participants who had stage 3-5 CKD and participated in Ramadan fasting.

Table 1. The clinical and labarotory features of the participants

Age, years, mean±SD	62.64±12.59
BMI, kg/m², mean±SD	29.17±4.93
Gender, male, n (%)	107 (55.7)
eGFR (CKD-EPI 2021), mean±SD	42.03±11.79
Mean Ramadan days, mean±SD	29.74±1.18
Smoking, n (%)	11 (5.7)
ACEi/ARB, n (%)	72 (37.5)
Beta blocker, n (%)	38 (19.7)
Alpha-blocker, n (%)	15 (7.8)
Physician consultation pre-Ramadan, n (%)	50 (26.04)
CKD etiology, n (%)	
DM	54 (28.1)
HT	110 (57.3)
PCKD	5 (2.6)
GN	8 (4.2)
Other	15 (7.8)
DM, n (%)	51 (25.5)
HT, n (%)	180 (93.7)
CVD, n (%)	33 (17.2)
CVE, n (%)	0 (0.0)
Lung disease, n (%)	6 (3.1)
OAD, n (%)	51 (26)
Insulin, n (%)	20 (10.4)
Polypharmacy, n (%)	27 (14.06)
Proteinuria, mg/day †	556 (0-5123)
CKD stage, n (%)	
Stage 3a	96 (50.0)
Stage 3b	66 (34.4)
Stage 4	25 (13.0)
Stage 5	5 (2.6)

Abbreviations: ACEi: angiotensin converting enzyme inhibitor, ARB: aldosteron receptor antagonist, BMI: body mass index, CVD: cardiovascular disease, CVE: cereberovascular event, DM: diabetes mellitus, eGFR: estimated glomerular filtration rate, GN: golmerulonephritis, HT: hypertension, PCKD: polyscystic kidney disease,, OAD: oral antidiabetic drug, †Expressed as range (minimum -maximum)

Out of the total 195 CKD patients, 50 received a consultancy just before Ramadan and were provided with relevant advice.

The study's results revealed a slight increase in estimated glomerular filtration rate (eGFR) from pre-Ramadan (43.54±11.04) to post-Ramadan month-6 (44.28±11.51), as illustrated in Figure 2 and Table 3. However, this difference was not found to be statistically significant (p=0.063) (Table 2). Additionally, Ramadan fasting demonstrated variable effects on different laboratory parameters, with significant changes observed in potassium (p=0.003), calcium (p=0.023), fasting glucose (p<0.001), total cholesterol (p=0.001), HDL cholesterol (p<0.001), and LDL cholesterol levels (p<0.001). On the other hand, other parameters did not display significant differences between the pre-Ramadan and post-Ramadan month-6 measurements (p>0.05) (Table 2).

Table 2. The comparison of the pre and post-Ramadan labarotory results

Parameter*	Pre-Ramadan	Post-Ramadan Month-6	P value
eGFR**	43.54±11.04	44.28±11.51	0.063
BUN (mg/dl)	54.42±24.12	56.34±25.17	0.876
Na^{+} (mmol/L)	139.98±2.84	139.66±9.63	0.673
K^{+} (mmol/L)	4.83±0.48	4.98±0.55	0.003
Ca^{++} (mg/dl)	9.19±0.53	9.26±0.48	0.023
Phosphorus (mg/dl)	3.79±0.60	3.79±0.70	0.997
PTH (ng/L)	102.57±61.54	102.18±74.10	0.921
Albumin (g/dl)	4.29±0.32	4.31±0.26	0.283
Uric acid (mg/dl)	6.60±1.79	6.62±1.73	0.726
Fasting Glucose (mg/dl)	119.48±39.90	111.14±25.98	<0.001
T. cholesterol (mg/dl)	171.93±42.35	162.39±41.50	0.001
Tryglyceride (mg/dl)	156.41±46.14	143.15±101.68	0.191
HDL cholesterol (mg/dl)	44.96±10.22	50.16±14.01	<0.001
LDL cholesterol (mg/dl)	116.48±28.91	106.74±28.94	<0.001
Hgb (g/dl)	12.50±1.53	12.52±1.63	0.816

*Expressed as mean±SD, **eGFR (CKD-EPI 2021 Formula) is given as ml/min/1.73 m², Abbreviations: BUN: eGFR: estimated glomerular filtration rate, HDL: high density lipoprotein, Hgb: hemoglobin, LDL: low density lipoprotein, PTH: Parathyroid hormone

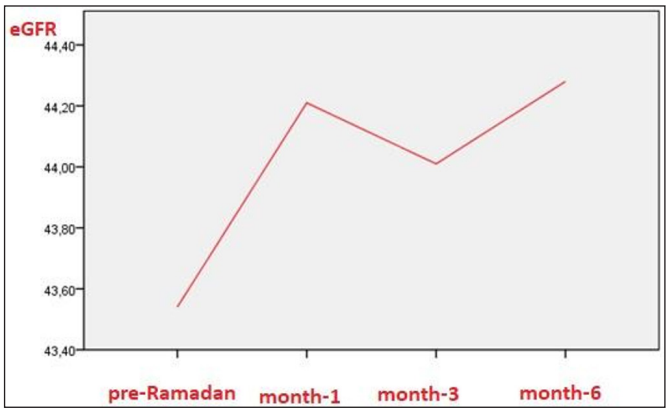

Figure 2. eGFR changes during 6-month, following Ramadan fasting, eGFR; estimated glomerular filtration rate (pre-Ramadan vs post-Ramadan month-6, p=0.063), eGFR (CKD-EPI 2021 Formula) is given as ml/min/1.73 m²

The impact of ACEi/ARB on eGFR change was analyzed, revealing no statistically significant effect (p=0.084). Initially, participants not taking ACEi/ARB had lower pre-Ramadan eGFR levels compared to ACEi/ARB users (eGFR; 41.64±12.28 vs. 45.29±10.50, p=0.030). However, after Ramadan, an improvement was observed among ACEi/ARB-free individuals, leading to the disappearance of the difference (eGFR; 43.62±12.30 vs. 45.38±10.50, p=0.310). Age, HT, DM, CVD, polypharmacy (p=0.581), and BMI were found to have no significant impact on eGFR change (p=0.780, p=0.389, p=0.780, p=0.836, p=0.829, and p=0.182, respectively). Surprisingly, the pre-Ramadan evaluation by a physician also had no impact on eGFR change (Delta eGFR [pre-Ramadan eGFR - post-Ramadan eGFR / pre-Ramadan eGFR]; -0.02±0.11 vs. -0.02±0.13, p=0.966). **Table 3** illustrates the changes in eGFR according to the stages of CKD, showing that there was no significant alteration in eGFR, even among patients with advanced-stage CKD. Pre-Ramadan proteinuria had no impact on post-Ramadan eGFR change (p=0.208 and r^2=0.08). However, the impact of Ramadan fasting on proteinuria progression could not be investigated due to lack of the data.

Table 3. eGFR changes following Ramadan fasting according to the CKD stages.

eGFR*	Pre-Ramadan	Post-Ramadan	P value
Stage 3a, n=96	50.23±6.83	50.88±7.68	0.963
Stage 3b, n=66	41.15±6.28	41.68±6.89	0.910
Stage 4, n=25	26.80±9.38	28.48±11.42	0.366
Stage 5, n=5	10.00±1.22	11.00±1.41	0.463

*eGFR (CKD-EPI 2021 Formula) is given as ml/min/1.73 m^2, Abbreviations: eGFR: estimated golmerular filtration rate.

DISCUSSION

The results of this study indicate that Ramadan fasting did not significantly affect the eGFR, even among patients in advanced stages of CKD. Importantly, the use of ACEi/ARB did not lead to worse outcomes in this context. Additionally, certain laboratory parameters related to metabolic features, including fasting glucose, total cholesterol, HDL cholesterol, and LDL cholesterol, exhibited significant improvement during the fasting period. This is the largest sample-sized longitudinal study in the literature and the only study including a small group of patients with non-dialysis stage 5 CKD. These findings will support future research to gain deeper insights into the effects of Ramadan fasting on renal function and to identify effective strategies for managing CKD in individuals who observe fasting practices.

As of the year 2020, the population adhering to the Islamic faith comprises approximately one-fourth of the global population.[6] Muslims annually observe a one-month fast from the time of dawn to sunset, with the total fasting duration varying based on the specific timing and geographic location of the observance, in accordance with the Islamic lunar calendar. Despite the widespread and extensive participation in this religious practice, its health-related consequences remain insufficiently understood. The lack of knowledge on the subject is further compounded by the absence of similar long-term mass religious practices in Western culture.[7]

The extended periods of fasting during Ramadan, which often last around 18 hours per day, have raised concerns regarding the potential deterioration of kidney function. Unfortunately, there is no single guideline published for CKD and Ramadan fasting. The International Diabetes Federation and Diabetes and Ramadan (IDF-DAR) Practical Guidelines for 2021 represent the sole acknowledged data concerning the prevention of fasting-related complications in patients with diabetes and CKD.[8] In this cohort, DM and HTN were the leading underlying causes of CKD, as previously reported in other Muslim countries.[9-12] The mean fasting duration in our study was 14-15 hours per day, which is similar to previous studies, and all patients fasted for almost one month.[11]

There are several small studies that have addressed the impact of fasting on the glomerular filtration rate (GFR).[1,2,13] However, the results of these studies are controversial. For instance, Wakil et al.[1] reported a non-significant reduction in GFR and an increase in urine N-acetyl-B-D-glucosaminidase levels, indicating potential renal tubular cell injury at the end of Ramadan fasting. In contrast, Mbarki et al.[2] found a higher risk of acute kidney injury (AKI) associated with Ramadan fasting, especially for patients with pre-Ramadan creatinine clearance of <60 mL/min/1.73 m^2. Nasrallah et al.[14] reported a link between elevated serum creatinine and Ramadan fasting, with a higher risk of creatinine elevation observed among those receiving renin-angiotensin-aldosterone system antagonists (RR=2). However, serum creatinine levels generally returned to baseline by the end of the fasting month. This study also demonstrated a higher occurrence of major adverse cardiovascular events among fasting CKD patients with pre-existing cardiovascular disease.

Numerous studies have reported that Ramadan fasting was not associated with an increased risk of declining renal function in patients with stages 2-4 CKD, even among kidney recipients.[4,13,15-17] However, the authors of these studies noted that elderly individuals might still be at a higher risk, and the amount of pre-fasting water consumption may play a significant role as a predictor of renal function. This study represents the largest sample size in the literature, and the study cohort was older compared to previous studies, yet GFR did not decrease

following Ramadan at the 6-month follow-up, consistent with previous studies.[11,17,18] Nevertheless, it is essential to acknowledge that this study was not designed to demonstrate the acute changes in GFR within the holy month of Ramadan.

Evidence-based risk factors for major complications during Ramadan fasting in individuals with diabetes indicate that age is a significant risk factor for hospitalization.[19] Abdullah et al.[19] suggested that a small subgroup of individuals with preexisting comorbidities may experience fasting-related kidney function issues. Kara et al.[13] also emphasized age as a risk factor for the deterioration of kidney function. However, in this current study, regression analysis demonstrated that age had no impact on the change in glomerular filtration rate (GFR) following Ramadan fasting.

The available literature on risk factors for GFR deterioration due to Ramadan fasting in CKD patients is limited. Paradoxically, the perception that prolonged fasting and thirst pose a risk for the deterioration of CKD in CKD patients is not supported by the evidence. This study indicates that traditional risk factors for CKD progression, such as DM, HT, CVD, and age, do not show any significant association with GFR changes in fasting patients. Furthermore, ACEi/ARB use was not found to impact GFR. It is possible that the acute hemodynamic changes experienced during Ramadan fasting may reverse after the conclusion of the holy month, at least in this particular cohort. Another explanation could be that the study participants had well-controlled or mild comorbidities that were not affected by fasting.

Data regarding patients with CKD stage 5 and Ramadan fasting is lacking as previous studies have often excluded this patient group.[4,20,21] In this study, a small group of patients with CKD stage 5 did not exhibit a significant change in GFR following Ramadan fasting.

Previous studies suggest that seeking consultation before Ramadan may lead to improved outcomes and better disease monitoring. However, this study did not find a significant impact of pre-Ramadan consultation on GFR changes. Since this was not a controlled study, participants may have received consultancy from different physicians or obtained information from various media sources.

Ramadan fasting has been associated with beneficial effects on metabolic parameters, such as blood glucose and lipid profile, as demonstrated in previous studies.[22,23] Consistent with these findings, our study also revealed similar improvements in lipid profile, with the exception of triglyceride levels. It is worth noting that fasting during Ramadan induces an acute increase in osmolarity and serum electrolytes while reducing body water composition.[24] In our study, we observed significant increases in potassium and calcium values during Ramadan fasting; however, the final values remained within the normal physiological range. These observations suggest that the changes in electrolyte levels during fasting were not of clinical concern and did not pose any adverse health effects.

Limitations of the Study

Sample size: The study's sample size may be relatively small, limiting the generalizability of the findings to a broader population of individuals with CKD observing Ramadan fasting.

Lack of control group: The absence of a control group of non-fasting individuals with CKD hinders the ability to compare the fasting group's outcomes to those not participating in Ramadan fasting, making it challenging to attribute specific effects solely to fasting.

Retrospective data: The study's retrospective nature may introduce inherent biases and limitations in data collection and analysis, potentially affecting the accuracy and completeness of the information obtained.

Single-center study: Conducting the study at a single center may limit the diversity of the study population and restrict the representation of individuals with CKD from different geographic regions or healthcare settings.

Short-term follow-up: The six-month follow-up period may not be sufficient to capture long-term changes or complications related to Ramadan fasting in individuals with CKD. A longer follow-up duration would provide more comprehensive insights into the effects of fasting on renal function over time.

Variability in fasting practices: Ramadan fasting practices can vary among individuals, with some adherents following strict fasting while others may modify their fasting patterns due to health conditions or personal preferences. The heterogeneity in fasting practices within the study population might introduce variability in the results.

Lack of dietary and fluid intake data: Detailed dietary and fluid intake information during Ramadan fasting was not recorded, which could potentially influence kidney function and confound the results.

Missing data: Incomplete or missing data on certain variables may limit the study's ability to analyze specific factors' impact on the outcomes.

External factors: Other external factors, such as climate, physical activity, or medication adherence, were not fully accounted for in the analysis and may have influenced the study results.

CONCLUSION

These findings suggest that, in our study cohort, Ramadan fasting does not appear to have adverse effects on kidney function. However, it is essential to consider individual variability in fasting practices and the potential influence of factors such as age, comorbidities, and medication use. Further research is warranted to explore the acute changes in kidney function within the holy month of Ramadan and to examine the effects of fasting on specific subgroups, such as elderly individuals and those with advanced CKD.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of by Zonguldak Bülent Ecevit University Non-interventional Clinical Researches Ethics Committee (Date: 10.06.2022, Decision No: 2022/14).

Informed consent: All patients included in the study signed informed consent.

Referee Evaluation Process: Externally peer reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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