

# Diabetes and Ramadan: Update New Guidelines

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## ABSTRACT

Fasting Ramadan exposes the diabetic patient to major metabolic complications: severe hypoglycemia, hyperglycemia, ketoacidosis and thromboembolic complications. A good assessment of the patient's risk level, individualized therapeutic education, regular self-monitoring and therapeutic adjustment make fasting possible and completely safe. Several recommendations and expert consensus have established proposals for optimizing the management of diabetes during Ramadan. We report recent, practical and simple recommendations from the International Diabetes Federation and the International Diabetes and Ramadan Alliance (IDF-DAR), to assist health professionals in the management of fasting diabetics regardless of their risk level. **Key words:** Diabetes, Ramadan, fasting, hypoglycemia, recommendations, self-monitoring of blood glucose.

## 1. INTRODUCTION

In 2019, the number of Muslims in the world has been estimated to be 1.9 billion, or about 24.7% of the world's population, of which more than 148 Million are diabetics [1]. Ramadan is a holy month that carries significant spiritual and socio-psychological weight, a source of piety and mental wellbeing for Muslims [2]. However, fasting exposes diabetics to various severe metabolic complications such as hypoglycemia, ketoacidosis, dehydration and thromboembolic complications [3-4].

The Epidemiology of Diabetes and Ramadan (EPIDIAR) study in 2001 showed that more than 40% of type 1 diabetics and nearly 80% of type 2 diabetics fasted for at least 15 days during Ramadan [5]. The CREED study in 2010 confirmed these numbers, reporting that 94% of T2DM patients fasted for at least 15 days and 64% fasted every day during Ramadan, the same study showed that in Algeria, 83.5% of diabetics fasted every day [6]. More recently the DAR-MENA (Diabetes and Ramadan-Middle East and North Africa) study completed by the DAR Global survey (2020) revealed that 86% of type 2 diabetics fasted for at least 15 days [7-8]. It is often difficult to convince even high-risk diabetics not to fast despite the exemption recommended in our religion (Sura El Bakarah, Verses 183-185) [9]. Recent recommendations and expert consensus have provided practical suggestions that make fasting during the month of Ramadan safe [10].

## 2. PHYSIOLOGY OF FASTING DURING RAMADAN

Ramadan leads to a major change in eating patterns, mealtimes, fluid intake, it also disrupts sleep and hormonal circadian rhythms [11].

**2.1. In healthy individuals:** The increase in glucose levels after a meal will stimulate insulin secretion, which triggers the storage of glucose as glycogen in the liver and muscles. During fasting, circulating glucose levels decrease and insulin secretion tends to decrease [12]. At the same time the secretion of glucagon and catecholamine increases, which stimulates glycogen utilization, and at the same time gluconeogenesis is increased [3]. If fasting is prolonged for several hours, glycogen reserves drop, and the low circulating insulin level allows the release of free fatty acids from the adipocytes. The oxidation of free fatty acids generates ketones that serve as energy sources for skeletal and cardiac muscle, liver, kidney and adipose tissue, thus saving glucose for continued use by the brain and erythrocytes [4].

**2.2 In non-diabetic subjects:** This process is regulated by a balance of insulin and counter-regulatory hormones that allow blood glucose levels to be maintained at physiological levels.

**2.3 In diabetic patients:** In type 1 diabetes, the response to hypoglycemia may be impaired by decreased adrenergic and glucagon secretion due to autonomic neuropathy, long-standing disease and recurrence of previous hypoglycemia [4-13]. In patients with severe insulin deficiency, prolonged fasting without insulin supply causes excessive glycogen utilization and increased gluconeogenesis and ketogenesis, leading to hyperglycemia and ketoacidosis.

Type 2 diabetics may have similar disturbances in response to prolonged fasting. The severity of the disturbances will depend on the degree of insulin resistance or insulin deficiency. Consequently the risks faced by diabetic patients during Ramadan are: hypoglycemia, hyperglycemia, ketoacidosis, dehydration and thrombosis [4-5-6].

## 2.4. Risks associated with fasting:

**2.4.1. Hypoglycemia:** The EPIDIAR study showed that fasting during Ramadan increases the risk of severe hypoglycemia by 4.7-fold in type 1, and 7.5-fold in type 2 [4-5]. Ahmedani et al. reported symptomatic hypoglycemia in 35.3% of T1DM and 23.2% of T2DM [13]. Factors favoring hypoglycemia are the number of hours of fasting, forgetting the meal before dawn (Suhoor) and the lack of adaptation of medications, exposing to an increased risk of hypoglycemia such as insulin and hypoglycemic sulfonamides [14].

**2.4.2. Hyperglycemia:** The incidence of severe hyperglycemia requiring hospitalization is five times higher in type 2 diabetics and three times higher in type 1 diabetics. Hyperglycemia is due to excessive reduction of hypoglycemic medicines to avoid hypoglycemia. Overconsumption of food and sweets increases the risk of hyperglycemia [5].

**2.4.3. Ketoacidosis:** The risk of ketoacidosis in type 1 diabetics fasting during Ramadan may be increased by reduced insulin doses due to reduced food intake, acute illness or undercurrent infection [15]. A recent prospective observational study conducted in several countries reported a higher proportion of ketoacidosis during the month of Ramadan compared to the previous month. The following month, the proportion of admissions for ketoacidosis was higher than the monthly average. The most common cause was poor adherence to treatment [16].

**2.4.4. Dehydration and thrombosis:** Dehydration is precipitated by lack of fluid intake during long hours of fasting and can become severe by excessive sweating in hot, humid climates or during strenuous physical activity. Osmotic diuresis favored by hyperglycemia leads to volume depletion.

The contraction of the intravascular space may contribute to a state of hypercoagulability due to an increase in coagulation factors, a decrease in endogenous anticoagulants and an alteration of fibrinolysis. Increased blood viscosity, caused by dehydration, combined with the procoagulant state of diabetes, may increase the risk of thrombosis, stroke and retinal vein occlusion [17-18-19].

## 3. INDIVIDUAL RISK STRATIFICATION IN DIABETES

Risk stratification must be individualized and take into account several elements updated by the authors (IDF-DAR): type of diabetes, patient treatment, individual risk of hypoglycemia, complications and comorbidities, socio-economic and working conditions and previous fasting experience (Table 1) [10-20].

**3.1 Modalities of risk stratification:** The scoring system was designed taking into account the various factors (Table 2) [10-20]. For a given individual, each risk element should be assessed and the score added up. The score obtained will determine the overall risk level for a person with diabetes who seeks to fast during Ramadan (Fig1) [10-20].

**3.2. Scores, risk level and corresponding recommendations:** The risk score plays a major role in the recommended fasting decision for each patient. (Fig1)

- Patients who are in the high-risk category with a score > 6 should not fast, as they are at very high risk of complications in fasting.

- Patients in the moderate risk category with a score between 3.5 and 6 should not fast, but the majority insists on fasting, education and therapeutic adjustment is required.

- Those at low risk with a score of <3 should be allowed to fast, as they are at less risk of complications from fasting during Ramadan.

However, circumstances may change, resulting in a change in risk, so risk stratification should be performed annually to assess the level of risk before Ramadan.

## 4. MEDICAL-RELIGIOUS PERSPECTIVE

Gaborit et al. reported in a study that diabetic patients often prefer to discuss Ramadan fasting with their IMAM than with their doctor++ +25%. Collaboration between health care providers and the IMAM is necessary to ensure the safety

of diabetics who want to fast [21]. In order to harmonize medical and religious advice, the FDI-DAR experts have developed new practical recommendations on diabetic fasting that have been approved by the regulatory religious authorities. The religious opinion on fasting for the three risk categories is described in (Table 3) [10].

## 5. ASSESSMENT AND THERAPEUTIC EDUCATION OF THE DIABETIC PATIENT BEFORE RAMADAN

All diabetic patients who wish to fast during Ramadan should receive specific education and medical assessment beforehand to avoid complications. This education should also include patients who do not wish to fast because they are at risk of hypoglycemia and hyperglycemia during Ramadan.

### 5.1. Pre-Ramadan consultation and individualized medical assessment:

The Pre-Ramadan consultation should be done 6-8 weeks before Ramadan in order to determine the patient's risk level and to adapt the treatment if necessary. It allows the metabolic balance of the patient to be assessed by measuring glycosylated hemoglobin and lipid profile. This assessment takes into account: the detailed history of diabetes, co-morbidities that may be aggravated by fasting, the experience of the previous Ramadan and the ability to self-manage the diabetes. The patient's risk category and the complications faced by fasting should be explained and specific medical advice given [22].

**5.2 Structured therapeutic education:** Bravis et al confirmed the benefits of pre-Ramadan education of the diabetic patient who planned to fast through the READ (Ramadan Education and Awareness in Diabetes) education program, diabetics who participated in this program showed a significant reduction in weight, less hypoglycemic events and stable HbA1c levels compared to those who did not participate in this program [23]. It involves both the diabetic and his or her family and should address: risk quantification, regular blood glucose monitoring, exercise, nutrition, dose adjustment, when to break the fast and recognizing symptoms of hypoglycemia or hyperglycemia. [24].

**5.3. Reinforce self-monitoring of blood glucose:** Self-monitoring of blood glucose (SMBG) should be performed several times a day and especially when symptoms of hypoglycemia or acute illness occur (Fig.2) [25-26]. Low-risk patients should perform SMBG at the following times: pre-SUHOOR, midday, pre-IFTAR and when symptoms of hypoglycemia or acute illness occur. Patients should be reassured that blood glucose testing does not invalidate religious fasting.

**5.4. Nutrition:** About 50% of fasting patients do not change their lifestyle (diet, physical activity) or their medication [5]. Diabetic patients should maintain a healthy and balanced diet during Ramadan, in order to maintain optimal glycaemic control and a constant weight even after Ramadan. Excessive intakes of high carbohydrate and high fat foods, especially during IFTAR, should be avoided. Slowly absorbed carbohydrates should be recommended during SUHOOR and high GI carbohydrates during IFTAR. It is recommended to increase fluid intake and avoid sugary drinks between IFTAR and IMSAK. The SUHOOR meal should be taken as late as possible, close to IMSAK - the start of the usual fasting.

A Ramadan Nutrition Plan (RNP) has been developed to enable caregivers to provide structured and appropriate medical nutrition therapy (MNT) to diabetic patients who fast during Ramadan. The MNT is an online application accessible to health professionals and even diabetics, offering examples of menus from different regions and nutritional advice adapted to the patients' profile [26-27].

**5.5. Physical activity:** Regular and adapted activity should be recommended during this month, avoiding intense exercise if there is a risk of hypoglycemia a few hours before breaking the fast [28]. Offer physical activity two hours after IFTAR. Prolonged prayers after the break of the fast "Tarawih" are part of the daily physical activity. [29].

**5.6. Breaking the fast:** The diabetic patient should break the fast immediately in case of:

- Hypoglycemia: blood glucose below 0.6 g/l,
- Hyperglycemia: blood glucose level above 3.0 g/l,
- If the blood glucose is below 0.7 g/l at the beginning of the fast with the use of medication with hypoglycemic risk (insulin, sulphonylureas or meglitinides) during the morning meal [4].

Breaking the fast if there are signs of hypoglycemia or an acute complication (dehydration; ketoacidosis...). Patients should avoid fasting if they have any other intercurrent medical condition. It is essential that diabetic patients and their families receive adequate and appropriate training in self-care, the warning signs of hyperglycemia and hypoglycemia (sweating, tremors, palpitations, pallor, faintness, dizziness, anxiety, visual disturbances, behavioral abnormalities, confusion, difficulty speaking, irritability), and the emergency

management of these serious complications [30].

## 6. THERAPEUTIC

The main concerns in the use of any antidiabetic treatment are glycaemic control and the risk of hypoglycemia.

**6.1. Metformin:** The risk of severe hypoglycemia in patients on Metformin is low. No dose modification is necessary. If taking Metformin once: take at the time of Iftar, if taking twice a day: take at the time of Iftar and at the time of SUHOOR. If taken three times a day, the morning dose should be taken before SUHOOR and the afternoon dose should be added to the dose taken at SUHOOR. If extended-release Metformin to be taken at time of Iftar. [4-31]

**6.2. Acarbose:** Although there are no randomized studies of Acarbose in people with diabetes fasting during Ramadan, no dose modification is necessary as the risk of hypoglycemia is low [10-31].

**6.3. Thiazolidinediones:** Pioglitazone: Due to the low risk of hypoglycemia with Pioglitazone. No dose modification is required during Ramadan. It potentiates the hypoglycemic effect of sulphonamides and insulin [32].

**6.4. Glinides:** Repaglinide is effective on postprandial glycaemia. Their short duration of action and low risk of hypoglycemia make their use during the fast interesting. The usual daily dose is 3 doses during meals, which can be reduced or redistributed to two doses during Ramadan depending on the importance of the meals [33].

**6.5. Hypoglycemic sulphonamides:** The risk of hypoglycemia with sulphonamides is higher than with other OADs. The risk varies from a medication to another, depending on the mechanism and duration of action. New generation sulphonamides (glimipiride, gliclazide,) have been shown to have a lower risk of hypoglycemia than first generation sulphonamides (Glibenclamide). [10] during the fast, sulphonamides require individualized adaptation by modifying the dose and the time of taking and respecting the hygienic-dietary rules. Prefer the latest generation sulphonamides. [10].

- 1 dose: take at the time of IFTAR, dose can be reduced in patients with good glycaemic control.

- 2 doses: take the same dose at IFTAR and half the dose at SUHOOR. [10].

### 6.6. New therapeutic classes

**6.6.1 Dipeptidyl peptidase-4 (DPP-4) inhibitors or gliptins:** DPP-4 inhibitors, or gliptins, have a lower hypoglycemic risk and improve glycaemic control compared to sulphonamides. They do not require treatment modification during Ramadan [34-35].

GLP1 receptor agonists (incretinomimetics) are effective in reducing weight, HbA1c levels during Ramadan and significantly less hypoglycemia. As long as liraglutide, exenatide, lixsenatide, have been appropriately dosed and titrated prior to Ramadan (at least 2-4 weeks), no further treatment modification is necessary. [10-36].

**6.6.2. Sodium-glucose co-transporter 2 inhibitors (SGLT2):** This class of therapy provides effective improvement in glycaemic control, weight loss and a low risk of hypoglycemia for type 2 diabetics during Ramadan but increases the risk of dehydration, hypotension, ketoacidosis and urinary tract infections. They should be avoided in cases of impaired renal function, They should be avoided in patients with impaired renal function, in the elderly or in patients taking diuretics. ISGLT2 should be initiated at least 2 weeks to one month before Ramadan. ISGLT2 should be administered at the time of Iftar and increased fluid intake should be provided outside of the fasting periods. They have a low risk of hypoglycemia and no dose adjustment is required during Ramadan [37-38].

**6.7. Type 2 diabetics on multiple therapies:** The risk of hypoglycemia in subjects on multiple antidiabetic agents is determined by many factors: medication, duration of diabetes, renal function, pre-Ramadan glycaemic control, presence of co-morbidities, etc. Adjustment of antidiabetic doses should be individualized and based on ongoing glycaemic control [39].

**6.8. Insulin therapy** Slow-acting and rapid-acting analogues compared to human insulin are recommended during fasting as analogues limit the risk of hypoglycemia and post prandial hyperglycemia. Opt for a long-acting basal scheme that is prandial with a short-acting before (IFTAR and SUHOOR) [40-41]. The premix insulin scheme is not recommended as it is a rigid diet: post prandial hyperglycemia and late hypoglycemia after SUHOOR. [41-42].

### Insulin adjustments proposed during fasting [10]

- Single daily basal injection regimen:

- PH/Detemir/Glargine100/Glargine300/ Degludec, the dose should be reduced by 15-30% and taken at IFTAR.

- Two-day basal injection regimen: NPH/Detemir/Glargine100, take usual dose at Iftar, reduce evening dose by 50% and take at SUHOOR.
- Rapid-acting insulin regimen: maintain usual dose at Iftar, remove midday dose, reduce SUHOOR dose by 25-50%.
- Premix insulin regimen: 1 injection/day: normal dose at IFTAR, 2 injections/day: normal dose at IFTAR, reduce SUHOOR dose by 25-50% Three injections/day: remove midday dose and adjust doses at IFTAR and SUHOOR [10].

Monitoring blood glucose levels several times a day is necessary.

## 7. POPULATIONS AT RISK

**7.1. Type 1 diabetes:** T1DM can be allowed to fast with a well-structured pre-Ramadan education program, the risks of fasting can be reduced [10]. These patients should have pre-Ramadan education, close medical supervision and more frequent blood glucose monitoring (intensified SMBG), especially in the late afternoon or in response to any symptoms or clinical events. The use of the new continuous interstitial glucose monitoring devices is particularly indicated in this case. [4-43-44]. The new second generation long-acting insulin analogues (glargine U-300 and degludec) are preferred as they have been shown to provide better safety and glycaemic control in fasting [45]. Patients on insulin pumps would have better safety and improved HbA1c during the fasting period. The basal rate during the day can be reduced and the preprandial bolus at the end of the fast can be increased, supplemental insulin injections according to the SMBG are allowed during the fasting period [46].

**7.2. Pregnancy and fasting during Ramadan:** Fasting during pregnancy appears to cause a high risk of morbidity and mortality for the fetus and its mother [47]. ASG and intensive insulin therapy are often required, making fasting very difficult. A pre-Ramadan medical assessment is necessary for any pregnant woman who insists on fasting. Their management should be done in high-risk, multidisciplinary pregnancy clinics, based on appropriate diet and intensive insulin therapy, with strict blood glucose monitoring and adjustments of insulin doses that should necessarily be more frequent [40]. The diabetic pregnant woman should break the youngster in case of malaise, blood glucose < 0.70 g/l or a decrease in fetal movements. [48-49-10].

**7.3. Covid19-Diabetes and fasting:** The COVID-19 epidemic represents an additional concern for people with diabetes who wish to fast. The presence of T2DM and hypertension are among the most important risk factors for the severity of SARS-CoV-2 infection (50-51). Therefore, diabetics planning to fast require careful assessment of their risk of fasting. Strict control of blood glucose is imperative, reinforced by clear and firm advice to stop fasting immediately if the patient develops symptoms of COVID-19, the importance of hydration, regular capillary blood glucose monitoring, plasma ketone monitoring, as there is evidence that ketosis and ketoacidosis are more common in people with diabetes and COVID-19, and consultation with the treating physician [52].

There is some evidence to suggest that people with strong religious faith may have better blood glucose control [53], in which case people with diabetes who fast may gain some protection against complications of COVID-19 infection.

During Ramadan, the Covid-19 vaccine is permitted under Sharia law and does not invalidate fasting [54].

## 8. POST-RAMADAN CONSULTATION

A post-Ramadan consultation is recommended to re-evaluate treatment regimens, assess the impact of youth on the patient's metabolic profile and discuss the experiences of youth during Ramadan [40].

## CONCLUSION

Diabetes and Ramadan is an important area of scientific research, many questions on the subject remain to be clarified, requiring randomized and multicenter clinical trials, particularly, the impact of therapeutic education and new therapeutic classes on the incidence of complications of fasting on diabetics. Taking into account the epidemic situation of COVID-19, the use of teleconsultation is a considerable contribution to the management of these patients.

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