

Ramadan Fasting and Diabetes in Adolescents and Children: A Narrative Review

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Abstract

Although children in general and patients with type 1 diabetes mellitus, in particular, are exempted from fasting during Ramadan, many elect to observe the fast. There is a sizeable amount of opinion and research data that warrants revisiting. This is a narrative nonsystematic review to explore the views and supporting data on Ramadan fasting and to examine the safety of fasting and its impact on diabetes control and management in children and adolescents. The key areas covered include epidemiology, the physiology of fasting, risk stratification, counseling strategy, nutrition advice, insulin therapy adjustment with a particular focus on multiple injection regimen, and insulin pump therapy. Findings from various studies and expert opinions were appraised and presented to illustrate points of agreements and differences. This review should enhance knowledge and form the basis to clear some doubts and differences of opinions surrounding the issue of diabetes and Ramadan fasting in young people. It should also empower healthcare professionals to develop consensus based on the most up-to-date advice and the best possible support to patients and families regarding fasting during Ramadan.

Keywords: Adolescents, children, diet, fasting, hyperglycemia, hypoglycemia, insulin, metabolism, Ramadan, technology, type 1 diabetes

INTRODUCTION

Ramadan fasting is one of the cardinal articles of Islam commonly known as “the five Pillars of Islam”.^[1,2] Fasting is obligatory for all healthy adult and adolescent Muslims.^[1,2] Fasting is ordained from the time of completing the puberty which varies from 12 to 16 years of age. Fasting starts from early dawn (*Sohur*) to sunset (*Iftar*). During this period, a fasting person has to abstain from eating and drinking. Islam has allowed many categories of people to be exempted from fasting, for example, prepubertal children, travelers, the sick, the elderly, pregnant, and lactating women and individuals with chronic illnesses such as type 1 diabetes mellitus (T1DM).

Sick individuals and children are exempted from fasting Ramadan. However, many patients insist on following the fast, often without the approval of their physicians.^[3,4] Ramadan fasting represents a significant shift in meal timing and content for practicing Muslims. This naturally affects the bodily homeostasis, metabolic environment, fluid balance, and interaction of foods, drugs, and disease.

Fasting by T1DM patients might predispose to acute complications due to the loss of fine balance between insulin action and carbohydrate supply in different directions in the two different times of the fasting cycle.^[5] The global literature production on health aspects of Ramadan fasting is notably relatively low in general as shown in recent review of the whole of publications in one year (2017)^[6]. Similarly, a more focused recent bibliometric analysis quantified the global production on Ramadan and diabetes over the last three decades also showed a low volume of scholarly work.^[7] There are several review articles and clinical practice guidelines in general with a predictable emphasis on adults.^[8-12] However, there are no comprehensive guidelines specifically addressing

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fasting safety or its impact on diabetes control in children and adolescents. Hence, we aimed to undertake this comprehensive review to narrate the available evidence and expert opinion thematically. This exercise may be particularly useful to inform discussion groups aiming to develop guidelines about this particular high-risk group.

METHODOLOGY

This is a narrative, nonsystematic review to explore the impact and management of adolescents and children with diabetes during Ramadan fasting. A literature search was conducted using two online databases (PubMed and Google Scholar) with the following search terms: “Diabetes,” “Ramadan fasting” and “adolescents” and “children” in various combinations. Retrieved records were reviewed and summarized primarily by SAB and AMH with additional contribution from all authors. All types of articles were included in the review process with no regard to the type of the study. The article aimed to explore the impact and management of fasting on adolescents and children with diabetes during Ramadan. The manuscript was developed and revised through several rounds of multilateral electronic communications. No statistical analysis was performed on the original data. All authors approved the final version.

EMERGING CONCEPTS

The key areas covered include safety of Ramadan fasting, risk stratification, management strategy, nutritional advice, insulin therapy adjustment with a particular focus on T1DM patients on multi-dose insulin injections or insulin pump therapy and conventional monitoring methods. The findings are presented thematically.

Should type 1 diabetes mellitus fast in Ramadan?

There is a striking difference of opinion between experts regarding the appropriateness, feasibility, and safety of fasting by adolescents with diabetes. Many experts are of the view that patients with T1DM who fast during Ramadan are at a very high risk to develop adverse events, and accordingly, they should be advised to make use of the religious allowance or “Fatwah’s” that they should not fast at all based on the Islamic Fiqh Academy^[2,10,11] or The Mufti of Egypt.^[12] This group warns that the risks of diabetic ketoacidosis (DKA), severe hypoglycemia, hyperglycemia, dehydration, and thrombotic episodes are increased. Lack of proper prefast assessment, management, and diabetes education have been stumbling blocks in facilitating Ramadan fasting in T1DM patients in general.^[13]

On the other hand, some experienced physicians believe that fasting during Ramadan is safe for T1DM patients, including adolescents and older children, with good glycemic control who can do regular self-monitoring and are under close professional supervision.^[14] The strategies to ensure the safety of T1DM adolescents who are planning to fast include the following: Ramadan-focused medical education, pre-Ramadan medical assessment, following a healthy diet and

physical activity pattern, modification in insulin regimen, and blood glucose (BG) monitoring as advised by the physician. Some experts uphold the opinion that recent studies have demonstrated that individuals with T1DM who are otherwise healthy and stable, provided enough evidence that they can fast during Ramadan if they comply with the Ramadan focused management plan and are under close professional supervision. Mohsin *et al.* elaborated how to assess, counsel, monitor, and manage people with T1DM who wish to fast during Ramadan.^[15]

Physiology of fasting in children and adolescents

Several studies focused on the changes in glucose homeostasis during Ramadan fasting.^[16-22] The salient findings are summarized in Table 1. It is noteworthy that some of these studies were mixed or conducted in adults; however, they remain valuable for the present discussion. The collective aims of these studies were to establish the BG patterns, variability and timing, and risk of hypoglycemia and hyperglycemia [Table 1]. However, the studied groups of patients were far from homogeneous in age, metabolic status, and therapeutic regimens. A typical plasma glucose curve during Ramadan has been illustrated using flash glucose monitoring (FGM) and continuous glucose monitoring (CGM) methodology. BG rises predictably and invariably after the first evening meal to variable durations, mounts a smaller postprandial rise after the predawn meal and demonstrates a progressive declining leading to the end of the fasting period [Figure 1].^[20] However, it is the order of magnitude of these changes in relationship to meals and medications that has been the focus of the management maneuvers.

The ability and safety of fasting during Ramadan in adolescents with T1DM was investigated by Kaplan and Afandi using CGM in 21 adolescents (mean age 15 ± 4 years) who had diabetes for 6 ± 3 years.^[18] Patients adjusted the pump basal rate according to the eating pattern during Ramadan. The averages of all daily readings were calculated to express the BG values every 5 min and the values during fasting and eating hours were compared. Eighteen were on the insulin pump, and three were on MDI regimen using insulin analogs. Patients were able to fast on 85% of the potential days, and 76% could fast 25 days or more. No severe hypoglycemia, DKA, or emergency room visits were reported. The average BG during fasting was predictably lower than that during the eating hours. Hypoglycemia and hyperglycemia were observed in 16.7% and 29.3% of the 24-h CGM readings, respectively. Hypoglycemia occurred more during fasting hours than the eating hours (14.2% vs. 2.5%, $P < 0.05$), whereas hyperglycemia was observed more often in the eating than in fasting hours (17% vs. 12%, $P < 0.05$). A wide BG fluctuation during fasting and eating hours and some episodes of unreported hypoglycemia were noted in the CGM data. The authors asserted that frequent BG monitoring is essential to recognize the incidence of hypoglycemia and take the proper action to control it. Furthermore, El-Hawary *et al.* compared three insulin regimens (regular insulin/NPH, regular insulin/

Table 1: Studies providing insights into glucose and metabolic homeostasis during and around Ramadan fasting during different modalities of monitoring

References	Authors	Methodology; sample size)	Conclusions
[16]	Lessan <i>et al.</i>	CGM; 63 (DM 56; 7 healthy)	The main change in glycemic control with Ramadan fasting in patients with diabetes is in the pattern of excursions
[17,18]	Afandi <i>et al.</i> , Kaplan and Afandi	CGM; 21: Ramadan versus pre-Ramadan	There was wide BG fluctuation during fasting and eating hours, with significant periods of unrecognized hypoglycemia during fasting and correlation between pre-Ramadan glycemic control and subsequent glucose fluctuation during fasting in adolescents with T1DM
[19]	El-Hawary <i>et al.</i>	Fructosamine; CBG; 53	Fasting during Ramadan is feasible and is associated with significant improvement in fructosamine level in children with T1DM using different insulin regimens
[20]	Beshyah <i>et al.</i>	FGM (8 mixed)	Comprehensive demonstration of glucose changes. The visually illustrated data give insights into glucose homeostasis in diabetes and related disorders throughout whole day of Ramadan
[21]	Pallayova <i>et al.</i>	Mixed study CGM and CBG (18 nondiabetic)	Glucose exposure and variability increased after Ramadan in nondiabetic adults. Physiological glucose response to dietary patterns was not clinically relevant
[22]	Musleh <i>et al.</i>	CBG (23 T1DM on either MDI or CSII)	Adolescents with T1DM wishing to fast during Ramadan may contemplate this under medical supervision. Use of insulin pump may help patients to fast. Adequate education and good glycemic control prior to Ramadan is associated with better outcome during Ramadan

BG: Blood glucose, DM: Diabetes mellitus, T1DM: Type 1 diabetes mellitus, MDI: Multi-dose injection, CSII: Continuous subcutaneous insulin infusion, FGM: Flash glucose monitoring, CBG: Capillary BG, CGM: Continuous glucose monitoring

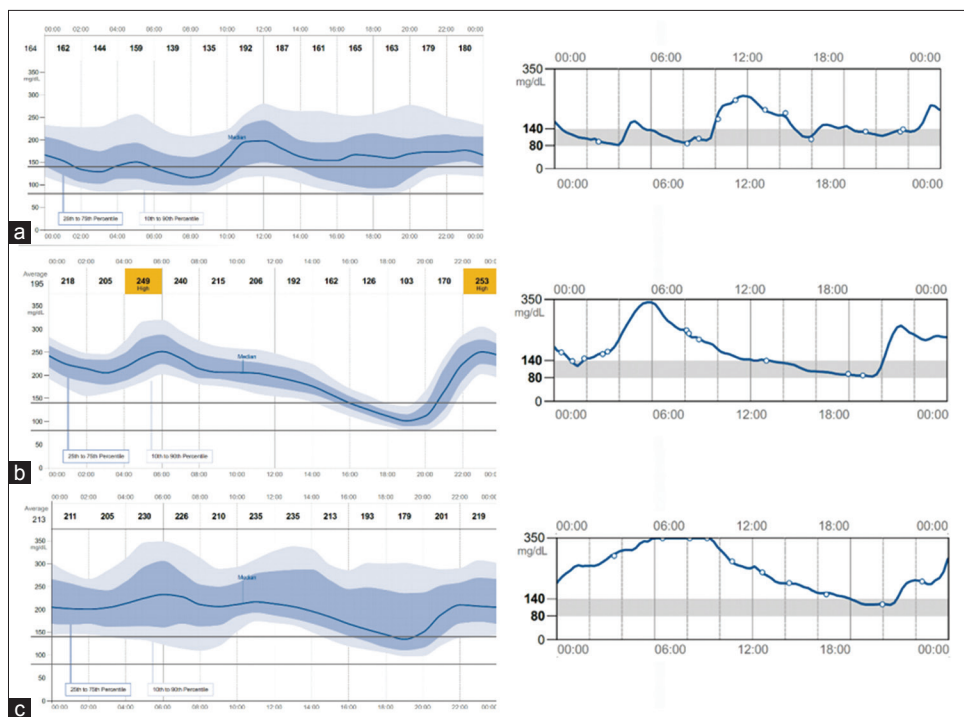


Figure 1: The contrasting metabolic environments reflected in plasma glucose levels before Ramadan (a), during Ramadan fasting (b) and after Ramadan fasting (c) illustrated by ambulatory glucose profile on the left and a representative single day curve of interstitial glucose levels using Flash Glucose Monitoring technology of Free Style Libre (Abbotts). Redrawn from Beshyah *et al.* (ref 20)

insulin glargine, and premixed insulin) in 53 children.^[19] They were recruited 3 months before Ramadan and were provided with intensive education; 28 completed the fasting. A significant drop in post-Ramadan fructosamine ($P < 0.001$) was observed. BG at three-time points, pre-*Iftar*, pre-*Sohur*, and mid-day were higher in the first insulin regimen compared to the other two ($P = 0.004$). Similarly, Musleh *et al.* prospectively

observed 21 T1DM adolescents (median age 14 years).^[22] The fasting days, the reasons for not fasting were noted, and BG and insulin doses were recorded in specially prepared dairies. Patients were able to fast 80% of the total possible days. The reasons for not fasting were hypoglycemia (29%), hyperglycemia (19%), or other reasons (52%). There was a minimal increment in the mean glycated hemoglobin (HbA1c)

after Ramadan (from 8.3% to 8.5%) but none of the participants developed severe hypoglycemia or DKA. Although this was a small study, those on insulin pump managed to fast more days (82.8% vs. 77.3%). Afandi *et al.* related the CGM data during fasting in 21 adolescents (15 ± 4 years), with T1DM for 6 ± 3 years, to their preRamadan diabetes control. They used CGM during fasting for a minimum of 3 days. Hypoglycemia, hyperglycemia, and severe hyperglycemia were captured. Patients were categorized as well-controlled, or poorly controlled according to the prefasting HbA1c ($\leq 8\%$ or $>8\%$, respectively). The percentages of hypoglycemia, hyperglycemia, and severe hyperglycemia were significantly higher in the poorly controlled group, whereas a higher percentage of normoglycemia was evident in the well-controlled group. The overall duration of hypoglycemia, hyperglycemia, and severe hyperglycemia in the poorly controlled group were longer than in the controlled group. In another study, glycemic excursions during Ramadan fasting were evaluated by Lessan *et al.* who investigated the short-term safety of this practice in different groups of patients with diabetes.^[16] CGM was performed before, during, and after Ramadan fasting in 56 patients with diabetes and 7 healthy volunteers. There was a significant difference in mean CGM curves during Ramadan in patients with diabetes showing a slow fall during fasting hours followed by a rapid rise in glucose level after *iftar*. The magnitude of this excursion was the greatest in the insulin-treated group. Pallayova *et al.* also using CGM studied the physiological effects of Ramadan fasting in young nondiabetic adults.^[21] CGM was captured before, in the middle, and after Ramadan to assess glucose exposure and variability. A large number of data points were obtained from 18 nonobese nondiabetic young adults. The CGM profiles showed an increase in the hyperglycemic area under the curve (AUC)^[17] after Ramadan compared to both before ($P = 0.004$) and during Ramadan ($P = 0.003$), along with an increased glucose variability after Ramadan ($P = 0.014$).

Attitude, complications, and ability to fast

The attitude toward fasting, frequency of complications, and impact on glycemic control were investigated in 65 children with T1DM.^[23] Questionnaires were filled, HbA1c levels were recorded, and log books indicating symptomatic hypoglycemia and hyperglycemia leading to breaking fast were obtained. Majority of patients were willing to fast, and 75% were encouraged by parents to do so; 57% and 26% fasted more than half and all of the month, respectively. Just over half (52%) had at least one episode of hypoglycemia, 29% had hyperglycemia, and one episode of ketoacidosis occurred. All patients broke fast in response to symptomatic hypoglycemia/hyperglycemia. The authors reported no significant difference in the frequency of complications between the pump or the multiple daily injection (MDI) groups. The mean HbA1c increased from 8.6% to 8.8%, but the difference was not statistically significant.

Diabetes self-management education for Ramadan

Eid *et al.* evaluated the feasibility of promoting safe Ramadan fasting through diabetes self-management education (DSME)

and determined the effect of such education on hypoglycemic episodes.^[24] The DSME sessions started 2–3 weeks before Ramadan and included one experimental fasting day during the 1st week and one during the 2nd week. Participants' HbA1c, serum fructosamine levels, and self-monitoring of BG (SMBG) logs were collected. Two-thirds of the 21 participants who were intending to fast completed the program. Their mean HbA1c was $6.7 \pm 1.6\%$, and SMBG results showed no significant difference in mean BG levels before and after Ramadan. Serum fructosamine after Ramadan decreased by 10%. The mean number of hypoglycemic events before Ramadan decreased in Ramadan. Differences between Group 1 (those without hypoglycemia, $n = 8$) and Group 2 (those with hypoglycemia, $n = 6$) were not significant for all three variables.

Dietary habits and nutrients intake

The effects of fasting on the dietary habits and nutrients intake were examined in 54 adolescents (13–18 years old) with T1DM who were permitted by their physicians to fast and had no medical complications.^[25] They were evaluated before, during, and after Ramadan. The participants fasted a mean of 21.7 days, had 0.45 kg weight loss, and their energy and macronutrients intake increased significantly during Ramadan. The authors concluded that changes in lifestyle, physical activity, and dietary pattern are characteristics of the month of Ramadan and these affect both diabetic and nondiabetic participants. They emphasized that adherence of adolescents with T1DM to dietary and nutritional guidelines are vital but may sometimes be difficult to attain and maintain.

Safety of fasting during Ramadan in adolescents with diabetes

In addition to the above studies, Zabeen *et al.*^[26] evaluated the safety of fasting in 33 children and adolescents with T1DM in a prospective observational study. Patients with their caregivers received intensive education and instructions were provided by diabetic educators, dieticians, and physicians on insulin adjustment, home BG monitoring and dietary adjustments before Ramadan. The majority (60.6%) of the youngsters were able to complete their fasting during Ramadan. Two groups were examined, i.e. those who completed fasting versus patients who broke the fast. BG, HbA1c, body weight, and insulin dose before and after Ramadan in the two groups showed no significant difference. Hence, the authors concluded that children older than 11 years of age with T1DM on conventional twice-a-day regimen could fast safely during Ramadan provided they receive proper prefasting education and intensive follow-up.

Diabetic ketoacidosis

A critical appraisal of the literature noted that the increased risk of DKA has been suggested in the older writings and reiterated ever since.^[27] The authors suggested that from physiological principles, DKA is not readily precipitated by the “stress-free” metabolic environment associated with Ramadan fasting with the exception of cases involved in classical risk factors for metabolic decompensation. Furthermore, recent

studies could not document any increase in observed DKA during Ramadan fasting in retrospective, prospective, and database reviews. However, no age-based subgroup analysis was included in the review^[27] nor in the recent series.^[28] Future analyses should consider the data on an age basis. Isolated case reports include a 15-year-old Muslim boy with T1DM who presented with DKA during the day-time fasting of Ramadan month when DKA occurred due to omitting pre-lunch insulin combined with dehydration and overeating during the permitted sunset-to-sunrise time.^[29] Furthermore, a case euglycemic DKA was reported in newly diagnosed T1DM of 14 years old boy due to starvation during Ramadan fasting.^[30] The importance of evaluation of acid-base state, urine glucose, and ketone values at in all newly diagnosed T1DM during Ramadan cannot be overemphasized.

Hypoglycemia

Risk of hypoglycemia during Ramadan is a core concern and is discussed in different contexts throughout this review. The frequency, timing, and severity of hypoglycemia were elucidated by Afandi *et al.*^[31] elucidated further in 25 adolescents with T1DM (mean age was 16 ± 3 years) using the FGM system. Differences in percentage and the total duration of hypoglycemia were compared between different times of the day and night related to the eating pattern in Ramadan. The mean glucose level was 11.1 ± 4.7 mmol/L, and the overall time spent in hypoglycemia was $5.7\% \pm 3.0\%$. The average daily time spent in hypoglycemia was 1.39 h per patient. Over two-thirds of hypoglycemia occurred between 11:00–19:00 and similar proportion of hypoglycemia were between 61 and 70 mg/dl. Similar to adults, hypoglycemia remains the most feared complication from fasting in insulin-treated patients. All educational programs must stress the need to stop fasting without delay when hypoglycemia occurs.

Insulin therapy during fasting

Multiple daily injections

A large volume of work has now accumulated on the use of insulin during Ramadan fasting.^[32-36] The published data on insulin therapy using MDI are summarized in Table 2. Al-Khawari *et al.*^[33] examined the ability and safety of fasting in young people with T1DM on multiple injections versus twice-daily premixed insulin regimen.^[33] All patients showed a tendency to high BG at the time of commencing their fast. Those on twice daily insulin continued to have hyperglycemia during the day while those on basal-bolus insulin showed a steady fall in BG toward normal by sunset time. Although there was a greater tendency to hypoglycemia in the basal-bolus group, this was successfully prevented by reducing the dose of basal insulin by 10%–20%. The authors recommend that it is safe for adolescents with diabetes to fast during Ramadan provided they (a) cut their basal insulin by the proposed amount and (b) continue to monitor their BG regularly. Furthermore, Kadiri *et al.* compared insulin lispro with regular human insulin concerning BG control and frequency of hypoglycemia in patients with T1DM who wished to fast during the month of

Ramadan.^[34] Insulin lispro or regular human insulin was given together with NPH insulin, twice daily before the morning and evening meals, for 2 weeks each in an open-label, randomized, cross-over design, and 64 patients completed the protocol. SMBG was undertaken in the morning and evening, and 1 h and 2 h after the post-*Iftar* on three consecutive days at the end of each treatment period. The 2-h BG excursion after the postsunset meal was significantly lower with insulin lispro than with regular human insulin. Daily insulin doses did not differ between treatments but compliance with a recommended time of injection was better with insulin lispro. Hypoglycemia incidence (23% of patients on insulin lispro vs. 32% of patients on regular human insulin, $P = 0.004$). Frequency (expressed as episodes/patient/30 days) was less on insulin lispro than regular human insulin (0.8 vs. 2.3; $P < 0.001$). Both postprandial glycemic excursions and hypoglycemic episodes were better on the insulin analog.

Insulin pump therapy

Several reports on the use of continuous subcutaneous insulin infusion (CSII or insulin pump therapy) during Ramadan fasting were published over the past decade.^[37-42] The published data on insulin pump therapy are summarized in Table 3.

The first report on using insulin pump in children and adolescents with T1DM during Ramadan fasting was by Bin-Abbas from Saudi Arabia in 2008.^[37] Five adolescents on pump therapy showed interest in fasting, their results of BG levels and the rate of hypoglycemic episodes were compared with four adolescents on conventional insulin therapy. Although a small study, the authors claimed significantly lower levels of HbA1c and lower risks of hypoglycemia. Furthermore, early work by Hawli *et al.*^[38] evaluated the need for changes in basal insulin regimen in five patients with T1DM fasting during Ramadan. Patients used regular human insulin were appropriately instructed to break the fast after any episode of hypoglycemia, severe hyperglycemia, or any hyperglycemia associated with ketonuria. BG concentrations did not change significantly with fasting. SMBG decreased at 4 p.m. and increased in the evening and morning (10 p.m. and 8 a.m., respectively). Furthermore, the basal insulin requirement decreased in four patients during the fast. No cases of DKA or severe hypoglycemia were reported. Benbarka *et al.*^[39] reported their experience with insulin pumps during Ramadan in 63 adolescents and young adults with T1DM who were using insulin pump for 20 ± 10 months. Forty-nine (22 ± 7 years) fasted, and 14 elected not to fast. Patients who fasted have diabetes for 9.6 ± 5.6 years, and 39 of them fasted the whole month with no problems. Nearly half of the patients decreased their basal insulin by 5%–50% of their pre-fasting doses; 17 patients had nonsevere hypoglycemia requiring breaking the fast. Unusual hyperglycemia was reported in 9 patients (18.4%).^[39] Twelve patients had fructosamine levels measured both before and immediately after Ramadan and showed postfasting improvement (4.0 ± 0.6 – 3.6 ± 0.6 mmol/L. $P = 0.007$). The same group reported a similar study with the additional use of CGM augmentation.^[40] They confirmed

Table 2: Summary of the studies observing or investigating multiple daily injection insulin regimens for patients with diabetes who fast during Ramadan

References	Author; patients	Insulin type/regimen	Study design	Observations/conclusions
[32]	Al Alwan and Banyan; 20 (12 only fasted; T1DM)	MDI, one basal and 2 prandial insulins; adjusted from the pre-Ramadan regimen	Observational prospective study	Fasting is feasible for children older than 8 years with long-standing T1DM to safely fast during Ramadan with proper education and follow-up
[33]	Al-Khawari <i>et al.</i> ; 22; T1DM	Intensive MDI (basal-bolus) versus conventional (premixed insulin BID)	Observational, prospective study	It is safe for adolescents with diabetes to fast during Ramadan as long as they reduce their basal insulin by this amount and continue to monitor their BG regularly
[5]	Kassem <i>et al.</i> ; 17; T1DM	Ultralente and regular insulin BID, dose reduced	Open-label interventional study	T1DM patients wishing to fast should be switched to long acting insulin such as ultralente around 85% of their initial insulin dose and it should be composed of around 70% ultralente and 30% rapid insulin, divided equally between <i>Sohur</i> and <i>Iftar</i>
[34]	Kadiri <i>et al.</i> ; 64; T1DM	Insulin lispro versus regular human insulin with NPH insulin, BID	Open-label, randomized, cross over design	Patients with T1DM may be better managed with insulin lispro. Glycemic control, measured by postprandial glycaemic excursions, was improved and hypoglycemia was significantly reduced
[35]	Strich <i>et al.</i> ; 57; T1DM	28 on MDI and 30 on CSII; They halved the basal insulin dose	Observational; TDD was compared in those who completed fasting versus those who broken it	TDD: 0.19±0.16 U/kg in those who completed the fast and 0.34±0.15 U/kg in those who broken it. The recommended TDD during Ramadan fasting is 0.2 U/kg/day
[36]	Kalra; 6; T2DM	IDeg and IDegAsp	Observational study; single center. <i>Suhor</i> dose reduced and <i>Iftar</i> dose increased	IDeg and IDegAsp are effective, safe, and well-tolerated means of achieving glycaemic control in T2DM who fast Ramadan

T1DM: Type 1 diabetes mellitus, T2DM: Type 2 diabetes mellitus, MDI: Multi-dose injection, BG: Blood glucose, TDD: Total daily dose, CSII: Continuous subcutaneous insulin infusion, IDeg: Insulin degludec, IDegAsp: Insulin degludec aspart, BID: Twice daily

that the advantages provided by insulin pump use in patients with diabetes were enhanced by the use of CGM in 21 patients. All fasted for a median of 29 days and adjusted their insulin as per their usual practices. The total insulin administered during Ramadan was not different from that in the pre-Ramadan period, and no major hypoglycemic episodes occurred. More recently, the use of low-glucose suspend (LGS) feature of insulin pumps was shown to reduce exposure to hypoglycemia significantly without compromising safety in 60 patients (aged 15.6 ± 2.7 years).^[41] One group used the sensor with LGS feature, and other turned off LGS feature. The AUC <70, AUC <60 mg/dL ($P = 0.0001$) and >240 mg/dL ($P = 0.006$) were all reduced with the LGS feature. None in the LGS group broke the fast compared to 15 in the second group ($P = 0.001$). No episodes of severe hyperglycemia or DKA were noticed in either group.

Should basal insulin dose be decreased to reduce the risk of hypoglycemia?

Deeb *et al.*^[42] addressed the specific question of whether lowering the basal insulin dose during Ramadan reduces the frequency of symptomatic hypoglycemia as was proposed by previous workers.^[39,40] Seventy-five children and adolescents with T1DM aged 14.5 years intended to fast during Ramadan. The days fasted, hypoglycemia, and basal insulin doses were recorded. Logbooks were examined, and glucometers and insulin pumps were downloaded.

Sixty-eight patients' results were analyzed (41 on pump and 27 on MDI). Mean HbA1c was $7.9 \pm 1.2\%$ and $8.4 \pm 1.3\%$ for the pump and the MDI, respectively ($P = 0.007$). Thirty-nine patients had hypoglycemia leading to breaking fast. The mean number of episodes of breaking fast was 3 (1–8). Thirty-five of the 68 patients had reduced basal insulin. However, there was no significant difference in the frequency of hypoglycemia between those who decreased and those who did not decrease the basal insulin dose ($P < 0.10$). Fifteen patients on MDI and 24 patients on pumps had at least one episode of breaking fast. Six and 18 of the patients on MDI and pumps, respectively, reduced basal insulin ($P > 0.10$).

Multiple daily injections versus insulin pump

The benefits and risks of CSII or MDI in patients with diabetes who fast during Ramadan were examined by two groups recently using systematic review and meta-analysis.^[43,44] Loh *et al.*^[43] pooled data from 17 observational studies involving 1699 patients treated with either CSII or non-CSII regimens. Whereas, Gad *et al.*^[44] assessment included a total of 9 studies. Loh *et al.*^[43] concluded that the CSII regimen had lower rates of severe hypoglycemia and hyperglycemia/ketosis, but a higher rate of nonsevere hyperglycemia than premixed/MDI regimens. They suggested that appropriate patient selection with regular supervised fine-tuning of basal insulin rate with intensive glucose monitoring may mitigate the residual

Table 3: Summary of studies involving insulin pump therapy during Ramadan

References	Authors; patients; location	Study design	Pump adjustments	Outcome
[37]	Bin-Abbas; 9 adolescents; T1DM; KSA	Small case series, uncontrolled, observational (5 on pump; 4 on MDI)	Patients on insulin pump reduced basal rate insulin by 10%-15%; One patient on insulin pump suspend it for 2 h	A significant reduction in HbA1c, mean BG, hypoglycemia on pump in comparison to MDI
[38]	Hawli <i>et al.</i> ; 5 adolescents with T1DM; Lebanon	Using an insulin pump with close SMBG and weekly follow-up with the endocrine team	Basal insulin reduced by 5.5%-25.0% in 4 patients but did not change in 1 patient	Patients were able to fast without DKA or severe hypoglycemia
[39]	Benbarka <i>et al.</i> ; 63 mixed adolescents and adults with T1DM, UAE	Prospective observational, single-center study	Half of patients reduced basal insulin by 5%-50% of prefasting doses; 17 had hypoglycemia requiring breaking the fast	Fasting during Ramadan is feasible in patients with T1DM using an insulin pump, with adequate counseling and support
[40]	Khalil <i>et al.</i> ; 21 mixed adolescents and adults with T1DM, UAE	Prospective observational, single-center study	Total insulin during Ramadan was not different, but basal insulin was reduced in the day by 5%-20% and increased at night	Insulin pump use provides advantages in patients with diabetes that is enhanced by the CGMS
[41]	Elbarbary; 60 T1DM, Egypt	The effect of the LGS algorithm on hypoglycemia during Ramadan	25 used the sensor with LGS feature and 35 used the sensor but turned off the LGS feature	Usage of LGS significantly reduced exposure to hypoglycemia without compromising safety
[42]	Deeb <i>et al.</i> ; 75 T1DM, UAE	Prospective comparison of insulin pump (41) and MDI (27) (log books, pumps and meters were examined)	Basal insulin was reduced during in 65 versus 24 during Ramadan	Hypoglycemia was not different between pumps and MDI. Reducing basal insulin during fasting did not decrease the risk of hypoglycemia

The patients included were children and adolescents exclusively or partially. BG: Blood glucose, T1DM: Type 1 diabetes mellitus, KSA: Kingdom of Saudi Arabia, UAE: United Arab Emirates, MDI: Multi dose injection, LGS: Low-glucose suspend, SMBG: Self-monitoring of BG, DKA: Diabetic ketoacidosis, HbA1c: Glycated hemoglobin, CGMS: Continuous glucose monitoring system

hypoglycemia risk during Ramadan. However, Gad *et al.*^[44] were more conservative and concluded that studies assessing the effect of CSII or MDI in patients with T1DM who fast during Ramadan are limited to observational studies and show no difference in the change in HbA1c, weight, or lipids during Ramadan. The differences in conclusions calls for more carefully conducted prospective studies for head-to-head comparisons.

What is the possible role of newer insulin?

Two groups attempted to answer this question.^[42,43] Although the experience described here was in adult patients, it could be translated to children and adolescents as the agents are used by young patients. Kalra^[36] documented the utility and safety of insulin degludec (IDeg) and insulin degludec aspart (IDegAsp) in persons with type 2 diabetes mellitus (T2DM), observing Ramadan fast. A single-center observational study conducted on six persons who either switched to IDeg or IDegAsp a month before Ramadan or changed the time of administration of IDegAsp at the onset of Ramadan. Participants were kept under regular monitoring and counseled before, during, and after Ramadan. Four persons, who changed from premixed insulin to IDegAsp, experienced a 12%–18% dose reduction after 14 days. At the onset of Ramadan, the *Sohur* dose was reduced by 30%, and this remained unchanged during the fasting month. The *Iftar* dose had to be increased by 4 units. One person

who shifted from NPH to IDeg demonstrated a 25% dose reduction at 20 days, without any further change in insulin requirement during Ramadan. One person who changed the time of injection of IDegAsp from morning to night reported no dose change. No major hypoglycemia was reported. Furthermore, Hassanein *et al.*^[45] compared the efficacy and safety of (IDegAsp and biphasic insulin aspart 30 (BIAsp 30) before, during, and after Ramadan fasting in patients with T2DM in a multinational, randomized, treat-to-target trial, patients with T2DM who intended to fast and were on basal, pre- or self-mixed insulin ± oral antidiabetic drugs for ≥90 days were randomized (1:1) to IDegAsp twice daily (BID) or BIAsp 30 BID. These data suggest that IDeg and IDegAsp are effective, safe, and well-tolerated means of achieving glycemic control in individuals with T2DM who wish to fast. Further studies in young patients with T1DM are needed.

Monitoring of blood glucose during fasting

Capillary blood glucose

Capillary BG remains the most widely used method of monitoring. Pragmatically, measurements during Ramadan is based on the same principles of SMBG outside Ramadan with the times being related to meals and medications with allowance for the difference in the glucose profiles during and outside Ramadan [Figure 1]. To assess the adequacy of postprandial control, readings are recommended 2 h after

Iftar, and for the predawn meal, a measurement on waking up should be enough as some patient go back to sleep after the dawn prayers. To guard against hypoglycemia, testing in the last 2 h of the fasting period is recommended. Additional midday is useful if morning readings were 100–120 mg or when any symptoms of hypoglycemia are experienced or suspected. Several studies used different combinations of all of these which filtered through various recommendations.^[9-12]

Continuous glucose monitoring systems

Kaplan and Afandi^[18] assessed the impact of fasting on interstitial glucose (IG) in adolescents with T1DM using CGM and concluded that adolescents with T1DM have a similar wide fluctuation in IG during fasting in Ramadan as they do outside Ramadan. CGM (minimum 2.5 days) was done on adolescents with T1DM during Ramadan fasting and in the months around Ramadan to compare the differences in mean IG, and in the duration of hypoglycemia, hyperglycemia, and severe hyperglycemia. Fourteen adolescents aged 15 ± 4 years with diabetes for 6 ± 4 years, and mean HbA1c $8.6 \pm 1.1\%$ were studied. No difference in the mean IG or the duration of hypoglycemia, hyperglycemia, and severe hyperglycemia between Ramadan and nonRamadan period.

Using the flash glucose monitoring (FGM), the first comprehensive demonstration of glucose changes during Ramadan fasting using FGM was reported in a small cohort included individuals with different glucose intolerance states.^[20] Also, Al-Agha *et al.*^[46] reported on 51 participants from a pediatric diabetes clinic during Ramadan. They were able to fast for 67.0% of the total days eligible for fasting, whereas they did not fast on 33% of the days due to either hypoglycemia (15.4%) or nondiabetes-related reasons (17.6%). None had severe hypoglycemia or DKA. Estimated HbA1c did not change. Furthermore, Afandi *et al.*^[31] elucidated the frequency, timing, and severity of hypoglycemia in 25 adolescents with T1DM while fasting the month of Ramadan who fasted Ramadan were monitored using the same FGM system. Percentage and the total duration of hypoglycemia were extracted from the FGM downloads, and the differences were compared between different times of the day and night according to the eating pattern 18 in Ramadan. The mean age was 16 ± 3 years, and mean glycated hemoglobin was $8.6\% \pm 1.2\%$, mean glucose level was 200 ± 84 mg/dl (11.1 ± 4.7 mmol/L), and the overall time spent in hypoglycemia was $5.7\% \pm 3.0\%$. The average daily time spent in hypoglycemia was 1.39 h^[19,20] per patient. The incidence of hypoglycemia was 0% from 19:00 to 23:00 p.m. and 69% from 11:00 to 19:00. Analysis of hypoglycemia revealed^[20,21] that 65% was between 61 and 70 mg/dl and 8% lower than 50 mg/dl. As the use of FGM increases, more confidence and perhaps safety may be felt by patients, and more insights into glucose homeostasis at different times of the day during fasting may be gained.

Telemonitoring

Lee *et al.*^[47] evaluated the benefits of a telemonitoring-supplemented focused diabetic education compared with

education alone in participants with T2DM who were fasting during Ramadan. They identified 37 participants and randomly allocated them to either a telemonitoring group or Ramadan-focused preeducation only. The authors observed no significant differences in glycemic control at the end of the study. However, participants viewed telemedicine as a more convenient alternative; although, technological barriers remain a concern.

CONCLUSIONS

Current limitations

Management of adolescents and children with diabetes during Ramadan fasting remains a major bioethical and clinical challenge. Risks may be increased if no proper preRamadan assessment, management, and targeted diabetes education is provided.^[36]

The literature on Ramadan, in general, has for long included less evidence than consensus and too many opinions and less actual evidence.^[48,49] This is possibly more obvious in pediatric than adult practices for various ethical and biological reasons. The volume of current literature on the impact and management of Ramadan fasting in children and adolescents with diabetes is increasing but not large enough to address such an important issue relative to the number of people involved.^[6,7] Some of the conclusions are based on experience with adults and extrapolation to children and adolescents. Available data suggest that Ramadan fasting at this age group may be possible and appears to be safe provided that family and healthcare professionals provide proper education and supervision. However, there is no place for complacency. A sound medical advice should be based on assessment of the person's maturation, status of glycemic control, and individual's ability to undertake self management.

There are several limitations to the Ramadan fasting studies in adolescents and children. The small numbers in many of the studies published so far is a major factor influencing the interpretation of results. It remains a challenge to recruit a "good" number at this age group for ethical, social and pragmatic reasons. This challenge may be overcome by carefully conducted multi-center trials using some of the individuals who choose not to fast as the control group. Such trials should enable assessment of the risks of hypoglycemia and hyperglycemia while using modern technology and newer insulin preparations. Such multicenter studies, if conducted using unified protocols and predetermined outcome measures, should enable pooling of data, take account of all potential confounders and address several questions simultaneously. Furthermore, more comprehensive outcome measures, rather than focusing on hypo and hyperglycemia, need to be included in the evaluation of overall control. Assessments of diabetes-related quality of life targeting detection of fear of hypoglycemia on the one hand compared to the potential for low self-esteem when facing peer-pressure in those who choose not to fast. It is strongly arguable that a single measurement during the fasting month may not be

enough to reflect the whole month. Factors such as lack of knowledge early in Ramadan contrasted with the balance between confidence, experience or complacency in the last few weeks may all be operative. The amount of physical exercise, schooling demands, and sick day rules are different between countries where Ramadan-working hours are applied versus other countries where they are not. The impact of knowledge, attitude, and practices during Ramadan of the treating physicians, diabetes educators, patients and other family members, and interplay thereof must be significant.^[27]

Future directions

Recent developments such as the use of insulin pumps, insulin analogs, and recognition of the importance of structured diabetes education and assessment should help select the patients best suited for the rigors of fasting.^[36] These may alter the traditional approach of doctors toward Ramadan fasting in both adults and adolescents with T1DM. Sophisticated therapeutic options like smart insulins may potentially provide safer and more convenient opportunities for the management of T1DM during Ramadan. Also, other therapies adjuvant to insulin therapy may change the scene.

These challenges cannot be addressed under the current fragmented Ramadan research arrangements mostly driven by personal interest.^[48,49] Furthermore, the required volume and high quality of data cannot be readily collected in busy clinics by otherwise fully committed practicing clinicians. Specifically, research is needed for this high-risk group of children and adolescents as well as other groups such as pregnant women, older adults, and patients with acute, advanced and chronic medical conditions. Funding must be made available for dedicated research fellows working under the guidance of experts to address impartial questions independent of third party agenda. Ramadan research should be identified by academia of Muslim-majority countries as a priority and a prime example of ethnically-sensitive care. Ramadan research should feature in institutional strategic plans rather than left as a marginal subject driven by personal interests.

However, for translation of the findings of research into clinical practice, focused education is needed for patients, physicians, family members, and community leaders. With the management of diabetes during Ramadan fasting in children and adolescents in mind, an online survey of physicians' perceptions and practices in the Arab Society for Pediatric Endocrinology and Diabetes (ASPED) countries revealed gaps in knowledge, perceptions, and practices.^[50] This was not much different from the knowledge gaps found in physicians charged with the care of adults with diabetes detected in a previous survey.^[51] Physicians and their supporting staff need to be ready for the job of dispelling myths, explaining religious rules, advising on lifestyle modifications, and making the necessary changes in medications.^[52,53] This should be provided over and the above the standard diabetes care including support, monitoring, and timely intervention.

Authors' contributions

All authors contributed to the conception, drafting, and revising of the manuscript. They all approved its final version.

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There are no conflicts of interest.

Compliance with ethical principles

Not applicable. No human or animal studies by the authors were reported.

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