



# BMJ Open Impact of Ramadan fasting on kidney function and related outcomes in chronic kidney disease and kidney transplant recipients: a systematic review and meta-analysis

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## ABSTRACT

**Objectives** Ramadan fasting is an Islamic religious practice involving abstinence from food and drink from dawn to sunset. Its consequences on kidney-relevant outcomes in patients with chronic kidney disease (CKD) and kidney transplant recipients remain unclear.

**Design** Systematic review and meta-analysis.

**Data sources** MEDLINE, Embase, Global Health, CINAHL (EBSCOhost), Scopus, Web of Science and Google Scholar were searched up to 18 September 2023.

**Eligibility criteria** We included observational studies among non-dialysis CKD and kidney transplant recipients who fasted during Ramadan and examined changes in kidney function.

**Data extraction and synthesis** Standardised methods were used by two independent reviewers to screen, select and extract data. Outcomes included changes in serum creatinine (SCr), estimated glomerular filtration rate (eGFR), proteinuria, blood pressure, electrolytes and adverse events—all pre- and post-Ramadan. Results were pooled using random effects modelling.

**Results** We included 32 observational studies with a total of 2592 participants. 21 studies reported on participants with CKD and 11 studies reported on kidney transplant recipients (studies variably including non-fasting control arms). Meta-analysis of 25 studies revealed that Ramadan fasting was not associated with changes to SCr for the following groups according to study design: CKD *with* a non-fasting arm (mean difference (MD)=0.82 µmol/L; 95% CI -7.22, 8.86; I<sup>2</sup>=38%); transplant *with* a non-fasting arm (MD=-0.17 µmol/L; 95% CI -2.50, 2.15; I<sup>2</sup>=0%) and CKD *without* a non-fasting arm (post-pre MD=13.84 µmol/L; 95% CI -3.78, 31.47; I<sup>2</sup>=88%). For transplant studies *without* a non-fasting arm, lower SCr was associated with the post-Ramadan period (post-pre MD=-5.40 µmol/L; 95% CI -10.78, -0.02; I<sup>2</sup>=0%). In the 18 studies that reported on eGFR, fasting during Ramadan was not associated with an effect on eGFR for any of the groups.

**Conclusion** We report inconsistent effects of Ramadan fasting on kidney function in CKD or kidney transplantation. Results should be interpreted with caution due to the significant limitations of the underlying studies.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This systematic review was conducted with methodological rigour including a comprehensive literature search, dual independent abstract screening, study selection and risk of bias assessment.
- ⇒ The review covered a broad spectrum of parameters of interest including changes in CKD markers or risk factors, most notably serum creatinine, eGFR and proteinuria.
- ⇒ Studying the effects of Ramadan fasting on kidney function is not amenable to randomisation, so the highest level of evidence underlying this systematic review is de facto derived from observational studies.
- ⇒ Selection bias is a critical limitation of the observational literature informing this systematic review as most studies did not have a non-fasting control group and those that did are likely to have excluded high-risk participants in the fasting arm.
- ⇒ There is significant geographic homogeneity of study sites, therefore limiting the generalisability of the results at the extremes of latitude.

## INTRODUCTION

Ramadan is the holiest month of the year for Muslims,<sup>1-3</sup> and fasting during Ramadan is a significant religious practice and a key pillar of Islam. Ramadan fasting involves abstinence from food and drink, from dawn to sunset. On average, the fasting period lasts between 12 hours and 14 hours but may extend up to 22 hours depending on the season and geographic latitude.<sup>4-7</sup>

In 2023, of the total global population, approximately 25% (2 billion people) identify as Muslim. In an increasingly globalised and interconnected world, physicians practising in all regions may be confronted with questions concerning the safety of Ramadan

fasting. Travellers, children, women who are menstruating/pregnant/breastfeeding and anyone with illness are exempt from fasting. Despite this exemption, many still participate in the fast, including patients with chronic kidney disease (CKD) and kidney transplant recipients.<sup>8</sup>

Reports of physiological outcomes in kidney disease are mixed. Some studies even suggest temporary improvement in estimated glomerular filtration rate (eGFR) and reduced proteinuria in patients with CKD or kidney transplant recipients,<sup>4 9</sup> while others report negative kidney and cardiovascular health outcomes.<sup>10 11</sup>

We conducted a systematic review of the effect of Ramadan fasting on kidney function in CKD and kidney transplant recipients. We examined associations between fasting and changes in CKD markers or risk factors (eg, serum creatinine (SCr), eGFR, proteinuria, blood pressure, electrolytes, blood glucose and weight/body mass index), adverse health outcomes (eg, all-cause hospitalisation, cardiovascular events and dialysis) and impact on quality of life.

## METHODS

### Overview

This systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P).<sup>12</sup> Our protocol was registered (CRD42018088973) and previously published.<sup>1</sup>

### Data sources and search strategy

A literature search to identify all full-text peer-reviewed studies involving adult non-dialysis CKD participants or kidney transplant recipients was conducted; the exposure of interest was fasting during Ramadan. Databases including MEDLINE, Embase, Global Health, CINAHL (EBSCOhost), Scopus, Web of Science and Google Scholar were searched up to 18 September 2023 (online supplemental table 1). English and non-English language publications were reviewed (including German, Turkish, Arabic and Persian). References of identified texts (eg, systematic or narrative reviews) were also screened. Grey literature was not searched. Two reviewers independently performed title and abstract screenings. Full-text articles of studies considered potentially relevant by one or both reviewers were retrieved and assessed for eligibility.

### Study selection

Using predetermined eligibility criteria, each potentially relevant study was independently assessed by two reviewers. Disagreements were resolved by a third reviewer. Randomised clinical trials (RCTs) or observational studies involving adult participants (age ≥15 years) with CKD or kidney transplant recipients meeting the following criteria were eligible for inclusion: (a) at least one arm of the study observing a single Ramadan fast and (b) at least one change in kidney function as reported by SCr or eGFR, change in proteinuria, blood pressure,

electrolytes, health-related quality of life, hospitalisations, adverse events or mortality. Studies both with and without a non-fasting control arm were included. The presence of CKD was based on the generally accepted standard of eGFR of <60 mL/min/1.73 m<sup>2</sup> (SCr alone is an accepted alternative for the purposes of diagnosis or monitoring, but concordance is imperfect<sup>4 9 10 13</sup>) or classified as CKD by study authors that could have been based on other definitional criteria based on standard frameworks (eg, Kidney Disease Improving Global Outcomes [KDIGO] or Kidney Disease Outcomes Quality Initiative [KDOQI] depending on study era). Studies of dialysis patients were excluded.

### Data extraction and risk of bias assessment

One reviewer extracted the data using the data extraction database, and a second reviewer independently checked the extracted data for accuracy. Items recorded in the database included study characteristics (country, year, design and sample size); participant information (demographics, kidney function (SCr and/or eGFR), CKD status, comorbidities and medications used); exposure arm information (Ramadan dates and fasting duration and non-fasting arm details if applicable) and outcomes (timing and results). The primary outcome was a change in kidney function, defined as a change in SCr or eGFR between the pre- and post-Ramadan periods. Secondary outcomes included: (a) changes in proteinuria, serum albumin and protein, blood pressure, blood glucose concentrations, electrolytes and weight/body mass index (BMI) between the pre- and post-Ramadan periods, (b) electrolyte disorders such as hyperkalaemia, (c) episodes of acute kidney injury (AKI), (d) all-cause hospitalisations, (e) dialysis, (f) cardiovascular events (myocardial infarction, stroke), (g) mortality and (h) quality of life. Authors were contacted when data were missing.

Two reviewers independently assessed all studies for methodological validity using the Downs and Black criteria.<sup>14</sup> Disagreements were resolved by a third reviewer. Evaluating criteria included study design, approach to recruitment, sample size calculation, description of the study population by characteristics (including age, sex, CKD stage or measure of kidney function and diabetes), reporting of country and season (or Ramadan dates specifically), statistical consideration of confounding variables (including age, sex and baseline kidney function via model adjustment, stratification or matching) and reporting of missing primary outcome measurements. Source of funding was also extracted where possible.<sup>15</sup>

### Statistical analysis and data synthesis

Analyses were performed using Stata/MP, V.18.0 (StataCorp, LLC). Missing SD were imputed as outlined by Wiebe *et al.*<sup>16</sup> Results were pooled where possible according to the following four population and study design groups: CKD and transplant studies with and without a non-fasting arm. We calculated the mean difference (MD) and corresponding SE for each study prior

to pooling. For studies with both fasting and non-fasting arms, we calculated the MD based on the difference-of-differences (ie, the difference between the change in pre- and post-Ramadan measurements in the fasting arm and the change in pre- and post-Ramadan measurements in the non-fasting arm). For studies that included a fasting arm only, we calculated the MD based on the difference between pre- and post-Ramadan measurements. To further distinguish studies without a non-fasting arm, we refer to the latter type of MD as a 'post-pre MD'. For studies that reported multiple pre-Ramadan measurements, we selected the latest measurement in the pre-Ramadan period. Similarly, when multiple post-Ramadan measurements were reported, we selected the first available measurement after the conclusion of Ramadan. We accounted for correlation<sup>17</sup> when calculating these statistics, setting  $r=0.5$  if a correlation could not be calculated or was not reported.

Results were pooled using random effects models<sup>18</sup> where clinical and methodological heterogeneity were reasonable. Statistical heterogeneity was quantified using the  $I^2$  statistic.<sup>19 20</sup> *A priori*, we planned (where possible) to examine the primary outcome for the following subgroups: CKD stage, baseline comorbidities (cardiovascular disease and diabetes), latitude, season and risk of bias items. Due to the small number of studies (and lack of subgroup information) in each of the four population/study design groups described above, we could not examine subgroups nor assess publication bias or explore meta-regression.<sup>21–23</sup>

Data informing this systematic review are available on request from the corresponding author.

### Patient and public involvement

Patients and members of the public were not involved at any stage of the project.

## RESULTS

### Study selection

Our search yielded a total of 3735 citations (figure 1). Full texts of 144 citations were screened, and 32 studies met the inclusion criteria. Reviewers disagreed about the inclusion of 8% of studies ( $\kappa=0.81$ ). Characteristics of included studies are detailed in online supplemental tables 2 and 3 (studies *with* and *without* a non-fasting arm, respectively). All studies were observational (prospective:  $n=29$ ; retrospective:  $n=3$ ) and conducted between 1994 and 2023. Two studies<sup>24 25</sup> were in abstract form only. 21 studies reported on participants with non-dialysis CKD: seven studies included both fasting and non-fasting arms and 14 studies included a fasting arm only. 11 studies reported on kidney transplant recipients: five included both fasting and non-fasting arms and six studies included a fasting arm only. In general, CKD was defined as stages 2 to 5. Some studies explicitly indicated that participants on dialysis were excluded; for the remaining studies, we assumed that dialysis participants were excluded based

on our examination of the text, reported SCr and eGFR values at baseline, or contacting the study author (online supplemental tables 4 and 5).

Geographic distribution and details of Ramadan seasonality (affecting daily temperature and fasting duration) are outlined in detail in the online supplemental materials.

Select baseline patient characteristics and pre-Ramadan SCr values are outlined in online supplemental table 6 according to population and study design. Risk of bias was considered high in all but four studies where this risk was considered moderate (online supplemental figure 1 and material).

### Serum creatinine and estimated glomerular filtration rate

We meta-analysed 25 studies reporting SCr and 18 studies reporting eGFR separately by population (ie, CKD and transplant) and presence/absence of a non-fasting arm (figures 2 and 3). With the exception of transplant studies without a non-fasting arm, there were no changes observed in SCr pre- and post-Ramadan. Fasting was not associated with any effect on SCr in CKD studies with a non-fasting arm ( $n=5$  studies;<sup>2 6 26–28</sup> MD=0.82  $\mu\text{mol/L}$ ; 95% CI  $-7.22$ , 8.86;  $I^2=38\%$ ). Pre-Ramadan SCr values were significantly different between fasting and non-fasting arms (baseline MD= $-28.65 \mu\text{mol/L}$ ; 95% CI  $-54.98$ ,  $-2.32$ ;  $p=0.03$ ,  $I^2=89\%$ ); heterogeneity was very large.

Fasting was not associated with an effect on SCr in transplant studies with a non-fasting arm ( $n=4$  studies;<sup>29–32</sup> MD= $-0.17 \mu\text{mol/L}$ ; 95% CI  $-2.50$ , 2.15;  $I^2=0\%$ ). Pre-Ramadan SCr values were not significantly different between fasting and non-fasting arms (baseline MD= $-1.54 \mu\text{mol/L}$ ; 95% CI  $-7.05$ , 3.98;  $I^2=4.9\%$ ).

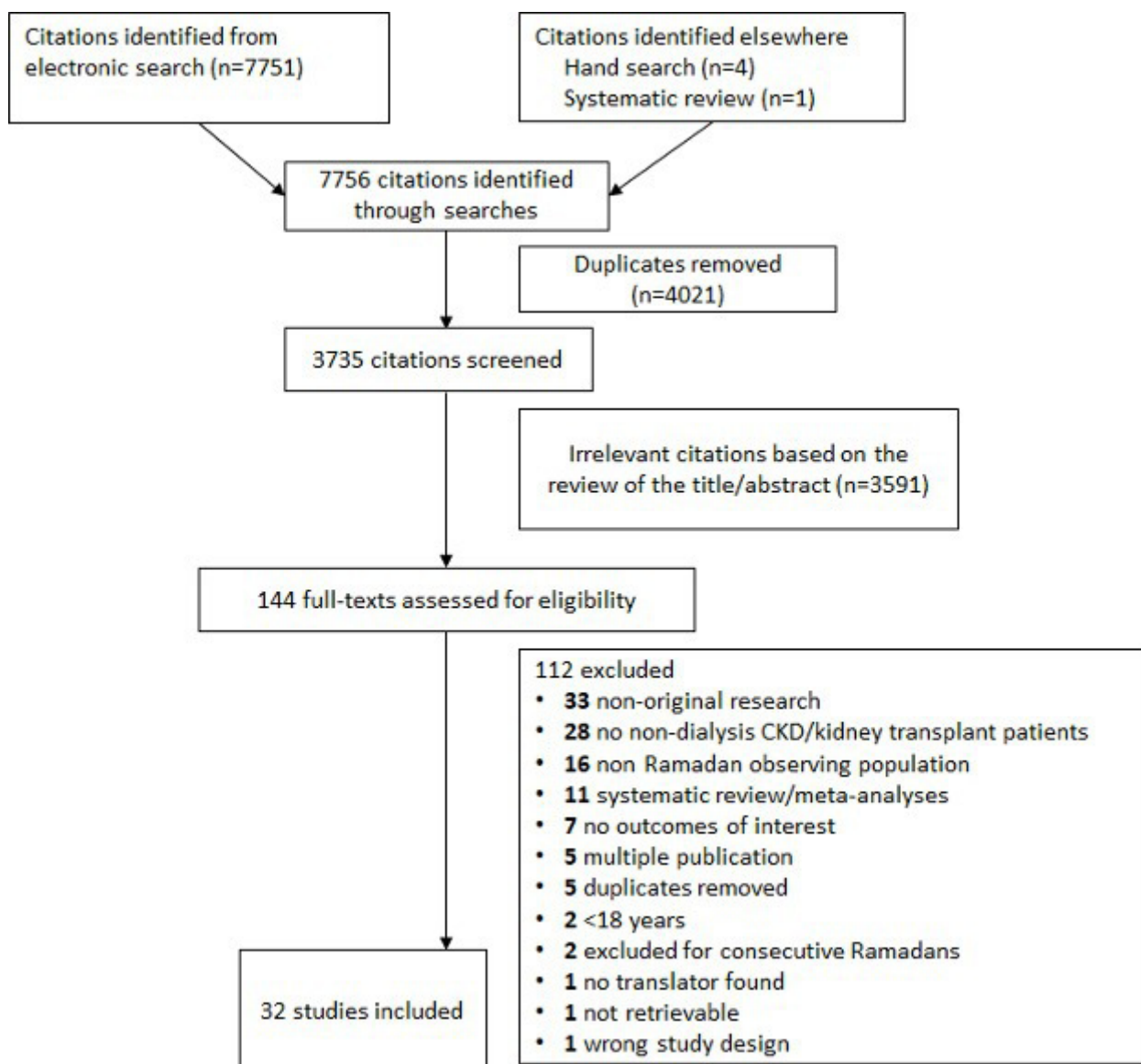
There was no significant difference in pre- and post-Ramadan SCr in CKD studies without a non-fasting arm ( $n=10$  studies;<sup>9 25 33–40</sup> post-pre MD=13.84  $\mu\text{mol/L}$ ; 95% CI  $-3.78$ , 31.5;  $I^2=88\%$ ).

For the six transplant studies<sup>41–46</sup> without a non-fasting arm, a modestly lower SCr was associated with the post-Ramadan period (post-pre MD= $-5.40 \mu\text{mol/L}$ ; 95% CI  $-10.78$ ,  $-0.02$ ;  $p=0.049$ ,  $I^2=0\%$ ).

Fasting during Ramadan was not associated with any effect on eGFR in CKD studies with a non-fasting arm ( $n=6$  studies;<sup>2 3 6 26–28</sup> MD=0.23  $\text{mL/min/1.73 m}^2$ ; 95% CI  $-1.64$ , 2.10;  $I^2=21\%$ ) nor transplant studies with a non-fasting arm ( $n=3$  studies;<sup>30 31 47</sup> MD=0.03  $\text{mL/min/1.73 m}^2$ ; 95% CI  $-1.14$ , 1.20;  $I^2=0\%$ ). There was a significant difference between arms in pre-Ramadan eGFR in the CKD studies (baseline MD=5.12  $\text{mL/min/1.73 m}^2$ ; 95% CI 0.25, 9.98 with very large between-study heterogeneity of  $I^2=86\%$ ) but not in transplant studies (baseline MD=1.04  $\text{mL/min/1.73 m}^2$ ; 95% CI  $-3.56$ , 5.64;  $I^2=16\%$ ).

There was no significant difference between pre- and post-Ramadan eGFR in CKD studies without a non-fasting arm ( $n=9$  studies<sup>9 10 24 34 36–40</sup>; post-pre MD=1.04  $\text{mL/min/1.73 m}^2$ ; 95% CI  $-0.26$ , 2.35;  $I^2=6\%$ ). No transplant studies without a non-fasting arm reported on eGFR.





**Figure 1** Flow diagram of study selection. CKD, chronic kidney disease.

## Secondary outcomes

### Proteinuria

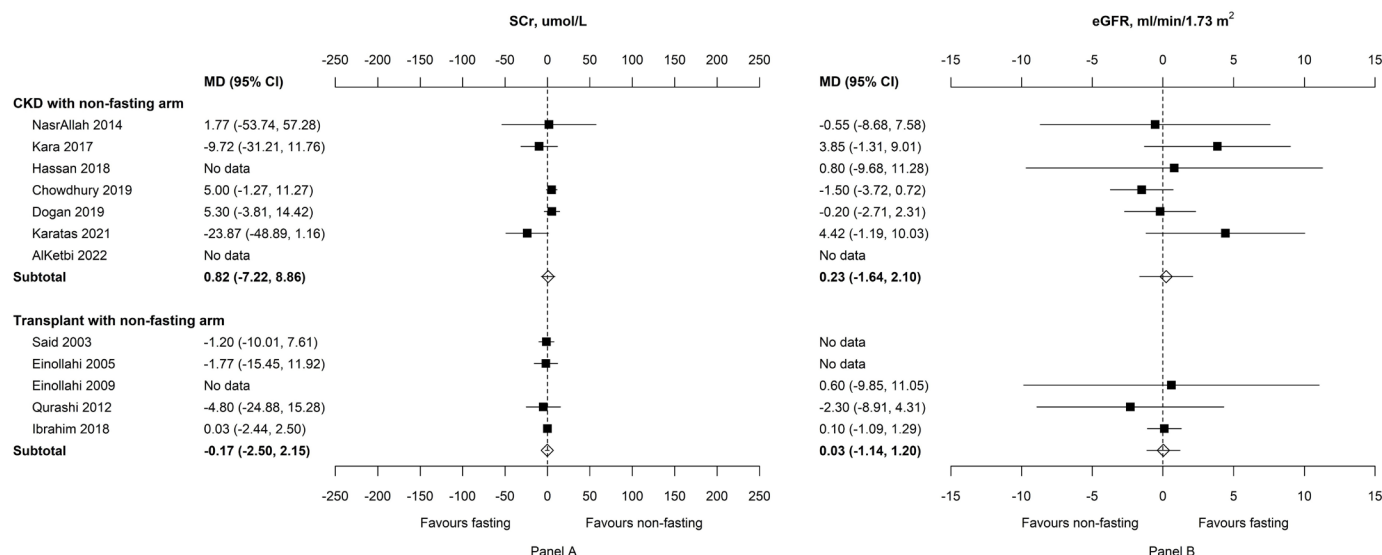
Among the 32 included studies, 13 reported on at least one measure of proteinuria.<sup>2 6 9 10 27 28 30 34 36 39 42 43 46</sup> We observed heterogeneity in terms of the measure and unit of proteinuria. There were too few studies to allow for meaningful pooling per study type; most results revealed non-significant changes in proteinuria with fasting. A detailed description of all secondary outcomes (proteinuria, serum albumin, total protein, measures of blood pressure, blood glucose or HbA1c, weight or BMI, electrolytes and adverse events) can be found in the online supplemental material.

## DISCUSSION

The aim of this review was to summarise the effects of Ramadan fasting on kidney function and related outcomes in CKD and/or kidney transplant recipients.

Literature on this topic is lacking with no evidence-based guidelines to help clinicians advise patients of the potential risks. On the basis of this systematic review, we found that Ramadan fasting was associated with no change in kidney function or even a counterintuitive reduction in SCr, depending on the study design. However, the literature underlying this review must be viewed with caution owing to significant limitations in the included studies.

Our review has identified a major knowledge gap in this field with the absence of high-quality published data to guide patients with kidney disease who want to fast during Ramadan, both in terms of immediate outcomes (ie, changes in kidney function or proteinuria) and/or long-term outcomes (ie, progression of CKD, risk of future AKI, cardiovascular disease and mortality), as well as quality of life (which has not been assessed in any of the included studies).<sup>2 6 9 35 48 49</sup> In fact, patients who might be considered at highest risk of fasting and for whom understanding

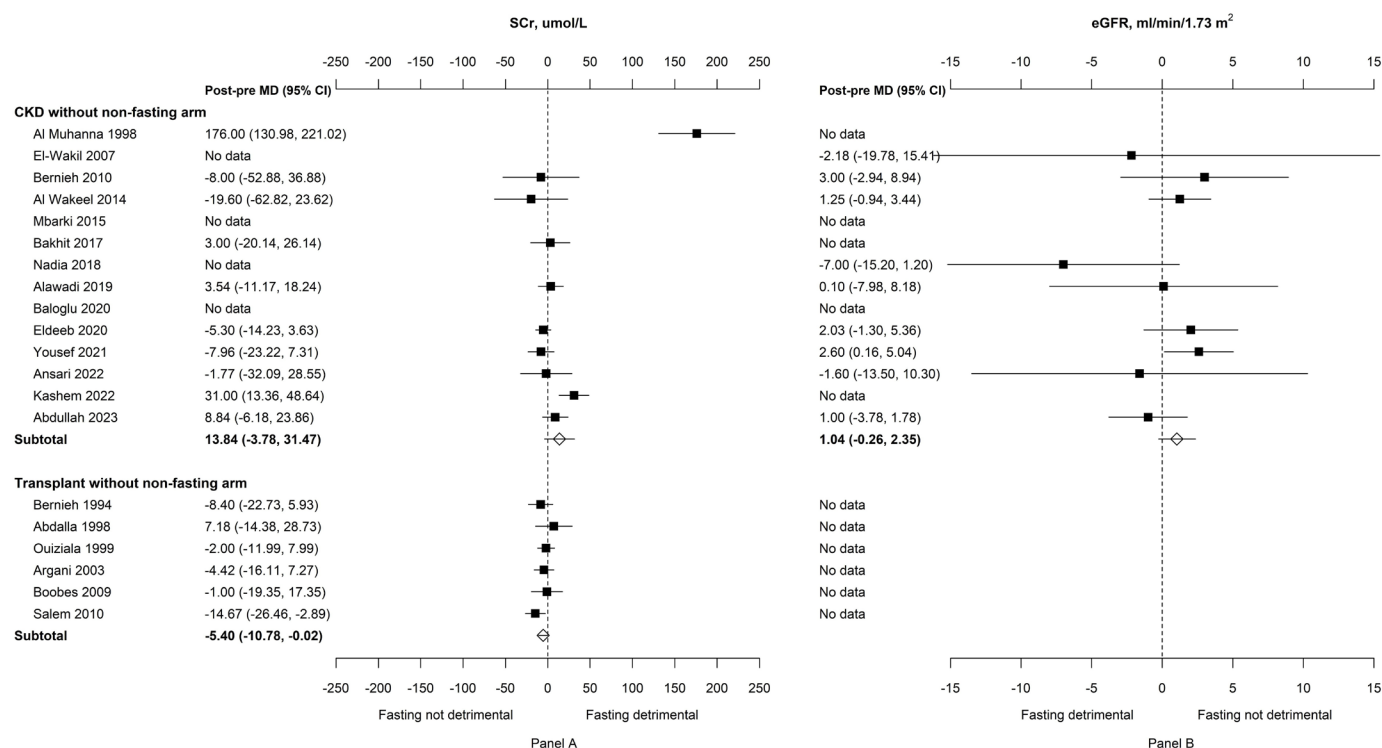


**Figure 2** Forest plot of serum creatinine and estimated glomerular filtration rate in studies with a non-fasting arm. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MD, mean difference; SCr, serum creatinine. MD (ie, the difference between the change in pre- and post-Ramadan measurements in the fasting arm and the change in pre- and post-Ramadan measurements in the non-fasting arm).

this risk is most clinically relevant (presumably those with most advanced kidney failure who are also expected to be on the most number of risk modifying medications—ACE inhibitors, ARBs, SGLT2 inhibitors, diuretics, immunosuppressive drugs, etc, which themselves increase the risk of kidney injury during volume contraction as may occur with fasting), especially those residing at extremes of geographic latitude where fasting in certain years may

be upwards of 22 hours, will not be helped by the findings of this literature nor this systematic review.

This is important as Muslims now constitute about a quarter of the world's population, and fasting during Ramadan is a central pillar of Islam. Current estimates suggest there are approximately 2 billion Muslims mostly concentrated in Africa, the Middle East and South Asia, but also increasingly living in very northern or southern



**Figure 3** Forest plot of serum creatinine and estimated glomerular filtration rate in studies without a non-fasting arm. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MD, mean difference; SCr, serum creatinine. MD (ie, the difference between pre- and post-Ramadan measurements).

regions where the duration of the fast may vary considerably. While it is generally accepted that anyone with a chronic disease may be exempt from fasting depending on their individual circumstances, many choose to fast regardless, prioritising the fast over health concerns.<sup>50</sup> Pre-Ramadan consultation, especially for patients with chronic diseases or multimorbidity is advocated by the International Diabetes Federation and the Diabetes and Ramadan International Alliance (IDF-DAR) and widely adopted by medical associations and societies.<sup>51</sup> This seems prudent but the value of such consultation is entirely predicated on specialty-specific literature to guide a discussion of potential risks. Mahmood *et al* provide thoughtful suggestions as to how such consultation be conducted in primary care and by specialists and how to integrate patients' values and perspectives with evidence-based guidance where possible and expert opinion where evidence is lacking.<sup>52</sup> The authors indicate that most literature pertains to diabetes management during Ramadan with less robust guidance for cardiac disease, epilepsy, adrenal disease or occupational health. Presumably, there is even less or no guidance with regard to other medical conditions. With respect to kidney disease, Malik *et al* propose a three-tier risk stratification system for approaching CKD in alignment with a similar paradigm proposed by the IDF-DAR for the management of diabetes.<sup>53</sup> Low-moderate risk patients with stable CKD stages 1–3 are advised to consult their medical practitioners for individualised risk discussion; high-risk patients with CKD stage 1–3 and unstable kidney function are advised they *should* not fast and very high-risk patients with stages 4–5 (non-dialysis) CKD are advised they *must* not fast. These authors concede, and our current systematic review substantiates, that these recommendations are based on the authors' consensus opinion and clinical experience rather than on objective evidence from well-conducted clinical studies. This is entirely related to the limitations of the available literature.

Our own review (to our knowledge, the first conducted with methodological rigour) is subject to the same limitations as the underlying literature. First, the topic of interest (effect of Ramadan fasting on kidney function) is not amenable to experimental studies of any kind or design. The Ramadan fast is a fundamental religious observance (counted among the five pillars of the Islamic faith) and is compulsory for all adults with the capacity to participate. It is therefore untenable that an RCT will be feasible (or even acceptable) to be conducted in the context of a person's expression of their faith. It is therefore unsurprising that there has been no single RCT ever conducted to investigate the effect of Ramadan fasting on the markers of kidney function; thus, all studies were observational/quasi-experimental and subject to well-recognised biases.<sup>54</sup> Selection bias is almost certain among the more-than-half of all included studies which did not include a non-fasting control group. In those studies, participants' clinicians' judgement would have suggested fasting was safe for everyone—anyone with a

high pretest probability of experiencing an adverse effect of fasting on their kidney function would presumably have been excluded from participating in the first place. Thus, patients at highest risk for whom recommendations are most relevant are almost certainly under-represented in these studies, if at all. For studies that did include a non-fasting control arm, the bias is even more relevant: the non-fasting control group is very likely disproportionately enriched by participants whose clinicians advised against fasting, presumably due to the perceived fragility of their kidney function. In fact, our analysis would substantiate this assumption since non-fasting control CKD subjects were shown to have higher pre-Ramadan creatinine values—182  $\mu\text{mol/L}$  versus 150  $\mu\text{mol/L}$ . Any comparisons between the fasting group and the non-fasting control are much more likely due to the participants' underlying medical condition rather than their fasting status (ie, a function of selection bias and confounding). Second, the number of included studies was small and the sample size per study was also small with inconsistent reporting of markers of kidney function, proteinuria, blood pressures, demographic variables, underlying kidney disease, medications, adverse events, etc. As such, we were not able to stratify the analyses into type and severity of kidney disease or other determinants of deteriorating kidney function in order to identify higher-risk groups and inform meaningful trade-offs. Third, the underlying literature is significantly limited by homogeneity in the geographic distribution of study sites. In fact, all but five studies were performed in the Middle East or North Africa. This impacts the generalisability of these results to regions in the extremes of the Northern and Southern Hemispheres where daylight hours and thus the duration of fasting can vary considerably with the seasonality of Ramadan. Finally, unlike RCTs, observational studies typically are not registered and can be subject to publication bias and selective outcome reporting.<sup>55</sup> Overall, this review is limited by the quality of the included studies and there remains a critical need for high-quality observational studies or even randomised trials to answer outstanding clinical questions that address important patient-relevant outcomes.

In conclusion, this review did not find a convincing impact of Ramadan fasting on the predefined study outcomes in CKD and among transplant recipients. However, the underlying literature is of such low quality that the potential for missing an important link between Ramadan fasting and kidney function is considerable. Kidney function in relation to Ramadan fasting is conceivably modified not only by patient-specific factors (ie, age, comorbidities, medications, etc) but also by the duration of fasting per day, itself a function of where (ie, latitude) and when (ie, seasonality) a person fasts; few, if any, of these factors are considered in the literature underlying this review, and we are unable to make evidence-based recommendations or stratify into specific risk groups. Until high-quality studies that rigorously evaluate the effect of fasting on kidney function in high-risk individuals are conducted, we recommend patients engage with

their care team for a conversation about the theoretical risks, personal risk tolerance, trade-offs, a monitoring strategy of laboratory and biophysical parameters, and a predefined threshold to break the fast and/or seek medical attention.

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**Contributors** RPP, AKB and SH conceived the original idea for this study. MAO, JK and AL reviewed the articles for inclusion/exclusion, risk of bias and methodological validity. AL, AKB and RPP wrote the first draft of the manuscript. AL, AKB, JK, MAO, TC, SH, ZH, MEQ, UQ, SS and RPP reviewed the manuscript for intellectual content and approved the final submitted version of the manuscript. RPP is the guarantor of this manuscript.

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**Data availability statement** Data are available upon reasonable request. Data informing this systematic review are available upon request from the corresponding author.

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