Original Research Article

Ramadan Fasting in Chronic Kidney Disease Patients: Single Centre observation

Abstract

Background–According to Islamic rules, a Muslim is requested to abstain from food, water, smoking, medications, and sexual activities from dawn until dusk, every day during the month of Ramadan. While Islam rules allow patients with appreciable illnesses not to fast, many Muslims, with chronic diseases, tend to stick to fasting, even against medical advice. However, there is no consensus among treating physicians regarding the fasting of Ramadan of patients in various stages of chronic kidney disease (CKD), especially those who insist on fasting regardless of their health problems.

Aim of the work

We aimed to observe the practice of Ramadan fasting of CKD patients of different disease stages and its effect on CKD progression.

Methods and subjects

The study observed sixty-three patients who were followed regularly at the Nephrology Outpatient Clinic in Mansoura Military Hospital, before, during, and after the month of Ramadan during summer in the years 2016-2019 to evaluate the effect of fasting on the patients and their kidneys.

Results

The examined CKD patients included 47 males and 16 females who comprised 50 patients who practised fasting and 13 patients who did not fast the months of Ramadan according to their own will. Their ages ranged between 27 and 77 years. Forty-nine patients did not progress to end-stage renal disease (ESRD), while the remaining fourteen patients ended with dialysis during the study.

Neither urea nor creatinine changes had statistically significant differences between patients who had and who had not fasted. In addition, differences in creatinine slope values between those who fasted did not show any statistical significance.

Fourteen of the studied patients progressed to the need for dialysis; their mean age was 62 years. Of them, those who fasted included 3 patients of stage 4 and 6 patients of stage 5. Furthermore, the frequency of patients who started dialysis directly after Ramadan (six patients; 66.7%) were lower in the fasting group.

Of the studied patients, seven had renal stones and opted to fast. All of them experienced occasional attacks of lion pain that increased during the first two weeks of fasting but decreased in the last two weeks of the month of Ramadan.

Conclusion

Comparedto non-fasting,Ramadan fasting does not cause a significant extra risk of renal disease progression.

Introduction

Every year during - the month of Ramadan - a Muslim is requested to fast every day from the beginning of dawn until dusk. Fasting during the holy month of Ramadan is of strong-willed importance amongst Muslims and is the fourth pillar of Islam that is considered compulsory for all healthy adult Muslims. While Islam does arrange for its supporters with serious illnesses not to fast, Ramadan is not only abstinence from food and drinking, but also from smoking, medication, and sexual intercourse **(1)**. Ramadan fasting is not, a prolonged or continuous fasting, but consists of alternate fasting and re-feeding periods **(2)**. For this reason, it represents a "unique metabolic model **(3)**. Ramadan duration is variable since the lunar Islamic year contains 354 days (instead of 365, as in the Gregorian or solar year). For this reason, the Ramadan month occurs 11 days earlier every year and may fall in any seasons of the year, making a full circle in a span of 33 years. Therefore, the mean fasting duration is usually 12-14 h, but depending on the place and the year season it can last also up to 18 h **(4)** or even 22 h, in the extreme latitudes**. (2).**

Fasting is an eating pattern that alternates between periods of fasting and eating. Sometimes, extended periods without food and drink could put the fasting individuals in a risky situation, particularly with the coexistence of associated comorbidities, e.g., uncontrolled diabetes mellitus, severe HTN, and advanced CKD requiring dietary restrictions…etc. Fasting could potentially be associated with some stressful physiological states including energy deficits and volume disturbance. In addition, the dietary habits followed by many Muslims during Ramadan fasting may be associated with the hazards of specific types of food. In fact, Ramadan fasting could be conceived as a specific mode of starvation (time-restricted feeding pattern) with abstinence from food and drink (dry fasting) that ranges, between 8 and 18 hours according to the geographical area and the season during which the month of Ramadan coincides, as the Islamic calendar follows the lunar rather than the solar calendars. However, there are some probable beneficial effects of fasting including spiritual impact and potential weight reduction that could benefit obese patients possibly leading to improvement of insulin resistance and glucose and lipid metabolism **(5)**. Additionally, prolonged carbohydrate deprivation may lead to the generation of ketosis, a metabolic state that occurs when the human body burns fat for energy instead of glucose and is potentially induced by fasting. Moreover, both fasting and calorie restriction are known to have a role in the up-regulation of autophagy; a vital self-degradation or clean-up process that aids the removal of misfolded or gathered proteins, as well as recycling of damaged cell components, which is induced in a wide variety of tissues and organs in response to food deprivation **(6).** Ketosis may have possible health-related effects including weight loss, improvement of glucose metabolism, and steatohepatitis, although it is sometimes associated with dyslipidemia. On the other hand, ketosis can produce temporary side effects (keto flu) such as headache, fatigue, irritability, trouble sleeping, nausea, stomach-ache, dizziness, sugar cravings, cramps, sore muscles, bad breath (ketosis breath), metabolic acidosis and constipation **(7, 8, 9).**

CKD classification based upon glomerular filtration rate (GFR) and albuminuria (AER): It is divided into five grades according to GFR and three stages according to albuminuria **(10) (11).** Nephrologists around the world have to carry their duties towards their Muslim CKD patients who desire to achieve their religious obligation of fasting during the month of Ramadan. Many Muslims, with chronic diseases, insist on fasting against medical advice **(12)** and guidelines would help clinicians to support patients in the decision-making

practice. Medical research on Ramadan is a developing field and many studies are observational in nature and findings not generalized regarding the risks of fasting with CKD patients. The majority of the studies included stable CKD-non dialysis(CKD-ND) Stage 3 patients and only a small number of CKD-ND Stage 4 and an even smaller number of CKD-ND Stage 5 patients **(13)**.

Fasting can induce a high risk of kidney stones because many people fail to hydrate their body well, however, there is still no strong evidence if Ramadan fasting can induce renal stone formation in susceptible patients or not. Regardless of such controversies, nearly all studies are in agreement that consuming adequate amounts of water from dusk to dawn reduces the potential risk of dehydration in developing renal stones **(14)**

The few studies that have been conducted on the effect of Ramadan on patients with CKD have found inconsistent results **(15, 16, 17).** Still, there is no definite recommendation regarding fasting during Ramadan in the various stages of chronic kidney disease and many patients insist on fasting regardless of their health problems. It would be helpful if we could rely on definite scientific regulations on the impact and limitations of fasting in different stages of CKD.

Aim of the work

We aimed to observe the practice of Ramadan fasting of CKD patients of different disease stages and its effect on CKD progression.

Subjects and methods

The study was conducted on sixty-three patients who followed regularly at the Nephrology Outpatient Clinic in Mansoura military hospital, before, during, and after the month of Ramadan during summer in the years 2016-2019 and evaluated the effect of fasting and its fate. Of them, sixteen patients were followed at our clinic for four successive years of fasting. All patients had CKD in different stages as confirmed by the CKD EPI formula of calculating the estimated GFR. Patients' collected data included age, gender, marital status, special habits, and associated comorbidities. Urine volume was recalled and recorded before, during, and after the month of Ramadan. In addition, clinical examination, with special attention to vital signs and stigmata of volume disorders, as well as blood urea and haemoglobin, plasma creatinine, and serum potassium were carried out every few months

during the follow-up period. In particular, the laboratory data were recorded before, during, and after Ramadan. The changes in serum creatinine and blood urea were calculated as the difference between post- and pre-Ramadan blood creatinine and urea values. The frequency of deterioration of kidney function was identified by the occurrence of any increase in creatinine and or urea. The patients' needs for starting haemodialysis, if any, were observed, and the exact time to start HD after Ramadan was recorded.

Statistical analysis

After the collection, the data were analysed using the statistical package of social science (SPSS, IBM) software version 24**.** Categorical data were expressed as numbers and percentages and were analysed by the Chi-square test. Normality was tested using Shapiro Wilkinson or Kolmogorov-Simiranov tests, as appropriate. Scale data were expressed as means ± SD or medians (IQ) as appropriate. Parametric data were analysed using one-way ANOVA, while Kruskal-Wallis tests were used to analyse non-parametric data. The P-value was considered significant if it was < 0.05.

Each patient's creatinine readings were divided into a set of readings that were taken beforeor at the start of Ramadan fasting (pre-fasting) and another set of creatinine data that were takenafter Ramadan fasting (post-fasting). Pre-fasting and post-fastingcreatinine data were enteredinto slope calculation using the Excel program (pre-fasting and post-fasting creatinine slopes). Then, the difference between both slopes was calculated.

Results

This study included 63 CKD patients including 47 males and 16 females that were divided into 50 patients (24 CKD stage 1,2,3 and 26 CKD stage4,5) who voluntarily practise Ramadan fasting and 13 patients (7 CKD stage 1,2,3 and 6 CKD stage4,5) who voluntarily opted for not to practice Ramadan fasting. Their ages ranged between 27 and 77 years (table 1). In this group of patients, 61 (96.8) were married and 24 (38.1) were smokers. Diabetes, hypertension, and ischemic heart disease were evident in 36 (57.1%), 50 (79.4%), and 23 (37.1%) of them, respectively. The fasting group of patients comprised 38 (76%) males, while the non-fasting group contained 9 males (69.2%); gender distribution was not statistically significantly different between both groups.

Of the total studied group, fourteen patients (22.2%) progressed to ESRD while forty-nine patients (77.7%) showed a non-progressive CKD course during the study. Five patients (38.5%) of the non-fasting group progressed to ESRD and started haemodialysis therapy

during the observational period of the study, while nine patients (18%) of the fasting group showed progression to ESRD; a difference that did not reach statistical significance (table 2).

Table (3) shows some important basal clinical and laboratory data of the patients. It reveals that the mean age was statistically insignificantly lower in the fasting group however; the median duration of hypertension was statistically significantly lower in the fasting than non-fasting groups of patients. It is noticeable that the basal creatinine level in patients with CKD stage 4 was lower in the fasting than non-fasting groups (2.8±0.74 vs. 5.18±3.01, respectively; p=0.496). on the other hand, in patients with CKD stage 5, the fasting had a higher basal creatinine level than the non-fasting group (8.29±3.19 vs. 4.35±0.91, respectively; p=0.227). Additionally, basal laboratory data showed no statistically significant difference between the faster and non-faster groups (Table 3).

Table (4) describes the changes in serum urea and creatinine in both the fasting and non-fasting groups of patients, as well as the frequency of progression to ESRD in different CKD stages. As shown in this table, neither urea nor creatinine changes were statistically significantly different between the fasting and non-fasting groups. Patients with CKD stages 4 and 5 were studied separately; two of the fasting group with stage 4 (11.8%) progressed while fifteen (88.2%) did not progress to ESRD. In patients with CKD stage 5, the difference between patients with non-progressive CKD course and those who ended with dialysis in relation to fasting showed no statistically significant difference (Table 4).

Both pre-and post-Ramadan mean creatinine slopes were statistically significantly higher in the fasting than in the non-fasting groups (Table 5-a). On the other hand, the difference in slope values between pre- and post-Ramadan creatinine showed no statistically significant difference in both fasting and non-fasting groups (Table 5-a). In Table 5-b, the frequency of distribution of patients with increased versus those without increased post from pre-Ramadan creatinine slopes showed no statistically significant difference between the fasting and non-fasting groups of patients. Additionally, the frequency of patients who started dialysis directly after Ramadan was non-significantly different in the non-fasting (80%) than in the fasting (66.7%) groups of patients (p=>0.99; Table 6).

Concerning the 14 CKD patients who had a progressive course reaching ESRD after the month of Ramadan (table 7), they had a mean age of 62years, they were mostly males (n=10; 76.9%, nine of them (64.2%) were non-smoker, four (28.5%) had lower limb edema and 66.7% had positive HCV virology. Diabetes mellitus (DM), hypertension (HTN and ischemic heart disease (IHD) were present in 9 (64.2%), 12 (85.7%), and 4 (28.5%) of them, respectively (table 7). There were no statistically significant differences in age, BMI, duration

of associated comorbidities, or duration of CKD in both CKD groups whether progressed to ESRD or not however, there were statistically significant lower serum creatinine and blood urea and higher haemoglobin levels in the group of CKD not progressed to ESRD (Table 7). There were no statistically significant differences in gender or in the frequencies of smoking, DM, HTN, or IHD between fasting and non-fasting groups (table 8). In the same context, no laboratory data showed a statistically significant difference between fasting and non-fasting groups (Table 9).

Of the studied patients, seven had renal stones and opted for the fasting group. All of these seven patients experienced lion pain that increased during the first two weeks of fasting but decreased in the last two weeks of the month of Ramadan. (Unshown Data).

Tables

Tables (1) General descriptive tables

Gender n (%)	**Females**	**16 (25.4%)**
	Males	47 (74.6%)
Age n=63 **Mean±SD/ Median (Q1-Q3)**		59.1±10.2 / 61.0 (52.0-67.0)
Marital Status n (%)	**Unmarried**	2 (3.2%)
	Married	61 (96.8%)
Smoking **n (%)**	**Non-Smoker**	39 (61.9%)
	Smoker	24 (38.1%)
Body mass index(BMI) n=56 **Mean±SD/ Median (Q1-Q3)**		29.7±5.7 / 30.0 (25.6-34.3)
Mode of Fasting n (%)	**Non-fasting**	13 (20.6%)
	Fasting	50 (79.4%)
Fate of CKD **n (%)**	**CKD course not progressive to ESRD**	49 (77.8%)
	CKD course progressive to ESRD	14 (22.2%)
Duration of CKD (months) n=39 **Mean±SD/ Median (Q1-Q3)**		23.7±9.4 / 21.0 (19.0-25.0)
DM n=63 n (%)	**Yes**	36 (57.1%)
Duration of DM (years) n=33 **Mean±SD/ Median (Q1-Q3)**		13.26±10.14 / 12.0 (6.0-18.0)
HTN n=63 n (%)	**Yes**	50 (79.4%)
Duration of HTN (yrs) n=45 **Mean±SD/ Median (Q1-Q3)**		11.3±9.2 / 10.0 (4.0-20.0)
IHD n=62 n (%)	**Yes**	23 (37.1%)

Duration of IHD (yrs) n=15 Mean±SD/ Median (Q1-Q3)	6.9±6.9 / 3.0 (2.0-12.0)
Urine output Pre-Ramadan n=46	1.398±0.375 / 1.5 (1-1.5)
Urine output Post-Ramadan n=46	1.391±0.385 / 1.5 (1-1.5)
Basal haemoglobin(HB)n=62 (Mean±SD/Median (Q1-Q3))	11.3±2.1 / 11.0 (9.9-12.9)

Table 2: Demographic data between fasting and non-fasting groups

		Mode of Fasting				**P**
		Non-fasting		Fasting		
		n	%	n	%	
Gender	Female	4	30.8%	12	24.0%	0.723
	Male	9	69.2%	38	76.0%	
Marital Status	Unmarried	0	0.0%	2	4.0%	1.000
	Married	13	100.0%	48	96.0%	
Smoking	Non-smoker	7	53.8%	32	64.0%	0.535
	Smoker	6	46.2%	18	36.0%	
Fate of CKD	CKD course not progressive to ESRD	8	61.5%	41	82.0%	0.141
	CKD course progressive to ESRD	5	38.5%	9	18.0%	

P value was measured by Fisher-Exact test.

Table 3: Clinical and laboratory data between fasting and non-fasting groups

	Non Fasting	**Fasting**	**p**
	Mean±SD or Median (Q1-Q3)	*Mean±SD or Median (Q1-Q3)*	
Age	66.0 (56.5-71.0)(n=13)	60.5 (51.5-66.0)(n=50)	0.063
Body mass index(BMI)	34.3 (23.0-36.0)(n=13)	29.3 (25.6-31.5)(n=43)	0.443
Duration of DM	13.5 (6.0-18.0)(n=10)	10.0 (5.0-18.0)(n=23)	0.516
Duration of HTN	15.0 (9.0-21.0)(n=13)	6.0 (3.0-14.3)(n=32)	0.038
Duration of IHD	7.8±8.3(n=4)	6.5±6.7(n=11)	0.455*
Basal Haemoglobin(Hb)	10.59±1.95 (n=13)	11.48±2.14 (n=49)	0.181*
Basal blood urea	64.0 (50.5-111.6)(n=13)	68.8 (46.0-99.0)(n=47)	0.612
Basal Creatinine	3.0 (1.7-5.0)(n=13)	2.4 (1.7-3.7)(n=49)	0.337
Basal Serum potassium	4.5 (3.8-5.2)(n=13)	4.9 (4.2-5.2)(n=48)	0.202
Basal Creatinine (Stage 1,2,3 CKD)	2.0114±0.82583 (n=7)	1.6421±0.62583 (n=24)	0.203
Basal Creatinine (Stage 4 CKD)	5.18±3.01 (n=2)	2.8±0.74 (n=19)	0.496
Basal Creatinine	4.35±0.91 (n=4)	8.29±3.19 (n=7)	0.227

(Stage 5 CKD)			

p value was measured using T test, while the rest of the parameters were tested using Mann-Whitney

Table 4:Changes of laboratory data infasting versus. non-fasting groups:

		Mode of Fasting				P
		Not fasting		Fasting		
		n	%	n	%	
Urea Change	No change	2	22.2%	11	25%	1
	Increased	9	81.8%	33	75%	
	Temporary increase	2	22.2%	14	42.4%	0.289
	Persistent increase not reaching ESRD	2	22.2%	10	30.3%	
	Persistent increase reaching HDx	5	55.6%	9	27.3%	
Creatinine Change	No change	2	18.2%	11	25%	1.000
	Increased	9	81.8%	33	75%	
Creatinine change	Temporary increase	2	22.2%	14	42.4%	0.322
	Persistent increase not reaching ESRD	2	22.2%	10	30.3%	
	Persistent increase reaching HDx	5	55.6%	9	27.3%	
Stage-4 Fate of CKD	CKD course not progressive to ESRD	1	50.0%	15	88.2%	0.298
	CKD course progressive to ESRD	1	50.0%	2	11.8%	
Stage-5 Fate of CKD	CKD course not progressive to ESRD	0	0.0%	2	22.2%	1.000
	Ended with dialysis CKD course progressive to ESRD	4	100.0%	7	77.8%	

P value was measured by Fisher-Exact test.

Table (5-a): Slope difference in serum creatinine in fasting and non-fasting groups

	N	**Mean**	**SD**	**Median**	**Min**	**Max**	**IQ**		**P1**	P1
							Q1	**Q3**		
Slope-pre-creatinine	7	-0.0014	0.0034	0.0000	-0.0067	0.0019	-0.0057	0.0011	0.032	*0.398 #0.105
Non-fasting Fasting group	30	0.0026	0.0074	0.0020	-0.0133	0.0267	0.0000	0.0042		
Slope-post creatinine	8	-0.0034	0.0066	-0.0050	-0.0100	0.0103	-0.0085	-0.0003	0.09	
Non-fasting Fastinggro	36	-0.0001	0.0073	0.0000	-0.0233	0.0233	-0.0033	0.0014		

up									
Slope value difference in creatinine Non-fasting Fasting group	7	-0.0022	0.0096	-0.0067	-0.0100	0.0170	-0.0088	0.0024	0.698
	25	-0.0020	0.0112	-0.0023	-0.0267	0.0367	-0.0067	0.0012	

Table (5-b): frequency of increased versus non- increased Slope pre and post Ramadan creatinine in fasting and non-fasting groups

		Mode of Fasting				**p**
		Non-fasting		Fasting		
		n	%	n	%	
Frequency of increased versus non-increasedSlope pre and post Ramadan creatinine	***Increase in Creatinine Slope***	5	71.4 %	16	66.7 %	1.000
	No or decrease in creatinine slope	2	28.6 %	8	33.3 %	

P1 was measured using Mann-Whitney test. P2 was measured using Wilcoxon Signed Ranks Test.

* P value was measured using Fisher-Exact test.

Table (6): Number of patients in relation to timing to start dialysis after Ramadan

Patient started dialysis		**Mode of Fasting**				**Total**
		Non-fasting		Fasting		
		n	%	n	%	
Timing to start dialysis after Ramadan	Directly started Dialysis after Ramadan	4	80.0%	6	66.7%	1.000
	delayed Dialysis	1	20.0%	3	33.3%	

* P value was measured using Fisher-Exact test.

Table 7: Clinical and laboratory data in the studied patients regarding CKD course

		N	**Mean ± SD Median (Q1-Q3)**	**Min**	**Max**	**p**
Body Weight Mean±SD	CKD not progressed to dialysis	44	85.51±18.5			0.877
	CKD progressed to dialysis	13	86.39 ±14.85			
BMI Mean±SD	CKD not progressed to dialysis	43	29.22± 5.9			0.277
	CKD progressed to dialysis	13	31.21 ± 5.96			

Average HB Mean±SD	CKD not progressed to dialysis	49	11.46 ± 2.24			0.01
	CKD progressed to dialysis	13	9.72±1.38			
Average blood Urea Mean±SD	CKD not progressed to dialysis	40	65.03 ±26.9			< 0.001
	CKD progressed to dialysis	13	125.39±33.51			
Age Median (Q1-Q3)	CKD not progressed to dialysis	49	61 (27-77)	52.00	66.00	0.778
	CKD progressed to dialysis	14	62 (45-75)	50.00	67.75	
Duration of DM Median (Q1-Q3)	CKD not progressed to dialysis	24	10 (1-52)	6.00	15.00	0.215
	CKD progressed to dialysis	9	15 (5-27)	8.00	19.00	
Duration of HTN Median (Q1-Q3)	CKD not progressed to dialysis	33	7 (1-30)	3.50	18.00	0.424
	CKD progressed to dialysis	12	10 (2-32)	4.25	20.00	
Duration of IHD Median (Q1-Q3)	CKD not progressed to dialysis	11	3 (1-20)	2.00	10.00	0.895
	CKD progressed to dialysis	4	8.5 (0-0.50)	0.50	18.75	
Duration of CKD in months Median (Q1-Q3)	CKD not progressed to dialysis	27	21 (12-47)	19.00	23.00	0.258
	CKD progressed to dialysis	12	22.5 (10-58)	18.75	32.75	
Average Serum Creatinine Median (Q1-Q3)	CKD not progressed to dialysis	49	2.17 (0.55-4.4)	1.5200	3.5767	< 0.001
	CKD progressed to dialysis	13	8.54 (4.07-12.3)	5.8317	10.3150	
Average Serum potassium Median (Q1-Q3)	CKD not progressed to dialysis	48	4.83 (3.2-20.14)	4.3575	5.1838	0.965
	CKD progressed to dialysis	13	4.96 (2.7-5.8)	4.2500	5.1750	

P was measured using T test or Mann-Whittney test as appropriate

Table 8: Demographic data in group of patients ended by dialysis after month of Ramadan

		Mode of Fasting				**P**
		Not fasting		Fasting		
		n	%	n	%	
Gender	Female	3	60.0%	1	11.1%	0.095
	Male	2	40.0%	8	88.9%	
Smoking	Non-smoker	4	80.0%	6	66.7%	1.000
	Ex-smoker	1	20.0%	3	33.3%	
Edema Lower Limb	Yes	2	40.0%	3	33.3%	1.000
	CKD progressed to dialysis	5	100.0%	9	100%	
DM	Yes	3	60.0%	6	66.7%	1.000

HTN	Yes	5	100.0%	8	88.9%	1.000
IHD	Yes	1	20.0%	2	22.2%	1.000

Table 9: Clinical and laboratory data in group of patients ended by dialysis after month of Ramadan.

Mode of Fasting	Non- fasting				Fasting				p
	N	Median	IQ		N	Median	IQ		
			Q1	Q3			Q1	Q3	
Age	5	57.0	49.0	65.0	9	65.0	51.0	69.0	0.364
Body Weight	5	88.0	84.5	95.5	8	81.5	70.0	100.8	0.560*
BMI	5	35.5	30.7	36.5	8	30.8	26.6	31.8	0.127
Duration of DM	3	15.0	6.0		6	16.5	8.8	18.5	0.905
Duration of HTN	5	10.0	6.0	21.0	7	15.0	3.0	20.0	1.000
Duration of IHD	1	2.0	2.0	2.0	3	15.0	0.0		0.506*
Start of dialysis	5	42948	42842	43298	8	43313	42690	43436	0.354
Basal HB	5	9.5	8.1	9.9	8	9.5	8.5	10.5	0.435
Basal Blood Urea	5	106.5	69.0	122.5	8	131.1	107.1	188.9	0.284
Basal Creatinine	5	5.0	4.3	7.8	8	8.8	4.1	10.2	0.435

Discussion

Previous studies that evaluated the effect of fasting on renal function changes in CKD patients are few and they were either small or uncontrolled **(15)**; the majority included stable CKD Stage 3 patients and only a smaller number comprised CKD stage 4 and CKD-ND stage 5 patients **(13)**. In the present study, we aimed to extend the general experience in this field by investigating the effect of Ramadan fasting practice on the progression of kidney dysfunction in different stages of CKD, relying on studying the changes in creatinine slope, as well as the factors that could have played a role in the instigation of haemodialysis.

The studied patients in the present work were in different stages of CKD. Of them, ~80% insisted on fasting voluntarily, usually against the advice of their treating nephrologists who usually advise against fasting to their CKD patients, especially in the hot summer months as the duration of fasting is around 16 hours, exposing the patients to potential dehydration. The observation of keenness to fast CKD patients was also noticed by Bernieh and his associates (2010). The latter authors evaluated 31 CKD patients of stages 3 to 5 who decided to fast during Ramadan which occurred during the autumn season of 2005 with a daily fasting duration of about 12 hours. Fasting was completed in all patients successfully

with good tolerance and safety **(15)**. However, a medical authority has suggested that patients with kidney disease be advised to take precautions if they choose to fast during the month of Ramadan; they should avoid spending significant time outside in high temperatures when they are fasting and they should also avoid eating salty foods **(18).**

In our study, 54.4% of the patients who fasted and 36.4% of those who did not fast had an increase in both serum creatinine and blood urea, although the differences between both groups were not statistically significant. Furthermore, the difference in slope values between pre- and post-Ramadan creatinine showed no statistically significant difference in the fasting and non-fasting groups. Moreover, the frequency of distribution of patients with increased, versus those without increased, post- compared to pre-Ramadan creatinine slopes, showed no statistically significant difference between the fasting and non-fasting groups of patients. These interpretations are supported by many previous studies **(16, 17, 19, 20)**. On the other hand, Kara and his group (2017), noted a significant increase in serum urea levels during the last seven days of Ramadan, which returned to basal levels after the following month. In contrast, AL Muhanna, (1998), presented data from 36 patients with CKD (GFR < 35 mL/min/1.73 m2) which revealed a more significant decrease of GFR during Ramadan fasting **(21)**. In the same context, a study of 106 CKD patients with GFR of 27.7- mL/min/1.73 m2 who fasted Ramadan showed significant adverse effects with fasting, and the plasma creatinine remained elevated in 23% of them three months after the end of Ramadan **(22)**. Moreover, Amaar and his group noticed that Ramadan fasting during the summer months was associated with worsening renal function in patients with CKD stage 3 or higher, and they advised that clinicians need to warn CKD patients against Ramadan fasting **(23)**.

Some studies showed different observations related to Ramadan fasting in special etiologic groups of patients. Ekinci et al. reported no significant deterioration of renal function in autosomal dominant polycystic disease patients with early CKD stage following Ramadan fasting **(24)**. In addition, 15 CKD stage 3b patients were included in El-Wakil et al. research who reported increased tubular cell damage marker (N-Acetyl-B-D-glucosaminidase) in the urine of the fasting group without statistically significant differences in the kidney function parameters between the patients and the control groups after Ramadan fasting **(3)**. In an observational study by Baloglu et al., 23% of the studied CKD patients stages 2-3 developed ARF with fasting, and the authors suggested that good hydration and regular check-ups could reduce ARF risk **(25)**.

In the current research, fourteen patients started dialysis after Ramadan, and they were analyzed separately. Nine patients with CKD stage 4 and 5 who progressed to the need of dialysis were in fasting while five were not in the fasting group. Fasting did not constitute an extra risk in both CKD stages 4 and 5 in our study, as the frequency of patients who started dialysis directly after Ramadan was non-significantly different in the non-fasting (80%) than in the fasting (66.7%) groups of patients. This finding was reinforced by Bakhit and his associates who found that the creatinine rise was not significantly different in the fasting and the non-fasting CKD patients, suggesting that the increased creatinine was possibly due to spontaneous CKD progression rather than the effect of fasting **(23)**. Moreover, in a retrospective study of 1199 patients who had not been exempted from Ramadan fasting for two years (2016 and 2017), fasting significantly reduced the risk of developing ARF, especially in patients with comorbid conditions, indicating that Ramadan fasting has no negative effects on most patients with comorbid conditions **(26)**.

In this work, there was no gender difference between fasting and non-fasting while, the mean age and the median duration of hypertension were lower in the fasting than non-fasting groups, possibly suggesting better tolerance to fasting with younger age and lower duration of hypertension. This is in harmony with Baloglu et al who revealed that fasting with HTN was a significant predictive risk for developing ARF **(25)**.

Fasting can impose a high risk of kidney stones because many people might fail to hydrate their bodies well by drinking enough water in the fasting-breaking period between sunset and dawn. However, there is still no strong evidence that Ramadan fasting can cause renal stone formation in susceptible patients; it is well-established that dehydration and low urinary volume are the main risk factors for the development of renal stones. **(27, 28)**. Many studies support that some CKD patients may be susceptible to stone formation and urinary tract infections and consuming adequate amounts of water after breaking their fast is the key if they want to fast **(14, 29)**. In our research, seven of the sixty-three patients in the fasting group had renal stones. All of these seven patients experienced lion pain, which increased during the first two weeks of fasting but gradually decreased in the last two weeks. Our observations were in accordance with those of Abdolreza and his associates who compared the number of patients hospitalized for renal colic between the four periods; 2 weeks before Ramadan, the first 2 weeks of Ramadan, the second 2 weeks of Ramadan, and 2 weeks after Ramadan. Their investigations showed that the hospitalizations for renal colic were highest in the first two weeks of Ramadan, while hospitalizations for renal colic continued, albeit decreased, until two weeks after Ramadan **(30)**. The authors of the latter research suggested

that changes in dietary habits (mainly, the reduction in water intake) may be responsible for increased hospitalizations due to abdominal pain during the first 2 weeks of Ramadan. Additionally, Al Mahayni and his colleagues found that patients fasting during Ramadan were twice as likely to develop ureteral stones as compared to stones elsewhere in the urinary tract, particularly when the month of Ramadan falls in summer **(30)**. Many studies suggest that patients with a history of renal stones should increase their water intake by 2 liters to prevent renal stone formation **(31,32, 33)**. On the other hand, many researchers have observed no significant change in the incidence of renal colic during the Ramadan months **(34, 35, 36)**.

Conclusion

It seems that Ramadan fasting does not impose a significant extra risk of renal disease progression compared to non-fasting. However, it remains unsettled whether to abide by the patients' desire to fast to satisfaction of his religious demands.

Study limitations and recommendations

Our sample size is small, and larger prospective studies are recommended. We recommend advising the patients to well hydrate themselves after fasting time to decrease kidney deterioration. We also advise frequent check-ups to rule out AKI during the month of Ramadan.

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