CHAPTER 9

Management of Type 1 diabetes when fasting during Ramadan

Adults Chapter lead:
Wan Mohamad Wan Bebakar

Authors:
Khadija Hafidh
Rakesh K. Sahay
Mohamed Hassanein

Adolescents Chapter lead:
Reem Mohammad Alamoudi

Authors:
Nancy Samir Elbarbary
Walid Kaplan
Bachar Afandi

CHAPTER 9

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WHAT IS KNOWN?

- Fasting in adolescents and adults with T1DM carries a high risk.
- Insulin analogues are better than conventional Natural Protamine Hagedorn insulin (NPH) or regular twice daily regimens.
- Insulin pumps are beneficial when fasting.
- Education is still not available to many people with T1DM – both adolescents and adults.

WHAT IS NEW?

- Risks associated with fasting is not the same for all people with T1DM — adolescents and adults.
- New studies have shown that some people with T1DM may have a lower risk and can safely fast during the month of Ramadan if certain needs are met.
- New research on the impact of daily life on glycaemic control shows that fasting attitudes and outcomes vary considerably among different countries.
- Evidence suggest that Continuous Glucose Monitoring (CGM) can aid safe fasting and sensor augmented pumps have allowed individuals to fast for most if not the whole month.

WHAT IS MISSING?

- Adequately powered randomised clinical trials comparing different treatment regimens and algorithms for dose adjustments for adolescents and adults with T1DM who seek to fast during Ramadan.
- Research on the impact of daily life on glycaemic control — this can vary considerably among different countries. Likewise, further research on fasting plans is needed with consideration of the type, duration, and intensity of physical exercise; demands of schooling; dietary habits; the season in which Ramadan falls; and the duration of fasting.
- A validated risk score stratification method for adolescents and adults to help conduct safe fasting.
- Research into quality of life, focusing on the psychological effects of facing peer pressure in those who choose not to fast and on the effects of acute complications during fasting.

1. INTRODUCTION

Fasting during Ramadan is an integral part of Islam and though there are exemptions made for people that suffer illness, it remains a personal choice. People living with diabetes generally have to take extra precautionary measures during Ramadan, particularly in the case of Type 1 diabetes mellitus (T1DM).

Fasting for extended periods of time can increase the risk of people with T1DM experiencing the effects of poor glycaemic control including hypoglycaemia, hyperglycaemia, diabetic ketoacidosis (DKA) and dehydration, among other challenges. However, it is also important to recognise that these additional risks are not evenly distributed, and different approaches for the management of T1DM during Ramadan may need to be taken among adolescent and young individuals and adults.

Much of the literature on fasting during Ramadan in people with T1DM has been based on adolescent and young individuals and, therefore, the guidance and recommendations have predominantly been targeted towards these age groups. Though, recently a few studies have been carried out on older populations and advice for adult individuals with T1DM who are seeking to fast during Ramadan can now be offered.

For the purposes of this chapter, we will have adolescents and young individuals together as one group and adults as a separate group. The terms adolescents and young individuals will be used interchangeably. The guidance offered to adults in this chapter do not necessarily apply to the elderly and specific guidance for the elderly will be offered in **chapter 12: Management of diabetes among the elderly when fasting during Ramadan**.

1.1 Safety, Risks, and complications of fasting

1.1.1 Adolescents and Young Individuals

According to Islam, fasting during the month of Ramadan becomes obligatory for children from the age of puberty, however, much like in adults, those with medical conditions that can be compromised by fasting are exempt from this obligation. Medical societies and experts have generally discouraged individuals with T1DM, in particular adolescents, from fasting **[1]** and T1DM continues to be listed as a high-risk factor for fasting **[1, 2]**. In spite of this, many adolescents, and even pre-pubertal children, with T1DM insist on fasting, against the advice of their healthcare providers **[3, 4]**. The recommendation to fast varies among different countries, reflecting different cultural perspectives and views held by treating physicians. Fasting intentions can also differ among specific age groups, as shown in a recent survey of the Middle East and North Africa region, with adolescents reporting a higher intention to fast than adults - 75.4% vs 69.6% (p=0.034) **[5]**.

Over the past decade, several studies have evaluated fasting among adolescents with T1DM and its associated safety during the month of Ramadan. It has been shown that the majority of individuals can fast for longer than 15 days, and over 60% fasting for the whole month **[6, 7]**. Kaplan *et al*. compared continuous glucose monitoring (CGM) data during Ramadan fasting and in the month before and after Ramadan, and found no differences in the mean interstitial

glucose (IG), or in glucose fluctuation **[8]**. Additionally, El-Hawary *et al*. reported a statistically significant drop in fructosamine after the end of Ramadan in a cohort of 28 adolescents of who managed to fast the whole month of Ramadan **[9]**. On the other hand, studies have reported wide fluctuations in IG, and extended periods of unrecognised hypoglycaemia from CGM data **[7]**. This has raised some concerns about the implementation of safety instructions or the breaking of a fast at the onset of the hypoglycaemia when reliant solely on glucose readings from self-testing. These findings indicate the need for close monitoring and an increased education on appropriate decision-making.

Some studies have evaluated the use of specific insulin regimens to minimise the risk of hypoglycaemia during fasting; for example the use of rapid insulin analogues compared to regular human insulin **[10]**. Others have investigated the actual treatment regimens; for example, the use of continuous subcutaneous insulin infusion (CSII) compared to the conventional or multiple daily injection regimens **[11-13]**. Additionally, the use of advanced technological features has resulted in a significant reduction in the exposure to hypoglycaemia and enhanced the ability of individuals with T1DM to fast for the whole month of Ramadan, specifically the low-glucose suspend (LGS) feature of insulin pumps has proven to be particularly useful **[14]** (please see **Table 1**). A recent global study was able to show that the timing of hypoglycaemia during Ramadan was important. Almost 80% of participants reported that they experienced hypoglycaemia during the first week of Ramadan, higher than other weeks of Ramadan. The same was seen for hyperglycaemia. On the other hand, it was also found that 1 in 10 adolescents did not change their behaviours after discovering hypoglycaemia **[5]**. This highlights the important of pre-Ramadan education in helping to avoid these events altogether and in understanding appropriate responses when these events are discovered (see **chapter 7: Pre-Ramadan Assessment and Education**). Nevertheless, further research is still needed on patient reported outcomes such as a measure of quality of life to help understand the experiences of individuals with T1DM more closely.

The above factors, when available, may reduce risk of hypoglycaemia but they do not eliminate it and individuals still require close supervision and monitoring. The risks of hypoglycaemia in people living with T1DM that have reduced access to advanced medical care and medical supervision remain significantly high and fasting cannot be encouraged.

TABLE 1: **A COMPARISON OF STUDIES EVALUATING THE SAFETY OF FASTING DURING RAMADAN IN CHILDREN AND ADOLESCENTS WITH T1DM**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
1. Insulin pump 2. MDI (glargine plus short-acting insulin)	Kaplan & Afandi (2015) **[7]**	N=21 Observational study Mean age was 15 ± 4 years Two groups based on regimen (18 on Insulin pump; 3 on MDI) Country: United Arab Emirates	Hypoglycaemia observed in 14.2% of the fasting hours and 2.5% of the eating hours $p<0.05$ No severe cases of hypoglycaemia were reported	Hyperglycaemia (>300 mg/dL or 16.7 mmol/L) was observed in 12% of the fasting hours and 17% of the eating hours $p<0.05$	Large fluctuations in blood glucose Consequently Symptomatic hypoglycaemia resulted in breaking the fast in 15% of the days	Though 76% of patients fasted ≥25 days, there were periods of wide blood glucose fluctuation during fasting and eating hours., with periods of unrecognised hypoglycaemia
1. MDI 2. Insulin pump (All used CGM)	Kaplan *et al.* (2017) **[8]**	N=40 Observational study Mean age 15 ± 4 years Country: United Arab Emirates	There were no notable differences in the duration of hypoglycaemia during Ramadan compared to times outside of Ramadan	There were no notable differences in the duration of hyperglycaemia during Ramadan compared to times outside of Ramadan	There was a subgroup effect found in subjects with a HbA1c ≤ 8% (64 mmol/mol) where the duration of hypoglycaemia during Ramadan was lower than times outside of Ramadan - 6.2% and 9.6% or 44 – 81.4 mmol/mol respectively; $p<0.001$	Adolescents with T1DM have the same scope of BG fluctuations during Ramadan than outside of Ramadan. Subgroup effects in this study support the emphasis placed on pre-Ramadan glycaemic control However, these associations may be spurious and need confirming

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1. MDI 2. insulin pump (All used CGM while fasting for a minimum of 3 days)	Afandi *et al.* (2017) **[15]**	N=21 Observational study Mean age 16 ±3 years Patients were categorised as well-controlled and poorly controlled if the pre-fasting HbA1C was ≤8% and >8%, respectively (well-controlled N=7; poorly controlled N=14) Country: United Arab Emirates	Hypoglycaemia was statistically significantly higher in the poorly controlled group than in the well-controlled group	Hyperglycaemia was statistically significantly higher in the poorly controlled group than in the well-controlled group	NA	The episodes of hypoglycaemia and hyperglycaemia were higher in the poorly controlled group than in the well-controlled group. Likewise, the overall durations of hypoglycaemia, hyperglycaemia and severe hyperglycaemia were longer in the poorly controlled group than those in the well-controlled group Good glycaemic control before Ramadan can reduce the potential risks of complications during Ramadan
1. MDI 2. Insulin pump	Kholoud Mohamed et *al.*, (2019) **[16]**	N=50 children and adolescents with T1D Retrospective cohort study Mean age 12.7 ± 2.1 years Two groups based on regimen (27 MDI; 23 Insulin pump) Country: Kuwait	There were no statistically significant differences observed between the two insulin regimen groups in the frequency of hypoglycaemia Together, patients with HbA1c ≤ 8.5% had less-frequent hypoglycaemic attacks than those over 8.5% (p=0.01)	There were no statistically significant differences observed between the two insulin regimen groups in the frequency of hyperglycaemia	Patients with HbA1c ≤ 8.5% were able to fast more days during Ramadan than those over 8.5%	Fasting for children with T1DM is safe and feasible There was an indication supporting the need for good glycaemic control prior to Ramadan for favourable diabetes outcomes during Ramadan

1.1.2 Adults

As mentioned, fasting during Ramadan becomes obligatory from the age of puberty but those individuals that are unhealthy can be exempted. In circumstances where any missed days cannot be compensated for after Ramadan, *Fidya* can be paid. The general consensus has been that people living with T1DM are at risk of complications when fasting and can be exempted from undertaking it during Ramadan (see **chapter 5: Risk stratification of people with diabetes before Ramadan**). Though the risks of complications and the intentions to fast **[5]** are not exactly the same in adults when compared to adolescents the complications of T1DM that may arise are.

The body of research that has been conducted on safe fasting during Ramadan in adults is relatively small, but in recent times there have been a few studies that have studied older individuals. These studies can be relevant and help provide specific guidance for adults (see **Table 2**).

Al Awadi *et al*., in an observational study conducted in the United Arab Emirates, was able to show that there were no statistically significant differences in the frequency of hypoglycaemia prior to and during Ramadan. Though data were not reported on hyperglycaemia, it was shown using laboratory tests that fasting could improve glycaemic control **[17]**.

Further, Al-Ozairi *et al*., showed, in a study investigating the use of MDI and insulin pump regimens, that participants were able to reduce rates of hypoglycaemia during Ramadan when compared to before Ramadan (p=0.001) without any reported severe hypoglycaemic events. They also found that glucose variability improved in insulin pump users. Much like in the studies conducted on adolescents with T1DM, an important emphasis was placed on education prior to Ramadan wherein all participants in this study had previously attended the Dose Adjustment for Normal Eating course in Kuwait **[18]**. (For further information on Pre-Ramadan Education, please see **chapter 7: Pre-Ramadan Assessment and Education**) Amoudi *et al*., in a larger prospective study of 156 participants, again demonstrated improvements upon glycaemic variability in those that used insulin pumps compared to MDI. There were no significant differences in hypoglycaemia between both groups and no reported DKA events in the study **[13]**.

Likewise, Al fadhil was able to observe similar results when investigating people that were on a basal bolus regimen and found that CGMS were important to successful and confident fasting during Ramadan **[19]**. These findings were wholly supported by Al Awadi *et al*., who in another study, investigated individuals on several different insulin regimens **[17]**.

On the other hand, Malek *et al*., looked into people with T1DM in Algeria in a multicentre study; they showed that people that they classified as high or very high risk were most likely to experience hypoglycaemia and break their fast. Of concern was the finding that SMBG was reduced while fasting during Ramadan **[20]**. This highlights the need to provide support and help increase motivation among people that are high or very high risk that fast during Ramadan. As noted in **section 9.1.1**, a global survey study reported that a majority of participants experienced hypoglycaemia, where most of these occurrences took place in the first week of Ramadan **[5]**.

TABLE 2: **A COMPARISON OF STUDIES EVALUATING FASTING DURING RAMADAN IN ADULTS WITH T1DM**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
1. Basal bolus 2. Insulin pump	Al-awadi *et al.* (2020) **[21]**	N=24 Prospective observational study Mean age 23.3 ± 7.85 years Country: United Arab Emirates	There were no statistically significant differences in the number of hypoglycaemic events before and during Ramadan	Data not reported	The average laboratory HbA1c prior to Ramadan was 8.2% (66 mmol/mol) and it reduced to 7.9% (63 mmol/mol) post Ramadan p=0.01 Conversely, the average sensor estimated HbA1c was 7.9% (63 mmol/mol) prior to Ramadan and increased to 8.5% (69.4 mmol/mol) in Ramadan	Fasting may be safe in selective patients There were conflicting results on glycaemic control before and during Ramadan Larger randomised trials are needed to establish any recommendations
1. CSII 2. MDI and FGM	Al-Ozairi *et al.* (2020) **[18]**	N=43 Prospective observational study Mean age 31.7 years Two groups based on regimen (21 CSII; 22 MDI) Dose Adjustment for Normal Eating (DAFNE) course attendants Country: Kuwait	In total, the rate of hypoglycaemia was reduced during Ramadan when compared to before Ramadan (0.53 and 0.81 respectively; p=0.001) There were no severe hypoglycaemic events	No statistically significant differences to report	A measure called the coefficient of variation (CV) was calculated to measure glucose variability The CV was seen to reduce during Ramadan when compared to before Ramadan in the CSII group – this reduction was maintained after Ramadan	This study demonstrated the importance of education prior to Ramadan Providing a good level of education patients with T1DM on CSII or MDI can safely fast during Ramadan

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TABLE 2: **A COMPARISON OF STUDIES EVALUATING FASTING DURING RAMADAN IN ADULTS WITH T1DM**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
Multiple regimens	Malek *et al.* (2019) **[20]**	N=65 (T1DM) Prospective multicentre observational study Mean age 45.8 ± 17.69 Country: Algeria	In this study there were relatively few cases of hypoglycaemia (12 cases) Patients that were categorised as high-very high risk were the most likely to experience hypoglycaemia	Hyperglycaemia was observed in 10 cases and was an important reason for stopping fasting	There were no real differences observed in HbA1c before and after Ramadan However, mean glycaemia (mg/dL) was lower after Ramadan when compared to before Ramadan; p=0.005	31% of patients stopped fasting due to reasons including complications due to T1DM SMBG was reduced when fasting It was deemed that there needs to a much greater emphasis on education
1. All patients except one were on basal bolus insulin (1 patient used an insulin pump) All used CGMS	Al fadhli (2018) **[19]**	N=24 Observational study Mean age 22 ± 6 Country: Kingdom of Saudi Arabia	Hypoglycaemia rates were lower during fasting and there were no reports of severe episodes The average time spent in hypoglycaemia was 0.60 ± 1.5 hours 4 patients broke their fast due to mild hypoglycaemia	The average time spent in hyperglycaemia, post-*Suhoor*, was 3.63 ± 4.3 hours Hyperglycaemia rates were higher than that of hypoglycaemia Approximately half of the time, patients were experiencing hyperglycaemia (≥ 180 mg/dL or 10 mmol/L) and 13% of the time experiencing severe hyperglycaemia (≥ 300 mg/dL or 16.7 mmol/L)	Sensor glucose levels were lower during fasting than when during the eating hours; 188.4 mg/dL (10.5 mmol/L) and 212.5 mg/dL (11.8 mmol/L) respectively p<0.001	Patients with T1DM that fasted during Ramadan experienced wide fluctuations in glucose levels There was a greater tendency towards hyperglycaemia CGMS was successfully used and can increase confidence in fasting during Ramadan

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TABLE 2: **A COMPARISON OF STUDIES EVALUATING FASTING DURING RAMADAN IN ADULTS WITH T1DM**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
Multiple regimens: (rapid acting; intermediate-acting; basal bolus; premix; Insulin pump)	Al Awadi *et al.* (2020) **[17]**	N=136 Prospective observational study Mean age 32 years Countries: Middle East and North Africa	Incidence of hypoglycaemia did not change from before Ramadan to during Ramadan This was also the case for severe hypoglycaemia	Incidence of hyperglycaemia did not change from before Ramadan to during Ramadan This was also the case for severe hyperglycaemia	The mean HbA1c levels reduced during Ramadan when compared to before Ramadan (-0.6%; p<0.001) Likewise, Fasting plasma glucose decreased by 21.2 mg/dL or 1.2 mmol/L p<0.001 and post-prandial plasma glucose decreased by 22.8 mg/dL or 1.3 mmol/L p<0.001	Nearly half of patients in this study fasted for the whole duration of Ramadan During Ramadan mean glycaemic control Improved with no increases in severe hypoglycaemic events These may be due to pre-Ramadan education and careful dose adjustments (80% had dose reductions)
1. MDI 2. Insulin pump	Al Amoudi et *al.* (2017) **[13]**	N=156 Prospective cohort study Mean Age (23.4± 6.1 years) Two groups based on regimen (95 MDI; 61 Insulin pump) Country: Kingdom of Saudi Arabia	No statistically significant difference was observed in the rate of mild or severe hypoglycaemia between groups	The mean rate of hyperglycaemia was higher in the insulin pump group compared to the MDI group; p=0.03	No differences in glycaemic control were observed between both groups; measured using fructosamine and A1c levels	More patients on the insulin pump than in patients on the MDI regimen managed to fast the whole month of Ramadan without the need to break their fast 31.2% and 22.1% respectively; p=0.41 The use of an insulin pump regimen was associated with less glucose variability; p=0.02

Taken together, these findings suggest a similar outlook in adults to adolescent and young people when fasting during Ramadan. However, a stronger effort needs to be made to investigate adults with T1DM, this can be through actively studying adults in prospective studies or randomised controlled trials or generally including more adults into the cohort of participants when conducting studies. This will allow for a greater depth of understanding and for systematic reviews and meta analyses to highlight specific differences or similarities between adults and adolescent and young individuals with T1DM.

Various studies have demonstrated that both adolescents and adults can achieve safe fasting during Ramadan with no worse outcomes than prior to Ramadan.

1.1.3 Complications that can arise during fasting

Though there are differences that need to be acknowledged between adolescents and adults, the complications of T1DM that can arise during fasting are by and large the same **[5]**. Fasting during Ramadan for people with T1DM can be dangerous if not conducted properly and the complications of doing so must be considered.

The period of fasting, that can reach over 20 hours in some countries, imposes a high risk of dehydration to all people living with T1DM. Conceivably, this risk would be even higher in children and adolescents, due to their higher surface area to volume ratio **[22]** and their relatively greater rate of physical activity. To the best of our knowledge, no study has been conducted to assess the associated risk of dehydration during fasting in adolescents with T1DM, nonetheless, all precautions should be taken to minimise the risk of this complication.

Furthermore, based on a large population-based retrospective survey conducted across 13 countries, adult individuals with T1DM reported a higher incidence of severe hypoglycaemia and diabetic ketoacidosis (DKA) during Ramadan compared to other months of the year **[2, 4]**. However, several subsequent studies conducted in countries with advanced medical care have shown no difference in severe hypoglycaemia or DKA between Ramadan and non-Ramadan days in adolescent with T1DM **[6, 7, 23-25]**. Kaplan *et al*., in a study of CGM data, reported no difference in the duration of hypoglycaemia during Ramadan and the month before or after Ramadan among adolescents with T1DM **[8]**. Similar findings were recently reported by Lessan *et al*. **[26]**. This was explored in further detail by Afandi *et al*., where they reported an average daily duration of hypoglycaemia whilst fasting during Ramadan of 1.39 hours per individual, with almost 70% of hypoglycaemic episodes occurring in the final 6 hours of fasting **[27]**. Another study, highlighted the importance of glycaemic control prior to Ramadan, showed that hypoglycaemia, hyperglycaemia, and severe hyperglycaemia were significantly higher in individuals with poor glycaemic control **[15]**. In a recent global survey of individuals with T1DM that were intending to fast, it was shown that the majority of adolescents and adults that fasted experienced day-time hypoglycaemia, highlighting its importance as a complication in

certain individuals. Although fewer individuals reported hyperglycaemia (approximately 45% of adolescents and adults), it also was an important complication **[5]**. **Table 3** summarises the some of the key parameters in those with T1DM who fasted during Ramadan **[5]**.

TABLE 3: **KEY PARAMETERS OF THOSE WITH T1DM WHO FASTED RAMADAN (N=1054, 71% OF SURVEY POPULATION) highlights from the DaR global survey [5]**

Duration of Fast	26.8% fasted for full 30 days	45% fasted 22-29 days due to diabetes related illness	28.2% fasted 21 days or less due to diabetes related illness
Hypoglycaemia	39.3% reported no symptoms of hypoglycaemia	48% reported symptoms of hypoglycaemia over 1-7 days	12.8% reported symptoms of hypoglycaemia over 8-30 days
Hyperglycaemia	55.2% reported no episodes of hyperglycaemia (BG>300 mg/dl)	28% had hyperglycaemia over 1-7 days	16.8% had hyperglycaemia over 8-30 days
Severe events leading to hospital admission	93.2% did not require Emergency Room or hospital admission for hypoglycaemia/hyperglycaemia		6.8% required Emergency Room or hospital admission for hypoglycaemia/ hyperglycaemia

Overall, it is important to carefully select those with T1DM who are prone to developing complications and advise them not to fast.

1.2 Risk stratification of people living with T1DM during Ramadan

People that have T1DM that wish to fast during Ramadan have generally been placed in a, blanket, 'high' or 'very high' risk category and this has made it difficult for medical professionals to advise and support people that wish to fast during Ramadan. As mentioned, fasting during Ramadan is an important aspect of a Muslim's life and remains a personal choice and so - must be respected. Moreover, Hussain *et al*, argued that people with T1DM need a more flexible approach to risk stratification when planning to fast during Ramadan **[28]**. Though, it is important to note that this does not directly advise people with T1DM to fast and may not be accessible or applicable to everybody living with T1DM. (For further information on Risk stratification please see **chapter 5: Risk stratification of people with diabetes before Ramadan**).

That risk stratification for a person with type 1 diabetes wishing to fast should be individualised and dependent on a range of different factors including:

- Pre-Ramadan glucose control
- The duration of T1DM – for example those newly diagnosed may be within the 'honeymoon period'
- Hypoglycaemia risk
- Level of hypoglycaemia awareness
- The level of diabetes related education
- Motivation for self-monitoring of blood glucose (SMBG)
- The ability to take appropriate decision making

- The feasibility of, and access to, continuous glucose monitoring and advanced insulin delivery technology
- The presence of diabetes related complications and/or associated autoimmune disorders such as Coeliac disease and thyroid disorders

Where all of the above have been considered and satisfied, people with T1DM can be advised that they are able to fast, only if they are willing to be educated on decision making around breaking their fast and comply to strict glucose monitoring and, where applicable, dietary and medication adjustments. Where these conditions are not met, or not feasible, fasting would pose a high risk and should not be encouraged.

1.3 Criteria for Fasting during Ramadan in people with T1DM

The findings from research studies that have been discussed thus far apply to individuals with access to advanced medical care, good education programmes and appropriate support. We believe that people with T1DM who have these privileges and wish to fast during the month of Ramadan can be allowed to do so, after proper risk scoring (see **chapter 5: Risk stratification of people with diabetes before Ramadan**), alongside the fulfilment of the following conditions:

- **A pre-Ramadan clinical evaluation and a full review of an individual's glucose profile should be completed. If poor glycaemic control is found (HbA1c >9% or 75 mmol/mol and or wide glucose fluctuation), the insulin treatment regimen should be adjusted as necessary and re-evaluated once again before the start of fasting.**

- **Individuals with T1DM, regardless of their age, and their carers or guardians should be taught about the potential adverse effects of fasting, including hypoglycaemia, hyperglycaemia and dehydration, and appropriate preventative measures to minimise the risks of these occurring. Additionally, the rationale for the revised insulin regimen should be explained and emphasised.**

- **There should be a nutritional assessment reviewing carbohydrate (CHO) intake and recommendations about the proper food options for the two main meals of the day. Carbohydrate counting techniques should also be discussed. An emphasis needs to be placed on the importance of a scheduled time for meals rather than following a looser erratic and frequent eating pattern. Also, an adequate intake of sugar-free beverages, especially with the pre-dawn meal, should be stressed.**

- **While there is still a debate about the best insulin regimen for during fasting, a basal insulin dose reduction by 10-30% has been recommended by the majority of experts and medical societies. More importantly, an individualised regimen should be considered and based on a review of the individual's glucose profile within the first few days of fasting.**

- **Frequent glucose testing is fundamental to ensure early recognition of abnormal glucose readings and that the proper measures in controlling them are taken. The use of CGM or FGM is superior to the traditional BG monitoring and should be the method of choice if available.**

- **Fasting should be broken immediately with hypoglycaemia (< 70mg/dL; 3.9 mmol/L) in individuals using MDI, both symptomatic or asymptomatic. Those using CSII may try suspending the pump if glucose drops below 90mg/dL (5 mmol/L) but should also break the fast if glucose is < 70 mg/dL (3.9 mmol/L).**

The allowance to fast cannot be generalised across to all individuals with T1DM, especially those where the aforementioned criteria are not met. We acknowledge that data on the safety of fasting is incomplete and may be prone to selection-bias in that individuals that are not willing to fast or those that show poor glycaemic control are not represented in these studies. It is therefore not possible to quantify or be assured of the exact risk related to fasting, and an individualised risk assessment remains the most appropriate method.

1.4 Blood glucose monitoring for people with T1DM during Ramadan

People with T1DM who choose to fast must regularly check their blood glucose levels through SMBG or CGM. The benefits of real-time CGM was demonstrated in a study of adolescents with T1DM where it showed that it can be effective in lowering HbA1c; reaching a target level of HbA1c; reducing glucose variability; reducing mild to moderate hypoglycaemia; and increasing the Time in Range (TIR) **[29]**. However, it is worth noting that the effectiveness of CGM, in children and adolescents with T1DM, may depend on the duration of sensor use **[30]**.

The use of these advanced methods to monitor blood glucose trends can be a valuable tool to detect hypoglycaemia and prevent glycaemic excursions during Ramadan fasting **[7]**. The use of CGM during Ramadan or in the month before or after the Ramadan, is also key for therapy adjustments **[8, 31, 32]**. Other systems such as flash glucose monitoring (FGM) have also been proved to be useful tools in studying T1DM **[27]**.

Importantly, most CGM studies during Ramadan have been performed in countries with similar durations of fast. These findings have not been replicated in countries with longer daylight times fasting hours and intentions of fasting **[5]** and so guidance should not be generalised. When CGM is not feasible, frequent and regular SMBG is necessary for an appropriate adjustment of insulin dosing.

Telemedicine, necessitated by the Coronavirus disease 2019 (COVID-19) crisis, has thus far shown strong results and remains an important tool that health care providers rely on to treat 'high-needs' individuals such as adolescents or adults living with T1DM. Insulin pumps, CGMs, and most blood glucose meters have the ability to be downloaded onto either the manufacturer's platform or a uniform secondary service. The downloading of device data enables patients and

their caregivers to visualise the glucose profile, through seeing summary statistics and trends in glycaemic data. It also provides an opportunity for clinicians and diabetes educators to review such data remotely between visits and make more frequent dosing adjustments. However, technological barriers remain a concern in those living in remote or rural locations.

- **Frequent glucose testing is fundamental to ensure safe fasting.**
- **The use of CGM or FGM is superior to SMBG monitoring, and should be the method of choice if feasible.**
- **Fasting should be broken immediately with hypoglycaemia (glucose < 70mg/dL; 3.9 mmol/L).**

1.5 Physical activity for people with T1DM during Ramadan

It is recommended that a relatively moderate level of activity be maintained during Ramadan, with the consideration to avoid strenuous activity in the hours before the sunset meal, where hypoglycaemia is most likely **[33]**.

Similar to meal routines, exercise patterns in Ramadan differ between countries, cultures, the need for school attendance, and the season that Ramadan comes in. Sleep patterns are also affected. In a study where Ramadan time coincided with the summer vacation, more than 90% of individuals with T1DM reported sleeping until 4.00 pm, and were only mildly active between 9.00 pm to 1.00 am **[34]**.

Evidence on the impact of fasting during Ramadan on athletic performance and treatment guidance for athletes when fasting is scarce. In a review of the available literature **[35]**, Shepard concluded that changes in training, fluid intake, diet, and sleep patterns can be managed but do not go far enough to attenuate the risk; he recommended that athletes with T1DM seek a medical exemption from fasting, but if they choose to fast then an individualised plan to optimise performance and ensure safety is needed. A consensus guiding nutritional management for athletic performance in people with T1DM has been outlined **[36]**, however, it requires an adaptation for athletes choosing to observe Ramadan fasting in order to the meet the different fluid, energy, and electrolytes requirements **[33]**.

Research is limited on the exercise patterns of people with T1DM during Ramadan. Generally, their activity patterns tend to vary, particularly so in adolescents where sport can be planned or spontaneous. Pre-Ramadan diabetes education should discuss physical activity, with a plan for appropriate insulin adjustment, hydration and hypoglycaemia treatment in an individualised manner **[33]**.

1.6 Nutritional care and meal planning for people with T1DM during Ramadan

Individualised nutritional assessments, education, and meal planning are all essential for safe fasting. Any proper assessment of people with T1DM should consider an individual's energy requirements, most commonly eaten foods, personal timing of the *Suhoor* (pre-dawn) and *Iftar* (after sunset) meals, insulin regimen type and time of administration in relation to meals, and exercise patterns **[33]**.

An individual's mealtime routine and type of food that is consumed during Ramadan can vary tremendously due to cultural differences but also other reasons owing to the fact that variation can also be seen even within households of the same culture. Amoudi *et al*. studied the different habits of 156 T1DM patients (aged 14-50 years old) in a middle eastern country; it was found that while the majority of patients consumed a large meal at the sunset prayer call, many others only consumed a small meal or a snack of dates and yogurt or soup, and had their main meal later, within a time range of 30 minutes to 4 hours after sunset. The insulin timing in relation to *Iftar* also varied, with some splitting their doses and others taking it with the main meal **[34]**. This certainly has implications on post-prandial glucose levels and should prompt physicians and educators to include this when providing education.

Commonly eaten types of food during Ramadan tend to be high in fat and sugar. This was demonstrated by Eltoum *et al*. who subsequently recommended that people with T1DM lower their saturated fat and sugar intakes during this period **[37]**.

A late evening meal (around 10-11 PM) is a common habit among people with T1DM; this could be a small snack or even the main meal for those who had a small *Iftar*. The timing of *Suhoor* was also been found to be quite variable **[34]**; ideally it should be eaten within in the last predawn hour, however many individuals tend to prefer eating it earlier allowing them a little bit of time to correct for hyperglycaemia before dawn and may even have another snack that is not covered with insulin. It is strongly recommended that the predawn meal is eaten as close to dawn as possible to minimise the fasting period. Lean protein and carbohydrates low on the glycaemic index (GI) are particularly important at the predawn meal to enhance satiety during the day. Caution with the insulin dose at predawn is essential to minimise any risk of hypoglycaemia and avoid any need for the disruption of fasting. Another important consideration is the proper distribution of fluid intake during the non-fasting hours to maintain adequate hydration **[33]**, a common habit of binging large amounts just before dawn is discouraged.

An assessment of individual patient habits during Ramadan will help to tailor patient education programmes and in making timely and proper decisions regarding therapy **[38]**. For those using intensive insulin therapy, education on carbohydrate counting is recommended to allow for the adjustment of the prandial insulin dose to match carbohydrate intake at *Iftar*, *Suhoor* or the supper meal. Daily consistency in carbohydrate intake at *Iftar* and *Suhoor* is necessary for those on a twice daily injection regimen. Continual snacking overnight after *Iftar* should be discouraged **[33]**. Pre-prandial bolus insulin is preferable to insulin administered during or after the meal **[39]**. Frequent SMBG monitoring, or preferably CGM, is recommended to allow for appropriate insulin adjustments**[1]**.

In younger individuals, an appropriate energy intake to maintain growth and development is necessary **[40]**. The IDF and Diabetes and Ramadan (DAR) International Alliance recommend that for adults the calorie load during fasting should be similar to the rest of the year to prevent weight gain (please see the **chapter 7: Pre-Ramadan Assessment and Education**). In children and adolescents with T1DM, both weight gain **[41]** and weight loss **[42]** have been reported. Weight loss can be explained by the reduced caloric intake with fasting, however it has also been associated with deterioration in glycaemic control **[42]**. Weight, as well as types of food and the appropriate insulin coverage of meals, need monitoring during Ramadan.

A moderation in traditional sweet intake and fried foods are strongly recommended, particularly at the sunset meal. This should be covered by prandial rapid-acting insulin to prevent postprandial glycaemic excursions. The use of an extended bolus delivered by an insulin pump, where some of the insulin is delivered promptly and the remainder over 2 to 6 hours, enables bolus insulin to match the glycaemic effect of the meal. This is particularly useful for high-fat meals such those consumed at *Iftar*. CGM is a useful tool to show the impact of meals consumed during Ramadan. It can guide changes in the timing of insulin administration and the insulin dose to match the profile of high fat foods **[33]**.

Taken together, it is essential to design an individualised meal plan well before Ramadan. The plan should be to help individuals maintain an adequate caloric intake and help avoid excessive weight changes. Furthermore, this meal plan should take into account the insulin regimen, the type of food consumed, and meal timing. During Ramadan continuous glucose monitoring and daily adjustments are required to achieve good glucose control and avoid excursions.

1.7 Management of adolescent individuals with T1DM during Ramadan

1.7.1 Insulin regimens

Most studies investigating the efficacy and safety of different insulin regimens in adolescents are observational studies with small sample sizes making evidence-based guidance difficult See **Table 1**. Therefore, an individualised approach is key, and the choice of treatment regimen largely depends on culture; access to specialist care; medication; and supportive diabetes technology, if these are available.

The most widely used insulin regimens in adolescents are:

- Basal-bolus regimens – meal adjusted Multiple Dose Injection therapy
- Continuous subcutaneous insulin infusion (CSII) with or without sensors
- Conventional, twice daily NPH/Regular short acting (human) insulin
- Premixed insulins (the least frequently used and generally not recommended for T1DM)

All of the above options are yet far from replicating physiological insulin secretion; MDI and CSII remain the closest options available **[43]**.

1.7.2 Basal-bolus regimen (MDI)

This regimen, using a long-acting insulin analogue and a premeal rapid acting insulin analogue, is associated with a lower risk of hypoglycaemia when compared to conventional, twice-daily, insulin regimens **[1]**, and is the preferred treatment option for paediatric and adolescent individuals with T1DM **[44]**.

Basal insulin: Long-acting analogues

The safety and efficacy of **first-generation** basal insulin analogues (such as glargine U-100), in individuals with well controlled T1DM, who fasted with an average range of 17-19 h/day, have been demonstrated in a number of observational studies **[41, 45-49]**. However, some saw an observed significant decline in plasma glucose, with a tendency towards hypoglycaemia, that occurred mostly towards the end of the fasting period. To minimise the risk of hypoglycaemia, many studies suggested a reduction of the basal insulin during Ramadan [41, 44, 50-53]. In some studies, the pre-Ramadan basal dose was reduced by 20% and given earlier in the evening **[11, 41, 48, 50]** while in other studies a reduction of up to 40% was needed **[2, 8, 51]**.

Basal insulin should, ideally, be administered earlier in the day. This is to reduce the exposure to active insulin during the last hours of fasting; this is supported by CGM studies showing that approximately 70% of the hypoglycaemic events occurred in the last 6 hours of fasting **[15]**. A general recommendation has come to the fore — Ramadan fasting should be started with a reduction of basal insulin and taken at *Iftar* or earlier in the evening in order to help prevent hypoglycaemia **[54]**. Though, this notion has been challenged with recent studies reporting no difference in the incidence of hypoglycaemia between T1DM individuals who reduced or did not reduce their dose of basal insulin in a retrospective study **[6]** and in a treatment timing ranomised cross-over study, utilising FGM **[55]**. Interestingly, a less recent study even suggested an increase in insulin dose **[56]**.

This clearly demonstrates that until greater clinical evidence accumulates, a greater emphasis must be placed on individualisation. A careful intensification of metabolic control prior to Ramadan must be achieved through close monitoring using frequent SMBG or CGM/FGM and this will help inform adjustments in basal insulin dosage.

The new, second generation, long-acting insulin analogues (glargine U-300 and degludec), have been reported as safe and effective, with no major risk of hypoglycaemia and good glycaemic control in two studies in type 2 diabetes [57, 58] **among adult individuals observing Ramadan. However, further research is needed to replicate these findings in young individuals with T1DM.**

Bolus insulin

The exact dose adjustment needed to achieve safe fasting while avoiding hyperglycaemia remains controversial. Alalwan *et al*. successfully used a pre-*Iftar* dose equal to that of a pre-Ramadan lunch dose and a pre-dawn dose equal to a pre-Ramadan evening dose of rapid acting insulin **[48]**.

An evaluation of the contents of a meal and blood glucose readings are important for proper insulin dose estimation. In current practice, most paediatric endocrinologists base a bolus (rapid-acting) insulin dose on the meal carb-count. The insulin to carbohydrate ratio (ICR) measure is highly dependent on insulin sensitivity and may vary between different meals and the time of day and, therefore, should be well adjusted before Ramadan.

Moreover, taking the bolus of rapid-acting insulin 20 minutes before a meal results in a significantly better postprandial glucose control than when the meal insulin bolus is given just prior to the meal or after meal initiation. The timing of this dose is especially important for high-fat and high-protein meals, which are often associated with *Iftar* **[59]**.

A premeal high blood glucose level in the evening may require an extra dose of insulin as a corrective measure **[41]**. This correction dose is calculated using the insulin sensitivity factor (ISF) and the target blood glucose level. It should not be given more frequently than every 3 hours so that insulin stacking, and consequent hypoglycaemia can be avoided.

TABLE 4: **STUDIES EVALUATING THE USE OF BASAL-BOLUS INSULIN IN ADOLESCENTS DURING FASTING IN RAMADAN**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
1. Conventional BID pre-mixed insulin regimen 2. Basal Bolus	Al-Khawari *et al*. (2010) **[41]**	N=22 Observational study Mean age was 13.9 years (range 9–18) Two groups based on regimen (conventional N=9; Basal Bolus N=13) Countries: UK, Kuwait	Greater number of cases in patients on basal/bolus than in those on conventional insulin 61.5% and 44% respectively	Twice daily insulin had hyperglycaemia during the day whilst those on basal-bolus insulin showed a steady fall in blood glucose towards normal by the time of breaking their fast	The mean HbA1c of patients on conventional insulin was 8.8% or 73 mmol/mol and was 10.2% or 88 mmol/mol in patients on Basal/bolus prior to starting the fast Patients on conventional insulin continued to have hyperglycaemia during the fast but not in those on basal/bolus	The dose of basal insulin was recommended to be reduced by 10-20% in order to ensure safe fasting during Ramadan

table continued on next page ▶

TABLE 4: **STUDIES EVALUATING THE USE OF BASAL-BOLUS INSULIN IN ADOLESCENTS DURING FASTING IN RAMADAN**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
1. Insulin MDI in both the fasting and non-fasting groups	AlAlwan *et al.* (2010) **[48]**	N=20 Observational study Ages ranged from 8-14 years Patients divided into a fasting (N= 12, mean age 12.4 years) and a Non-fasting group (N=8, mean age 10.5 years) Country: KSA	1 child in the fasting group withdrew due to hypoglycaemia	-	No change in HbA1c before and after Ramadan in the Fasting group A slight change in HbA1c before and after Ramadan of -0.2%, which was not statistically significant	The Pre-*Iftar* dose given was equal to that of the pre-Ramadan lunch dose of rapid acting insulin The Pre-*Suhoor* dose given was equal to that of the pre-Ramadan evening dose of rapid acting insulin. The Pre-Ramadan Basal dose was reduced by 20% and given in the evening. Fasting during Ramadan can be conducted relatively safely
1. Glulisine, Lispro or Aspart 2. NPH – BID	Kadiri A *et al.* (2001) **[10]**	N=64 Open label randomised, crossover study in Young adults	Hypoglycaemia lower with lispro than regular insulin - 23.4% vs 48.4%; p=0.004	The 2-hr BG after *Iftar* was significantly lower in those treated with lispro p=0.026	No statistically significant changes in HbA1c	It was deemed Lispro is better than regular insulin in managing diabetes during Ramadan
1. MDI of Ultralente and Regular short acting insulin	Kassem *et al.* (2005) **[50]**	N=17 Observational study Mean age was 18.8 years Country: Lebanon	No episodes of severe hypoglycaemia	-	No statistically significant changes in HbA1c	Insulin regimens should be switched to long lasting insulins for patients with T1DM wishing to fast The dose was recommended to be 85% of their initial insulin dose and composed of 70% Ultralente and 30% rapid insulin, and divided equally between *iftar* and *Suhoor*

table continued on next page ▶

TABLE 4: **STUDIES EVALUATING THE USE OF BASAL-BOLUS INSULIN IN ADOLESCENTS DURING FASTING IN RAMADAN**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
1. Insulin (conventional BID regimen)	Zabeen *et al.* (2014) **[42]**	N=33 Observational study Ages ranged from 11-18 years Country: Bangladesh Split into groups of children that completed fasting and those that did not	2 (10.0%) patients developed hypoglycaemia in those completing their fasting compared with 3 (23.1%) in those that did not complete their fast No severe episodes were reported	-	No statistically significant changes were observed in either group	Children can safely fast during Ramadan given that there is adequate education in place prior to Ramadan and intensive monitoring during Ramadan

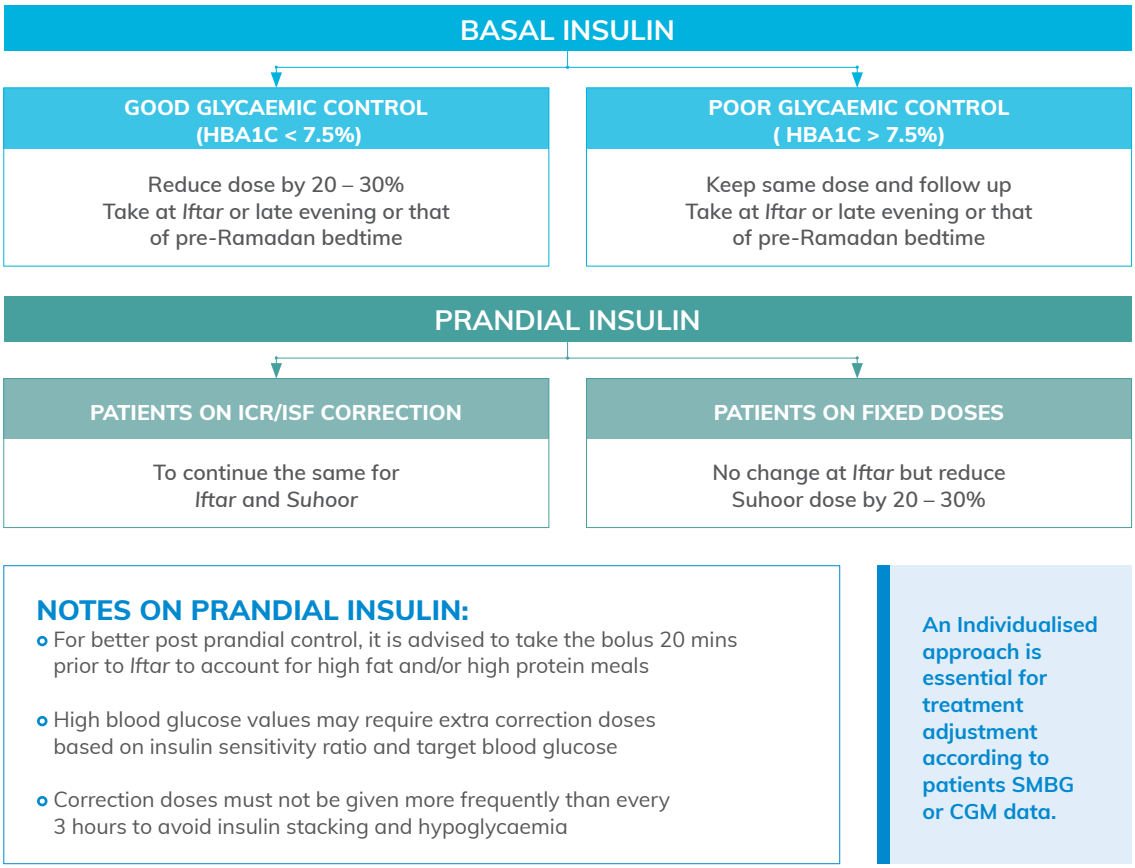

FIGURE 1

The recommended use of MDI therapy in adolescents with T1DM that are fasting during Ramadan

1.7.3 Conventional insulin treatment

It has been shown, in adolescents, that the use of **long acting insulin analogues** are preferred over intermediate acting insulin through providing a steady fall in blood glucose concentration towards normal levels by sunset time **[60]**. Al-khawari *et al*. reported children on a conventional twice daily regimen are more prone to hyperglycaemia, with or without ketones than those on a basal-bolus regimen. Further, children on twice daily regimens continued to show hyperglycaemic values during the daytime, while those on basal-bolus insulin showed a steady fall in their blood glucose concentration up until the time of breaking their fast **[41]**, (see **Table 4**).

The duration of action and the timing of the peak effect of intermediate acting Neutral Protamine Hagedorn (NPH) and the regular (human) insulins should be considered when adjusting insulin doses alongside the content and portions of food and the hours of fast. The need for two to three daily injections allows less flexibility and freedom in lifestyle and nutritional choices. **The use of conventional regimens is discouraged in individuals with T1DM who fast during Ramadan. However, if this is the only conceivable option then adjustments should be carried out as shown in Figure 2.**

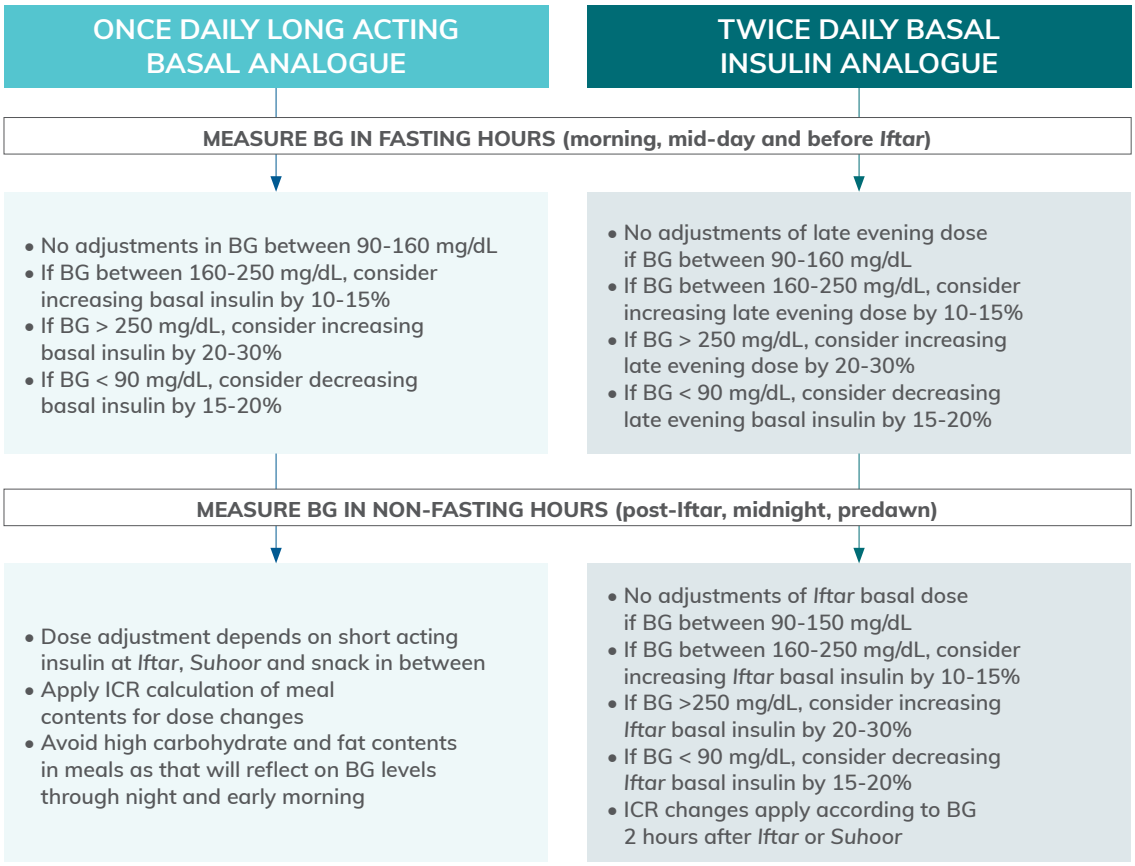

FIGURE 2

Schematic adjustments of insulin and/or food considerations during fasting and non-fasting hours

NOTES FIGURE 2

1. These adjustments depend on blood glucose trends and excursions (i.e. persistent increase of BG levels in all suggested timings for measurement without proceeding hypoglycaemias)
2. An insulin regimen should be adopted and individualised according a patient's needs

Regimens that use **premixed insulin twice daily** require a fixed intake of carbohydrates, at set times, to counteract the two peaks of activity of the associated insulin profile. This may be difficult to use safely when fasting, especially with adolescents who tend towards having more erratic eating habits, and is therefore not advised **[29]**.

- **Basal-bolus regimen is preferred over conventional twice daily regimens in adolescents with T1DM.**
- **Basal insulin should be adjusted according to fasting blood glucose levels, to reduce hypoglycaemia during fasting.**
- **Bolus insulin before *Iftar* and *Suhoor* using ICR and ISF-based corrections are recommended in order to control postprandial and evening hyperglycaemia.**
- **Premixed insulin regimens are incompatible with safe fasting and should be discouraged.**

1.7.4 Continuous subcutaneous insulin infusion pump (CSII)

Insulin pump therapy has proved to be beneficial in all paediatric groups with T1DM **[61]**. Achieving the targeted glycaemic control, reduction of severe hypoglycaemia with no significant increase in BMI, reverting hypoglycaemic unawareness, improved flexibility, quality of life, decreased total daily insulin doses, episodes of DKA and glycaemic variability have all been reported as advantages with the use of insulin pump **[62, 63]**.

The use of technology can be a valuable asset in improving diabetes control without increasing the risk of hypoglycaemia and hyperglycaemia during Ramadan. The combined risks of hypoglycaemia from prolonged daytime fasting and hyperglycaemia from excessive night-time eating, can be more easily managed by adjustments of an insulin pump's settings than by multiple insulin dose–injection therapy. The ability to lower the basal insulin infusion rate or even suspending it, helped individuals with diabetes avoid major hypoglycaemic events during fasting **[44]**. Despite these benefits, its widespread use is limited in many countries primarily due to cost and access.

A number of studies **[11, 13, 63]** have shown the benefits of insulin pumps when fasting. In adolescents with T1DM, the use of subcutaneous insulin infusion was frequently associated with fewer hypoglycaemic episodes and an improvement in diabetes control **[11]**. Amoudi *et al*. reported significant better glycaemic variability, and an association with less hypoglycaemia (not statistically significant) in pump users **[13]**. In a retrospective study, Deeb *et al*. found no differences in hypoglycaemia events in adolescents between pump and multiple daily injection users **[6]**. A recent study showed that, fasting in children above the age of 10 years with T1DM is feasible and safe in both pump and non-pump users, and well-controlled individuals are less likely to develop complications. It was concluded that the education of families and their children before Ramadan, along with an intensive monitoring of fasting children during Ramadan are more crucial than the type of regimen used **[16]**.

Most studies of CSII in young individuals and adolescents during Ramadan **[8, 11, 14, 15]** reduced the dose of **basal insulin by 10–25%** during fasting. Some studies propose an increase of the basal rate during eating hours and then reducing it throughout the fasting period, especially towards the final few hours of fasting; even up to a 40% reduction **[8, 14, 15]**. However, Deeb *et al*. found no difference in hypoglycaemia frequency when the basal rate was reduced **[6]**.

A recent systematic review and meta-analysis of young individuals with T1DM showed that a CSII regimen had lower rates of severe hypoglycaemia, hyperglycaemia or ketosis, but a higher rate of non-severe hyperglycaemia than that of premixed or MDI regimens. These findings suggest that the appropriate selection of individuals is key. This paired with a regular, supervised fine-tuning of the basal insulin rate and intensive glucose monitoring might help mitigate the risk of hypoglycaemia during Ramadan **[12]**.

In addition, a great benefit of new technology is the extra information provided through the use of integrated pump-sensor technology, allowing for a greater understanding of when to change basal settings during fasting and non-fasting hours. For more simpler pumps, temporary adjustments to basal insulin are made through algorithms that respond to fluctuations in blood glucose levels.

Boluses covering predawn and sunset meals should be based on the usual Insulin Carbohydrate Ratio (ICRs) and Insulin Sensitivity Factor (ISFs) **[8, 14, 15]**. A useful advantage of insulin pump therapy, is that the bolus dose can be delivered by three different mechanisms:

1. immediately, known as a standard or normal bolus
2. gradually over a certain duration of time, called an extended or square bolus
3. a combination of the previous two, known as a combo or dual wave bolus

Foods that are higher in fat, as observed in traditional *Iftar* meals, may need an extended or combination bolus to compensate for the delay in the rise of blood glucose due to the high levels of fat in the meal **[64]**.

Bolus calculators, either on insulin pumps or through mobile phone applications, for MDI users can be a useful tool in determining any corrections to dosing. Their **use is associated with improved glycaemic control in individuals with T1D** and should be encouraged for all **[65]**.

BASAL INSULIN	BOLUS INSULIN
Reduce basal insulin by 20-35% in the last 4-5 hours before *Iftar* Increase dose by 10-30% after *Iftar* up to midnight	Prandial insulin bolus is calculated based on usual ICR and insulin sensitivity factor

NOTES ON BOLUS INSULIN:

- Bolus doses on insulin can be delivered in three different patterns:
  - Immediately, knows as standard or normal bolus
  - Slowly over a certain period of time (extended or square bolus)
  - A combination of the two, a combo or dual wave bolus
- Meals higher in fat content may need an extended or combo bolus as the rise in glucose following the meal will be delayed by the fat content
- It is recommended to use bolus calculators in determining carbohydrate and correction dosing to avoid insulin stacking and hypoglycaemia

FIGURE 3
Highlights the different recommendations for adolescents with T1DM on insulin pump therapy

An individualised approach is essential for treatment adjustment according to a patient's SMBG or CGM data.

1.7.5 Sensor-augmented pumps: Low-glucose suspend (LGS) and Predictive low-glucose insulin-suspend (PLGS) pumps

Studies from Benbarka *et al*. and Khalil *et al*. both reported encouraging experiences with insulin pumps augmented by CGM during Ramadan **[47, 66]**. The advent of the Low Glucose Suspend (LGS) function, has allowed insulin to be automatically suspended for up to 2 hours when sensors detect a fall in glucose levels below a pre-set threshold **[67]**. Elbarbary investigated the LGS algorithm using insulin pumps in adolescents with T1DM during Ramadan and observed significant reductions in the exposure to hypoglycaemia which enabled individuals to fast through the whole month without interruption due to complications **[14]**.

More recently, Predictive Low Glucose Suspend (PLGS) pumps have the ability to suspend insulin administration before blood glucose reaches hypoglycaemic values **[68]**. In two-cases, PLGS insulin suspension was associated with a significant reduction in the number of hypoglycaemic events with no serious adverse effects in adolescents with T1DM. In addition, other promising results include a significant reduction in the time spent below a glucose

level of 70 mg/dL (3.9 mmol/L), an increase in the time spent within target levels, no severe hypoglycaemic or DKA events, and everybody keeping their fast **[69]**.

The results from these case reports are encouraging in that they point towards the ability to safely fast using advanced insulin delivering technology. Importantly similar studies using a larger sample size are needed to confirm these findings.

TABLE 5: **A REVIEW OF STUDIES THAT HAVE EVALUATED THE USE OF INSULIN PUMP THERAPY IN ADOLESCENTS WITH T1DM WHEN FASTING DURING RAMADAN**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
1. Insulin pump	A Hawli (2009) **[70]**	N=5 Observational study Country: Lebanon	No cases of severe hypoglycaemia	Blood glucose concentrations did not change significantly when fasting	No statistically significant change of mean (HbA1c) before or at the end of Ramadan	Patients on an insulin pump regimen were able to fast during Ramadan without severe complications
1. Insulin pump With low glucose suspend (LGS)	Elbarbary (2016) **[14]**	N=60 Prospective observational study Mean age 15.6 ± 2.7 years Country: Egypt Split into two groups where some had the LGS function on (N=25) and the rest had the LGS function off (N= 35)	A total of 2716 LGS alerts occurred with 48.6% coming between 4pm and 7pm. The mean duration of LGS events was 26.5 min, 38% lasted for <5 min and 5.3% lasted for 120 min. LGS usage showed a meaningful reduction p<0.001	No episodes of severe hyperglycaemia occurred LGS usage showed a meaningful reduction p=0.006	No statistically significant changes in the mean HbA1c% 7.5±0.67 vs. in either group	LGS significantly reduced exposure to hypoglycaemia No patients in the LGS on group broke their fast whereas 15 did in the LGS off group Regimen proposal to adjust insulin pump during fasting

Automated insulin delivery (closed loop)

Automated insulin delivery (closed loop) not only suspends insulin delivery but can also increase insulin delivery based on its sensor glucose values. These systems improve the time in range (TIR), including minimising hypoglycaemia and hyperglycaemia **[71, 72]** . Though commercial availability remains limited, access to these systems is anticipated to improve and, therefore, increasing the ability to safely fast during Ramadan for adolescents with T1DM.

Hybrid closed-loop automated insulin delivery systems have also been of benefit to people with T1DM. Do-It-Yourself Artificial Pancreas Systems (DIY APS) are a form of hybrid closed-loop systems that use open-source algorithms, which determine the delivery of insulin in response to IG levels and other individually personalised variables. In a recent report, a T1DM patient shared her experience of using a Do-It-Yourself Artificial Pancreas System (DIY APS) during Ramadan fasting. There were reported benefits to her quality of life and her ability to self-manage diabetes **[73]**.

On the whole, the need for flexibility and customisability for a fasting person with T1DM make Hybrid closed-loop automated insulin delivery systems a good option.

Insulin pump therapy or basal-bolus regimens?

There have been several studies conducted in the literature that have investigated the use of insulin pump therapy and basal-bolus treatment regimens during Ramadan (see **Table 6**). Some of these studies have found favourable outcomes in individuals using insulin pump therapy compared to those using basal-bolus regimens. Al-Agha *et al*. were able to show that pump therapy was associated with a lower likelihood of breaking the fast due to complications of hypoglycaemia during Ramadan (p=0.03). They also highlighted that the use of FMGS is important for safe fast in adolescents **[24]**. Likewise, in an earlier study Bin-Abbas found that the ability to use the LGS function in insulin pumps were very helpful towards achieving fewer hypoglycaemic events than compared to those on conventional insulin. It was also shown that conventional insulin users were more likely to break their and had poorer glycaemic control **[11]**. Interestingly, in contrast to these findings Deeb *et al*. found no difference between MDI and insulin pumps with regards to hypoglycaemia, hyperglycaemia or glycaemic control **[6]**.

The general outlook in the literature is that insulin pump technology seems extremely promising but greater research is needed before direct recommendations can be made. More randomised trials powered to detect differences between insulin pump therapy and basal-bolus regimens are needed. In addition, there remains the issue of access with regards to technology; for many, insulin pump therapy may not be available or even appropriate. So as mentioned, the recommendations need to place an emphasis on individualisation.

TABLE 6: **A REVIEW OF STUDIES THAT HAVE EVALUATED THE USE OF INSULIN PUMP THERAPY AND BASAL-BOLUS REGIMENS IN ADOLESCENTS WITH T1DM WHEN FASTING DURING RAMADAN**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
1. Insulin pump 2. MDI	Deeb *et al.* (2017) **[6]**	N=65 Observational study Median age 14.5 years (range 10.2-18.9) Two groups based on regimen (27 MDI; 38 Insulin pump) Country: UAE	No real difference was observed between both groups for the number of severe episodes of hypoglycaemia	No real difference was observed between both groups for the number of severe episodes of hyperglycaemia	There were not any notable changes to HbA1c levels	The use of an insulin pump does not appear to be different from MDI in the frequency of occurrence of complications The majority of adolescents with T1DM were able to fast during Ramadan with 57% fasting more than 14 days
1. Insulin pump 2. Conventional Insulin (CI) BID Regimen	Bin-Abbas (2008) **[11]**	N=9 Observational Ages ranged from (15-19 years) Country: KSA Two groups based on regimen (Insulin pump N=5; CI N=4)	Events counted per patient per Month: More events with BID than with insulin pump 29 and 16 respectively p<0.002 Three adolescents on CI therapy had to break their fast because of hypoglycaemia. None of the insulin pump group broke their fast	The mean blood glucose was lower in the insulin pump group compared to in the CI group (123 mg/dL or 6.8 mmol/L; 192 mg/dL or 10.7 mmol/L respectively) P<0.001	Mean HbA1c was lower in those using the insulin Pump compared to those on BID, 7.8% and 9.1% respectively p<0.001	A reduction of 10-15% of basal insulin in patients with an insulin pump was used A suspension of the insulin pump can be carried out to avoid hypoglycaemia Those on a CI regimen were more likely to break their fast, however it was noticed that adolescents may find it difficult to break their fast even if they do feel unwell

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TABLE 6: **A REVIEW OF STUDIES THAT HAVE EVALUATED THE USE OF INSULIN PUMP THERAPY AND BASAL-BOLUS REGIMENS IN ADOLESCENTS WITH T1DM WHEN FASTING DURING RAMADAN**

Insulin Regimen	Author(date)	Sample size and study details	Findings related to Hypoglycaemia	Findings related to Hyperglycaemia	Findings related to Glycaemic control	Key Findings
1. MDI 2. Insulin pump (All used FGMS)	Al-Agha *et al.* (2017) **[24]**	N=51 Prospective cohort study Mean age: 14.2 ±2.6 years Two groups based on regimen (33 MDI; 18 Insulin pump) Country: Kingdom of Saudi Arabia	In all: patients broke their fast on 33% of total fasting days – hypoglycaemia was the reason 15.4% of the time The mean number of hypoglycaemic episodes, during fasting hours, per day was 0.56 compared to 0.18 non-fasting hours p=0.0001 10% of these episodes were asymptomatic The percentage of patients that broke their fast due to hypoglycaemia were lower in those using an insulin pump compared to MDI; 41.9% and 60.9% respectively; p=0.03 No severe hypoglycaemia	The mean number of hyperglycaemic episodes during fasting hours was 1.24 per day, which was higher than that of during non-fasting hours 0.7; p=0.0001	There were not any notable changes to HbA1c levels	It was found that there was some evidence of an association between type of treatment and hypoglycaemia as the reason for breaking the fast. Pump users were less likely to break their fast than insulin users due to hypoglycaemia FGMS can be successfully used in adolescents with T1DM

- **CSII therapy can be used safely and effectively in adolescents with T1DM during Ramadan to facilitate safe fasting.**
- **LGS and PLGS systems can reduce both the severity and duration of hypoglycaemia when fasting.**
- **Utilising bolus calculators with different types of bolus delivery can be useful for adjusting post-prandial insulin doses with different meal contents.**

1.8 Management of adults with T1DM during Ramadan

Differences arise in the monitoring and adjustments in the dosing of insulin in adults with T1DM wishing to fast during Ramadan. The individual needs of individuals and the subsequent type of insulin regimens dictate the different recommendations for dose adjustments and blood glucose monitoring.

1.8.1 Basal-bolus regimen (MDI)

Those adults that are fasting during Ramadan and under a basal bolus or an MDI regimen with analogue or conventional insulin are advised to self-monitor using a 7-point glucose monitoring method – a check of blood glucose levels when fasting; post-breakfast; pre-lunch; post-lunch; pre-dinner; post dinner; and midnight. Doses of long acting insulins such as **glargine** or **Degludec** should be advised to reduce their dose by 30-40% and take the dose at *Iftar*. The dose of the rapid acting analogue should remain the same around *Iftar*, unless a reduction is warranted based on the 2-hour post-*Iftar* blood glucose levels, and the dose at *Suhoor* may be reduced by 30-50%. The use of short acting insulin analogues (glulisine, lispro, or aspart) were found to be associated with fewer hypoglycaemic events and an improvement in postprandial glycaemia when compared to regular insulin in a randomised control trial among adults with T1DM that were fasting during Ramadan **[10]**.

1.8.2 Premixed insulins

As was the case in adolescents, the use of premixed insulin is not advised. Adults should be shifted onto a basal bolus regimen with either conventional or analogue insulins **a few months prior to Ramadan**. However, those that insist on continuing on with a premixed insulin regimen can be allowed to do so with proper adjustment and blood glucose monitoring **(see Table 7)**. The pre-Ramadan dose of morning insulin may be shifted to the dose of the pre-*Iftar* and 50% of the pre-Ramadan evening dose can be shifted to the pre-*Suhoor* dose.

1.8.3 Continuous subcutaneous insulin infusion pump (CSII)

Those on insulin pump or CSII regimens should be advised to reduce the dose of basal insulin by 20-40% in the final 3-4 hours of their fast and increase their basal dose by 10-30% in the first few hours of *Iftar*. The dose of bolus insulin has to be adjusted on the same principles of carbohydrate counting as during the other times (see **1.6 Nutritional care and meal planning for people with T1DM during Ramadan**). The benefits of CSII have been summarised in **section 1.7.4 Continuous subcutaneous insulin infusion pump (CSII)**.

These findings are summarised in Table 7 (see **Table 7**).

TABLE 7: **RECOMMENDATIONS FOR INSULIN DOSE ADJUSTMENTS BASED ON TYPE OF REGIMEN**

Type of Insulin Regimen	Adjustment for fasting during Ramadan	Methods of monitoring during Ramadan
CSII / Insulin Pump	Basal rate adjustment o 20-40% decrease for the last 3-4 hours of fast o 10-30% increase for the first few hours after *Iftar* Bolus doses o Same principles as prior to Ramadan	**CGM**
MDI (basal bolus) with analogue insulin	Basal insulin o 30-40% reduction in dose and to be taken at *Iftar* Rapid Analogue Insulin o Dose at *Suhoor* to be reduced by 30-50% o Pre-lunch dose to be skipped o The dose around *Iftar* to be adjusted based on the 2-hour post-*Iftar* glucose reading	**7-point glucose monitoring**
MDI (Basal bolus) with conventional insulin	NPH insulin o The usual pre-Ramadan morning dose to be taken in the evening during Ramadan o 50% of the pre-Ramadan dose to be taken at *Suhoor* Regular insulin o Dose at evening meal remains unchanged o *Suhoor* dose to be 50% of the pre-Ramadan evening dose o Afternoon dose to be skipped	**7-point blood glucose monitoring or 2-3 staggered readings throughout the day**
Premixed (analogue or conventional)	o Shift the usual pre-Ramadan morning dose to *Iftar* o 50% of the pre-Ramadan evening dose at *Suhoor*	**At least 2-3 daily readings and whenever any hypoglycaemic symptoms develop**

1.9 When to break the fast during Ramadan – all people with T1DM

In general, it should be recommended that all people with T1DM fasting during Ramadan monitor their blood glucose levels closely and carefully.

ALL INDIVIDUALS SHOULD BREAK THEIR FAST IF:

- **Blood glucose <70 mg/dL (3.9 mmol/L)**
  – re-check within 1 h if blood glucose 70-90 mg/dL (3.9 - 5.0 mmol/L)
- **Blood glucose >300 mg/dL (16.7 mmol/L)****
- **Symptoms of hypoglycaemia or acute illness occur**

** In people with previously well controlled diabetes, these targets can be adapted and individualised.

SUMMARY

- Fasting Ramadan for people with T1DM is generally associated with a high risk of hypoglycaemia and hyperglycaemia.
- With well-structured pre-Ramadan education programmes, the risks of fasting can be reduced, and suitable individuals can be allowed to fast under strict monitoring and after appropriate insulin dose adjustments.
- Approaches to treatment adjustments should be individualised. The following should be considered: pre-Ramadan diabetes control; previous Ramadan experience; availability of recourses; the level of education; and the motivation for self-care.
- Different demographic characteristics affecting duration of fast, access to insulin and glucose monitoring must be considered in any risk assessment for the safety fasting.
- Insulin analogues are preferred over conventional insulin regimens if fasting is considered.
- Frequent SMBG is essential and if feasible, through CGM or FGM.
- Advanced insulin technology seems very promising in allowing for safe fasting.
- There is a lack of research and guidance for adults with T1DM that are seeking to fast during Ramadan and further research needs to be conducted in this age group.
- Overall, further research, including randomised clinical trials, are needed to assess clinical outcomes during fasting in Ramadan to help produce the best treatment options for adolescents and adults with T1DM.

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