Chapter 4.
Risk Stratification of Individuals with Diabetes before Ramadan

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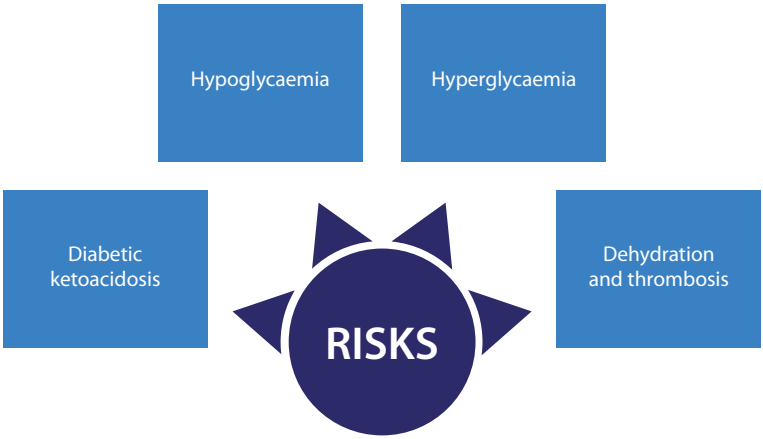
4.1 Risks associated with fasting in people with diabetes

During Ramadan, the normal diet changes considerably and physical activity levels fall during the daytime compared with other times of the year. These changes can result in metabolic disturbances and also lead to alterations in the timing and doses of diabetes medication. Ramadan lasts for 29–30 days, and over the next few years will fall during the summer months in a majority of countries. As discussed in Chapter 3, Muslims with diabetes who choose to fast face a number of challenges. Key risks associated with fasting are shown in ***Figure 1*** [1]. Summer fasting periods last up to 20 hours per day and are often undertaken in hot and humid conditions which can exacerbate the risks. Dehydration, in particular, is a serious risk associated with fasting [2].

Figure 1. Key risks associated with fasting for patients with diabetes [1]



The major risks, hypoglycaemia and hyperglycaemia, are the same challenges that people with diabetes face on a daily basis; however, studies have shown that fasting may increase the occurrence of these events. In the EPIDIAR study (see Chapter 2 for details), higher rates of severe hypoglycaemia were recorded in people with type 1 or type 2 diabetes mellitus (T1DM/T2DM) during Ramadan compared with before Ramadan (4.7-fold or 7.5-fold increases, respectively) (***Figure 2***) [3]. A study in Pakistan, carried out by Ahmedani et al, found that of the 388 patients with diabetes who chose to fast, symptomatic hypoglycaemia was reported by 35.3% and 23.2% of patients with T1DM and T2DM, respectively [4]. Lower figures were observed in the CREED study, where only 8.8% of patients with T2DM reported a hypoglycaemic event; a majority of these episodes, however, required further assistance or breaking of the fast [5].

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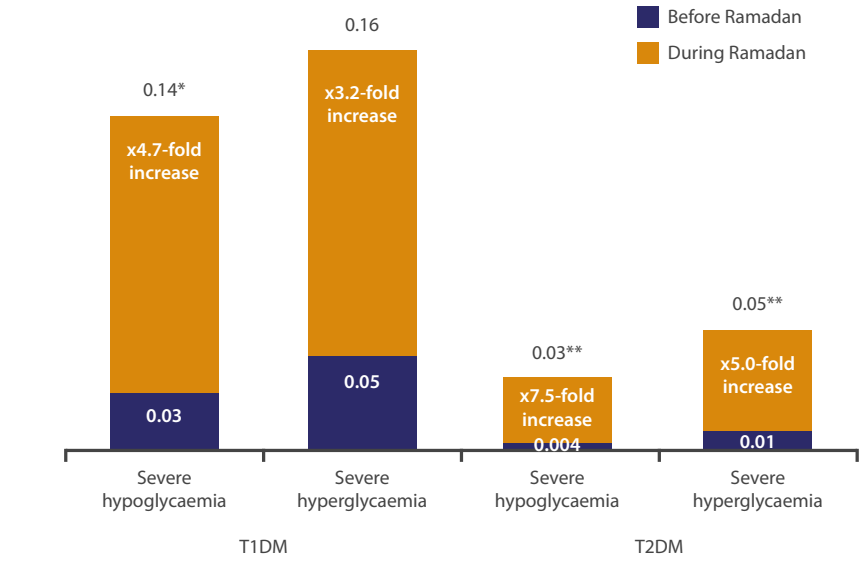
Figure 2. EPIDIAR study: mean numbers of severe glycaemic events/month during Ramadan compared with before Ramadan [3]



*p<0.05; **p<0.0001
T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus

Higher hyperglycaemia rates have also been reported during Ramadan. Among patients with T2DM in the EPIDIAR study, rates increased 5.0-fold for hyperglycaemia with or without diabetic ketoacidosis (DKA) [3]. In the Ahmedani study, symptomatic hyperglycaemia was observed in 33.3% and 15.4% of patients with T1DM and T2DM, respectively [4]. In another study, performed in the United Arab Emirates, the rate and duration of hospital admission for DKA during Ramadan and the following month (Shawal) were compared. Although there were no significant differences in DKA rates between Ramadan and Shawal, the observed incidence for the two months was higher than the average monthly rate. The mean length of hospitalisation was significantly longer for patients admitted during Ramadan than for those admitted during Shawal [6]. Most of the patients admitted (75%) had not received any guidance on diabetes management during Ramadan.

Type of anti-diabetic medication can influence hypoglycaemic risk during fasting (see Chapter 8 for details and recommendations). In addition, meals eaten during

Ramadan are often large and contain fried and sugary food which can have an impact on blood glucose control [2]. Fluctuations in blood glucose levels, particularly postprandial hyperglycaemia, have been linked with oxidative stress and platelet activation as well as the development of cardiovascular disease in people with diabetes [7-9].

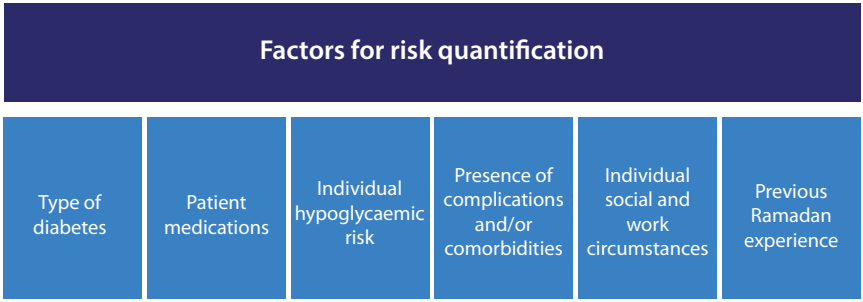
Healthcare professionals must be conscious of the risks associated with fasting and should quantify and stratify the risks for every patient individually in order to provide the best possible care

Taking all these risks into account it is easy to see why religious regulations, as well as medical recommendations, allow exemption from fasting for some people with diabetes [1, 10, 11]. However, for many such individuals, fasting is a deeply spiritual experience and they will insist on taking part, perhaps unaware of the risks they are taking. Healthcare professionals (HCPs) caring for these patients must be conscious of the potential dangers and should quantify and stratify the risks for every patient individually in order to provide the best possible care.

4.2 Risk quantification

As noted in Chapter 2, it has been estimated that more than 100 million people with diabetes fast during Ramadan [5] and this number will continue to grow. The latest predictions from the International Diabetes Federation (IDF) suggest that in the Middle East and North Africa region alone, the number of people with diabetes will more than double from 35.4 million to 72.1 million over the next 25 years, with a similar rise expected in Africa and South-East Asia [12]. However, it should be noted that a majority of the Muslim diabetes population are able to fast, as shown by the CREED study where 63.6% were able to complete the full month of Ramadan fasting [5]. Safety of fasting is paramount and various elements should be considered when quantifying the risk for such patients (***Figure 3***).

Figure 3. Factors for risk quantification [2]



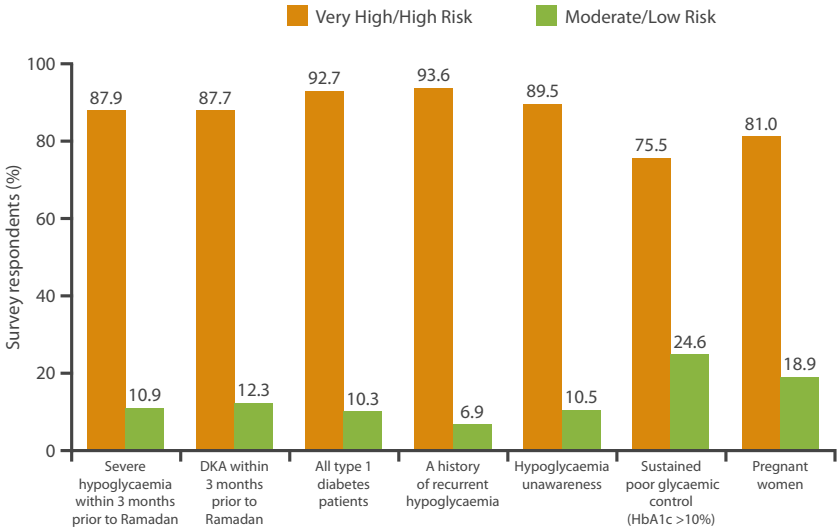
This assessment exercise must be carried out on an individual basis for each patient looking to fast during Ramadan, and the care given must be personalised according to the patient's specific circumstances.

4.3 Risk stratification

The 2005 American Diabetes Association (ADA) recommendations for management of diabetes during Ramadan and its 2010 update categorised people with diabetes into four risk groups – very high risk, high risk, moderate risk and low risk [1, 10]. These risk categories have been endorsed by the Islamic Organization for Medical Sciences and the International Islamic Fiqh Academy, who published a decree accepting and approving the ADA's risk categories and outlined recommendations for who should not fast based on the probability of harm [11].

In the CREED study, 62.6% of physicians referred to guidelines for the management of fasting. Of these, 39.0% reported using the ADA 2005 recommendations and 41.2% consulted the 2010 guidelines [5]. A recent study involving nearly 200 physicians mainly from the Middle East and North Africa revealed that the vast majority stratified patients in accordance with the categories defined in the ADA 2005 and 2010 recommendations. These findings suggest that these recommendations are in line with real-world practice (***Figure 4***) [13].

Figure 4. Survey showing risk classification of clinical conditions by physicians [13]

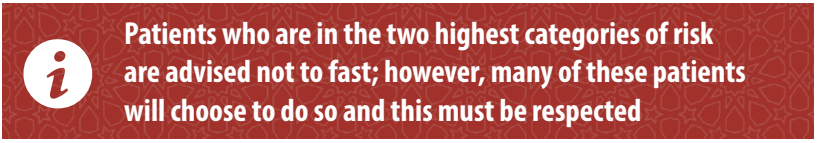


DKA, diabetic ketoacidosis; HbA1c, glycated haemoglobin

Surprisingly, the numbers of days fasted by the highest and the lowest risk group only varied by 3 days, indicating that either these risk categories are not efficiently applied by HCPs or that people with diabetes are ignoring these medical recommendations despite the fact that they are recognised by religious leaders [5]. Hence, there is a clear need to reconsider the various risk categories and to provide a level of flexibility that would help the individual with diabetes and their HCPs to make a decision regarding fasting during Ramadan.

Table 1 summarises the new risk categorisations defined by the IDF and Diabetes and Ramadan International Alliance (IDF-DAR). Patients should not fast if the probability of harm is high. However, if high risk patients choose to fast, against medical advice, then conditions that need to be fulfilled by these individuals are included in the recommendations. It should be remembered that although medical-based evidence is scarce in this field, safety for the person with diabetes is of the utmost importance. Indeed, this approach matches the essence of the religious regulations of Islam and has been approved by the Mofty of Egypt, the highest religious regulatory authority in Egypt (see Chapter 5 for further details).

Patients who are in the two highest categories of IDF-DAR risk should not fast; however, as previously mentioned, many of these patients will choose to do so and this must be respected. This important personal decision should clearly be made in light of guidelines for religious exemptions and after consideration of the associated risks in consultation with HCPs. Patients who insist on fasting need to be aware of the risks associated with fasting, and of techniques to decrease this risk. It is also worth highlighting that the initial risk assessment could change in time according to a number of factors. For example, a person with T2DM with poor glycaemic control is considered to be at high risk. If control improves pre-Ramadan and the choice of treatment does not include multiple insulin injections, then such a person would be considered to be at moderate risk.



Once a patient has been made aware of the risks associated with fasting, they should be provided with an individualised management plan and be advised on the measures they can take to minimise these risks. This includes attending a pre-Ramadan assessment, regular self-monitoring of blood glucose levels (SMBG), structured education, medication adjustments and nutritional and exercise advice [10].

Table 1. IDF-DAR risk categories for patients with diabetes who fast during Ramadan

Risk category	Patient characteristics	Comments
Category 1: very high risk	One or more of the following: • Severe hypoglycaemia within the 3 months prior to Ramadan • DKA within the 3 months prior to Ramadan • Hyperosmolar hyperglycaemic coma within the 3 months prior to Ramadan • History of recurrent hypoglycaemia • History of hypoglycaemia unawareness • Poorly controlled T1DM • Acute illness • Pregnancy in pre-existing diabetes, or GDM treated with insulin or SUs • Chronic dialysis or CKD stage 4 & 5 • Advanced macrovascular complications • Old age with ill health	If patients insist on fasting then they should: • Receive structured education • Be followed by a qualified diabetes team • Check their blood glucose regularly (SMBG) • Adjust medication dose as per recommendations • Be prepared to break the fast in case of hypo- or hyperglycaemia • Be prepared to stop the fast in case of frequent hypo- or hyperglycaemia or worsening of other related medical conditions
Category 2: high risk	One or more of the following: • T2DM with sustained poor glycaemic control* • Well-controlled T1DM • Well-controlled T2DM on MDI or mixed insulin • Pregnant T2DM or GDM controlled by diet only or metformin • CKD stage 3 • Stable macrovascular complications • Patients with comorbid conditions that present additional risk factors • People with diabetes performing intense physical labour • Treatment with drugs that may affect cognitive function	
Category 3: moderate/low risk	• Well-controlled T2DM treated with one or more of the following: – Lifestyle therapy – Metformin – Acarbose – Thiazolidinediones – Second-generation SUs – Incretin-based therapy – SGLT2 inhibitors – Basal insulin	Patients who fast should: • Receive structured education • Check their blood glucose regularly (SMBG) • Adjust medication dose as per recommendations

*The level of glycaemic control is to be agreed upon between doctor and patient according to a multitude of factors

CKD, chronic kidney disease; DAR, Diabetes and Ramadan International Alliance; DKA, diabetic ketoacidosis; GDM, gestational diabetes mellitus; IDF, International Diabetes Federation; MDI, multiple dose insulin; SGLT2, sodium-glucose co-transporter-2; SMBG, self-monitoring of blood glucose; SU; sulphonylurea; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus

The importance of risk stratification is reflected in the central role it has taken in two recently proposed management strategies – the PRE-approach (Presentation, Risk stratification, Education), and the 5 R's (Respect, Risk stratification, Revision of therapy, Regular follow-up, Reappraisal of strategy) [14, 15].

4.4 Special populations

4.4.1 Type 1 diabetes

People with T1DM will be advised not to fast because of the risks of severe complications. However, recent studies involving young adults suggest that if the patient is stable, otherwise healthy, has good hypoglycaemic awareness and complies with their individualised management plan under medical supervision, then many of these patients can fast safely [16]. One study involving 33 adolescent children with T1DM found that 60.6% completed the fast without any serious problems [17]. These children and their caregivers were given intensive training and education on insulin adjustment, SMBG, and nutrition before Ramadan and were closely monitored during the month-long fast. In total, five cases of mild hypoglycaemia and no cases of DKA were recorded [17]. Another study involving 21 adolescents with T1DM also found that a majority (76%) could fast for at least 25 days [18]. However, the use of continuous glucose monitoring equipment in this study demonstrated that blood glucose levels fluctuated and some episodes of hypoglycaemia went unrecognised, suggesting that regular SMBG during fasting is vital. The findings also highlighted the importance of thorough attention to hypoglycaemia unawareness in these circumstances [18].

While the results of these studies are encouraging, they cannot be generalised to all people with T1DM. Strategies to ensure safety of individuals with T1DM who choose to fast include: Ramadan-focused medical education, pre-Ramadan medical assessment including robust assessment of hypoglycaemia awareness, following a healthy diet and physical activity pattern, modification of insulin regimen, and frequent SMBG or continuous glucose monitoring [16].

4.4.2 The elderly

Many older people have enjoyed fasting during Ramadan for many years and they should not be categorised as high risk based on a specific age but rather on health status and their social circumstances. Many elderly people, especially those who have suffered with diabetes for a prolonged period, will have comorbidities that impact on the safety of fasting and present additional challenges to the HCPs managing them. Assessments of functional capacity and cognition need to be performed and the care provided should be adapted accordingly [19]. The current risk categorisation

considers those with old age combined with ill health as very high risk, however, old age on its own is not considered as an additional risk factor for fasting. The choice of anti-diabetic agents, which carry varying risks for hypoglycaemia, should also be considered.

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4.4.3 Pregnant women

Three quarters of Muslim pregnancies overlap with Ramadan and the risk to both the mother and foetus mean that pregnant women are exempt from fasting. However, many of these women will choose to fast. The possible effects of fasting on mother and foetus have been summarised in the *South Asian consensus statement on women's health and Ramadan* [20]. The risk categories proposed by the IDF-DAR (***Table 1***) take into consideration the differences between pregnancy in pre-existing diabetes and gestational diabetes mellitus (GDM). Some important factors to consider include:

- Pregnancy in pre-existing diabetes affects the pregnant woman throughout the duration of pregnancy, compared to the relatively shorter duration of GDM which normally develops during the second or third trimester
- The type of diabetes medication the woman with diabetes uses pre-pregnancy: incretins or thiazolidinediones are considered relatively low risk with regards to safety for fasting. However, during pregnancy, the vast majority of women with T2DM would be treated with insulin, metformin or glibenclamide. Insulin and glibenclamide carry a higher risk of hypoglycaemia if fasting [21, 22]
- Many are concerned about hypoglycaemia in Ramadan, however, for pregnant women hyperglycaemia is associated with increased risk for both mother and baby [10]. For this reason pregnant women with pre-existing diabetes or GDM are advised not to fast until further research data are available to support any change in risk category.

Summary

- With the correct guidance, many people with diabetes can fast safely during Ramadan but they must be under close supervision and be made aware of the risks.
- The risks associated with fasting include hypoglycaemia, hyperglycaemia, DKA, dehydration and thrombosis; physicians must quantify the risks and stratify each individual patient accordingly.
- The new IDF-DAR risk stratification approach defines three risk categories: very high, high and moderate/low.
- Patients who fast against the advice provided by their HCPs should follow experts' detailed guidance to avoid the development of serious complications.

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