

CHAPTER 13

Risks of fasting during Ramadan: Cardiovascular, Cerebrovascular and Renal complications

Chapter lead:

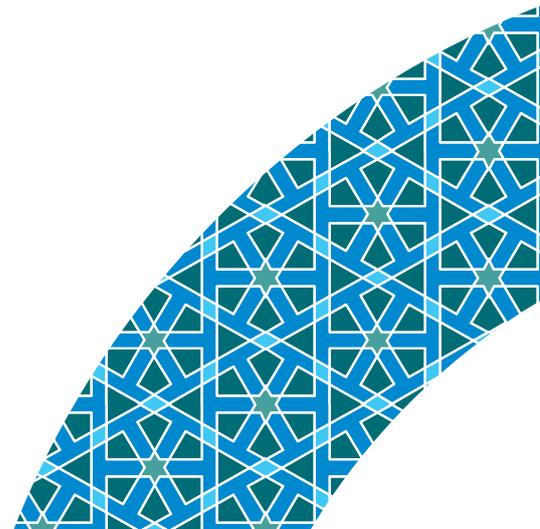
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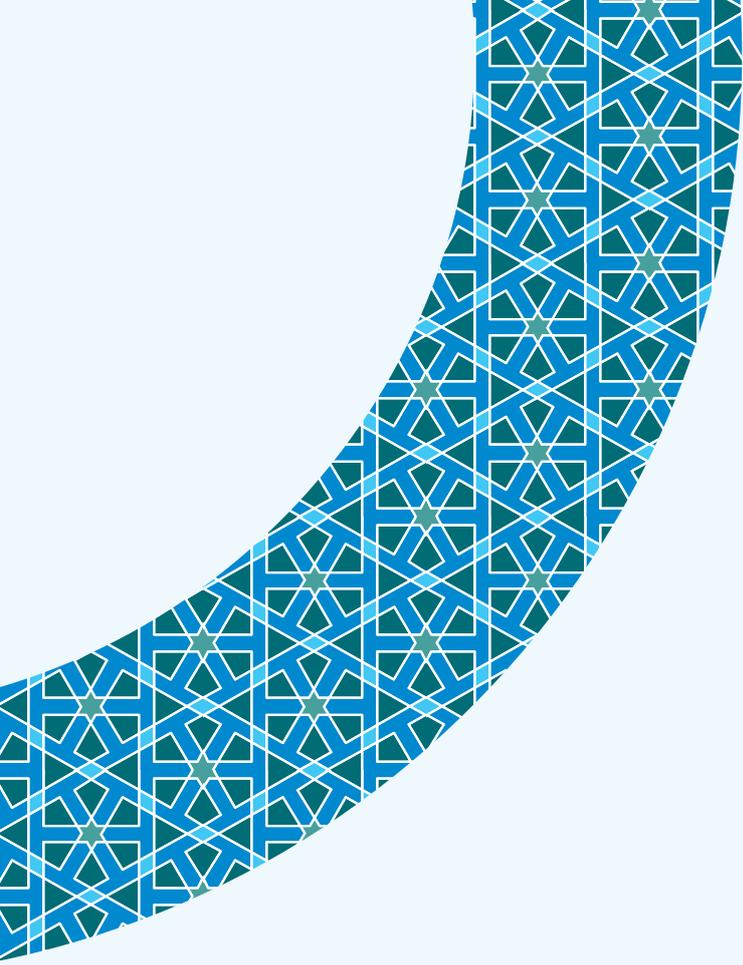
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WHAT IS KNOWN?

- Diabetes is a risk factor towards cardiovascular disease (CVD) and stroke.
- Individuals with pre-existing CVD or stroke and diabetes are at greater risk of complications when fasting and should be cautious.
- Individuals with chronic kidney disease (CKD) stage 3 and diabetes are of high-risk for fasting during Ramadan.
- Individuals with chronic kidney disease (CKD) stage 4-5 and diabetes are of very high-risk for fasting during Ramadan.
- Fasting in these individuals should generally be discouraged.

WHAT IS NEW?

- New research has been conducted highlighting the effect of fasting on CVD and stroke. However, further evidence is yet needed from study populations with pre-existing type 1 and type 2 diabetes and CVD and/or stroke in order to make specific recommendations regarding fasting during Ramadan.
- Individuals with diabetes and unstable CVD or stroke are high risk and should be discouraged from fasting.
 - Those that choose to fast must receive individualised guidance from a diabetes specialist and cardiologist or neurologist and must undertake pre-Ramadan education on safe fasting with diabetes (see **chapter 7: Pre-Ramadan Assessment and Education**)
- There is some evidence showing fasting could be conducted safely during Ramadan in individuals with stable CKD, on dialysis or having undergone a kidney transplant. However, more research is needed on individuals with pre-existing type 1 and type 2 diabetes in order to make specific recommendations regarding fasting during Ramadan.
- Individuals with stage 3 or higher CKD and diabetes are at high risk of fasting and should be discouraged from doing so.
 - Those that choose to fast should consult a diabetes specialist, keep hydrated and avoid foods with a high potassium or phosphorous content.

WHAT IS MISSING?

- Further research is needed into the effects of CVD, stroke and CKD in individuals with type 1 and type 2 diabetes.
 - These studies should also include information on social backgrounds, ethnicity and climates.
 - Likewise, this research should also include the effects of fasting in individuals that have any associated complications of diabetes including poorly controlled glycaemia, frequent episodes of hypoglycaemia (with and without unawareness), hypertension and in individuals on different treatment regimens.
- Further studies need to be conducted that investigate the effect of fasting on neuropathy and retinopathy in people with diabetes.

1. INTRODUCTION

Macrovascular disease can occur as a complication of diabetes; it affects the larger blood vessels including the coronary arteries, aorta and arteries within the brain and limbs and can lead to cardiovascular disease (CVD) or cerebrovascular disease including stroke. Likewise, microvascular disease can also occur whereby the smaller vessels that branch off of the larger arteries are affected and this can cause issues such as a loss of renal function.

People with diabetes that choose to fast during Ramadan could potentially exacerbate these complications, if conducted unsafely, and therefore these individuals are classified as high risk [1]. This chapter outlines the guidance for individuals with diabetes that have these complications and includes specific guidance for those with:

1. Cardiovascular and Cerebrovascular complications;
2. Chronic kidney disease (CKD).

2. MACROVASCULAR COMPLICATIONS

Impact of fasting during Ramadan for people with diabetes on cardiovascular disease (CVD)

Diabetes has been frequently associated with an increased risk of CVD [2, 3]. In addition, people with diabetes also have a heightened risk of stroke [4]. Importantly, the practice of unsafe fasting including a high intake of carbohydrates, low levels of activity, poor sleeping patterns, inadequate hydration, and missing doses of essential medicines could have an impact on the risk of CVD or stroke in people with diabetes [5, 6].

On the other hand, when fasting is conducted safely (see **chapters 9** and **10**) these risks could be mitigated. It has been demonstrated that proper glycaemic control can reduce the number of cardiovascular events [7]. Likewise, fasting has also been shown to significantly increase levels of nitric oxide (NO) and decrease markers of oxidative stress [8, 9], with a variable effect on lipoprotein levels, high sensitivity C-Reactive protein (hsCRP) levels and blood pressure [10, 11].

The last two decades have seen an increase in the awareness of the risks that diabetes poses to CVD. However, it is important to understand the impact that fasting during Ramadan has on the risk of CVD.

2.1 Fasting during Ramadan and congestive heart failure (CHF)

One particular form of CVD is congestive heart failure (CHF); **Table 1** has summarised several studies that have investigated the effect of fasting during Ramadan on the risk of CHF in people with diabetes.

A multi-centre study conducted in the Gulf region found no difference in the proportion of patients that were hospitalised for heart failure with diabetes during Ramadan and outside of Ramadan, 52% and 48.4% respectively [12]. Similarly, in a study of patients with heart failure,



18 had worsening symptoms due to non-compliance with dietary advice and medications while 209 remained stable or improved. Diabetes was found not to be associated with the worsening of symptoms [13]. A retrospective review of clinical data also found that there were no differences in the number of hospitalisations when comparing the month prior to Ramadan, the period of Ramadan and the month after Ramadan [14].

TABLE 1: STUDIES INVESTIGATING THE EFFECT OF FASTING DURING RAMADAN ON CONGESTIVE HEART FAILURE (CHF)

Author (Date)	Sample size and study details	Study population and CHF measures related to Ramadan	Key outcomes
Amar M. Salam et al. (2018) [12]	N=4,157 patients hospitalised – 306 (7.4%) during Ramadan; 3851 (92.6%) outside of Ramadan Prospective observational study Location: 7 countries in the Middle East	All participants were hospitalised for acute heart failure Outcomes of hospitalisation during Ramadan and outside of Ramadan were investigated	No significant differences between hospitalisations during Ramadan and outside of Ramadan were found, 52% and 48.4% respectively (p=0.23) Diabetes was not a risk factor for in hospital mortality, Odds Ratio 1.05 p=0.78
Rami M. Abazid et al. (2018) [13]	N=249 – 227 fasted for the entire month of Ramadan Prospective observational study Mean Age 54 years old (±12.83) Location: Kingdom of Saudi Arabia	Patients that were hospitalised with chronic heart failure Symptoms related to CHF were investigated	Diabetes was not associated with the worsening of symptoms during hospitalisation
Swaidi et al. (2006) [14]	N=2160 Mean Age 64.2 years old (±11.5) Retrospective review Location: Qatar	Patients that were admitted to hospital with CHF during Ramadan, the month prior to Ramadan and the month after Ramadan – 56.5% had diabetes The number of hospitalisations were investigated in each period	No significant differences in the number of hospitalisations were between the three periods

2.2 Fasting during Ramadan and acute coronary syndrome (ACS)

Acute coronary syndrome (ACS) is a term that refers to a range of conditions that involve a restriction of blood flow to the coronary arteries. Such conditions include unstable angina and myocardial infarction (MI). **Table 2** has outlined several studies that have investigated the effect of fasting during Ramadan on the risk of ACS in people with diabetes.

Evidence suggest that there is no clear association between fasting during Ramadan an increase in acute cardiac events [15, 16]. Suwaidi *et al.* demonstrated no true differences in the percentage of people with diabetes that were admitted with ACS before (51%), during (56%) and after (59%) Ramadan [17]. Indeed, echocardiographic and angiographic measurements found no clear differences between people that were fasting and people that were not fasting during Ramadan [18].

In addition, there were some protective effects of fasting during Ramadan found in some studies. Temizhan *et al.* found a significant reduction in the number of ACS events during Ramadan when compared to times outside of Ramadan [19]. Likewise, Burazeri *et al.* found protective associations between a composite measure of religiosity and ACS in a cross-sectional study [20].

TABLE 2: STUDIES INVESTIGATING THE EFFECT OF FASTING DURING RAMADAN ON ACUTE CORONARY SYNDROME (ACS)

Author (Date)	Sample size and study details	Study population and ACS measures related to Ramadan	Key outcomes
Chamsi-Pasha <i>et al.</i> (2004) [21]	N=86 Prospective observational study Location: Kingdom of Saudi Arabia	All participants were patients with stable cardiac disease Measures were taken of biochemical markers and all patients were monitored for any deterioration	There were no significant changes to biochemical markers or deterioration measured using the Ney York Heart Association classifications
Khafaji <i>et al.</i> (2012) [10]	N=56 Prospective observational study Location: Qatar	All participants in the study were stable but had suffered from CVD Electrocardiography, angiography and biochemical measurements were assessed before, during and after Ramadan	All participants finished the total duration of fasting without any cardiac or non-cardiac events
Al Suwaidi <i>et al.</i> (2006) [22]	N=465 Prospective observational Location(s): Various medical centres Kuwait, Qatar, United Arab Emirates, Bahrain	All participants were outpatients with acute heart disease Clinical assessments were performed before, during and after Ramadan	91.2% of patients were able to fast for the duration of Ramadan; only 6.7% felt worsening symptoms due to fasting Most participants were stable and able to safely fast
Mousavi <i>et al.</i> (2014) [15]	N=148 Prospective observational study Location: Iran	Fasting and non-fasting groups were compared for symptoms of coronary artery disease	There were no differences among both groups in terms of occurrences of chest pain No differences were observed in the composite measure of chest pain and dyspnoea
Turker <i>et al.</i> (2012) [18]	N=151 - 55 fasting during Ramadan; 96 non-fasting Cross-sectional study Location: Turkey	All participants in the study were diagnosed with acute ST-elevated MI The diurnal variation in MI was measured during the period of Ramadan	No clear differences were found between those that fasted and those that didn't during Ramadan in echocardiographic and angiographic measurements
Temizhan <i>et al.</i> (1999) [19]	N=1665 Retrospective study from 1991 - 1998 Location: Turkey	All participants were hospitalised with acute myocardial infarction ACS events were measured before, during and after Ramadan	There was a significant reduction seen in the number of ACS events during Ramadan when compared to before or after Ramadan (p=0.03)

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TABLE 2: STUDIES INVESTIGATING THE EFFECT OF FASTING DURING RAMADAN ON ACUTE CORONARY SYNDROME (ACS)

Author (Date)	Sample size and study details	Study population and ACS measures related to Ramadan	Key outcomes
Burazeri et al. (2008) [20]	N=936 Cross-sectional study Location: Albania	467 nonfatal ACS patients were compared to 469 controls and assessed for ACS using a composite measure made up of the frequency of prayers, mosque attendance, and fasting	A protective effect was observed in the composite score on the odds of having ACS; odds ratio 0.45 (95% CI 0.26-0.77)
Al Suwaidi et al. (2004) [17]	N=8446 Retrospective clinical review Location: Qatar	Patients that were hospitalised with unstable angina or MI Percentages of hospitalisations in the months prior to Ramadan, during Ramadan and after Ramadan were assessed	The number of admissions with ACS was not significantly different in either of the three periods

2.3 Fasting during Ramadan and cardiac arrhythmias

There have been few studies assessing the impact of fasting during Ramadan on cardiac arrhythmia and further research into this condition is needed. A retrospective review from 1991 – 2010 looking into patients that were hospitalised with atrial fibrillation found no significant differences in the time periods of admission when comparing times prior to, during and after Ramadan. There was even the finding in a subgroup of patients that had underlying ischemic heart disease that showed a reduction in hospitalisations during Ramadan [23]. Al Suwaidi et al. also found no additional cardiac arrhythmia episodes in patients with hypoglycaemia that utilised continuous glucose monitoring (CGM) during Ramadan [14].

3. MACROVASCULAR COMPLICATIONS

Fasting during Ramadan and stroke

Diabetes is an independent risk factor for stroke and the effect of fasting during Ramadan in people with diabetes needs to be established. There have been several studies that have investigated this and are outlined in **Table 3**.

Assy et al. in a cross-sectional designed study found that people with type 2 diabetes mellitus (T2DM) were no more likely to be hospitalised for ischaemic or haemorrhagic stroke during Ramadan than in the months before or after Ramadan [24]. Moreover, El-Mitwalli et al. confirmed these results in a longitudinal study in Egypt [25]. A retrospective review by Bener et al. also reported similar findings in Qatar where 50% of the cohort had diabetes, although no subgroup analyses were shown to see this effect in those with diabetes [26].

Conversely, others found the opposite showing fasting during Ramadan was associated with a significantly higher risk of stroke. Selcuk et al., in a retrospective review, found a greater frequency of ischaemic stroke during Ramadan than compared to before or after Ramadan [27]. Yazdeen et al. found in a cohort that were primarily middle aged that was some evidence that fasting was associated with a higher risk towards stroke ($p=0.03$) [28]. Zimhony et al. built

on this in a study in Israel and found that the risk of stroke was greatest during the first fortnight of Ramadan [29].

It is clear that there are conflicting findings on the impact of Ramadan on the risk of stroke. Some have found that there is a greater risk during Ramadan and others have found no difference in the risk. Greater research is needed in randomised cohorts where confounding can be removed and the specific effects of fasting on the risk of stroke can be assessed. Also, studies should aim to follow up individuals that have pre-existing stroke and diabetes and assess whether these patients can safely fast during Ramadan.

TABLE 3: STUDIES INVESTIGATING THE EFFECT OF FASTING DURING RAMADAN ON STROKE

Author (Date)	Sample size and study details	Study population and stroke measures related to Ramadan	Key outcomes
Assy et al. (2019) [24]	N=220 Longitudinal cross-sectional study across different time periods Location: Egypt	People with T2DM were asked to participate in this study The frequency of hospitalisations was assessed in all individuals during the time periods of before, during and after Ramadan	No significant differences were noted in the frequency of hospitalisations due to stroke (ischaemic or haemorrhagic) between all time periods
Selcuk et al. (2003) [27]	N=793 Retrospective review of clinical data Location: Turkey	Patients that were hospitalised for ischaemic or haemorrhagic stroke were reviewed Measures were taken during the time periods of before, during and after Ramadan	Approximately 20% of patients had diabetes It was found that there were greater ischaemic stroke hospitalisations during Ramadan than before or after Ramadan (statistically significant)
Zimhony et al. (2018) [29]	N=4727 564 from the Bedouin population Retrospective clinical review Location: Israel	All patients reviewed were admitted to hospital with acute ischaemic stroke Stroke incidence was compared to the time period of Ramadan	Overall, there was a statistically significant association between stroke incidence and the time period of Ramadan; this effect was higher during the first fortnight of Ramadan
Yazdeen et al. (2016) [28]	N=120 Case control study; 1:1 split Location: Iraq	Patients that were middle aged and had clinical or radiological features of stroke were included The rates of stroke were assessed for an association with fasting during Ramadan in both groups and compared	Fasting was a significant risk factor towards stroke; 66.7% of cases and 40% in controls (p=0.03) This was also confirmed using logistic regression
El-Mitwalli et al. (2009) [25]	N=517 Prospective longitudinal study Location: Egypt	Patients that were admitted to the stroke unit of hospitals were recruited into the study Measurements were taken before and during Ramadan	No statistically significant differences were found across the time periods in ischaemic or haemorrhagic stroke

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TABLE 3: STUDIES INVESTIGATING THE EFFECT OF FASTING DURING RAMADAN ON STROKE

Author (Date)	Sample size and study details	Study population and ACS measures related to Ramadan	Key outcomes
Saadatina et al. (2008) [30]	N=162 Retrospective study Location: Iran	All patients admitted to neurological centres participating in the study were included The month of onset was assessed with the incidence of cases	The mean number of diagnoses was 5.5 during fasting months and approximately 2 during non-fasting months Analyses also showed a statistically significantly increased risk of cerebral venous sinus thrombosis when fasting during Ramadan when compared to outside of Ramadan
Bener et al. (2006) [26]	N=335 Retrospective clinical review Location: Qatar	Patients that were hospitalised for stroke were included in the study from 1991 – 2003 The frequency of hospitalisations was compared before, during and after Ramadan	Almost 50% of the cohort had diabetes There were no clear differences found in the frequency of hospitalisations based on the time periods of before, during and after Ramadan
Akhan et al. (2000) [31]	N=1579 Retrospective study Location: Turkey	All patients admitted to the participating sites for stroke between 1991 – 1995 A comparison of the frequency of stroke was made during Ramadan and other months	No statistically significant differences were found in the frequency of stroke across the two groups of during Ramadan and outside of Ramadan

4. CONSIDERATIONS AND RECOMMENDATIONS (CVD AND STROKE)

It is important to caveat the results shown above with their limitations. Many of these studies assessed hospitalisations in retrospective reviews and these have inherent biases; those that were most ill or likely to suffer macrovascular complications of CVD or stroke may have not made it into hospital. There could also be factors that confounded the association between Ramadan and macrovascular complications.

Additionally, many studies did not specifically assess the act of fasting during Ramadan and its association with CVD or stroke and only looked at aggregate data during time periods in and around Ramadan. This makes it difficult to truly assess the impact of fasting. It is also important to note that there were not many studies that directly investigated the impact of fasting during Ramadan in a population of individuals with diabetes, much less the different types.

It is recommended that all people with diabetes and pre-existing CVD, that are seeking to fast during Ramadan should receive a specific risk assessment and individualised advice.

Further randomised controlled studies in populations that have diabetes, including type 1 and type 2 diabetes need to be conducted in order to gain a better understanding of the risks of CVD or stroke in people with diabetes and the true effect of fasting during Ramadan.

Individuals with diabetes that have macrovascular complications such as stable or unstable CVD or stroke should remain classified as high risk. These individuals should generally be discouraged from fasting.

THOSE THAT ARE IN THE HIGHER RISK CATEGORIES FOR FASTING AND STILL CHOOSE TO FAST MUST:

- Receive a thorough risk assessment from their diabetes specialist, cardiologist and/or neurologist well in advance of Ramadan.
- Obtain individualised advice based on their current health status and treatment regimes.
- Receive pre-Ramadan education and understand how to properly conduct safe fasting with diabetes (see **chapter 7: Pre-Ramadan Assessment and Education**).
- Practice safe fasting as discussed in these guidelines wherever applicable.
- Receive pre-Ramadan screening.
- Make appropriate adjustments to therapies in accordance with their symptoms of CVD or stroke. For example, diuretics, antihypertensives, anti-diabetes medication and insulin regimens will need adjusting to give the greatest chance of achieving safe fasting during Ramadan.
- Make a concerted effort to stay hydrated and get an adequate amount of sleep and nutrition prior to conducting fasting.



5. MICROVASCULAR COMPLICATIONS

Impact of fasting during Ramadan for people with diabetes on Chronic Kidney Disease

An important microvascular complication that can arise as a result of diabetes can be chronic kidney disease (CKD) [32]; CKD can be categorised into different stages reflecting the severity of the disease, this classification has been described elsewhere [33]. The International Diabetes Federation and Diabetes and Ramadan International Alliance (IDF – DaR) guidelines stratify people with diabetes that have CKD by risk. Previously people with diabetes and CKD stage 3 were classified as high risk and those stage 4 or 5 were classified as very high risk [1]. In the new risk stratification, both are discouraged from fasting.

Kidney disease remains a huge issue to people with diabetes and in particular in countries that have large Muslim populations [32, 34], (see **chapter 2: Epidemiology of diabetes and fasting during Ramadan**).

Despite the associated risks, many people with diabetes and CKD may still wish to fast during the month of Ramadan and recommendations need to be made to help allow these individuals to practice the fast safely [35].

5.1 Fasting during Ramadan and Renal function

There have not been many studies conducted that have investigated the direct effect of fasting during Ramadan in people with diabetes on renal function. However, some studies that have investigated this, directly or indirectly, have been summarised in **Tables 4** and **5**.

El-Wakil *et al.* showed in a comparative prospective study that those with CKD were more likely to have increased levels of urinary NAG compared to healthy individuals that fasted during Ramadan. Importantly, they showed that the increase in urinary NAG levels were associated with blood glucose levels, highlighting the importance of glycaemic control among those with diabetes [36]. Mbarki *et al.* also showed that individuals with CKD that fasted during Ramadan could experience deterioration in renal function, particularly in those with an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73m² [37]. Bakhit *et al.* also showed that the higher the stage of CKD the worse the renal outcomes during Ramadan [38]. Importantly, others also noted that CKD can lead to an increased risk of CVD in individuals that fast during Ramadan [39].

On the other hand, Bernieh *et al.* showed an improvement in eGFR during and after Ramadan with no significant changes to biochemical measures such as urinary electrolytes, protein or osmolarity [40]. Kara *et al.* also showed similar outcomes in a comparative study of people that fasted compared to those that did not. They also highlighted that the elderly individuals could be at a higher risk of deterioration in kidney function [41], (for further information on elderly individuals please see **chapter 12: Management of diabetes among the elderly when fasting during Ramadan**). A meta-analysis conducted on the mean difference of the eGFR before and after Ramadan among several different studies; no clear or meaningful difference was found (mean difference 0; 95% CI -0.19 – 0.19) [35].

TABLE 4: STUDIES SHOWING WORSENING OUTCOMES IN RENAL FUNCTION IN PARTICIPANTS THAT FASTED DURING RAMADAN

Author (Date)	Sample size and study details	Population	Key findings
El-Wakil et al. (2007) [36]	N=21 15 with CKD and 6 healthy volunteers Prospective study Location: Egypt	All cases of CKD were evaluated pre-Ramadan and during Ramadan and the mean change eGFR was measured and compared to the healthy volunteers Roughly 20% of cases of CKD were caused by diabetes	Tubular injury correlated significantly with glycaemic control – NAG/creatinine and urinary protein/creatinine levels were correlated with percentage change in blood glucose ($p=0.001$)
Mbarki H et al. (2015) [37]	N=60 Prospective study Location: Morocco	All participants were diagnosed with CKD, approximately 8% had insulin-requiring diabetes Patients were separated into three groups based on renal function and evaluated before, during and after Ramadan	A total of 11.7% of patients that fasted during Ramadan experienced acute renal failure The main risk factor for deterioration in renal function was the presence of an eGFR < 60 mL/min/1.73m ²
NasrAllah and Osman (2014) [39]	N=106 Prospective study	All participants were patients that presented to a clinic with CKD Participants were split into two groups: 52 fasting and 54 non-fasting eGFR and biochemical measurements were taken before, during and after Ramadan and a mean difference was calculated	There was a worsening of kidney function during Ramadan and a hint that CKD could progress with worsening outcomes after Ramadan – creatinine levels rose by 60% during Ramadan and remained after Ramadan in 23% of individuals There was an increase in the risk of CVD in among that fasted during Ramadan 4 individuals continued fasting despite worsening outcomes
Bakhit et al. (2017) [38]	N=65 Prospective study Location: Kingdom of Saudi Arabia	All participants had CKD stage 3 or higher; 38% also had diabetes Clinical and biochemical measurements were taken before, during and after Ramadan	Around a third of participants that fasted during Ramadan experienced worsening renal function, this effect was increased by the stage of CKD Increases in the levels of creatinine were sustained after Ramadan



TABLE 5: STUDIES SHOWING STABLE OUTCOMES OR IMPROVEMENTS IN RENAL FUNCTION IN PARTICIPANTS THAT FASTED DURING RAMADAN

Author(s) (Date)	Sample size and study details	Population	Key findings
Bernieh et al. (2010) [40]	N=31 Prospective study Location: United Arab Emirates	Out-patients to a participating site that had stage 1-5 CKD were enrolled into this study 61% of the cohort had diabetes Clinical and biochemical measurements were taken before, during and after Ramadan	There was an improvement seen during and after Ramadan in eGFR (p=0.017) There were no statistically significant differences in urine electrolytes, protein or osmolarity
Hassan S et al. (2018) [42]	N=57 Prospective comparison study Location: Israel	All participants were with CKD stage 2, 3 or 4 There were 31 that fasted and 26 that did not fast Clinical and biochemical measurements were taken before, during and after Ramadan	eGFR did not change throughout the three time periods in fasting participants Changes in biochemical measurements were noted during Ramadan but returned back to normal after Ramadan It was concluded that participants in this study with CKD of stages 2–4 could fast throughout the month of Ramadan with no significant deterioration of renal functions
Kara E et al. (2017) [41]	N=94 Prospective study Location: Turkey	All participants had stable CKD of stages 3-5 45 individuals fasted and 49 did not fast during Ramadan; 32% of the cohort had diabetes Clinical and biochemical measurements were taken before and after Ramadan	There were no reported changes to BMI, systolic or diastolic blood pressure in both time periods in those that fasted No differences were seen in either fasting group for changes to eGFR between time periods It was found that elderly individuals were associated with a greater degree of deterioration in kidney function
Al Wakeel et al. (2014) [43]	N=39 Prospective study Location: Kingdom of Saudi Arabia	Participants included people with CKD of stage 3 or higher Clinical and biochemical measurements were taken before, during and after Ramadan	There were no notable changes in the progression of CKD or eGFR between the time periods Biochemical and clinical measurements remained relatively stable including creatinine, urine protein and blood pressure

5.2 Fasting during Ramadan in individuals on dialysis

There have been several studies conducted in individuals that have undergone dialysis, and many have found that fasting can be safely conducted during Ramadan without any added complication. Several studies have also taken into account the effect of diabetes. These studies have been summarised below.

Al-Wakeel *et al.* showed, in a study of 31 participants on peritoneal dialysis, that fasting was not associated with mortality or morbidity [44]. A study in 40 participants on haemodialysis that fasted on non-dialysis days found that fasting had no effect on weight gain, blood-pressure or electrolytes [45]. Likewise, another study on participants that underwent haemodialysis and fasted during Ramadan, showed that there was no excess mortality or morbidity as a result of fasting [46]. A large prospective, multi-centre, comparative study of individuals on haemodialysis was conducted in Saudi Arabia. More than half of the study participants had diabetes. It was found that there were no differences in pre- and post-dialysis blood pressure, serum potassium, albumin or cardiovascular events between those that fasted and those that did not fast during Ramadan [47].

A study conducted in Malaysia, in which approximately half of the participants had diabetes, found that fasting during Ramadan was associated with a reduction in weight and improvements in serum albumin and phosphate levels [48]. Another more recent study from Malaysia found that fasting in participants that were on haemodialysis was associated with reductions in BMI, inter-dialytic weight gain and improvements in serum phosphate, urea and creatinine levels, though serum albumin levels were found to fall. It was concluded that participants in their study only experienced transient changes during Ramadan and fasting could be conducted safely [49]. Similarly, Kazneh *et al.*, in a study conducted in Palestine of which almost half of participants had diabetes (46%), found fasting during Ramadan was associated with increases in inter-dialytic weight gain, even after adjusting for diabetes and other socio-demographic factors. Diabetes was associated with some biochemical changes but these were deemed clinically negligible [50].

5.3 Fasting during Ramadan in individuals that have undergone a renal (kidney) transplant

There have also been many studies that have looked into the effect of fasting during Ramadan in individuals that have undergone a kidney transplant, see **Table 6**. Generally, the consensus was that fasting can be conducted safely in these individuals, but more research is needed into people with diabetes that also have had kidney transplants to make more specific recommendations.

Ghalib *et al.* found that eGFR did not change from levels before Ramadan after fasting during Ramadan, even after adjusting for diabetes and age. They also found no differences in biochemical measurements between participants that fasted and those that did not fast [51]. These results were similar to that found by Ibrahim *et al.* who conducted a retrospective study in the Kingdom of Saudi Arabia [52]. A prospective study in Iran found that fasting was not associated with acute rejections of transplants or other complications [53].



Quarashi *et al.* also showed that fasting did not affect eGFR in different groups of baseline eGFR (categorised low, moderate and high), but did find that post-transplant periods of those that fasted were longer than those that did not fast [54]. Said *et al.* showed in a prospective study, that there were no associations between fasting during Ramadan and changes to serum creatinine levels but did find that those with type 1 diabetes mellitus (T1DM) had a tendency for higher blood glucose levels. Importantly, they also found two cases of acute rejection and three cases of chronic graft dysfunction [55].

TABLE 6: STUDIES ASSESSING THE SAFETY OF FASTING DURING RAMADAN IN INDIVIDUALS WITH KIDNEY TRANSPLANTS

Author(s) (Date)	Sample size and study details	Population	Key findings
Ghalib M <i>et al.</i> (2008) [51]	N=68 Prospective study Location: Kingdom of Saudi Arabia	Participants that underwent kidney transplants were prospectively followed for three consecutive Ramadans The study sample were split into two groups – 35 fasting and 33 non-fasting 28% of the sample had diabetes The eGFR and other clinical and biochemical measures were compared between the groups across all time periods The measurements were also compared within the same group from baseline	It was found that the eGFR in the fasting group did not differ from baseline even after adjusting for age and diabetes status There were no statistically significant differences observed between groups for eGFR, mean arterial pressure or in urinary protein excretion No rejection episodes were seen Conclusions based on those with <150 µmol/L creatinine
Abdulla AH <i>et al.</i> (1998) [56]	N=23 Prospective study Location: Kingdom of Saudi Arabia	All participants had undergone kidney transplant – 17 with normal renal function and 6 with impaired but stable renal function All participants had undergone their transplant at least 1 year before entering the study Biochemical measurements were taken before, during and after Ramadan	There were no statistically significant differences in all measurements at any time point
Einollahi <i>et al.</i> (2005) [57]	N=39 Prospective study Location: Iran	All participants had undergone kidney transplants and the groups were split into fasting (19) and non-fasting (20) All fasting individuals had consecutively fasted for three years Biochemical measurements were taken before, during and after Ramadan	There were no significant differences in the changes to serum creatinine levels across the time periods between fasting and non-fasting groups All fasting participants had stable renal function and safely practiced fasting during Ramadan

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TABLE 6: STUDIES ASSESSING THE SAFETY OF FASTING DURING RAMADAN IN INDIVIDUALS WITH KIDNEY TRANSPLANTS

Author(s) (Date)	Sample size and study details	Population	Key findings
Einollahi et al. (2009) [53]	N=82 Prospective study Location: Iran	All participants had undergone a kidney transplant There were two groups of people fasting (41) and non-fasting (41) 11% of participants had diabetes Clinical and biochemical measurements were taken before, during and after Ramadan	There were no acute complications, acute rejections or differences in serum creatinine and eGFR levels between both groups across all time periods
Ibrahim et al. (2003) [52]	N=565 Retrospective study Location: Kingdom of Saudi Arabia	All participants had undergone a kidney transplant at least one year before fasting outcomes were measured and presented for follow up at a renal transplant clinic Participants were split into two groups – 280 who fasted and 285 that did not fast eGFR and other biochemical measurements were taken from baseline and during and after Ramadan	There were no statistically significant differences found between the fasting and non-fasting groups for eGFR, urinary protein levels or in mean arterial pressure after adjusting for age and diabetes There were no acute rejection episodes reported in either group
Said et al. (2003) [55]	N=145 Prospective study Location: Kuwait	All participants had undergone a kidney transplant and had at least 6 months of stable function The sample was split by those that fasted (71) and those that did not fast (74) 10% of participants had T1DM and 16% had T2DM Biochemical measurements were taken before during and after Ramadan and then for a period after the study for follow up	There were no differences in the change in serum creatinine between both groups across all time periods Blood pressure remained the same and was similar in both groups There was a tendency for higher blood glucose in those with T1DM There few two cases of acute rejection and three cases of chronic graft dysfunction

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TABLE 6: STUDIES ASSESSING THE SAFETY OF FASTING DURING RAMADAN IN INDIVIDUALS WITH KIDNEY TRANSPLANTS

Author(s) (Date)	Sample size and study details	Population	Key findings
Qurashi T et al. (2012) [54]	N=80 Prospective study Location: Kingdom of Saudi Arabia	All participants had undergone kidney transplants 43 fasted during Ramadan and 47 did not fast The eGFR and other biochemical was calculated before during and after Ramadan (1 month and 6 months after Ramadan) and compared between and within groups	Fasting did not adversely affect renal function Serum creatinine were similar when compared to baseline within groups This was also the case for eGFR; after subgrouping participants by levels of eGFR (low, moderate, high) no differences were found in eGFR All measurements of kidney function were also similar between groups Those that had fasted did have longer post-transplant times compared with non-fasters (p=0.0001)
Salem et al. (2010) [58]	N=25 Prospective study Location: Libya	All participants were stable and had undergone kidney transplants, all had normal graft function prior to the study All had a transplant prior to entering the study for at least 1 year (1.5-26 years) Clinical and biochemical measurements were taken before, during and after Ramadan	All participants completed the month of fasting, non-experienced abnormal symptoms Body weight, blood pressure and cyclosporine levels were stable during Ramadan Creatinine and urea levels remained similar through all periods
Boobes et al. (2009) [59]	N=22 Prospective study Location: United Arab Emirates	All participants had undergone a kidney transplant and had a post-transplant period for at least one year prior to entering the study 73% had a baseline eGFR of >50 mL/min/1.73m ² Clinical and biochemical measurements were taken before, during and after Ramadan	All participants managed to fast during the whole month of Ramadan Fasting was not associated with any adverse events No statistically significant changes were found across the time periods in weight, blood pressure or in measures of creatinine, urea and electrolytes

6. CONSIDERATIONS AND RECOMMENDATIONS (CKD, Dialysis and Kidney Transplants)

Many of the studies conducted in the area of CKD including individuals with a previous diagnosis of CKD, on dialysis and having undergone a kidney transplant were conducted in populations which included people without pre-existing diabetes. This is an important consideration and further research is needed specifically into individuals that have pre-existing diabetes, both T1DM and T2DM.

The general consensus among the studies was that individuals with stable renal function could safely fast with, at most, transient changes occurring during Ramadan that do not last after Ramadan. It remains to be seen whether these results are applicable to people with type 1 or type 2 diabetes and the risk for fasting remains high. Alongside poorly controlled diabetes fasting could be unsafe. It is, therefore, paramount the following recommendations are **considered**:

- All individuals with diabetes (both T1DM and T2DM) and CKD should discuss their intentions to fast during Ramadan with diabetes and renal specialists at least three months prior to Ramadan and attend Ramadan focused education (see **chapter 7: Pre-Ramadan Assessment and Education**). As a pre-requisite, the recommendations for the practice of safe fasting discussed in these guidelines must also be met where applicable.
- Individuals with stable renal transplants and diabetes (both T1DM and T2DM) may be able to fast safely providing they are monitored carefully by their transplant team before, during, and after Ramadan, and given careful advice on how to take immunosuppressive and anti-diabetes medication.
- Individuals with diabetes (both T1DM and T2DM) and CKD of stages 3-5, or on dialysis should be considered high-risk, and fasting should be discouraged.
- Those that are considered high risk and still choose to fast must:
 - be carefully monitored and have weekly reviews during Ramadan
 - make a concerted effort to stay hydrated outside of fasting periods
 - monitor electrolyte and creatinine levels at various points during Ramadan to ensure safe fasting is being conducted and whether it should continue
 - avoid foods with high potassium or phosphorous content.



SUMMARY

- Fasting during Ramadan with stable CVD does not increase hospitalisations or worsening of the underlying heart condition. However further research is needed into individuals with diabetes and pre-existing CVD to carry any specific recommendations to individuals with diabetes and CVD.
- Studies investigating the risks of fasting on stroke are conflicting and greater research is needed in individuals with diabetes with pre-existing stroke.
- Fasting during Ramadan with stable CKD or having undergone a kidney transplant does not increase eGFR and any biochemical changes are transient. This may also apply to individuals with diabetes, but further research is needed into individuals with pre-existing diabetes and CKD.
- Individuals that have undergone a kidney transplant or have stage 3-5 CKD are at high-very high risk of fasting during Ramadan. These will require careful monitoring and specialised tailored advice before fasting during Ramadan. The conditions required to safely fast in other chapters of these guidelines must be met as a pre-requisite.
- Larger prospective studies are needed; these include randomised trials and studies assessing the effect of fasting in individuals with diabetes and its complications on microvascular and macrovascular complications.

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