

# Use of automated insulin delivery systems in people with type 1 diabetes fasting during Ramadan: An observational study

Ali Aldibbiat<sup>1,2,3\*</sup> , Ahmed Alqashami<sup>4</sup>, Sufyan Hussain<sup>5,6,7</sup> 

<sup>1</sup>Dasman Diabetes Institute, Kuwait City, Kuwait, <sup>2</sup>Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK, <sup>3</sup>Department of Endocrinology, Prime Hospital, Dubai, United Arab Emirates, <sup>4</sup>T1D\_arabic, Riyadh, Saudi Arabia, <sup>5</sup>Department of Diabetes & Endocrinology, Guy's and St Thomas' Hospital NHS Trust, London, UK, <sup>6</sup>Department of Diabetes, School of Life Course Sciences, King's College London, London, UK, and <sup>7</sup>Institute of Diabetes, Endocrinology and Obesity, King's Health Partners, London, UK

## Keywords

Artificial pancreas systems, Fasting, Type 1 diabetes

## \*Correspondence

Ali Aldibbiat  
Tel.: +971-556082349  
Fax: +971-42721549  
E-mail address:  
Ali.Aldibbiat@endocrinehub.net

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## ABSTRACT

Fasting among people with type 1 diabetes imposes the risk of metabolic decompensation. Automated insulin dosing systems can allow better glycemic control without safety concerns. The utility in prolonged and repetitive fasting has not been studied. In this observational study, validated glycemic data were reviewed and analyzed from people with type 1 diabetes who observed fasting during Ramadan in 2019 and 2020 using automated insulin dosing systems. Six profiles met the inclusion criteria. The average age was  $33.7 \pm 4.8$  years, diabetes duration was  $23.5 \pm 7.9$  years, body mass index  $23.6 \pm 1.9$  kg/m<sup>2</sup> and glycated hemoglobin was  $6.3 \pm 0.2\%$  ( $45 \pm 5$  mmol/mol). The average glucose during Ramadan was  $7.0 \pm 0.5$  mmol/L ( $126 \pm 9$  mg/dL), coefficient of variation 28.5%, percentage of time in range 3.9–10 mmol/L ( $70$ – $180$  mg/dL)  $88.8 \pm 7.3\%$  and percentage time  $<3.9$  mmol/L ( $<70.0$  mg/dL)  $2.5 \pm 1.3\%$ . The number of fasting days was  $27.3 \pm 3.3$ , and the number of days where fasting was broken due diabetes was  $1 \pm 1.5$ /participant. No significant differences in glycemic outcomes were noted between Ramadan and non-Ramadan periods. In this first clinically validated study, automated insulin dosing systems showed a safe and effective management strategy to support prolonged and consecutive fasting in people with type 1 diabetes.

## INTRODUCTION

Recent advances in therapies and technology have had a major impact on type 1 diabetes management approach, and enabled a range of physical and metabolically challenging activities to be undertaken safely<sup>1,2</sup>. Fasting, which is an important part of several religions and health practices, can present a considerable metabolic challenge for people with type 1 diabetes. Fasting in Islam constitutes complete abstinence from food and water from sunrise to sunset on consecutive days for the duration of the lunar month of Ramadan<sup>3</sup>. Fasting among people with type 1 diabetes increases the risk for severe hypoglycemia, hyperglycemia and higher glycemic variability<sup>4,5</sup>. In medically high-risk conditions, such as type 1 diabetes, exemption from fasting is given<sup>3,6–8</sup>. However, observational studies report  $>40\%$  of Muslims with type 1 diabetes observe fasting despite medical exemption<sup>9</sup>, as fasting is considered an essential part of Muslims' spiritual fulfillment and mental well-being.

Therefore, healthcare professionals should determine optimal ways to empower people with type 1 diabetes to undertake fasting safely should they wish so<sup>10,11</sup>.

Advancements, such as continuous glucose monitoring (CGM), continuous subcutaneous insulin infusion and structured education, offer measures of safety for people with type 1 diabetes during Ramadan<sup>10,11</sup>. Sensor-augmented pump therapy and low-glucose suspend systems have shown further opportunities to improve safety in fasting among people with type 1 diabetes<sup>12</sup>. More advanced automated insulin delivery (AID) systems utilize continuous subcutaneous insulin infusion, CGM and a software controller to adapt insulin delivery in response to interstitial glucose dynamic changes<sup>13</sup>. Both open-source and commercial AID systems show improved glycemic outcomes and reduced hypoglycemia<sup>13,14</sup>, and have been successfully used in routine diabetes management and in different challenging circumstances, including pregnancy, sports and illness<sup>13,15,16</sup>. AID systems might provide a novel enabling strategy for people with type 1 diabetes wishing to fast during Ramadan<sup>17,18</sup>. This report details a

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retrospective observational study of adults with type 1 diabetes fasting during Ramadan with the support of AID systems.

## METHODS

Adults with established type 1 diabetes who observed fasting in Ramadan 2019 and 2020 using AID systems (commercial or open-source) were invited to participate in this project through a social media platform regardless of geographic location. The study was carried out in a real-world setting with no impact on routine clinical care. The study received ethical approval from the King's College London ethics committee (MRA-19/20-18831), and was carried out in accordance with the ethical principles in the Declaration of Helsinki 2013. Participants provided information about their demographics, duration of diabetes and diabetes treatment. The most recent clinical glycated hemoglobin (HbA1c) level (Diabetes Control and Complications Trial-aligned) before Ramadan was obtained, in addition to reports on any adverse events during the study. An active analysis method was used to obtain qualitative data on participants' experience from posts, comments and reactions on a shared messaging group involving study participants.

Glycemic data were obtained and validated by the authors from the Dexcom Clarity<sup>®</sup>, Nightscout or Diasend<sup>®</sup> platforms. Individually reported data, including glucose-related events, number of fasted days and fast-breaking events, were clinically validated. Glucose data were compared for each participant for the period of Ramadan and the 1 month preceding and after Ramadan. CGM-captured hypoglycemia was considered as one episode when glucose fell to  $<3.9$  mmol/L (70 mg/dL) for at least 15 consecutive minutes. Estimated HbA1c was calculated using a minimum of 14 days of CGM data employing the Nathan *et al.* formula<sup>19</sup>. Percentages of time in range (TIR) 3.9–10 mmol/L (70–180 mg/dL), time below range (TBR) 3.9 mmol/L (70 mg/dL) and 3.0 mmol/L (54 mg/dL), and time above range (TAR) 10.0 mmol/L (180 mg/dL) and 13.9 mmol/L (250 mg/dL), were calculated as averages of all individual mean percentages for each range for the respective period. Glucose variability was estimated by the calculation of the coefficient of variation of CGM readings. Data are presented as the mean  $\pm$  standard deviation, unless stated otherwise. Additional analysis was carried out on one profile where complete glucose, insulin and carbohydrate data for the month of Ramadan and another month outside of Ramadan were available. Data analyses were carried out using RStudio (version 1.3.959; RStudio, Boston, MA, USA) and GraphPad (GraphPad, San Diego, CA, USA), with two-sample Student's *t*-test used for analyses of parametric continuous variables.

## RESULTS

Six profiles were included with a total of 164 fasted days (3,936 h) using AID systems. Participant demographics and AID setups are summarized in Table 1. Three profiles were from the UK (fasting ~16–17 h/day) and three from Saudi Arabia (fasting ~15 h/day). All participants had excellent glycemic

levels before Ramadan with HbA1c  $6.3 \pm 0.2\%$  ( $45 \pm 3$  mmol/mol) and optimal TIR (Figure 1). Participants fasted an average of  $27.3 \pm 3.3$  days, with 50% completing the whole month. Fasting was broken due to diabetes-related events for two participants with a total of 6 days. During Ramadan, TIR, TBR and TAR were all within international recommended targets<sup>20</sup>, and glucose variability was excellent (coefficient of variation  $28.5 \pm 4.9\%$ ; Table 2; Figure 1). There was no significant difference between all these ranges during Ramadan in comparison with the months outside Ramadan (Table 2). Hypoglycemic episodes were minimal during Ramadan ( $0.8 \pm 0.3$  episodes/day) and did not differ statistically when compared with the months outside Ramadan. No episodes of severe hypoglycemia, diabetic ketoacidosis or hospitalization were reported during the study.

The additional subanalysis on the complete dataset from one profile (CamAPS FX) showed no difference in total daily insulin during Ramadan compared with outside Ramadan ( $34 \pm 5.2$  unit/day vs  $35.2 \pm 6.4$  unit/day respectively,  $P = 0.44$ ; Figure 2); however, bolus insulin was significantly lower during Ramadan ( $18.8 \pm 2.6$  units vs  $20.2 \pm 4.0$ ,  $P = 0.009$ ). Although carbohydrate intake during Ramadan was lower than outside Ramadan ( $193 \pm 43$  g vs  $249 \pm 36$ ,  $P < 0.001$ ), the insulin-to-carbohydrates ratio was significantly higher during Ramadan compared to outside Ramadan (1:11 vs 1:13 [insulin unit : grams carbohydrates],  $P = 0.017$ ), indicating a relative insulin resistance during Ramadan.

In the qualitative data analysis, participants expressed “enablement” by AID systems to undertake fasting safely with less disruption to daily activities. Peer support through the shared messaging group provided confidence, comfort and a cumulative learning experience for study participants.

## DISCUSSION

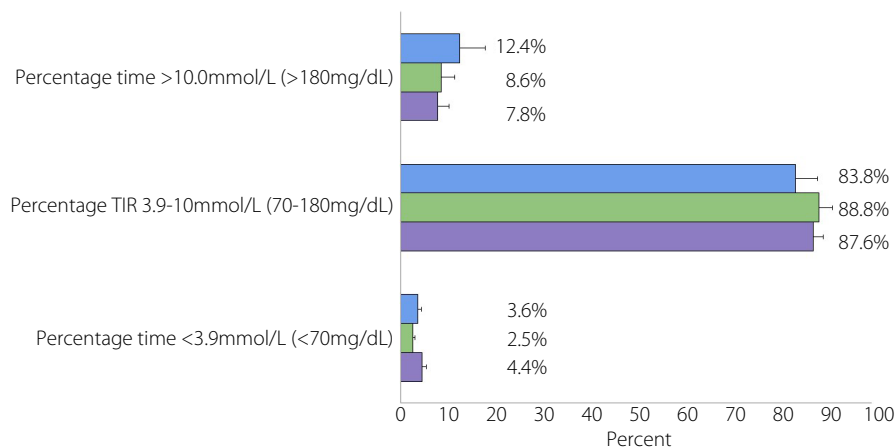
In the present study, we detailed the use of current AID systems in consecutive fasting for a month in well-managed and highly motivated people with type 1 diabetes who were able to maintain exceptional glycemia without safety concerns. Contrary to previous concerns<sup>5</sup>, overall hypoglycemic events in the study were minimal. This is in keeping with a previous observation using a first-generation commercial AID system (Medtronic-670G), where no change in TIR during Ramadan was reported<sup>18</sup>. However, in the present study, the glycemic measures achieved and maintained were superior (TIR 88 vs 72%<sup>18</sup>) in keeping with data showing improved efficacy with more advanced AID systems<sup>21</sup>.

The insights gained from the additional analysis showed a higher insulin-to-carbohydrates ratio. This is in keeping with a non-clinically validated, self-reported perspective on open-source system use during Ramadan where increased insulin requirements at iftar time was noted<sup>3</sup>. The higher insulin-to-carbohydrates ratio in the evening might have several contributing factors. Similar to exercise and hypoglycemia<sup>22</sup>, fasting elicits a complex adaptive metabolic and counter-regulatory

**Table 1** | Participants' baseline data, automated insulin delivery and continuous glucose monitoring setups, and Ramadan fasting outcomes

	Clinical variables (mean ± SD)
Age (years)	33.6 ± 4.8
Duration of type 1 diabetes mellitus (years)	23.5 ± 7.9
Sex (female)	16.7%
BMI (kg/m <sup>2</sup> )	23.6 ± 1.9
HbA1c (%)	6.3 ± 0.2
	<b>AID and CGM setup</b>
Insulin used	Fiasp 50%, NovoRapid 50%
AID system	Loop 50% (3), AAPS 33.3% (2), CamAPS FX 16.7% (1)
CGM modality	Dexcom G6 50% (3), G5 33.3% (2), Libre (+Bluetooth bridge) 16.7% (1)
	<b>Ramadan fasting outcomes</b>
No. days fasting completed <sup>†</sup>	27.3 ± 3.3
No. days fasting was broken due to diabetes <sup>‡</sup>	1 ± 1.5

<sup>†</sup>Days fasting completed are days when participants abstained from food or drink from sunrise to sunset safely during Ramadan. <sup>‡</sup>Days fasting was broken due to diabetes are days when participants started fasting from sunrise, but terminated their fasting due to a diabetes-related event; for example, hypoglycemia. AID, automated insulin delivery; BMI, body mass index; CGM, continuous glucose monitoring; HbA1c, glycated hemoglobin 1C.

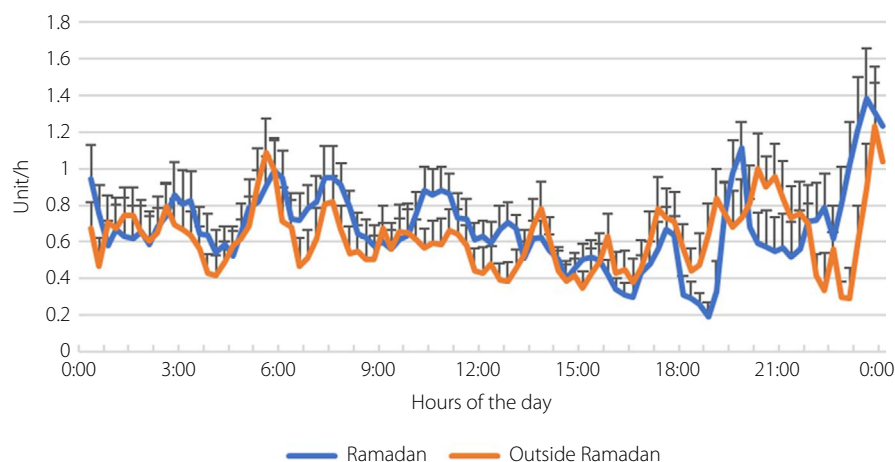


**Figure 1** | Time in range before Ramadan (blue), during Ramadan (green) and after Ramadan (purple). Data presented as the mean ± standard deviation, *n* = 5.

**Table 2** | Glucose data analysis before, during and after Ramadan for profiles using automated insulin delivery systems in people with type 1 diabetes

Glycemic outcomes	Before Ramadan	During Ramadan	After Ramadan	<i>P</i> -value
Glucose (mmol/L)	7.26 ± 1.2	7.03 ± 0.5	6.8 ± 0.6	0.5
CoV (%)	30.3 ± 4.4	28.5 ± 4.9	29.8 ± 3.1	0.6
eA1C %	6.2 ± 0.7	6.1 ± 0.3	6.0 ± 0.4	0.6
No. hypos/day	1.3 ± 0.6	0.8 ± 0.3	1.7 ± 1.0	0.1
% Time >13.9 mmol/L (<250 mg/dL)	2.3 ± 4.0	1.1 ± 2.0	1 ± 1.3	0.9
% Time >10.0 mmol/L (>180 mg/dL)	12.4 ± 13.5	8.6 ± 6.9	7.8 ± 8.9	0.8
% TIR 3.9–10 mmol/L (70-180 mg/dL)	83.8 ± 11.7	88.8 ± 7.3	87.6 ± 5.1	0.8
% Time <3.9 mmol/L (<70 mg/dL)	3.6 ± 1.9	2.5 ± 1.3	4.4 ± 2.5	0.1
% Time <3.0 mmol/L (<54 mg/dL)	0.6 ± 0.4	0.5 ± 0.4	1 ± 0.9	0.2

CoV, coefficient of variation; eA1C, estimated A1C; hypos, hypoglycemia; TIR, time in range.



**Figure 2** | Insulin profiles from one participant who used CamAPS FX during Ramadan (blue lines) and outside Ramadan (orange lines). Data presented as the mean  $\pm$  standard deviation ( $n = 27$ ).

response to maintain glucose and energy homeostasis. A rise in glucagon and generation of ketone is noted during prolonged fasts<sup>23</sup>. Furthermore, cortisol levels are increased in the iftar period, as well during Ramadan fasting, whereas background insulin requirement is the lowest with less insulin onboard at this time<sup>24</sup>. Prolonged periods of food abstinence might improve insulin sensitivity<sup>25,26</sup>; however, the aforementioned physiological responses to fasting lead to lipid oxidation, reduction in insulin-stimulated glucose uptake and the development of reversible insulin resistance at iftar time. Furthermore, lower exercise and activity levels during Ramadan, especially when meals are typically eaten, might be an added contributor.

As open-source AID systems use as a treatment option is unregulated, their safe and effective use in fasting adds to the growing literature on them and provides further reassurance for their use in keeping with recent reports<sup>14,27,28</sup>. This experience provides newer insights about how AID systems can support people with type 1 diabetes undergo considerable physiological challenges, such as fasting, and can aid healthcare professionals when counseling individuals planning on fasting with open-source AID systems.

It is important to note that the presented data are limited to the well-managed cohort included in this report. Furthermore, the heterogeneity of AID setups among study participants makes generalization of the results difficult. Randomized controlled trials of AID systems during Ramadan will help provide objective insights into the potential and wider utility of this approach. Larger case series or registries will help expand these real-world observations, and provide deeper understanding and guidance related to insulin dosing during fasting for people with type 1 diabetes, and the impact on diabetes and quality of life.

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#### DISCLOSURE

The authors declare no conflict of interest.

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Informed consent: All participants gave informed consent.

Approval date of registry and the registration no of the study/-trial: N/A.

Animal studies: N/A.

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