REVIEW ARTICLE

Ramadan fasting and chronic kidney disease: A systematic review

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Ramadan fasting represents one of the five pillars of the Islam creed according to the Sunnah and the second practice of faith for the Shiaa. Even though patients are exempted from observing this religious duty, they may be eager to share this particular moment of the year with their family and peers. However, there are no guidelines or standardized protocols that can help physicians to properly address the issue of patients with chronic kidney disease (CKD) fasting in Ramadan and to correctly advise them. Moreover, in a more interconnected and globalized society, in which more and more Muslim patients live in the Western countries, this topic is of high interest also for the general practitioner. For this purpose, we carried out a systematic review, including also articles written in Arabic, Turkish, and Persian languages. Our main findings are that:

1. recipients of kidney allograft can safely fast during Ramadan;
2. evidences for safety in patients with nephrolithiasis and CKD are instead mixed and controversial. On the other hand,
3. most studies have been carried out during Ramadan falling in cold seasons, and there is scarce information about Ramadan fasting in hot seasons.

For these reasons, the findings may be not generalizable and therefore cautions should be taken and applied; the physicians should carefully monitor their patients during the fasting period with an adequate follow-up, in order to avoid any injurious effect.

Key words: Chronic kidney disease, hemodialysis, Islam, kidney transplantation, peritoneal dialysis, Ramadan fasting, renal colic

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INTRODUCTION

The holy month of *Ramadan* (in Arabic and Farsi language, *Ramadhaan*), the 9th month of the Muslim lunar calendar (*Hijra*), is of great value and significance among Muslims, representing the month of the descent of the *Qu'ran*. For the Sunnis, Ramadan fasting (*as-sawm*) is considered one of the five Islamic pillars of the creed (*arkan al-Islam*), together with the faith declaration (*as-shahada*), the ritual prayers (*as-salah*), the pilgrimage to Mecca (*hajj*), and charity (*zakat*). For the Shiites, Ramadan is the second practice of the religious branches (termed also as practices of faith).

Ramadan is not only abstinence from food and drinking, but also from smoking, medication, and sexual intercourses (*Surat* 2 "*Al-Baqarah*", *ayyat* 183-187).

Ramadan fasting is not, however, a prolonged or continuous fasting, but consists of alternate fasting and feasting (re-feeding) periods.[1] For this reason, it represents a "unique metabolic model."[18] Predawn meal is termed as *suhoor*, while after-sunset meal is called *iftar*. Ramadan duration is variable, since the Islamic calendar is a lunar one and therefore the Islamic year contains 354 days (instead of 365, as in the Gregorian or solar calendar). For this reason, the Ramadan month occurs 11 days earlier every year, and may fall in any period of the year, making a full circle in a span of 33 years. Therefore, mean fasting duration is usually 12-14 h, but depending on the place and the year it can last also up to 18 h[2] or even 22 h, in the extreme latitudes.[1]

Prepuberal and puberal children, menstruating, pregnant and breast-feeding women, sick people, debilitated older subjects, travelers are exempted from this religious duty (*Surat* 2 "*Al-Baqarah*", *ayyat* 184-185). However, they could be willing to fast and share the spirituality of this month with their family and peers.[3]

The effects of Ramadan fasting on kidney physiology is not a mere academic topic or of limit interest for only the Arabic countries. In a globalized society, the physicians have to face with issues like the management of chronic

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kidney diseases (CKDs) in Muslim patients that want to fast during Ramadan, since more and more Muslims live in the Western societies.[4] However, information is sparse and no guidelines or standardized protocols exist.[3] For this purpose, we have carried out a systematic review, that could be helpful for general practitioners.

MATERIALS AND METHODS

We systematically searched ISI Web of Science (WoS), Scopus, MEDLINE/PubMed, Google Scholar, Directory of Open Access Journals (DOAJ), EbscoHOST, Scirus, and ProQuest. We used a proper string made up of a combination of key-words such as "fasting," "CKD" and "chronic renal failure."

Gray literature was also manually searched. Review articles or research manuscripts not pertinent with the aim of this systematic review were excluded, while all the other research articles (including editorials, letters, case reports) were retained.

No time and language filters were applied.

RESULTS

We identified 25 original articles describing 26 studies [Table 1, with the list of studies divided according to their main topic], and we coded them. Fifteen studies as described in 14 manuscripts focused on kidney transplant, 6 on renal colic, while 5 studies concerned CKDs. Most studies were original researches (20 articles), 3 were conference proceedings, 1 was a letter and 1 was a clinical case report. We summarized in Tables 2 and 3 the demographic characteristics, the clinical suggestions and interventions as well as the main findings, the investigated parameters and the used statistical techniques (when reported by the authors).

Most studies were prospective and observational, with the exceptions of that by Basiri *et al*., which is a retrospective, database-based study[12] as well as that by Al-Hadramy.[7]

Most studies did not find any differences between fasters and not fasters, or between before and after Ramadan fasting [Table 3].

The study by Bernieh *et al*. they found improvements during the fasting and after.[13]

Only three studies presented mixed evidences of an increased risk for fasting patients during Ramadan, and three clear negative evidences.

Table 1: Studies divided according to their main topic

Kidney pathology	References
Kidney transplant	Qurashi *et al*., 2012
	Mousavi *et al*., 2011
	Salem *et al*., 2010
	Boobes *et al*., 2009
	Einollahi *et al*., 2009
	Ghalib *et al*., 2008
	Einollahi *et al*., 2005
	Argani *et al*., 2003
	Said *et al*., 2003
	Abdalla *et al*., 1998 (first study)
	Abdalla *et al*., 1998 (second study)
	Ouziala *et al*., 1998
	Al-Khader *et al*., 1996
	Bernieh *et al*., 1994
	Rashed *et al*., 1989
Renal colic	Günaydın *et al*., 2012
	Miladipour *et al*., 2012
	Abdolreza *et al*., 2011
	Zghal *et al*., 2005
	Basiri *et al*., 2004
	Al-Hadramy, 1997
CKD	Al Wakeel *et al*., 2013
	Bernieh *et al*., 2010
	El-Wakil *et al*., 2007
	Al Muhanna, 1998
	Al-Khader *et al*., 1991

CKD = Chronic kidney disease

However, most of studies (11/26) were conducted in cold seasons, while only 3 in hot seasons, for the other 12 no information was available [Table 4]. For this reason, the findings may be not generalizable to hot seasons and therefore cautions should be taken and applied when fasting in those periods.

DISCUSSION

The need for evidence-based protocols

There is a strong need for evidence-based suggestions and guidelines.[3] An alarming letter was published, calling for caution in fasting patients during Ramadan and advising of a "R^2 syndrome" (religion and renal failure).[27]

Even though the content of this letter is a bit exaggerated, patients with kidney diseases should be properly advised and counseled before the beginning of Ramadan, as well as during and after the fasting period, about the proper dietary and pharmacological regimen and other behaviors to follow.

This could be done within a multidisciplinary team, made up of a nephrologist, a nutritionist, a psychiatrist or a psychologist. Patients should be carefully checked and assessed, considering both the clinical symptoms and the laboratory exams.

Table 2: Studies summarized according to the investigated parameters and the used statistical techniques

References	Investigated parameters	Statistical analysis
Al Wakeel *et al*., 2013	Weight, blood pressure, average daily urine output (as an estimate of residual renal function), weekly creatinine clearance, Kt/V (as an estimate of HD and PD treatment adequacy)	NA
Günaydın *et al*., 2012	Heart rate, systolic blood pressure, blood glucose, urine volume and density/specific gravity, urea, creatinine, leukocyte count in urine, erythrocyte count in urine, ketonuria	Student's *t*-test, Pearson correlation analysis
Miladipour *et al*., 2012	Total excretion of calcium, oxalate, uric acid, citrate, phosphate, magnesium, sodium and potassium in 24-h urine, urine volume, urine concentration of calcium, oxalate, uric acid, citrate, phosphate, magnesium, sodium, and potassium, uric acid supersaturation, calcium phosphate and calcium oxalate supersaturation	Student's *t*-test
Qurashi *et al*., 2012	MDRD GFR, e-GFR, serum creatinine	Student's *t*-test, Chi-square test, Wilcoxon signed-rank test
Abdolreza *et al*., 2011	Number of visits and admissions to ED, mean room temperature, humidity	ANOVA
Mousavi *et al*., 2011	Systolic and diastolic blood pressure, serum urea, creatinine, BUN	NA
Bernieh *et al*., 2010	Weight, systolic and diastolic blood pressure, hemoglobin, e-GFR, blood sugar, HbA1c, serum creatinine, proteinuria, urinary sodium, potassium, carbonate, urea, lipid profile (HDL, LDL, total cholesterol, triglycerides), osmolality, protein/creatinine ratio	ANOVA
Salem *et al*., 2010	Body weight, blood pressure, urine volume, serum urea, creatinine, cyclosporine A, creatinine clearance, urinary total count of leukocytes and erythrocytes, proteinuria	NA
Boobes *et al*., 2009	Weight, systolic and diastolic blood pressure, creatinine, urea, uric acid, albumin, lipid profile (HDL, LDL, total cholesterol, triglycerides), ciclosporine A, tacrolimus, hemoglobin, MDRD GFR, sodium, potassium and carbonate	Unpaired two tail Student's *t*-test
Einollahi *et al*., 2009	Body weight and BMI, e-GFR, hemoglobin, creatinine clearance, serum BUN, creatinine, uric acid, blood glucose, electrolytes, lipid profile	Paired Student's *t*-test, Pearson Chi-square test, Fisher exact test, Wilcoxon signed-rank test, Mann-Withney test, Spearman's correlation analysis
Ghalib *et al*., 2008	Body weight, MAP, plasma creatinine, proteinuria, GFR, average and maximum temperature, average humidity	Paired Student'S *t*-test, Chi-square test, Wilcoxon signed-rank test, multiple linear regression
El-Wakil *et al*., 2007	GFR, mean blood pressure, urinary NAG, urinary NAG/creatinine ratio, blood glucose, BUN, serum sodium, potassium, albumin, lipid profile (cholesterol, triglycerides), proteinuria, urinary protein/creatinine ratio	Paired Student's *t*-test, Mann-Withney test, Wilcoxon signed-rank test, Spearman's rank correlation analysis
Einollahi *et al*., 2005	Body weight, standing and lying blood pressure, serum levels BUN, serum creatinine, uric acid, lipids, and hemoglobin	Not described in the test (method section)
Zghal *et al*., 2005	Crystalluria and other urinalysis parameters	NA
Basiri *et al*., 2004	Number of visits and admissions to ED	Unpaired Student's *t*-test
Argani *et al*., 2003	Body weight, blood pressure, BUN and urea, serum sodium, serum potassium, blood glucose, hemoglobin, lipid profile (triglycerides, LDL, VLDL, HDL cholesterol and total cholesterol), complement level (C3, C4), serum immunoglobulins (IgA, IgG, IgM), B-cell count, T-cell count, serum uric acid, serum and urine creatinine, 24-h urine volume, proteinuria, 24-h urine protein/urine creatinine ratio	ANOVA, Friedman test
Said *et al*., 2003	Serum urea, creatinine, systolic and diastolic blood pressure, blood sugar	Pearson Chi-square, Fisher exact test, Wilcoxon signed-rank test
Abdalla *et al*., 1998	Lying and standing blood pressure, serum and urine sodium, sodium and urine creatinine, serum potassium, urea, cyclosporine A, urinary osmolality, FENa, haematocrit	Paired Student's *t*-test
Ouziala *et al*., 1998	Body weight, standing and lying blood pressure, serum sodium, potassium, chloride, calcium, phosphorus, uric acid, urea, creatinine, bicarbonate, total protein, lipid profile (triglycerides, cholesterol), bilirubin, aspartate amino transferase, alanine amino transferase, alkaline phosphatase, hemoglobin, white blood cells, proteinuria, FENa and hematuria, urine volume	Student's *t*-test
Al-Hadramy, 1997	Number of visits and admissions to ED for renal colic episodes, mean monthly temperature, pressure and relative humidity	Pearson product moment, correlation analysis, Student's *t*-test
Al-Khader *et al*., 1996	Body weight, blood pressure, urinary osmolality, FENa	NA
Bernieh *et al*., 1994	Body weight, standing and lying blood pressure, total leukocyte count, hemoglobin, serum potassium, sodium, urea, creatinine, total protein, glucose, albumin, cyclosporine A, lipid profile (cholesterol, triglycerides), FENa, urine volume, proteinuria	Student's *t*-test
Al-Khader *et al*., 1991	Body weight, blood pressure, urinalysis	NA
Rashed *et al*., 1989	Sodium urinary osmolality	NA

BMI = Body mass index; BUN = Blood urea nitrogen; ED = Emergency department; e-GFR = Estimated glomerular filtration rate; FENa = Fractional excretion of sodium; GFR = Glomerular filtration rate; HD = Hemodialysis; MAP = Mean arterial pressure; MDRD = Modification of diet in renal disease; NA = Not available; PD = Peritoneal dialysis; HDL = High density lipoprotein; LDL = Low density lipoprotein; VLDL = Very low density lipoprotein; NAG = N-acetyl-B-D-glucosaminidase

Table 3: Studies summarized according to the demographic characteristics of the sample and their clinical suggestions, interventions and main findings

References	Demographic characterstics	Main findings
Al Wakeel *et al*., 2013	Study design: Prospective cohort observational/interventional study Sample: 18 patients (10 female, 8 male) out of an initial cohort of 31 under PD; 8 on CAPD (2 at low membrane transport; 3 at low-average transport, and 3 at high-average transport by a PET), 10 on CCPD (1 at low membrane transport; 5 at low-average transport; 3 at high-average transport, and 1 at high transport by PET) Age: Mean age 41.8±15.7 years, in the range of 17-66 years Mean fasting duration: 14 h Patients monitoring: 3-4 weeks before Ramadan, during Ramadan (with a regular follow-up every 2 weeks), 4 weeks after Ramadan Inclusion criteria: Good and stable general health, autonomy and compliance to treatment Exclusion criteria: Poorly controlled diabetes, hypertension, angina, postural hypotension, co-morbidities, lack of autonomy and compliance to treatment Place: Riyadh (Saudi Arabia) Time: Ramadan 2009 (August-September)	Complication rates: 5/18 (27.8%): hypotension (in 2 cases), hypertension (1 case), pleural effusion (1 case), and lower-limb edema and fluid overload (1 case) Two patients developed peritonitis and therapy was discontinued No statistically significant changes in the biomarkers and parameters
Günaydın *et al*., 2012	Study design: Matched case-control prospective observational study Sample: 61 subjects (45 male, 16 female), 35 fasting (25 male, 10 female), 26 nonfasting (20 male, 6 female) as control group Age: Mean age 41.13 years Mean fasting duration: 18 h Patients monitoring: During Ramadan Inclusion criteria: Fasting subject, aged >18 years, with episodes of renal colic, accessing the ED Exclusion criteria: None Place: Ankara (Turkey) Time: Ramadan 2011 (August)	No significant changes apart from heart rate ($P = 0.007$). Some significant correlations between urea and creatinine ($r = 0.38$, $P = 0.003$), between urine erythrocyte and leukocyte numbers ($r = 0.29$, $P = 0.026$), and between fasting days and blood pressure ($r = 0.48$, $P = 0.015$) were observed. A correlation between urine density and dehydration was not observed
Miladipour *et al*., 2012	Study design: Prospective matched case-control observational study Sample: 57 men, 37 with recurrent kidney calculi (clinical symptoms confirmed with radiological imaging and calculi analysis), matched with a randomly selected group of 20 subjects with no history of kidney calculi Age: Mean age 41.66±6.80 years, in the range of 30-55 years. Mean fasting duration: 15 h Patients monitoring: 1 day before Ramadan, during Ramadan, 1 day after Ramadan Inclusion criteria: Subjects with a history of kidney calculi Exclusion criteria: Subjects with urinary tract anomalies, infections, obesity (BMI >30) and any co-morbidities (metabolic, gastrointestinal, liver, kidney, cardiovascular, or endocrine) or taking drugs Place: Tehran (Iran) Time: NA	Total excretion of calcium, phosphate, and magnesium in 24-h urine as well as urine volume during fasting were significantly lower. Urine concentration of calcium during fasting was significantly lower ($P < 0.001$), while urine concentrations of uric acid, citrate, phosphate, sodium, and potassium were significantly higher. Uric acid supersaturation was increased, while calcium phosphate supersaturation was decreased significantly during fasting
Qurashi *et al*., 2012	Study design: Prospective matched case-control observational study Sample: 43 fasters (20 male) versus 37 nonfasters (21 male) Age: Mean age 43.7±15.6 years for the fasting group versus mean age 41.8±15.4 for the nonfasting group Mean fasting duration: 12-14 h Patients monitoring: NA before Ramadan, during Ramadan, and 1 and 6 months after the end of Ramadan Inclusion criteria: Recipients of kidney allograft. Mean length of time after transplant in the two groups was 64.4±30.4 (for the fasters) and 27.7±36.7 months (for the nonfasters). Mean follow-up 7.6±1.3 months Exclusion criteria: NA Place: Riyadh (Saudi Arabia) Time: Ramadan 2011 (August)	No statistically significant differences

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Table 3: (*Continued*)

References	Demographic characterstics	Main findings
Abdolreza *et al*., 2011	Study design: Prospective observational cohort study Sample: 610 patients with renal colic (441 male, 169 female) Age: In the range 15-85 years (mean age 37.6 years) Patients Monitoring: 2 weeks before Ramadan, during Ramadan (the first and second 2 weeks), 2 weeks after Ramadan Inclusion criteria: Patients with episodes of renal colic Exclusion criteria: None Time: Ramadan 2008 (September) Place: Mashhad (Iran)	The number of admissions due to renal colic was higher during the first 2 weeks of Ramadan ($P<0.05$)
Mousavi *et al*., 2011	Study design: Clinical case reports Sample: 5 patients recipients of a kidney allograft (2 male, 3 female); 2 suffering from glomerulonephritis, 1 from diabetes mellitus Age: Mean age 32.6±6.7 years, in the range 25-40 years Mean fasting duration: NA Patients monitoring: NA Inclusion criteria: NA Exclusion criteria: NA Time: NA Place: Iran	No statistically significant changes
Bernieh *et al*., 2010	Study design: Prospective observational cohort study Sample: 31 CKD patients (19 male, 12 famale) from an initial cohort of 45 subjects, 14 in stage III, 12 in stage IV, 5 in stage V; 19 suffering from diabetes (50% of them managed with oral hypoglycemiants agents, 40% with insulin and 10% with both), 22 from hypertension Age: mean age 54.0±14.2 years, in the range of 23-81 years Mean fasting duration: NA Patients monitoring: 1 month before Ramadan, during Ramadan, 1 month after Ramadan Inclusion criteria: Patients with CKD (diabetes mellitus in 61% of the subjects, in 26% of the cases chronic glomerulonephritis, systemic lupus nephritis, and in 13% of the cohort unknown causes of CKD), with co-morbidities (hypertension in 71% of the cases) and hyperlipidemia (in 26% of the cases), age >18 years Exclusion criteria: Patients with kidney transplant, history of acute tubular necrosis due to dehydration, and renal colic, severe co-morbidities, pregnancy, needing to assume medications more than twice a day Time: Ramadan 2005 (October-November) Place: Al Ain (United Arab Emirates)	Weight reduction, and lower systolic and diastolic blood pressure were observed. e-GFR showed a significant improvement during the fast and the month after. The blood sugar was high during fasting with an increment in the HbA1c. There was better lipid profile, reduction of the proteinuria and FENa. No complications were observed
Salem *et al*., 2010	Study design: Prospective cohort observational study Sample: 25 patients recipient of kidney allograft (from an initial cohort of 100 subjects), 15 male and 10 female; mean posttransplantation duration of 8.5 years, with a range of 1.5-26 years, treated with cyclosporine, azathioprine or mycophenolate mofetil, and prednisolone; 5 patients suffering from hypertension (4 managed with nifedipine and atenolol, 1 with diltiazem.); the final list of patients includes 20 patients (5-4 male and 1 female - did not complete the follow-up) Age: mean age 41.7±9.8 years (range: 28-57 years) for the male subjects, mean age of 44.9±12.3 years (range: 32-62 years) for the female patients Mean fasting duration: NA Patients monitoring: 2 weeks before Ramadan, during Ramadan, 2 weeks after Ramadan Inclusion criteria: Good renal function Exclusion criteria: NA Time: Ramadan 2008 (September) Place: Tripoli (Libya)	No statistically significant changes

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Table 3: (*Continued*)

References	Demographic characterstics	Main findings
Boobes *et al*., 2009	Study design: Prospective cohort observational study Sample: 22 patients (10 male, 12 female). 18 (82%) patients received the organ from living nonrelated donors, 4 from living related donors. 19 patients were treated with a triple immunosupressive regimen. Some patients suffered from co-morbidities, such as hypertension (20 patients), dyslipidemia (9 patients) and diabetes mellitus (5 patients). The mean posttransplant period was 78.8±61.7 months (in the range: 14-250) Age: Mean age 47±11.6 years (age in the range: 25-69 years) Mean fasting duration: 12 h and half Patients monitoring: 3 months before Ramadan, 1 month before Ramadan, during Ramadan, 1 month after Ramadan Inclusion criteria: Recipients of kidney allografts with a transplanted organ from >1 year, with stable functions Exclusion criteria: Any acute illness before and during the Ramadan Time: Ramadan 2004 (October-November). Place: Al Ain (United Arab Emirates)	No statistically significant changes were observed apart from albumin (P=0.02; before-after Ramadan), triglycerides (P=0.0011; before-during Ramadan) and ciclosporine A level (P=0.03; before-after Ramadan). No complications or adverse effects were recorded
Einollahi *et al*., 2009	Study design: Prospective matched case-control observational study Sample: 41 fasting patients (16 of which with mild-to-moderate renal impairment; 30 male, 12 female) matched with 41 nonfasting subjects (24 male, 16 female). The recipients of kidney allograft received the organ from living related (6 and 5), living unrelated (28 and 35), and deceased donors (7 and 1), for the fasting and nonfasting group respectively Age: Mean age 41.9±11.9 years for the fasting group versus mean age 43.1±12.0 years for the nonfasting group Mean fasting duration: 14 h Patients monitoring: Before, during and after Ramadan Inclusion criteria: Healthy and physically fit to observe the fasting, transplantation at least 1 year prior to the study and stable renal function for at least 6 months prior to the study exclusion criteria: NA acute tubular necrosis due to dehydration, age below 18 years, poorly controlled hypertension, pregnancy, severe co-morbidities (such as chronic liver disease, advanced cardiac disorders, acute infection, diabetes mellitus or diabetes insipidus, active peptic ulcer or nephrolithiasis), polyuria (urine volume ≥2.5 l/day) Time: Ramadan 2007 (September-October) Place: Tehran (Iran)	No statistically significant changes were observed apart from the different values of GFR between recipients of kidney transplant with previously repeated fasting and those without (P <0.05)
Ghalib *et al*., 2008	Study design: Prospective matched case-control observational study Sample: 35 fasting patients recipients of kidney allograft (treated with mycophenolate mofetil, sirolimus, tacrolimus, prednisolone and cyclosporine A; 68.6% male) matched with 33 nonfasting subjects (75.8% male). Posttransplant time was 5.7±4.0 years for the fasting group and 4.5±4.6 years for the nonfasting group. A total of 14.3% (for the fasters) and 27.3% (for the nonfasters) received the kidney allograft <1 year. 28.6% of the fasting subjects suffered from concurrent diabetes, whilst 88.6% from hypertension Age: mean age 39.5±13.2 years for the fasting group versus mean age 41.5±14.0 years for the nonfasting group Mean fasting duration: 12-14 h Patients monitoring: During Ramadan and throughout the 3 years of this study Inclusion criteria: Good and stable renal functions Exclusion criteria: Impaired e-GFR/GFR, severe co-morbidities Time: Ramadan 2004 (October-November), Ramadan 2005 (October-November), Ramadan 2006 (September-October) Place: Riyadh (Saudi Arabia)	No statistically significant changes

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Table 3: (*Continued*)

References	Demographic characterstics	Main findings
El-Wakil *et al*., 2007	Study design: Prospective observational cohort study Sample: 15 predialysis CKD patients (9 female, 6 male); 6 healthy volunteers as control group. Patients were suffering from diabetes mellitus (21.4% of the cases), hypertension (21.4%), chronic pyelonephritis (21.4%), chronic glomerulonephritis (14.2%), polycystic kidney disease (14.2%) and obstructive uropathy (7.14%) Age: Mean age 53.0±15.6 years, in the range of 23-82 years Mean fasting duration: NA Patients monitoring: NA Inclusion criteria: Good and stable renal functions, creatinine clearances below 60 ml/min Exclusion criteria: Age <20 years, acute infections, diabetes insipidus, severe co-morbidities (such as cardiovascular disorders, chronic liver disease) Time: Ramadan 2001 (November) Place: Alexandria (Egypt)	Before fasting, BUN was higher in CKD patients (P=0.003), as well as serum potassium (P=0.01), urinary protein excretion (P=0.03). Serum albumin was lower in CKD patients (P=0.003), as well as GFR (P=0.004). After fasting, there was a significantly positive correlation between the NAG/creatinine values and the change in the blood glucose level (P=0.001), and urinary protein/creatinine ratio (P=0.02), as well as urinary protein/creatinine ratio and the percentage change in the blood glucose level (P=0.001). Moreover, urinary NAG was statistically significantly different between CKD patients and healthy controls (P=0.03)
Einollahi *et al*., 2005	Study design: Prospective matched case-control observational study Sample: 19 fasting patients (11 male, 8 female) matched with a group of 20 subjects who had not fasted in the last 3 years Age: 33.5±10.5 years for the fasting group versus mean age 38.3±10.2 years for the nonfasting group Mean fasting duration: 13-14 h Inclusion criteria: Transplantation at least 1 year prior to the study and serum creatinine values below 1.5 mg/dL Exclusion criteria: Acute tubular necrosis, nephrolithiasis, severe co-morbidities (such as active peptic ulcer, cardiovascular disorders), poorly controlled hypertension, diabetes mellitus, need for medications more than twice a day, and polyuria (urine volume>2.5 L/d) Time: NA Place: Tehran (Iran)	No statistically significant changes
Zghal *et al*., 2005	Study design: Matched case–control observational study Sample: 90 patients divided in 3 groups of healthy fasting individuals, healthy nonfasting individuals, and nonfasting patients with calcium lithiasis Age: NA Mean fasting duration: NA Patients monitoring: During Ramadan Inclusion criteria: Episodes of renal colic Exclusion criteria: NA Time: NA. Place: Tunisia	Crystalluria was higher in patients with lithiasis compared with healthy nonfasting individuals (58% vs. 11.4%), but was similar between healthy fasting participants and calcium lithiasis patients, as well as supersaturation of urinary oxalate, uric acid and brushit, but were similar between healthy fasting participants and calcium lithiasis patients. An increase in serum and urinary urea, as well as in uric crystal (12%) and in oxalate monohydrate or whewellite (4%) concentration was also observed
Basiri *et al*., 2004	Study design: Retrospective observational study, database-based Sample: 574 subjects (398 male, 176 female); 43 subjects fasting in Ramadan period (27 male, 16 female) Age: Mean age 36.4±14.0 years. Mean fasting duration: 12 h Patients monitoring: Not applicable Inclusion criteria: Subjects accessing the ED, with a history of renal colic Exclusion criteria: NA Time: Ramadan 2000 (November-December), Ramadan 2001 (November-December) Place: Varamin (Iran)	There was no statistically significant difference between frequency of admissions for renal stone colic episodes in Ramadan and mean admission during the year for the 2 years of the study. The mean admission in warm seasons instead was found to be significantly higher than in Ramadan (P=0.001)

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Table 3: (*Continued*)

References	Demographic characterstics	Main findings
Argani *et al*., 2003	Study design: Prospective observational cohort study Sample: 24 patients out of an initial cohort of 30 subjects (15 male, 15 female) Age: Mean age 39±4 years. Mean fasting duration: 12 h Patients monitoring: 1 month before Ramadan, during Ramadan (beginning of Ramadan, after 2 weeks of fasting, end of Ramadan), 1 month after Ramadan Inclusion criteria: Subjects recipients of kidney allograft, with a stable renal function, 30 months after the transplantation, with serum creatinine <1.8 mg/dL under triple immunosuppression and not taking drugs more than twice a day Exclusion criteria: Severe co-mobordities (such as cardiovascular disorders), diabetes mellitus Time: NA Place: Tabriz (Iran)	No statistically significant differences between the 2 groups were observed apart from the level of blood VLDL (P=0.019) and HDL (P=0.001) cholesterol, C3 (P=0.010), C4 (P=0.001) and IgM (P=0.020). HDL and C4 values increased after the fasting, whilst VLDL, C3, and IgM decreased
Said *et al*., 2003	Study design: Prospective matched case-control study Sample: 145 kidney transplant recipients divided in two matched groups of fasting (71) and nonfasting (74) subjects Age: In the range of 18-64 years; 37.3±11.9 years for the fasting subjects, 40.1±10.5 years for the nonfasting subjects Mean fasting duration: 12 h Patients monitoring: 1 year before Ramadan, during Ramadan, 1 year after Ramadan Inclusion criteria: Good and stable general health, serum creatinine level <200 μmol/L for at least 6 months before Ramadan Exclusion criteria: Active peptic ulcer disease or renal stone disease Time: Ramadan 2000 (November) Place: Kuwait	No statistically significant differences apart from the level of blood sugar (especially in patients suffering from diabetes type 1). The incidence of adverse effects was not statistically significant between the groups. However, cyclosporine toxicity was observed in 2 fasters, acute rejection in other 2 subjects, as well as urinary tract infections in other 2 patients (complication rates: 6/71, 8.5%)
Abdalla *et al*., 1998 (first study)	Study design: Prospective observational cohort study Sample: 23 transplant recipients (18 male, 5 female), 17 with a normal function and 6 with an impaired but stable function Age: Mean age 35.5 years (age in the range 20-60 years) Patients monitoring: 1 week before Ramadan, during Ramadan (2nd and 4th week of fasting), 1 week after Ramadan Inclusion criteria: Recipients of kidney allograft (9 had cadaveric transplant, 7 received allograft from living-related donors, and 7 had transplants from living nonrelated donors), managed with cyclosporine A and prednisolone. Mean posttransplant period was 2.0 (range: 0.6-6.3) years Exclusion criteria: Severe co-morbidities, serum creatinine >300 mMol/L Time: NA Place: Riyadh (Saudi Arabia)	No statistically significant changes apart from a small but statistically significant (P=0.017) increase in serum potassium. No complications were observed
Abdalla *et al*., 1998 (Second study)	Study design: Prospective observational cohort study Sample: 34 patients with a mean posttransplant period of 6.2 (range: 1.6-15.3) years, 8 of them had impaired function with a mean serum creatinine level of 193.6 (range: 142-263) mMol/L Patients monitoring: 1 week before Ramadan, during Ramadan, 1 week after Ramadan Inclusion criteria: Good and functional allograft Exclusion criteria: Severe co-morbidities Time: NA Place: Riyadh (Saudi Arabia)	No statistically significant differences

(Continued)

Table 3: (*Continued*)

References	Demographic characterstics	Main findings
Al Muhanna, 1998	Study design: Prospective observational cohort study Sample: 36 patients (18 male and 18 female), with moderate to severe renal failure Age: Mean age of 39±5 years Monitoring patients: during Ramadan, 2 weeks after Ramadan Time: NA Place: Dammam (Saudi Arabia)	There was a statistically significant elevation of serum creatinine, BUN, uric acid during the month of Ramadan and 2 weeks after Ramadan. There was a statistically significant deterioration of creatinine clearance and other biochemical parameters Complications rate: 25% (liquid and fluid accumulation, lower limb edema, weight gain, poor control of blood pressure)
Ouziala *et al*., 1998	Study design: Prospective observational cohort study Sample: 14 patients (9 male, 5 female) Age: Mean age 26.4 years (age in the range 18-32 years); transplantation 1-7 months before the beginning of the study Mean fasting duration: 11 h and half Inclusion criteria: Stable renal functions, <12 months from the transplantation, not high immunosuppressive regimen Exclusion criteria: Severe co-morbidities. Time: Ramadan 1997 (December-January) Place: Algiers (Algeria)	There was no significant change in serum values apart from, however, a significant elevation of total plasma proteins, urea, uric acid, hemoglobin, triglycerides, cholesterol, urinary sodium and potassium concentration (P<0.05). 5 patients (35.7%) showed changes in body weight
Al-Hadramy, 1997	Study design: Retrospective observational cohort study Sample: 447 male subjects with history of renal colic Inclusion criteria: Subjects accessing the ED (80,951 ED recorded visits) Time: Ramadan 1992 (March-April), Ramadan 1993 (February-March), Ramadan 1994 (February-March) Place: Jeddah (Saudi Arabia)	There was no statistically significant difference between frequency of ED visits and admissions in Ramadan and in Haj festival (*Tholhejah*) and mean admission during the 3 years of the study. A significant correlation was found between urinary stone colic and both temperature (r=0.67-0.76, P<0.0001) and atmospheric pressure (r=−0.64/−0.74, P<0.0001), but not with relative humidity
Al-Khader *et al*., 1996	Study design: Prospective cohort observational study Sample: 58 patients recepients of kidney allograft. No other information available Age: NA Patients monitoring: NA Inclusion criteria: NA Exclusion criteria: NA Time: NA Place: Riyadh (Saudi Arabia)	No statistically significant differences
Bernieh *et al*., 1994	Study design: Prospective observational cohort study Sample: 11 patients (7 male, 4 female) out of an initial cohort of 45 subjects; the patients were transplanted between 12 and 62 months before and the mean age of the grafts was 30+15.6 months Age: In the range 17-50 years Inclusion criteria: Stable renal functions. Hypertension does not constitute an exclusion criteria Exclusion criteria: Severe co-morbidities Time: Ramadan 1993 (February-March) Place: Saudi Arabia	There were no statistically significant changes apart from potassium (P=0.044) and blood pressure (P=0.013)
Al-Khader *et al*., 1991	Study design: Prospective observational cohort study Sample: 40 patients on HD, fasting on nondialysis days Inclusion criteria: Being on HD for at least 6 months Time: NA Place: Riyadh (Saudi Arabia)	An increase in serum potassium and interdialytic weight gain were observed. No complications such as pulmonary edema or hyperkalemia were recorded

(Continued)

Table 3: (*Continued*)

References	Demographic characterstics	Main findings
Rashed *et al*., 1989	Study design: Prospective matched case-control study Sample: 43 patients recipients of kidney transplant treated with azathioprine, prednisolone and/or cyclosporine A matched with 23 healthy controls Age: NA Inclusion criteria: Stable renal functions Exclusion criteria: Assumption of diuretics Time: NA Place: Doha (Qatar)	No statistically significant differences

BMI = Body mass index; BUN = Blood urea nitrogen; CAPD = Continuous ambulatory peritoneal dialysis; CCPD = Continuous cycling peritoneal dialysis; ED = Emergency department; e-GFR = Estimated glomerular filtration rate; FENa = Fractional excretion of sodium; GFR = Glomerular filtration rate; NA = Not available; NAG = N-acetyl-B-D-glucosaminidase; PD = Peritoneal dialysis; PET = Peritoneal equilibration test; CKD = Chronic kidney disease; HbA1c = Glycated hemoglobin; VLDL = Very low density lipoprotein; HDL = High density lipoprotein; HD = Hemodialysis

Table 4: Studies divided according to the Ramadan season in which they have been carried out

Ramadan season in which the study has been conducted	References
Hot seasons	Al-Wakeel *et al*., 2013
	Günaydın *et al*., 2012
	Qurashi *et al*., 2012
Cold seasons	Abdolreza *et al*., 2011
	Bernieh *et al*., 2010
	Boobes *et al*., 2009
	Einollahi *et al*., 2009
	Ghalib *et al*., 2008
	El-Wakil *et al*., 2007
	Basiri *et al*., 2004
	Said *et al*., 2003
	Ouziala *et al*., 1998
	Al-Hadramy, 1997
	Bernieh *et al*., 1994
No available information	Miladipour *et al*., 2012
	Mousavi *et al*., 2011
	Salem *et al*., 2010
	Einollahi *et al*., 2005
	Zghal *et al*., 2005
	Argani *et al*., 2003
	Abdalla *et al*., 1998 (First study)
	Abdalla *et al*., 1998 (Second study)
	Al Muhanna, 1998
	Al-Khader *et al*., 1996
	Al-Khader *et al*., 1991
	Rashed *et al*., 1989

Furthermore, psychological aspects, such as motivation, coping, self-regulation, and patient preferences and adherence/compliance to treatment should be investigated and taken into account.

Ramadan and kidney transplant

Summarizing all the studies dedicated to the relationship between Ramadan fasting and renal allograft, 463 patients who received kidney transplant have been investigated.

The concentration of immunosuppressive drugs tends to remain stable,[4] and biochemical parameters do not change significantly. No organ rejection or deterioration of kidney functions were observed. Only one author reported of adverse effects due to cyclosporine toxicity, acute rejection episodes, and urinary infections.[24] No kidney loss has been documented.

Ramadan and urolithiasis

Summarizing all the collected evidences, 1,262 subjects have been studied using both prospective studies and retrospective database-based surveys.

Ramadan fasting does not seem to deteriorate health condition in subjects with renal colic, does not cause

hypercalciuria and does not impair in a statistically significant and clinically relevant way the balance between lithogenic promotors (that is to say, oxalate, calcium, uric acid, phosphates) and inhibitors (citrate, magnesium). Moreover, any renal changes are fully reversible after 10 days from the end of the fasting.[7]

Ramadan and chronic kidney disease

Summarizing all the studies, 140 subjects with CKD have been investigated: 40 on hemodialysis, 18 on peritoneal dialysis (PD), 15 on predialysis, 67 on pharmacological treatment.

If needed, patients can choose between the two clinically available regimens of PD: modified continuous ambulatory PD (three exchanges during the night and icodextrin infusion), modified continuous cycling PD (exchanges over 6-7 h and icodextrin infusion) or continuous cycling peritoneal dialysis (CCPD). Continuous ambulatory peritoneal dialysis is generally preferred by younger patients, whilst CCPD by older subjects.[3]

No severe adverse effects have been recorded, apart from those described by Al-Muhanna.[10] However, the group of patients recruited in this study included also patients suffering from severe renal failure and this could have an impact on the findings of the author.

Recommendations against fasting

Patients suffering from acute tubular necrosis, polyuria (urine volume ≥2.5 L/day), uncontrolled or poorly controlled diabetes mellitus and insipidus or other dysmetabolic disorders, hypertension, angina, postural hypotension, acute infections, active peptic ulcer, significant co-morbidities (such as cardiovascular disorders and chronic liver disease) leading to marked limitations and amendments of daily activities, or with a history of noncompliance and adherence to therapy, dietary and drugs modifications should not fast during the month of Ramadan.

Clinical recommendations for patients willing to fast

Patients should take regularly their treatment twice daily (with *suhoor* and *iftar* respectively); if they should need to take drugs more than 2/die, they should consider switching to the former regimen (consulting their physician). If not possible, they should not fast.

They should break the fasting if the plasma creatinine increases by the 30% above the baseline values and/or if you observe clinical symptoms due to changes in serum potassium and sodium.[5]

Patients should be monitored during Ramadan and should be instructed to recognize some alarm symptoms such as an increase in weight (>2 kg from the baseline), lower limb or facial swelling, shortness of breath, dizziness, anorexia or hyporexia, fatigue, weakness or a sense of lethargy.[3] Body weight, blood pressure, biochemical parameters such as fluid and electrolytes should be regularly checked throughout the Ramadan. Patients should attend regular follow-up every 1-2 weeks, before, during and after Ramadan.

When breaking the fasting, they should avoid high-potassium and phosphorous diet (such as dates, apricots, fried food, nuts, cheese, soft juices and drinks, tea, coffee). Moreover, they should drink up to 1-2.5 L of water in order to re-hydrate themselves and compensate a fluid depletion, but avoid exceeding in liquid amount, thus occurring into fluid imbalance and overload.[3]

Water drinking is indeed a good method for preventing and treating both nephrolithias[28] and recurrent renal colic, as proven by a recent systematic review and meta-analysis of randomized clinical trials.[29] Most of the authors of the studies included in this systematic review agree that suggesting and advising patients to take an adequate amount of fluids during the breaks of the fasting is a good clinical practice. This confirms the conclusion of a previous narrative mini-review on the same topic.[30]

If they have a tendency to hyperkalemia, they should take some calcium resonium powder (30 g/die with lactulose once a day).

Anecdotal episodes of hyperkalemia due to free food and drink consumption after the break of fasting or hypokalemia due to PD regimen have been reported in the literature.[31]

Particular attention should be paid to infections, since some fasting patients are on immunosuppressive therapy.[11] According to the therapeutic regimen and combination of drugs, a prophylaxis should be taken into account, considering that the threshold for developing an infection in CKD fasting patients is lower than in healthy subjects.[11] Clinical consultations with pharmacologists and infectious diseases specialists are highly recommended in these cases.

CONCLUSIONS

There are no evidences that Ramadan is injurious for patients with CKD willing to fast,[1-31] even though further high quality research is welcome. Randomized clinical trials are particularly encouraged since there is a lack of evidence-based guidelines and protocols which correctly address the issue of the impact of the fasting on CKD patients and proper counsel and advise them.

In conclusion, if stable and at the least for the categories included in the reviewed studies, patient's eagerness to fast should be taken into account and even encouraged, since spirituality plays a key role in CKDs. The patient feels indeed himself/herself more active being involved in the religious activities, and less depressed and isolated.[3]

AUTHOR CONTRIBUTIONS

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Drafting the work or revising it critically for important intellectual content; Final approval of the version to be published; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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