

# Fasting during Ramadan in people with chronic kidney disease: a review of the literature

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**Abstract:** Chronic kidney disease (CKD) is common among Muslim patients, and many such patients are keen to fast during the month of Ramadan. Fasting for prolonged periods may be deleterious for patients with CKD, but the changing season of fasting means that the duration of fast is very variable between geographical locations. There is, furthermore, a paucity of evidence to guide patients and clinicians in management of fasting in people with CKD. In this article, we aim to review the available evidence for patients with CKD and fasting, including haemodialysis and renal transplantation. We suggest that all patients with CKD should be deemed high risk or very high risk for fasting. We conclude, however, that patients with stable mild/moderate CKD (stage 1–3) may be able to fast providing they are carefully monitored and counselled. We also suggest that patients with stable renal transplants may also be able to fast, providing they are monitored carefully by their transplant team. Patients on haemodialysis or peritoneal dialysis should not be encouraged to fast, but if they do so, they will need careful weekly monitoring. There is an urgent need for high-quality data for patients with CKD who plan to fast over Ramadan, to enable more guidance to be developed for this vulnerable group of patients.

**Keywords:** chronic kidney disease, dialysis, fasting, Ramadan

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## Introduction

The worldwide prevalence of chronic kidney disease (CKD) is rapidly rising.<sup>1</sup> CKD is associated with a number of other major diseases, which impact on global morbidity and mortality, including diabetes mellitus (DM), cardiovascular disease (CVD), hypertension, human immunodeficiency virus (HIV) infection and malaria. The Global Burden of Disease (GBD) 2015 study suggested that 1.2 million deaths, 19 million disability-adjusted life-years (DALYs) and 18 million years of life lost from cardiovascular diseases were directly attributable to reduced glomerular filtration rate (GFR).<sup>2</sup> The study also suggested an alarming 32% increase in global mortality from renal disease between 2005 and 2015.<sup>3</sup> Mortality from renal disease is, however, likely to be underestimated due to lack of robust epidemiological

data, and poor access to laboratory-based diagnosis in many parts of the world.

In addition to high mortality, kidney disease imposes a high economic cost on health systems. High-income countries spend around 2–3% of their annual healthcare budgets on the treatment of end-stage renal disease (ESRD).<sup>4</sup> In 2010, over 2.6 million people received dialysis worldwide, and the need for dialysis is projected to double by 2030.<sup>5</sup> A significant proportion of the cost of DM or hypertension is attributable to renal complications of these conditions. DM itself is associated with a high burden of microvascular and cardiovascular complications.<sup>6</sup> It is currently the most common cause of blindness and renal failure in many developed countries,<sup>7</sup> with diabetic nephropathy accounting for up to 50% of patients receiving

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renal replacement therapy (RRT), and a significant proportion of patients with CKD overall.<sup>6</sup>

It is estimated that there are around 1.9 billion Muslims around the world, many of whom fast during Ramadan, which is prescribed for all healthy Muslims beyond puberty.<sup>8</sup> While there are clear instructions regarding exemption from fasting for those who are sick or who may come to harm from fasting, a significant number of patients decide to fast irrespective of the opinion of medical or religious authorities. This poses a particular challenge for physicians treating patients with CKD. To address this challenge, a number of guidelines have been developed, but these mainly focus on people with DM and CKD.<sup>9</sup> These guidelines recognize that patients with CKD are very high-risk patients and need meticulous supervision with strict instructions on breaking the fast in the event of acute deterioration in health. Despite this, many patients with CKD do partake in fasting.<sup>10</sup>

There is a paucity of studies assessing the impact of fasting in patients with CKD. In this review, we aim to provide an overview on fasting in people with CKD, and draw some conclusions from the available published data.

### Epidemiology of CKD in Muslim countries

There has been an exponential rise in the prevalence of DM, CVD and hypertension in the Arab world. Middle Eastern and North African countries have seen the prevalence of DM grow at the second highest rate globally and the number of people with DM is estimated to increase by a startling 96.2% by the year 2035.<sup>11</sup> In a 2017 study, countries belonging to the Gulf Cooperation Council (GCC), Middle Eastern countries with high incomes, showed an average DM prevalence of 25.4%, while the average in non-GCC countries was 12.69%, clearly demonstrating the link between affluence and prevalence of type 2 DM.<sup>12</sup>

Most Muslims, however, live outside of the Arab world. In Bangladesh, estimated prevalence of diabetes is around 7.4%, predicted to rise to around 13% by 2030.<sup>13</sup> A recent study from Pakistan suggested a prevalence of almost 17%,<sup>14</sup> while Malaysia has an estimated prevalence of 20.8%<sup>15</sup> and Indonesia 7.0%.<sup>16</sup> Prevalence of CVD is rising rapidly in Muslim-majority countries,<sup>17</sup> as is hypertension.<sup>18</sup>

With the rise in prevalence of DM, CVD and hypertension in Muslim countries, a commensurate rise in prevalence of CKD is observed. The GBD Eastern Mediterranean region study showed that in 2015, 16,470 [95% confidence interval (CI) 13,977–18,961] people died from diabetes-related CKD, a 179% increase compared to 1990.<sup>2</sup> A study from 2010 suggested a prevalence of CKD in Saudi Arabia of just over 5%,<sup>19</sup> but a well-conducted study from Bangladesh of laboratory tests of patients suggested a prevalence of CKD stage 3 and below of 19% in 2006 and 17% in 2015, indicating a stable prevalence.<sup>20</sup> Data from Iran, however, suggest a significant rise of CKD prevalence from 1.1% in 2011 to 3.3% in 2016.<sup>21</sup> A population-based study from Malaysia in 2011 suggested a 9.1% prevalence of CKD, and dialysis use of 0.36%.<sup>22</sup> Furthermore, a recent report on the economic burden of CKD in Malaysia suggested that the total annual expenditure on ESRD by the public sector had grown by 94% in 7 years, to US \$785 million in 2016, constituting around 4.2% of total health expenditure.<sup>23</sup> Most epidemiological surveys from Muslim-majority countries suggest a significant rise in the burden of CKD, and a growing prevalence of ESRD, possibly due to better provision of dialysis facilities.<sup>24</sup>

### Fasting during Ramadan

A high proportion of Muslims around the world perform fasting for one lunar month each year, during the month of Ramadan. Fasting is compulsory for all healthy Muslims beyond puberty, and is espoused as a very honourable act; as a result, there is a strong desire to fast, particularly as many people may have spent the majority of their lives fasting during this month. This is the case even among those who are exempt due to health conditions.<sup>9</sup> The Muslim calendar is lunar, lasting 355 days per year. This means that the month of Ramadan can fall in any period of the Gregorian calendar, returning to its starting point every 33 years. As a result, the fast of Ramadan will traverse the seasons, and hence the fast can last from an average of 12–14h in equatorial regions, to up to 22h in certain geographical locations. The Muslim fast is an absolute one, with both food and water prohibited from dawn to dusk. The pre-dawn meal is called *suhoor*, while the post-sunset meal is called *iftar*. This prolonged fast can result in acute shifts in meal times and sleeping patterns, with resultant changes in

endocrine processes, leading to an increased risk of dehydration.<sup>9,25</sup>

Exemptions to fasting are clear. Prepubertal children, menstruating women, pregnant or breast-feeding mothers, those who are frail or too elderly and anyone with a medical condition that can cause harm in the event of fasting have clear medical and religious dispensation from fasting. There is a general consensus that a number of conditions such as DM or CKD fall into the category such a medical condition.<sup>9,25–27</sup> Despite this, however, it is well documented that many Muslims with these conditions continue to fast irrespective of the dispensation. For example, it was reported that 78.7% of patients with type 2 DM fasted for at least 15 days during Ramadan.<sup>28</sup> In another more recent study, more than 94% of patients with type 2 DM fasted at least 15 days during Ramadan and at least 60% fasted every single day.<sup>29</sup> In addition, a significant proportion of patients fast without consultation with their doctor.<sup>30</sup> As a result, episodes of severe hypoglycaemia and significant hyperglycaemia, among other complications, are frequent and potentially serious.<sup>31</sup> A similar exemption from fasting exists for people with CKD, particularly if a doctor is concerned that the CKD may worsen during fasting for prolonged periods.

### Guidelines for fasting in people with CKD

Guidelines exist for the advice and management of patients with DM who wish to fast.<sup>9,25</sup> The International Diabetes Federation and Diabetes and Ramadan International Alliance (IDF-DAR) guidelines are widely used to risk-stratify patients with diabetes who wish to fast into three categories: very high risk, high risk and moderate/low risk (Table 1).<sup>9</sup> Moderate-/low-risk patients are those with well-controlled type 2 DM who are on either lifestyle modification, oral antidiabetic medication or on basal insulin only. High-risk patients are those with type 1 DM (regardless of level of control), type 2 DM which is poorly controlled, type 2 DM on mixed insulin regimes, gestational diabetes, CKD stage 3, stable macrovascular disease, significant comorbid conditions that pose an additional risk factor, patients with diabetes performing intense physical activity, and concomitant use of drugs that affect cognitive function. Very high-risk patients are those with a severe hypoglycaemic event or unexplained hyperglycaemic emergency [diabetic ketoacidosis

(DKA) or hyperosmolar hyperglycaemic syndrome (HHS)] within 3 months of Ramadan, a history of recurrent hypoglycaemia, or of hypoglycaemia unawareness, poorly controlled type 1 DM, acute illness, pregnancy in a patient with preexisting DM or gestational DM on treatment, dialysis or CKD stage 4/5, advanced macrovascular complications and elderly patients who are frail.

These guidelines also provide religious opinion on each category, indicating that patients who are very high risk *must* not fast, those who are high risk *should* not fast and those who are moderate/low risk should heed medical advice. The guidelines provide clear advice on the management of patients in each category who wish to fast, even if this is against medical advice. All such patients should be offered structured education on management of diabetes during Ramadan. In addition, those who are high risk or very high risk should check their blood glucose regularly, will need meticulous medical supervision, be prepared to break their fast in the event of hypo/hyperglycaemia, be prepared to stop fasting altogether in the event of frequent hypo/hyperglycaemia and will need medication dose adjustment as per the recommendation of their physician. Those who have a moderate/low risk should check blood glucose regularly as well as adjust medication dose as per the recommendation of their physician. It is notable that these guidelines make it clear that people with diabetes and CKD are classified as either high risk or very high risk and therefore should not fast.

As far as we are aware, there are no national or international guidelines specifically for people with CKD on fasting during Ramadan. The only concerted effort to publish recommendations around fasting and CKD are from Bragazzi,<sup>32</sup> who undertook a meta-analysis of available data in 2014. He suggested some precautions for patients with CKD and fasting, including:

1. Patients should break the fast if plasma creatinine increases by 30% above baseline, or symptoms occur due to changes in serum potassium and sodium.
2. Patients should be monitored one or twice weekly and advised to aware of symptoms such as an increase in weight (>2 kg from the baseline), oedema, shortness of breath, dizziness, anorexia or weakness.

**Table 1.** Risk stratification and management of patients with DM who wish to fast.

Risk category	Risk factors	Advice for patients
Very high risk (must not fast)	Severe hypoglycaemic event within 3 months of Ramadan Unexplained DKA within 3 months of Ramadan, hyperosmolar hyperglycaemic syndrome within 3 months of Ramadan History of recurrent hypoglycaemia History of hypoglycaemia unawareness Poorly controlled type 1 DM, acute illness Pregnancy in a patient with preexisting DM or gestational DM on treatment Chronic dialysis or CKD stage 4/5 Advanced macrovascular complications Old patients who are frail	
High risk (should not fast)	Type 1 DM (regardless of level of control) Type 2 DM which is poorly controlled Type 2 DM on mixed insulin regimens Gestational DM CKD stage 3 Stable macrovascular complication Comorbid conditions that pose an additional risk factor Diabetic patients performing intense labour Concomitant use of drugs that affect cognitive function	Structured education Check blood glucose regularly Will need meticulous medical supervision Be prepared to break their fast in the event of hypo/hyperglycaemia, Be prepared to stop fasting altogether in the event of frequent hypo/hyperglycaemia Will need medication dose adjustment as per the recommendation of their physician
Moderate/low risk (listen to medical advice)	Well-controlled type 2 DM on either lifestyle modification, oral antidiabetic medication or on basal insulin only	Will need medication dose adjustment Check blood glucose regularly

CKD, chronic kidney disease; DKA, diabetic ketoacidosis; DM, diabetes mellitus.  
Adapted from IDF-DAR guidelines.<sup>9</sup>

- When breaking the fast, avoidance of high-potassium and phosphorous foods should be recommended and a high intake of water should be advised.

### Fasting in people with CKD

As stated above, there is a paucity of studies analysing the effects of fasting on renal function in patients with CKD, and many of the available data involve studies that are small and uncontrolled.

El-Wakil and colleagues reported on the effects of fasting on renal function in 15 pre-dialysis patients with an average GFR of 33 ml/min/1.73 m<sup>2</sup> (CKD stage 3b), in comparison to six healthy controls during Ramadan 2001.<sup>33</sup> While there were no differences in the change in GFR between the two groups, the authors found that patients with CKD demonstrated a rise in biomarkers associated with increased tubular cell

injury (urinary N-acetyl-B-D- glucosaminidase), suggesting that fasting may have a deleterious effect on renal tubular function in people with CKD, although the authors did recommend larger studies to confirm. A study from Morocco during Ramadan 2010 examined 60 patients with CKD who fasted for most of the month.<sup>34</sup> Overall, 11.7% developed acute renal failure as defined by a rise in serum creatinine  $\geq 5$  mg/L relative to the initial value, increase of serum creatinine  $\geq 50\%$  relative to the initial value or reduction of the GFR of  $\geq 25\%$  relative to the initial value. The main risk factor for developing acute renal failure was the presence of estimated GFR (eGFR)  $< 60$  ml/min/1.73 m<sup>2</sup>, though the authors admit that the sample size of the study (60 patients) did not allow for reliable conclusions. Similarly, in a study of 36 patients with severe CKD (average creatinine clearance  $< 35$  ml/min/1.73 m<sup>2</sup>), fasting during Ramadan was associated with a clinically and statistically

significant reduction in creatinine clearance.<sup>35</sup> A larger study of 106 patients with CKD (fasting group baseline eGFR of 27.7 ml/min/1.73 m<sup>2</sup>, nonfasting group baseline eGFR 21.5 ml/min/1.73 m<sup>2</sup>) reported some serious adverse effects of fasting in their cohort. These included a rise in serum creatinine by 60.4% by day 7, and six cardiovascular events in the fasting group (two cases of acute coronary syndrome, two exacerbations of chronic peripheral vascular disease requiring surgical interference, one case of severe heart failure and one minor nonhaemorrhagic stroke), albeit the majority of these patients (five out of six) had preexisting cardiovascular disease.<sup>36</sup> Three months after the end of Ramadan, serum creatinine remained elevated in 12 of 52 (23%) patients in the fasting group, although this was not significantly different from controls 19/54 (35%), suggesting that the deterioration in creatinine may have been due to progression of CKD, rather than the fast itself. A further prospective observational study of 65 patients fasting in Ramadan with CKD stage 3 or worse showed 33% of patients developed worsening renal function, as defined by a rise in creatinine of 26.5 µmol/L or greater.<sup>37</sup>

There are, however, further published studies which report opposing results. For example, Bernieh and colleagues reported a prospective observational cohort study of 31 patients with CKD (14 patients with CKD stage 3, 12 with CKD stage 4 and 5 with CKD stage 5), which showed a significant *improvement* in the eGFR from 29.7 ml/min/1.73 m<sup>2</sup> prior to fasting, to 32.7 ml/min/1.73 m<sup>2</sup> post-fasting, with an accompanying improvement in blood pressure control, better lipid profile and decreased urinary protein excretion, albeit with episodes of hyperglycaemia and overall increase in glycated haemoglobin (HbA<sub>1c</sub>).<sup>38</sup> Similarly, Hassan and colleagues found no difference in change of eGFR among 31 fasting and 26 nonfasting patients with CKD stages 2–4, but did report reduced levels of hydration as measured by bioimpedance spectroscopy, and reduction in baseline levels of brain natriuretic peptide (BNP), though BNP levels and hydration status returned to baseline within a month after the end of fasting.<sup>39</sup> Similarly, a Turkish study of 45 fasting and 49 nonfasting patients with CKD stages 3–5 found no significant differences in eGFR between fasting and nonfasting patients, although patients who were older (mean age 72 years) appeared to have a

higher risk of deterioration in renal function compared to those who were younger (mean age 64 years).<sup>40</sup> One study from Saudi Arabia examined 39 patients with CKD stages 3 and 4, and demonstrated no differences in clinical and laboratory parameters compared to nonfasting patients.<sup>41</sup>

Our own group have recently published data on fasting in summer months for a cohort of Muslim people with type 2 DM and CKD stage 3 during Ramadan 2018, where duration of fast was 19 h.<sup>42</sup> In this study, we compared 68 patients who fasted to 71 patients who did not, and found no significant changes in weight, blood pressure, creatinine, HbA<sub>1c</sub>, cholesterol and urinary protein creatinine ratio pre- and post-Ramadan, and no significant differences between the fasting and nonfasting groups. There was also no difference in adverse events, including acute kidney injury (AKI), hypoglycaemia or cardiovascular events, between the fasting and nonfasting groups.

It is interesting to speculate on the reason for differences seen between the various studies reported above. There is a great deal of heterogeneity between the study populations, including degrees of CKD, age, days fasted, duration of fast and period of observation. Among those studies of patients with greater degrees of renal impairment, however, it appears that fasting may have been shown to be more deleterious, although this does not apply to all studies.

### Fasting in people on dialysis

Al Wakeel and colleagues reported on the experience of managing 31 patients on peritoneal dialysis (PD) who wished to fast in Riyadh, Saudi Arabia during Ramadan 2009 (a fast of 14 h duration).<sup>43</sup> The authors report a method of meticulous supervision and substantial modification to the patients' treatment regimen including extra PD cycles at night, which led to some minor adverse effects (PD-related pleural effusion, peritonitis or mild fluid overload), but overall no serious morbidity or mortality occurred, and all patients were able to fast at least some days during Ramadan.

A larger number of studies have reported outcomes of fasting in patients on haemodialysis (HD). In a study of 40 patients established on HD for at least six months, those who fasted on



nondialysis days, were observed to have statistically but not clinically significant weight gain, and no differences in blood pressure control and electrolyte imbalances.<sup>44</sup> A further study of 34 fasting HD patients compared to 252 nonfasting HD patients showed no difference in the risk of harm from fasting,<sup>45</sup> with no excess in mortality or morbidity in the fasting group. Interestingly, the fasting group had an improvement in serum albumin, phosphorus and diastolic blood pressure compared to the nonfasting group. In a Malaysian study of 35 patients on HD, approximately half of whom had diabetes, Ramadan fasting was associated with reduced weight, improved serum albumin and phosphate levels.<sup>46</sup>

A larger prospective multicentre observational study of 635 patients on HD from five centres in Saudi Arabia (64.1% fasting) has shown some important and reassuring results.<sup>47</sup> The fasting group were more likely to be younger, working and more likely to miss dialysis. Nevertheless, the only clinically important parameter that differed from the nonfasting group was a slight elevation in serum phosphorous at the end of the fasting period ( $2.78 \pm 1.8$  versus  $2.45 \pm 1.6$  mmol/L;  $p=0.045$ ). No other differences in pre- and post-dialysis blood pressure, serum potassium, albumin or weight gain was seen, and no difference between the groups was seen in other morbidity or mortality, including cardiovascular events.

A recent 12-week multicentre study from Malaysia examined 87 patients on HD, 68 of whom were fasting for longer than 20 days.<sup>48</sup> Fasting led to significant reductions in body mass index (BMI) and other parameters of obesity, interdialytic weight gain and a significant improvement in serum phosphate, urea and creatinine levels, although serum albumin also fell. Energy and protein intakes remain unchanged and hand-grip strength improved significantly during Ramadan. The authors concluded that 'intermittent Ramadan fasting leads to temporary changes in nutritional status parameters and poses non-detrimental nutritional risk for patients on maintenance HD'.

A slight note of concern is suggested by data from a large retrospective study analysing 1841 patients over 24 years on HD in Karachi, Pakistan between 1989 and 2012.<sup>49</sup> Importantly, the study was not able to determine fasting status. Of 1841 patients registered, 897 (48.7%) had died. The study

showed higher mortality during the month of Ramadan, with 94 patients dying during Ramadan – 11% of the total number of deaths, significantly higher than any other Islamic month. The lack of fasting status, however, does not allow us to make conclusions on whether fasting may have contributed to the higher death rate during Ramadan months.

A further study suggesting some concern around fasting on HD showed that among 32 patients on HD who fasted during Ramadan, a significant increase in erythrocyte count, serum creatinine, blood urea, serum phosphorus, serum albumin and serum uric acid levels during the fasting period was seen (with hyperkalaemia in 25% and hyponatraemia in 15.6%), although there were no adverse events requiring hospitalization.<sup>41</sup>

Overall, however, data published on patients fasting on HD suggest that it appears relatively well tolerated, and is not associated with significant morbidity or mortality, although changes in electrolytes (especially potassium and phosphorus) need careful monitoring.

### Fasting in people with renal transplants

Renal transplantation has a major impact on the quality and length of life in people with ESRD. As many people feel clinically much better following transplantation, a number of studies have considered whether fasting is well tolerated after renal transplantation.

One study spanning three consecutive Ramadan fasts in Saudi Arabia examined the effects of fasting on 35 renal transplant patients who fasted all three months of Ramadan over three years, compared to 33 people with renal transplants who did not fast.<sup>50</sup> There were no significant differences between fasters and nonfasters in eGFR (eGFR  $56.4$  ml/min/ $1.73$  m<sup>2</sup> versus  $55.4$  ml/min/ $1.73$  m<sup>2</sup>), mean arterial blood pressure and urinary protein excretion between the two groups. A further study from Saudi Arabia of 23 renal transplant patients with an average post-transplant period of 2 years, 17 of whom had normal renal function and 6 of whom had impaired but stable function (creatinine  $<300$   $\mu$ mol/l), showed no significant differences in serum and urinary biochemical parameters before and after fasting.<sup>51</sup> In a study of 39 renal transplant patients, 19 fasting patients matched to 20 control patients, serum creatinine

levels before and after Ramadan were not significantly different (serum creatinine concentrations before and after Ramadan  $1.07 \pm 0.24$  versus  $1.08 \pm 0.22$  mg/dl ( $p > 0.05$ ) and  $1.00 \pm 0.24$  versus  $1.03 \pm 0.28$  mg/dl ( $p > 0.05$ ) in fasting and control groups, respectively).<sup>52</sup> Similarly, an Iranian study comparing 41 fasting renal transplant patients to 41 who did not fast showed no difference in creatinine levels, even among those patients with moderate CKD post-transplant.<sup>53</sup> A further Iranian study of 30 patients post-renal transplant showed stable creatinine and electrolyte profiles before and after Ramadan fasting.<sup>54</sup>

Circulating levels of immunosuppressant drugs are critical to monitor in people with renal transplants, and there is a theoretical concern that fasting may affect immunosuppressant drug levels. Trough levels of drug should be measured, and this will require drugs to be ingested ideally at the start of fasting, and drug levels taken 12h later, which may require some alteration to clinic schedules in some patients. Some studies have examined this issue specifically in fasting transplant patients during Ramadan. One study of 22 patients who fasted over Ramadan showed no significant difference in circulating ciclosporin or tacrolimus levels before, during or after Ramadan in fasting transplant patients.<sup>55</sup> Similarly, a study of 11 patients with renal transplants who fasted showed no change in ciclosporin levels during Ramadan.<sup>56</sup>

A larger study from Kuwait of 145 renal transplant patients with creatinine  $<200$   $\mu\text{mol/L}$  demonstrated no difference between fasting and nonfasting patients in relation to serum creatinine, urea, blood glucose levels or blood pressure values.<sup>57</sup> Similar results were found in a prospective matched case-control observational study comparing 43 fasting renal transplant patients with 37 nonfasting participants during August 2012 in Riyadh, Saudi Arabia. eGFR and serum creatinine levels were no different pre- and post-Ramadan fasting, and on subgroup analysis no significant differences in the eGFR, before and after  $19.6 \pm 1.3$  months, in the people with severe renal impairment (eGFR  $<45$  ml/min/1.73 m<sup>2</sup>) and moderate renal impairment (eGFR 45–75 ml/min/1.73 m<sup>2</sup>) was seen. There was, however, a significant high eGFR subgroup ( $>75$  ml/min/1.73 m<sup>2</sup>), although this was similar in the fasting and nonfasting groups.<sup>58</sup> The same group reported similar data at 2 years' follow up.<sup>59</sup>

Among 14 patients who were transplanted less than 12 months prior to Ramadan with stable renal function (mean creatinine 115  $\mu\text{mol/L}$ ), serum creatinine, sodium and potassium values were not different pre- and post-Ramadan fasting, although there was a significant rise in urea, haemoglobin, triglyceride and cholesterol levels.<sup>60</sup> In a cohort of 20 well-established renal transplant patients with an average of 8.5 years post-transplant and mean creatinine clearance of  $>100$  ml/min/1.73 m<sup>2</sup>, renal function, body weight, blood pressure, ciclosporin level and urine volume were stable in fasting patients in comparison to those not fasting.<sup>61</sup> Finally, a large study of patients from Riyadh, Saudi Arabia of 280 fasting patients post-renal transplant compared to 285 nonfasting renal transplant patients with mean baseline eGFR of around 72 ml/min/1.73 m<sup>2</sup> showed no difference in eGFR, mean arterial pressure or urinary protein excretion before or after Ramadan.<sup>62</sup> In this study, among those patients who did have a deterioration in eGFR after fasting, the main predictor of change in eGFR was a lower baseline eGFR. There were no adverse events, including cardiovascular events, graft or patient losses in either group.

A mini meta-analysis, consisting of studies involving CKD patients as well as renal transplant patients, concluded that fasting can be well tolerated.<sup>32</sup> Similarly, in a larger systematic review also consisting of studies involving CKD patients, renal transplant studies and studies reporting on the effects of fasting on incidence of renal colic also concluded that fasting can be well tolerated.<sup>63</sup>

## Conclusion

People of Muslim faith have a high risk of developing CKD. Fasting during Ramadan is physically arduous and may lead to deterioration in CKD in susceptible patients due to dehydration. While many patients may be able to justify being exempt from fasting due to medical conditions that put them at high risk of deterioration, it is widely recognized that many Muslims feel the spiritual need or social pressure to fast during Ramadan, even when they are not compelled to do so.

Health professionals advising patients with CKD on their risks of fasting need to be cognizant of a number of factors. First, there is little available robust evidence to guide clinicians, in the form of

randomized controlled trials or large-scale observational studies. Second, advice may have to be guided by the duration of fasting. For example, in equatorial countries the duration of fast varies little from year to year, and is stable at around 12–14h, whereas in temperate countries the duration of fast may vary from 8h in the winter to 20h in the summer. It may, therefore, be feasible for some low-risk patients to fast in the winter but not in the summer in some countries. Third, the clinician should give advice based on the best available guidance, which, at the moment, probably resides in the IDF-DAR guidelines that deal with patients with diabetes, but classify patients with CKD as ‘high’ or ‘very high’ risk. Clearly a person with diabetes *and* CKD will have higher risk of adverse events than those patients with CKD alone. Nevertheless, it seems reasonable for a clinician to suggest to a person with CKD that they should avoid fasting, and many patients may accept this advice. Patients who wish to fast despite advice to the contrary, however, should be supported to do so safely and without fear.

From the preceding literature review of the available material on fasting and CKD, and in the absence of high-grade evidence, some broad conclusions may be drawn:

1. It is widely accepted by religious and medical authorities that CKD is a high-risk state for fasting, and patients with moderate to severe CKD (stages 3–5) could be discouraged from fasting. In addition, patients with CKD and known CVD should be discouraged from fasting.
2. The theoretical risk of acute deterioration in renal function in people with moderate CKD (stage 3), however, is not borne out in many studies. Therefore, many patients with stable CKD stage 3 may be able to fast providing they are monitored before, during and after Ramadan. In addition to the advice offered by Braggazi,<sup>32</sup> advice to offer such patients might include:
  - a. Encouragement to drink plenty of fluids during the nonfasting period – perhaps a measured amount each day, depending on fluid status.
  - b. Regular daily measurement of weight may assist in helping the patient ensure they are adequately hydrated at the end of the fast.
  - c. Checking electrolytes and creatinine in the middle of the fasting month to help

those with advanced CKD to decide if they should continue fasting. Patients might be recommended to break the fast if plasma creatinine rises by 30% above baseline, or significant changes to serum potassium and sodium occur.

- d. Patients should be monitored once or twice weekly and advised to look out for symptoms such as an increase in weight (>2kg from the baseline), oedema, shortness of breath, dizziness, anorexia or weakness.
  - e. When breaking the fast, avoidance of high-potassium and phosphorous foods should be recommended and high intake of water should be advised.
3. While a number of studies of people on peritoneal or haemodialysis suggest that some people are able to fast, fasting among patients on dialysis should not be encouraged. If they decide to fast, they will require careful monitoring and weekly reviews will be required for such patients.
  4. People with stable renal transplants on stable immunosuppression are probably able to fast safely, providing they are monitored carefully by their transplant team before, during and after Ramadan, are encouraged to drink fluids during the nonfasting period and are given careful advice on how to take immunosuppressive tablets.

What is clear from the preceding review is the dearth of evidence available to clinicians to help guide patients with CKD. There is, therefore, an urgent need to undertake controlled studies of fasting *versus* nonfasting outcomes in patients with CKD to help guide clinicians and patients. This will require a concerted multicentre approach, similar to that seen in the management of diabetes during Ramadan by the DAR group, who have developed an evidence base to help clinicians guide patients with diabetes when fasting.

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