

Review Article**Fasting with diabetes during Ramadan: An updated review**

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ABSTRACT

Introduction: In reality, many Muslims have an intense spiritual urge to participate in fasting, even those who could get an exemption. There are many cultural variations in the Muslim population in different parts of the world, even in the same country with different social and family backgrounds. Thus, persons with diabetes should seek medical advice before planning to fast or proceed to fast during *Ramadan*.

Materials: This was a narrative, non-systematic review of the international literature from the major medical online database (PubMed and Google Scholar) in 2023. The term “*Ramadan* fasting” and “Diabetes” was used to search, and the relevant literature was captured and narrated in a concise thematic account.

Results: Practically, there are certain risks associated with fasting for patients with diabetes, which might exacerbate their existing illnesses. Along with the globally increasing prevalence of diabetes, there is an increased number of the population who intend to or fast. The article captured a wide array of topics related to *Ramadan* fasting by patients with diabetes, including its epidemiology, risk stratification, lifestyle modification, assessment of safety and efficacy profiles of pharmacotherapies, hypo or hyperglycemia, and the impact of diabetes education.

Conclusion: Fasting with diabetes poses a range of risks and thus pre-*Ramadan* risk stratification is essential. Particular attention should focus on the patient’s current risk factors, complications, comorbidities, and the roles of newer antihyperglycemic medicines and advanced technology for safer fasting practices to mitigate the risks of hypoglycemia and or hyperglycemic crises.

Keywords: diabetes, *Ramadan* fasting, hypoglycemia, Muslims, risks of fasting

INTRODUCTION

Ramadan fasting is obligatory for every physically and mentally healthy Muslim adults. This month, Muslims refrain from eating, drinking, and conjugal relations between dawn and sunset.¹ Most of the Muslim population intends to fast, even those exempted from fasting, such as the elderly, children, the infirm, and pregnant women.² Muslims think fasting may provide some health benefits, including an opportunity for a better lifestyle, facilitating weight loss and smoking cessation, and some favorable effects on the lipid

profile.^{3,4} Possible health hazards of fasting include hypoglycemia, hyperglycemia, dehydration, and acute metabolic complications such as diabetic ketoacidosis (DKA).² Hence, keen interest exists to look for an update on the trends epidemiology of *Ramadan* fasting, its consequences, and evidence of management.

Thus, this article aims to review and update the existing knowledge of *Ramadan* fasting. This is based on recent studies and evidence gathered in the past. We also make some recommendations on the management of diabetes patients during the month of *Ramadan*.

HIGHLIGHTS

1. Diabetes patient management, education, and risk assessment should be first priority of diabetic patients during *Ramadan*.
2. In light of this, individual diabetes care programs tailored to *Ramadan* should be provided to various risk categories.
3. All physicians and general practitioners should be aware that fasting during *Ramadan* can significantly modify the levels of several hormones, which may have an unfavourable (or favourable) impact on the health of patients with diabetes. On the other hand, fasting during *Ramadan* has several advantages for the physical and spiritual well-being of diabetes patients.

METHODS

This non-systematic narrative review article searched articles over 2023 by using the search term 'diabetes and *Ramadan*' in PubMed and Google Scholar with the aim to provide a reasonably updated evidence based approach to fasting with diabetes. One author prepared the initial draft, and others contributed intellectually to make it a final one after several modifications. No statistical analysis was conducted on the data included in the original articles, and detailed numerical presentations were avoided. All types of articles were included. Before submission, the draft was thoroughly discussed by the final round of corrections.

EPIDEMIOLOGY

Gradually the number of Muslims who fast during *Ramadan* is increasing, and currently, about 24% of the world's population is fasting for 29-30 days consecutively. Studies found that about 79% of Muslims with type 2 diabetes (T2DM) and about 43% of them with type 1 diabetes (T1DM) fast during *Ramadan*.⁵ Of those who fast during *Ramadan*, 64% fasted daily, and 94.2% fasted for at least 15 days.⁶ The medication timings of these individuals with diabetes must be adjusted to pre-dawn and post-sunset timings.⁷⁻⁹ The duration of abstinence from foods and drinks ranges from 12-20 hours a day (from dawn to dusk), depending upon the country's geographical area.

PATHOPHYSIOLOGY

There is a significant lifestyle changes during *Ramadan* fasting among people with T2DM (more than 95%),¹⁰ including changes in meal patterns (food intake) and sleeping patterns (duration and quality), impacting the circadian rhythm and physical activity.^{11,12} All these changes are likely to impair the glycemic control of patients with diabetes.

One of the studies evaluating the pathophysiological changes occurring during *Ramadan* described the immediate effect of fasting on biometric and biochemical parameters in persons with diabetes before and after the fasting month. The differences between T2DM and T1DM and their treatment modalities are significant in those who fasted and those who did not fast during *Ramadan*.¹³ All the participating (349) patients with diabetes had a mild and moderate risk for fasting. Metabolic risks were higher between pre-, during, and post-*Ramadan* periods. The modest reduction in weight in a few during *Ramadan* was regained soon after *Ramadan*, even exceeding it. In most patients with diabetes, fasting is associated with poorer glycemic control, body weight management, and blood pressure control. Second, the researchers assessed the impact of *Ramadan* fasting on glycemic control and fetuin-A. This glycoprotein affects insulin resistance (IR) among patients with T2DM among 37 patients in a prospective study.¹⁴ Anthropometric data and HbA1c, fasting blood glucose (FBG), and fetuin-A levels were measured at three-time points: before, during, and after *Ramadan* fasting. *Ramadan* fasting reduced fetuin-A

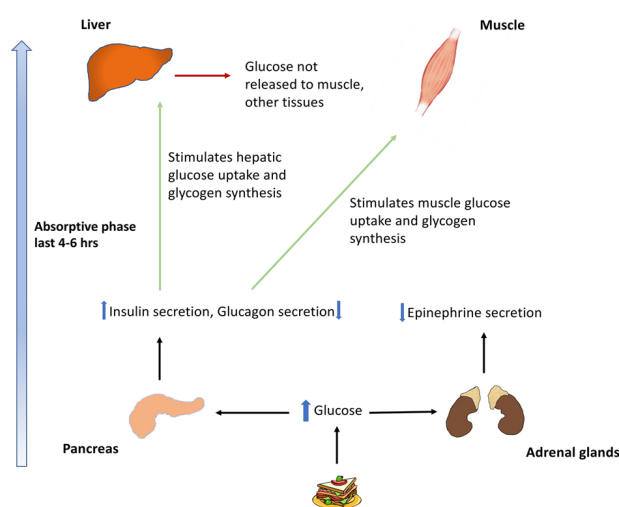


FIGURE 1 Pathophysiology of fasting with diabetes

TABLE 1 Risk stratification score card

Risk element	Risk score	Risk element	Risk score
1. Duration of diabetes (Years)		7. CAD complications/comorbidities	
A Duration of >10	2	Unstable CAD/HF	6
A Duration of < 10	1	Stable CAD	3
2. Presence of hypoglycemia		No CAD	0
Hypoglycemia unawareness	6	8. CVD/stroke	
Recent severe hypoglycemia	6	Unstable and mentally not oriented	6
Multiple monthly hypoglycemia	3	Stable and mentally oriented (can take food by mouth)	3
No hypoglycemia	0	No CVD	0
3. Level of glycemic control		9. Renal complication/comorbidities	
HbA1c levels > 10%	3	eGFR <30 mL/min	6
HbA1c levels 8-10%	2	eGFR 30-45 mL/min	4
HbA1c levels < 8%	1	eGFR 45-60 mL/min	2
4. Type of treatment		eGFR >60 mL/min	0
Premixed insulin	3	10. Frailty and cognitive function	
Basal bolus/split mixed	2	Impaired cognitive function or frail	6
Basal insulin/ insulin pump	1.5	>70 years old with no home support	3
Gliclazide//MR or glimepiride or repaglinide	1	No frailty or loss in cognitive function	0
Other therapy not including SU or insulin	0.5	11. Previous <i>Ramadan</i> experience	
5. Self-monitoring of blood glucose (SMBG)		Good experience	0
Indicated but not conducted or conducted sub-optimally	2	Bad experience	1
Conducted as indicated	1		
6. Acute complications			
DKA/HHS in the last three months	5		
No DKA/HONC	0		

DKA - diabetic ketoacidosis; HHS - hyperosmolar hyperglycemic State; eGFR- estimated glomerular filtration rate; CAD- coronary artery disease; CVD- cerebrovascular disease

Score <4	Low risk or less	Able to fast
Score 4-7	High risk	Fasting with supervision
Score >7	Very high risk	Must not fast

NB: This scoring was proposed by BES (not yet validated)

levels four weeks after the end of *Ramadan* compared with pre-*Ramadan*. Two weeks following *Ramadan* fasting, the authors found a mild reduction in body weight, BMI, FBG, and HbA1c levels which rebounded to baseline levels after *Ramadan* and even exceeded those. Fasting during *Ramadan* was associated with a significant decrease in fetuin-A level post-*Ramadan*.¹⁴

Management of diabetes during 'Ramadan'

Pre-Ramadan assessment & risk stratification

Changes in lifestyle and circadian rhythm, shifting in fluid and energy balance, and alteration in the timing of antidiabetic medications during *Ramadan* fasting result in metabolic disturbances. Fasting is associated with

increased glycemic variability and therefore increased risk of hypoglycemia, severe hyperglycemia (with or without diabetic ketoacidosis), dehydration, and thrombosis in diabetic patients.^{15, 16} Patients with diabetes and pre-existing CVD or stroke are at greater risk of complications when fasting. Unstable CVD or stroke patients are also at very high risk from fasting. Individuals with diabetes and CKD stage 3 are at high-risk of fasting while those with stage 4-5 are at very high risk from fasting during *Ramadan*. Patients on dialysis or those with a kidney transplant are also considered high risk from fasting.¹⁷ Therefore, every person with diabetes should be assessed individually before *Ramadan* using standardized risk stratification tools.

A pre-*Ramadan* individualized assessment should be performed by healthcare professionals 1-3 months (ideally 6-8 weeks) before the start of fasting to reduce these risks.^{18,19} To stratify risk and develop an individualized management plan, needs assessment of

detailed medical history, aspects of diabetes and ability to self-manage, presence of co-morbidities, individual's prior experience in managing diabetes during *Ramadan* fasting, individual's ability to self-manage diabetes, and other factors increasing the risk of fasting.

The risk stratification is based on several factors: type and duration of DM, risk or occurrence of hypoglycemia, level of glycemic control, self-monitoring of blood glucose (SMBG), acute metabolic complications, chronic microvascular/macrovascular complications/co-morbidities, pregnancy, frailty/mental stability, level of physical labor, previous *Ramadan* experiences and support, duration of fasting hours, climate, diabetes treatment regimens and polypharmacy with multiple glucose-lowering drugs, etc.^{20, 8}

BES recommends the IDF and DaR 2021 guideline risk calculation score and stratifies individuals into three risk categories, low, moderate, and high, with some modifications (TABLE 1).²¹ Considering risk scores and risk categories, BES recommends similar to IDF-DaR 2021 guideline recommendations.²²

T1DM and hyperglycemia DM are very high risk for Ramada Fasting

Pre-Ramadan Education and Monitoring

Pre-Ramadan education should include information on risk stratification, diet and exercise, drug adjustment, blood glucose monitoring, recognition of hypoglycemia, and other complications and situations when to break the fast.

Ramadan-focused education is needed to make people aware of the risks associated with diabetes and fasting and to teach them the strategies to minimize the risks.²² Education should be delivered in a culturally sensitive manner by trained healthcare professionals.^{17, 18, 24, 25} Persons with diabetes who have received structured *Ramadan*-focused education are more compliant with *Ramadan* diabetes management recommendations.²³ Educational programs are effective in maintaining and improving glycemic control during *Ramadan*.^{25, 25, 8, 26} and decreasing hypoglycemia episodes.²⁷ A combination of structured education and frequent blood glucose monitoring is essential for safe fasting during *Ramadan*.^{24, 28}

Pre-Ramadan education should target people with diabetes and healthcare professionals (HCPs). Educational campaigns should also target the general population.²⁹ Pre-Ramadan assessment and education should ideally be started 12 weeks before *Ramadan*.³⁰

Components of a *Ramadan*-focused education program are pre-Ramadan planning, risk stratification, medical nutrition therapy, fluid and electrolytes, exercise, drug adjustment, blood glucose monitoring, and breaking the fast.³¹

Monitoring blood glucose during Ramadan

Self-monitoring of blood glucose (SMBG) is essential for every diabetic patient who chooses to fast, and it should be emphasized that testing does not invalidate the religious fast. Monitoring depends on treatment regimens and patients' risk profiles. SMBG should be performed multiple times during the day and, most importantly, whenever symptoms of hypoglycemia or acute illness occur.³²

High-risk patients should perform SMBG multiple times a day. The regularity of the blood glucose checking depends on the frequency of insulin treatment and/or the risk of hypo or hyperglycemia. Low-risk patients and patients on metformin, DPP4 inhibitor, GLP1 analog monotherapy, or a combination of these drugs should also monitor their blood sugar. To get a true understanding of how blood glucose changes while fasting, patients should be encouraged to keep a *Ramadan* logbook detailing the measurement.¹

Time of SMBG: Good to do³³

- Pre-Suhoor - before taking meal (for adjustment of OAD, premixed insulin)
- Early morning - two hours after Suhoor (patients are in bolus, split, premixed regimen, OAD)
- Around 10 am - patients are in a split regimen, premixed insulin, OAD
- Mid-day- 11 am to 2 pm (premixed insulin, intermediate-acting insulin, OAD, basal insulin)
- Pre-Iftar meal - for every patient and dose adjustment for long-acting insulin analog, long-acting OAD
- Two hours after Iftar -bolus insulin, OAD
- At any time when there are symptoms of hypoglycemia/hyperglycemia or feeling unwell

Time of SMBG: Must to do³³

- Before *Iftar*
- Two hours after *Iftar*
- Mid-day

The frequency of SMBG should be daily for the first three days, every third day from next week onwards, and every alternate day in the last week.

Modification of diet and physical activity**Aims of MNT³⁴**

- Consume the same number of calories, with balanced proportions of macronutrients, during the non-fasting period (i.e., sunset to dawn).
- Distribute the carbohydrate intake equally among meals to minimize postprandial hyperglycemia and also hypoglycemia during the fasting period.
- Consider co-morbidities such as hypertension and dyslipidemia, and obesity.
- Avoid weight gain during *Ramadan*. Patients with T2DM who are overweight or obese may find that *Ramadan* provides a good opportunity to lose weight. Weight loss may result in a significant improvement in glycemic control and may reduce cardiovascular risk.

Dietary advice for patients with diabetes during Ramadan^{34, 35}

Large carbohydrate meals, and sugary drinks are to be avoided. Meal plan and dietary frequency should be followed as a healthy balanced diet accounting height, weight, and occupation as done during the pre-*Ramadan* period. Well-balanced meals should be ensured with 50%-60% carbohydrate, 20-30% protein, <20% fat (preferably mono-and polyunsaturated), low glycemic index, complex starchy carb, and high fiber foods. Proteins like egg, fish, meat, milk, and yogurt must be included, and carbohydrates like bread, beans, rice, plenty of vegetables, and salads can be added. A moderate number of fresh fruits is permitted. Foods high in saturated fats should be discouraged, like *ghee*, butter, *samosas*, *pakorras*, *puri*, *paratha*, or heavy fried meat. Sugary desserts like *jilapi*, *laddoo*, *barfi*, and other sweets must be avoided. Sweetened drinks are advised to avoid. Allowed number of fresh fruits can be taken as juice without added sugar. Small amounts of oil, especially vegetable oil (corn/soybean/olive oil),

should be encouraged while cooking.

Hydration and electrolytes balance can be maintained by drinking more or other non-sweetened beverages like coconut water, lemon water, etc. Small and six-times healthy balanced diet of pre-*Ramadan* should be accommodated in two to three times of meal frequency between *Iftar*, dinner, and *Suhoor*. The diet should be planned to keep the equal calorie and quality and consider the patient's condition, choices, desires, and customs according to pre-*Ramadan* eating patterns. *Suhoor* is advised to take close to *Fajar* prayer, and it will be the main meal the equivalent of lunch of the pre-*Ramadan* period. A meal plan for different caloric targets (1200, 1400, 1600, 1800, and 2000 kcal/day) may benefit.

Unhealthy nutrition habits (should be avoided)^{8, 36}

- Taking large meals at *Iftar* and desserts loaded with sugar after *Iftar* may result in severe postprandial hyperglycemia and weight gain.
- Taking significant amounts of highly processed carbohydrates at or between *Iftar* and *Suhoor* may also cause severe hyperglycemia.
- Having large and frequent snacks between the two main meals can contribute to longer periods of hyperglycemia.
- The temptation to take *Suhoor* early or avoid *Suhoor* meal or less amount of meal may result in hypoglycemia before *Iftar*, especially when fasting hours are longer than usual.
- Consumption of large portions of high glycemic index and high glycemic load carbohydrates at *Suhoor* can lead to post-prandial hyperglycemia.

Exercise recommendations during Ramadan fasting⁸

- Fasting people are advised to avoid exercise during fasting time.
- Rigorous exercise is not recommended due to the increased risk of hypoglycemia and dehydration.
- Physical exertion in *Tarawih* prayer can be considered a daily exercise activity.
- The rest of the exercise can be done before or after the *Tarawih* prayer on the house premises.

Modification of oral antidiabetic drugs (OADs)

The individualized management plan and therapeutic modification are the cornerstones of *Ramadan* fasting management.^{8, 36, 37} The type of medication the patient takes for diabetes management influences the potential risks.³⁷⁻⁴⁰ Adjustments of oral antidiabetic drugs in

patients with T2DM who are fasting during *Ramadan* can be made in the following ways.⁸

Modification of injectable medications

Management of patients with T2DM

Current recommendations aim at intensive glycemic management in patients with diabetes T1DM, which requires multiple daily insulin injections (three or more) or continuous subcutaneous insulin infusion through pump therapy.⁴¹⁻⁴² A few patients with T1DM insist on fasting during *Ramadan*, and most of them change their insulin regimens immediately before, during, and a few days after this month. Basal-bolus regimen is the preferred management protocol as it is considered safer, with fewer episodes of hyper- and hypoglycemia. As an alternative once- or twice-daily injections of intermediate insulin along with pre-meal rapid-acting insulin is the management of choice. It is unlikely that other regimens, including one or two intermediate-, long-acting, or premixed insulin injections, would provide adequate insulin therapy.⁴²⁻⁴⁴

Management of patients with T2DM

Necessary levels of basal insulin are required to prevent fasting hyperglycemia. One injection of a long-acting (or intermediate-acting) insulin can be useful in some patients as long as the dosage is appropriately individualized; however, most patients will require rapid- or short-acting insulin along with the basal insulin at meals, usually the evening meal typically comprises a larger caloric load.⁴⁵

Using a rapid-acting insulin analog instead of regular human insulin before meals in patients with T2DM who fast during *Ramadan* is associated with less hypoglycemia and smaller postprandial glucose excursions. Given their safety and tolerability, it is recommended that insulin analogs, both basal & bolus analogs, should be used during *Ramadan*.

Hypoglycemia, though less frequent, is still a risk, especially in elderly patients or who have required insulin therapy for a long duration. This can be reduced by using basal insulin analogs such as insulin detemir or glargine, degludec along, and rapid-acting insulin analogs such as aspart, lispro, or glulisine as a basal-bolus regimen.

TABLE 2 Modification of OADs during *Ramadan*¹¹

Name/category of drug	
Metformin	Daily total dose remains unchanged. Once daily dose should be taken at <i>Iftar</i> . For twice daily dose, should be taken at <i>Iftar</i> and <i>Suhoor</i> . For thrice daily dose, morning dose should be taken at <i>Suhoor</i> and combined lunch and evening dose at <i>Iftar</i> . Prolonged release preparation should be taken at <i>Iftar</i> .
Sulfonylurea	Switch to newer Sulfonylurea (Gliclazide, Gliclazide MR, Glimepiride) where possible. Glibenclamide should be avoided. For once daily dose, the total dose should be taken at <i>Iftar</i> . Dose may be reduced in patients with good glycemic control. For twice daily dose, full pre- <i>Ramadan</i> breakfast dose should be taken at <i>Iftar</i> and 50% of the dinner dose should be taken in <i>Suhoor</i> .
Meglitinides	Thrice daily dosing may be reduced/redistributed to two doses taken with <i>Iftar</i> and <i>Suhoor</i> according to meal sizes.
Acarbose	No dose modification. Pre- <i>Ramadan</i> morning dose is given at <i>Iftar</i> , lunch dose at dinner (if taken) and evening dose at <i>Suhoor</i> .
Thiazolidinediones	No dose modification but should be taken with <i>Iftar</i> .
DPP-4 inhibitors	No dose modification during <i>Ramadan</i> .
SGLT2inhibitors	SGLT2 inhibitors should be initiated at least one month prior to <i>Ramadan</i> for better tolerance. No dose modification. Dose should be taken with <i>Iftar</i> . Extra water should be ingested during non-fasting periods.

Note:

- At the start of *Ramadan*, up to dinner, OAD should be taken as per the pre-*Ramadan* schedule.
- At *Suhoor* of the first *Ramadan*, OAD should be omitted. The *Ramadan* schedule should be followed at the end of *Ramadan*, up to *Iftar*.
- On the Eid day breakfast, the pre-*Ramadan* schedule should be started.

TABLE 3 Insulin regimens and adjustments during Ramadan fasting

A) Basal insulin [Glargine (U 100 or U 300), Detemir, Degludec, NPH]	
Glargine, Detemir, Degludec; Usually at bedtime and single dose	The same dose and time as pre-Ramadan if blood sugar (in SMBG) is high; May be reduced if fasting blood sugar is within target
NPH (single or twice daily) (not preferred)	If single-same dose of dinner at <i>Iftar</i> if BG is high; Reduce by 15-30% if BG is within target. For twice daily- same dose of breakfast to be taken at <i>Iftar</i> (30-minute prior); reduce 15-30% if BG within target; Reduce dinner dose 15-30% at <i>Suhoor</i>
B) Rapid/short acting insulin: Bolus [(analogue-Aspart, Lispro, Glulisine)/ regular]	
Once, twice or thrice daily	The same pre-Ramadan breakfast dose should be taken at <i>Iftar</i> ; Reduce pre-Ramadan dinner dose by 20-50% for <i>Suhoor</i> in Ramadan; The lunch dose will be shifted to dinner if full dinner is taken (usually reduced)
C) Premix (analogue-30/70, 50/50; conventional 30/70, 50/50, 25/75): May be used once daily or twice in Ramadan with caution.	
Single dose	Once daily dose- same dose at <i>Iftar</i>
Twice daily (breakfast & dinner)	Twice daily doses-The pre-Ramadan breakfast dose will be same for <i>Iftar</i> , Pre-Ramadan dinner dose may be reduced by 20-50% for <i>Suhoor</i> (depending on prolong fasting, carb content)
D) Switching can be done from low premix (25/75 or 30/70) to high premix (50/50 at <i>Iftar</i> if carbohydrate is more during the <i>iftar</i> meal.	

Recommended changes to insulin regimen in patients with T2DM who fast during 'Ramadan'

Change of insulin regimen should be customized and individualized according to food habit and composition, especially during fasting.

Insulin dose titration algorithm during fasting

- IDF recommends a normal dose before the evening meal, omitting the lunchtime dose and reducing the morning dose by 25-50%.
- If fasting/ pre-meal blood glucose is < 3.9 mmol/L (70mg/dL) and is 3.9-5.0 mmol/L (70-90 mg/dL) morning/evening dose before the meal is to be reduced by 4U and 2U, respectively.
- Further, the guidelines recommend no dose change if fasting/pre-meal blood glucose is 90-130 mg/dL (5.0-7.2 mmol/L).
- However, if fasting/ pre-meal blood glucose is 7.2-11.1 mmol/L (130-200mg/dL) or >11.1 mmol/L (200mg/dL), increase the dose by 2U and 4U, respectively.⁵

TABLE 4 Insulin dose adjustment according to SMBG

Fasting/before breaking fast	Insulin units
<3.9 mmol/L (70 mg/dL) or symptoms of hypoglycemia	Break the fast and down-titrate
< 5.0 mmol/L (90 mg/dL)	-2 IU
5.0-7.0 mmol/L (90-126 mg/dL)	No change
> 7.0 mmol/L (126 mg/dL)	+2 IU

ADA recommends the administration of short or rapid-acting insulin in combination with basal insulin at meals, particularly at the evening meal, as an effective

strategy under fasting conditions. Rapid-acting insulin analog are associated with less hypoglycemia and smaller postprandial glucose excursions compared to regular human insulin before meals in patients with T2DM who fast during Ramadan.⁴⁶

These newer insulins have made possible the near-physiological replacement of prandial and basal insulin with many conveniences and have provided physicians with the appropriate tools to overcome the obstacles to improve metabolic control during fasting without increasing the risk for hypoglycemia and also improve diabetes outcomes.⁴⁷⁻⁵⁰

GLP-1 analog: (Liraglutide-0.6/1.2/1.8mg; Dulaglutide - 0.75/1.5 mg, Semaglutide-0.25/ 0.5/ 1mg; Lixisenatide- 10/20µgm; Exenatide-5/10µgm).⁵¹⁻⁵²

Combination of different antidiabetic agents

Combination of oral (OAD) and insulin

Only doses of insulin and oral secretagogues (SU and non-SU) need to be adjusted. Other oral agents need not require adjustment. A combination of insulin glargine and glimepiride may be used during Ramadan in patients with T2DM who wish to fast, provided glimepiride is given at the time of breaking the fast and insulin glargine titrated to provide FBG >6.7 mmol/L.⁶⁰

Combination GLP1 analog with OAD or insulin

Keep the dose of GLP1 analog liraglutide/ exenatide/ lixisenatide or weekly dulaglutide/ semaglutide will remain the same as the pre-Ramadan dose even used

with insulin. But insulin doses need to be adjusted accordingly. Similarly, SU needs to be changed; other OADs do not require adjustment.⁴³

Special Population

Fasting with hyperglycemia in pregnancy

Different studies have published contradictory conclusions on a healthy pregnancy and *Ramadan* fasting. While some studies have concluded that healthy non-diabetic pregnant women may fast without any threat to either the mother or the fetus,^{44,45} some authors have reported it decreased placental weight in pregnant women who fast as a potential threat (although without affecting the birth weight).⁴⁶ Regardless of such controversies in healthy pregnant women, the current consensus for fasting women with pre-existing T1DM or T2DM is that they are categorized as the high-risk fasting group and should not be allowed to fast during *Ramadan*.⁵⁰

TABLE 5 GLP 1 RA analog adjustment during *Ramadan*

Situation in pre- <i>Ramadan</i>	Action during <i>Ramadan</i>
Exenatide single dose before breakfast	Same dose before <i>Iftar</i>
Exenatide twice daily	Same as pre- <i>Ramadan</i> before <i>Iftar</i> /or <i>Suhoor</i>
Liraglutide	Same dose before <i>Iftar</i>
Dulaglutide/ semaglutide weekly	Same dose as before pre- <i>Ramadan</i> weekly

Management of diabetes among the older adults when fasting during Ramadan

- Previously, older adults with diabetes have been placed in the higher risk categories for fasting during *Ramadan* based on their age alone. Many older adults have enjoyed fasting during *Ramadan* for many years and should be allowed to continue if their health is stable.⁴⁴
- Age alone is often a risk factor for fasting during *Ramadan*.
- In older adults with diabetes, particular consideration needs to be given to any accompanying comorbidities.
- Many elderly individuals will still fast during *Ramadan*, and guidance is needed to help these individuals fast safely.
- The prevalence of fasting in elderly individuals is lower than in younger individuals.
- Comorbidities such as impaired renal functions, cardiovascular disease (CVD), dementia, frailty,

and a risk of falls need to be considered alongside age in risk stratification.

- The risk of diabetes-related complications is higher in elderly populations.
- Modifications to medications are essential for older adults wishing to fast.

The risk stratification of older adults with diabetes should not be based on age alone but on their health status and social circumstances.⁵¹

Future research on *Ramadan* fasting needs to include more elderly individuals with diabetes to make specific recommendations.

Complications of diabetes in the elderly

It is important to recognize that age in and of itself is not a good reason to categorize individuals as at high risk for fasting during *Ramadan*. Still, rather it is the associated implications of old age that need consideration. Indeed, more senior people who manage to fast can be more motivated than their younger counterparts - the DAR Global Survey found that 69% of those aged ≥ 65 years fasted for 30 days compared to 60% of those < 65 years.⁵²

However, people in the elderly age can often have other comorbidities alongside diabetes. Indeed, people with diabetes have a heightened risk of complications such as diabetic kidney disease, cardiovascular disease (CVD), and retinopathy.⁵³ Certainly, old age can be a risk factor for conditions such as dementia or recurrent falls, hip fractures, amputation, and visual impairment. In a study of elderly participants with diabetes and an added risk of CVD during *Ramadan*, it was found that there was an increased risk of impaired renal function.^{6, 50} Fasting during *Ramadan* also affected postural balance and attention in the elderly and may increase the risk of falls or fall-related injuries. Volume depletion is also an important issue, especially among those over 75. This increase in the risk of complications occurring in older adults with diabetes can directly impact the number of days fasted during *Ramadan*.⁴⁵

In elderly individuals with such comorbidities, there will inevitably be changes to their physical activity patterns, ability to self-manage blood glucose (SMBG), ability to take medications, feeding patterns, and general independence and family support. Therefore, pre-*Ramadan* education to elderly individuals with diabetes and their surrounding support network needs

to be clear and individualized covering all circumstances to prevent any unexpected outcomes from arising during the *Ramadan* fast.

Hyperglycemia

Hyperglycemia was defined as blood glucose levels > 16.6 mmol/L, 300 mg/dL). The DAR 2020 Global Survey also showed that hyperglycemia remains a large issue among older people.⁵² It was reported that there was a significantly higher proportion of elderly individuals with T2DM reporting hyperglycemia during *Ramadan* 2020, with 19.3% among those aged ≥ 65 compared to 15.6% among those aged < 60, $P=0.006$. Among all, the mean number of days with hyperglycemia was 8.1, similar in both age groups.⁵³

Management of elderly individuals with diabetes who fast during 'Ramadan'

People in older age groups fast during *Ramadan* for many reasons, and their wishes to do so must be respected. As mentioned, many elderly individuals that fast do so with a heightened risk of complications. These must be considered and taken into account when any individual's guidance or advice is offered.

Elderly individuals that do seek to fast during *Ramadan* must be given greater support than their younger counterparts. This can be through friends, relatives, or caregivers, but elderly individuals who plan to fast must have these support networks in place before conducting the fast. The heightened risk of complications arising during the *Ramadan* fast and the increased likelihood that individuals have accompanying comorbidities require extra care.

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.^{54, 55} In addition, people with diabetes also have a heightened risk of stroke.⁵⁶ 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 impact the risk of CVD or stroke in people with diabetes.^{57, 58}

On the other hand, when fasting is conducted safely, these risks could be mitigated. It has been

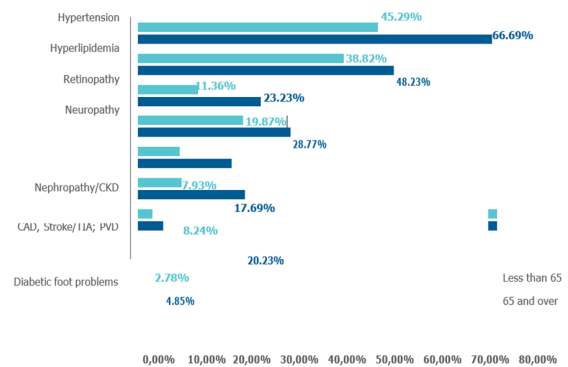


FIGURE 2 Reported complications among individuals with T2DM aged ≥ 65 and < 65; data adapted from the DAR 2020 Global survey⁵²

demonstrated that proper glycemetic control can reduce the number of cardiovascular events.⁵⁵ Likewise, fasting has also been shown to significantly increase levels of nitric oxide (NO) and decrease markers of oxidative stress,^{59, 60} with a variable effect on lipoprotein levels, high sensitivity C-Reactive protein (hs-CRP) levels, and blood pressure.⁵⁸ The last two decades have seen an increase in 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.

Fasting during 'Ramadan' and acute coronary syndrome (ACS)

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). Evidence suggests no clear association between fasting during *Ramadan* and increased acute cardiac events.^{61, 62} 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*.⁶³

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* compared to times outside of *Ramadan*.⁶² Likewise, Burazeri et al. found protective associations between a composite measure of religiosity and ACS in a cross-sectional study.⁵⁵

Fasting during 'Ramadan' and cardiac arrhythmias

Few studies have assessed the impact of fasting during *Ramadan* on cardiac arrhythmia, and further research is needed. A retrospective review looking into patients that were hospitalized with atrial fibrillation found no significant differences in the periods of admission when comparing times before, during, and after *Ramadan*. Al Suwaidi et al. found no additional cardiac arrhythmia episodes in patients with hypoglycemia that utilized continuous glucose monitoring (CGM) during *Ramadan*.⁶⁴

Fasting during 'Ramadan' and stroke

To date, the impact of *Ramadan* on the risk of stroke is controversial. Thus, good quality research is needed in randomized 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 with individuals that have pre-existing stroke and diabetes and assess whether these patients can safely fast during *Ramadan*.

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).⁶⁵ CKD can be categorized into different stages reflecting the severity of the disease; this classification has been described elsewhere.⁶⁶ 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 with stage 4 or 5 were classified as very high risk.^{67, 60}

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. 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*. They showed that the increase in urinary NAG levels was associated with blood glucose levels, highlighting the importance of

glycemic control among those with diabetes.⁶⁸ 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/1.73m².⁶⁹ Bakhit et al. also showed that the higher the stage of CKD, the worse the renal outcomes during *Ramadan*.³³ Importantly, others also noted that CKD could lead to an increased risk of CVD in individuals that fast during *Ramadan*.³² 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.^{70, 71} Kara et al. also showed similar outcomes in a comparative study of people who fast compared to those that did not.⁶⁹

Fasting during 'Ramadan' in individuals on dialysis

There have been several studies conducted on individuals that have undergone dialysis, and many have found that fasting can be safely conducted during *Ramadan* without any added complications. Several studies have also taken into account the effect of diabetes. These studies have been summarized below. Al-Wakeel et al. showed, in a study of 31 participants on peritoneal dialysis, that fasting was not associated with mortality or morbidity.³³ A study of 40 participants on hemodialysis who fast on non-dialysis days found that fasting did not affect weight gain, blood pressure, or electrolytes.³² Likewise, another study on participants that underwent hemodialysis and fast during *Ramadan* showed that there was no excess mortality or morbidity as a result of fasting.⁷¹ A large prospective, multicenter, comparative study of individuals on hemodialysis 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*.⁷²

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. 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.⁷³ These results were similar to that found by Ibrahim et al. who conducted a retrospective study in the Kingdom of Saudi Arabia.⁷⁴ A prospective study in Iran found that fasting was not associated with acute rejections of transplants or other complications.⁷⁵

Emergencies related to diabetes during 'Ramadan'

Hypoglycemia

Among diabetic people who fast during *Ramadan*, the rate of hypoglycemia is found to be 1.6 times higher compared with non-fasting periods.⁷⁶ The Epidemiology of Diabetes and *Ramadan* (EPIDIAR) study⁷ showed that fasting during *Ramadan* increased the risk of severe hypoglycemia (defined as hospitalization due to hypoglycemia), some 4.7-fold in patients with T1DM (from 3 to 14 events/100 people/month) and 7.5-fold in patients with T2DM (from 0.4 to 3 events/100 people/month). Inappropriate adjustment of medication and lifestyle is the main contributor to the development of hypoglycemia. Excessive physical activity may lead to a higher risk of hypoglycemia.⁷¹ If hypoglycemia develops, the patient should break the fast immediately and treatment should be started as per standard protocol to alleviate blood glucose level. Cause of hypoglycemia should be addressed (inadequate meal consumption at night or *Suhoor*, excess physical activity, renal or hepatic impairment, anti-diabetic drug/ dose adjustment) to prevent further development of hypoglycemia.

Hyperglycemia

The extensive EPIDIAR study showed a 5-fold increase in the incidence of severe hyperglycemia (requiring hospitalization) during *Ramadan* in patients with T2DM (from 1 to 5 events/100 people/month) and an approximately 3-fold increase in the incidence of severe hyperglycemia with or without ketoacidosis in patients with T1DM (from 5 to 17 events/100 people/month).⁷¹ Hyperglycemia may result from an inappropriate reduction of the dosage of medications in fear of hypoglycemia. An increase in food and/ or sugar intake also significantly increases rates of severe

hyperglycemia. During hyperglycemia, the patient should discontinue fasting until blood glucose level comes within safe range. Appropriate drug and dose adjustment should be done.⁶⁷

Diabetic ketoacidosis (DKA)

The risk of DKA is higher during *Ramadan* as fasting will result in hypoinsulinemia, hyperglucagonemia, ketone body formation and eventually development of DKA.⁷ Inappropriate reduction of insulin dose is often a major contributing factor.⁷ Patients who have moderate to severe hyperglycemia (average blood glucose 8.3 to 16.7 mmol/L) before fast, renal insufficiency, advanced micro-/macrovascular complications and other comorbid conditions are at increased risk to develop DKA or HHS. DKA and HHS are medical emergencies and should be treated as per standard protocol.⁶⁷

Dehydration and thrombosis

Dehydration (and thrombosis) often may develop due to limitation of fluid intake during the fast, hot and humid climates, hard physical labor, hyperglycemia and hypercoagulable state due to an increase in clotting factors and impaired fibrinolysis.⁷⁰ If dehydration develops, fasting should be discontinued. Adequate hydration should be maintained. During the correction of dehydration and also during the non-fasting period, the consumption of excessive caffeinated drinks should be avoided.

General prevention measures to avoid acute complications

The key components needed to be addressed to minimize acute complications related to diabetes during *Ramadan* fasting are risk assessment, providing structured *Ramadan*-focused education to people with diabetes, frequent blood glucose monitoring, appropriate and individualized advice on nutrition and exercise, appropriate drug and dose modification, and addressing comorbidities and personal circumstances.^{70, 71, 77}

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. Individuals with stable renal transplants and diabetes (both T1DM and T2DM)

maybe 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

Risk assessment

Those patients with diabetes with very high risk and high risk should be recommended not to fast. Emphasis should be given to frequent capillary blood glucose monitoring.⁷¹

'Ramadan'-focused diabetes education

Patients should be empowered with *Ramadan* focus structured education with the knowledge of recognizing symptoms of hypoglycemia, hyperglycemia, and other acute complications three months (at least one month) before the beginning of *Ramadan*.⁷¹

Self-monitoring of blood glucose (SMBG)

The patients should do frequent SMBGs in the first few days of fasting to become aware of their glycemic profile with changed meal intake and altered dosage of medications. Thereafter frequency of testing can be reduced.⁷⁰ SMBG should be done before *Suhoor*, 2 to 4 hours after *Suhoor*, between 11 am to 2 pm, before *Iftar*, and 2 hours after *Iftar*. SMBG Self-monitoring of blood glucose (SMBG) does not invalidate religious fasting. Low-risk patients should also perform SMBG during pre-*Suhoor*, midday, pre-*Iftar*, and whenever symptoms of hypoglycemia or acute illness occur.⁷⁶ High-risk persons should monitor SMBG more frequently during

fasting, with special attention during noon, afternoon, and before *Iftar* times.

Diet plan

Dietary recommendations should be individualized and tailored to the patient's lifestyle requirements, age, comorbidities, and other medical needs. Adherence to a diabetic diet is vital during *Ramadan* to avoid hypoglycemia, hyperglycemia, and dehydration. Excessively eating when the fast is broken and inappropriate dose modifications of medicines should be avoided. *Suhoor* meals should be taken as late as possible.⁷¹

Maintaining hydration

Hydration should be maintained between meals by drinking water and non-sweetened beverages.⁷⁶ *Iftar* should begin with water and 1-2 dates to raise blood glucose.⁷⁷ The dosage of antihypertensive medications should be adjusted to prevent hypotension.⁷⁶

Exercise

Excessive physical activity should be avoided, particularly a few hours before *Iftar*. *Tarawabi* prayer should be considered a part of physical activity.⁷¹

Drug and dose modification

Second generation Sulfonylurea (Gliclazide, Gliclazide MR, Glimepiride) is preferred due to the low risk of hypoglycemia compared to the first-generation, while the dose and timing of OAD should also be changed during *Ramadan*. With SGLT 2 inhibitors, extra water should be ingested during non-fasting periods to prevent dehydration. It should not be used in elderly patients with eGFR <20 ml/min/1.73 m² in conditions that may lead to hypotension. Analog insulins are preferred over conventional insulins due to the lower risk of hypoglycemia. The Analog basal-bolus regimen is the safest regimen to be used during *Ramadan* fasting.⁷⁷

Post- 'Ramadan' follow-up

At the end of *Ramadan*, up to the last *Iftar*, the *Ramadan* schedule of anti-diabetic medication and meal patterns should be followed. The pre-*Ramadan* medication and meal pattern schedule should be followed from *Eid* day. *Eid-ul-Fitr*, a festival day, marks the end of *Ramadan*, and patients with diabetes should be made aware of the

risks of dietary overindulgence during this time. A post-Ramadan follow-up meeting with a physician is advisable, ideally within 1-2 weeks after *Eid-ul-Fitr*, to assess how the patient handled the fasting, the level of glycemic control, the incidence of hypoglycemia, hyperglycemia, or any acute complication like DKA, HHS that would help the physician to make a patient-specific *Ramadan* plan for the next year.⁷⁷

The physician should assess the patient's body weight and BMI, check the SMBG records during *Ramadan* and days after the *Eid-ul-Fitr*, and measure HbA1c, serum creatinine, and lipid profile. Post-Ramadan follow-up should include necessary changes to the patient's medication regimen, meal planning, and physical activity plan. It should be stressed to the patient that a safe fast one year does not automatically make them low-risk for the next year due to the progressive nature of the disease.⁷⁷

To summarize, management of patients with diabetes in *Ramadan*, education and risk assessment should be given priority over any clinical decision-making or intervention. Accordingly, different risk groups should receive their personal *Ramadan*-specific diabetes management plans. It should be taken into consideration by all clinicians and general practitioners that *Ramadan* fasting can make great alternations to the levels of different hormones, and this may adversely (or favorably) affect the health of patients living with diabetes. On the other hand, there are several physical and spiritual health benefits to patients with diabetes which are conferred through *Ramadan* fasting. Therefore, it is imperative that people with diabetes consult with their clinicians prior to the commencement of *Ramadan* fasting on an annual basis.

Conclusion

This is an updated review article processed by searching recently published articles including all types of studies. However, this has the inherent limitations of a non-systematic review. It includes the results from all types of studies.

Fasting with diabetes during *Ramadan* draws the attention of endocrinologists/diabetologists, other concerned physicians, and relevant healthcare professionals. Despite cultural and geographical differences in fasting patterns, the overarching desire

for all patients and the physicians looking after them is safety, especially in avoiding hypoglycemia, dehydration, and other complications. In the management of diabetes during *Ramadan*, pre-Ramadan education should be emphasized first. All patients should be categorized according to standard risk stratification scales and treated accordingly. It should be taken into consideration by all clinicians and general practitioners that *Ramadan* fasting can make great alternations to the levels of different hormones, and this may adversely (or favorably) affect the health of patients living with diabetes.

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The authors have no conflict of interest to declare.

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