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A Real-World Prospective Study of the Effectiveness and Safety of Automated Insulin Delivery Compared With Other Modalities of Type 1 Diabetes Treatment During Ramadan Intermittent Fasting

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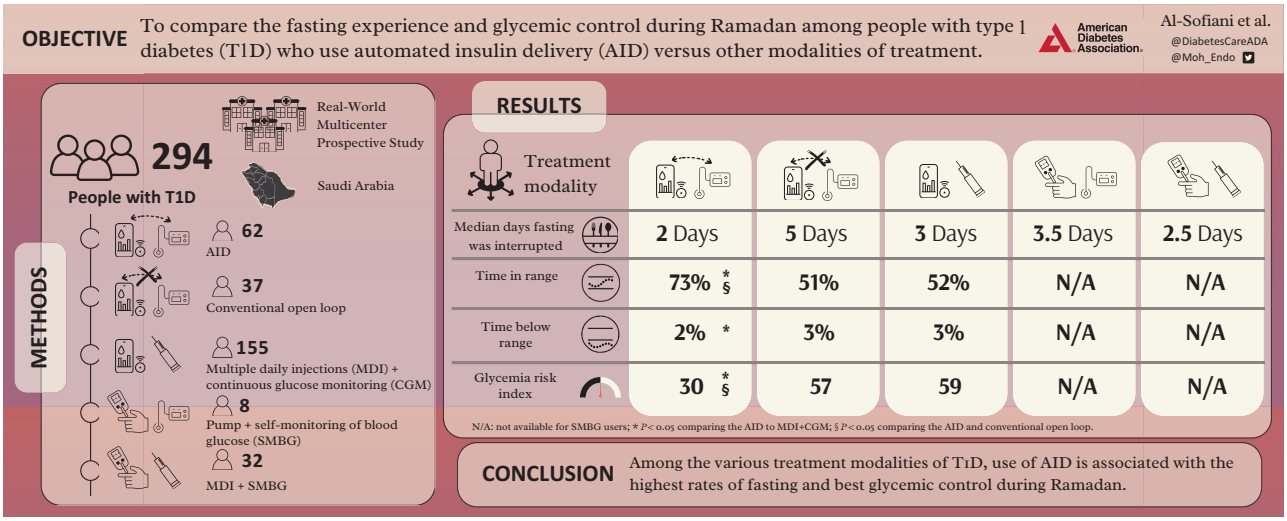

ARTICLE HIGHLIGHTS

- **Why did we undertake this study?**
  To our knowledge, no studies have compared the efficacy and safety of the various modalities of type 1 diabetes (T1D) treatment among people with T1D (PWT1D) who practice intermittent fasting during Ramadan.
- **What is the specific question(s) we wanted to answer?**
  Which modality of T1D treatment is associated with the highest rates of fasting and best glycemic control during Ramadan?
- **What did we find?**
  Use of automated insulin delivery was associated with the highest rate of fasting and best glycemic control during Ramadan.
- **What are the implications of our findings?**
  Our findings are relevant to PWT1D who practice intermittent fasting for any reason. Moreover, diabetes and Ramadan practical guidelines should consider assigning a lower risk score to PWT1D who use AID compared with other modalities of treatment.

A Real-World Prospective Study of the Effectiveness and Safety of Automated Insulin Delivery Compared With Other Modalities of Type 1 Diabetes Treatment During Ramadan Intermittent Fasting

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OBJECTIVE

To compare the fasting experience and glycemic control during Ramadan among people with type 1 diabetes (PWT1D) who use automated insulin delivery (AID) versus other modalities of treatment.

RESEARCH DESIGN AND METHODS

A total of 294 PWT1D who attempted fasting during Ramadan in 2022 were categorized on the basis of treatment modality into one of five groups: *1*) AID (*n* = 62); *2*) conventional pump + continuous glucose monitoring (CGM; *n* = 37); *3*) pump + self-monitoring of blood glucose (SMBG; *n* = 8); *4*) multiple daily injections (MDI) + CGM (*n* = 155); and *5*) MDI + SMBG (*n* = 32). Predictors of fasting most days of Ramadan (i.e., breaking fast ≤2 days because of diabetes) were analyzed using uni- and multivariable logistic regression.

RESULTS

The median numbers of days when fasting was broken because of diabetes were 2, 5, 3, 3.5, and 2.5 for AID, conventional pump + CGM, MDI + CGM, pump + SMBG, and MDI + SMBG users, respectively($P = 0.047$). Users of AID had a significantly greater time in range (TIR) and lower glycemia risk index, time below range, and time above range compared with users of conventional pumps and MDI(both $P < 0.05$). Likewise, 53% of AID users attained the double target of *1*) breaking fast ≤2 days because of diabetes and *2*) maintaining TIR ≥70% during Ramadan compared with only 3% of the conventional pump users and 44% of the MDI + CGM users (both $P < 0.05$). Compared with MDI + CGM users, AID users were twice as likely to complete fasting most days of Ramadan.

CONCLUSIONS

Use of AID is associated with the highest rates of fasting and best glycemic control during Ramadan fasting.

Ramadan is the ninth month of the Islamic lunar calendar, during which adult Muslims are required to fast for 29 or 30 consecutive days. It is estimated that >116 million Muslims with diabetes fast during Ramadan every year, including many people with

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type 1 diabetes (PWT1D) (1). Fasting during Ramadan includes refraining from eating and drinking from dawn to sunset. Fasting can stretch up to 20 h in some parts of the world. In addition to fasting, major changes in lifestyle, meal schedule, physical activity level, and sleep pattern take place during Ramadan (2–5). For PWT1D, fasting during Ramadan has been linked to an increased risk of hypoglycemia, hyperglycemia, diabetic ketoacidosis (DKA), dehydration, emergency room (ER) visits, and hospitalization (6,7). Therefore, PWT1D are generally considered at moderate to high risk for development of such conditions during fasting and are religiously exempt from fasting (7). Yet, many PWT1D attempt to fast during Ramadan, even if this is against the advice of their health care professionals (HCPs) (8,9).

The International Diabetes Federation and Diabetes and Ramadan International Alliance (IDF-DAR) developed a risk stratification calculator to define the risk of fasting for people with diabetes and guide HCPs in how to treat PWT1D during Ramadan (7). According to the IDF-DAR risk calculator, PWT1D are considered at moderate to high risk and are generally advised to not fast during Ramadan. The IDF-DAR risk calculator assigns the same risk score to users of multiple daily injections (MDIs) of insulin and users of pump therapy. Moreover, the IDF-DAR risk calculator does not account for the type of insulin pump used by the patient (7). More recently, advances in insulin pump therapies, including the introduction of automated insulin delivery (AID), have remarkably improved the glycemic control and quality of life of PWT1D (10,11). The algorithm used in these AID systems automatically adjusts basal insulin delivery every 5 min according to current and predicted glucose levels. As a result, AID users, compared with users of MDI and other treatment modalities of diabetes, often have better glycemic control with less hypoglycemia and hyperglycemia and enjoy a more flexible lifestyle (10,12,13).

It remains unknown whether the use of AID technology, compared with other modalities of diabetes treatment, in real-world settings is associated with a better fasting experience and improved glycemic control, among PWT1D who attempt to fast during Ramadan. Here, we report on the largest prospective study, to our knowledge, examining the safety and effectiveness of AID during the month of Ramadan, and, to our knowledge, the first study to compare these outcomes in users of AID versus users of other modalities of diabetes treatment during Ramadan.

RESEARCH DESIGN AND METHODS

Study Design and Participants

This was a prospective, noninterventional, study of PWT1D who attempted to fast during Ramadan in 2022. We included PWT1D who were seen at our endocrine clinics during the months preceding Ramadan and who agreed to share their health information and fasting experience. We recruited PWT1D from five medical centers in Riyadh and Madinah, Saudi Arabia (King Saud University Medical City, Dr. Suliman Al-Habib Medical Group, Dallah Hospital, Madina Medical Center, and Taibah University). The fasting hours (i.e., daytime) in Riyadh and Madinah ranged from 13 h and 30 min to 14 h and 20 min during Ramadan in 2022. The 294 participants who completed the study were categorized on the basis of their treatment modality into the following five groups:

1. AID (n = 62): This group included users of any of the three AID systems available in Saudi Arabia at the time of the study (Medtronic MiniMed 780G, MiniMed 670G, and Tandem Control-IQ).
2. Conventional pump + continuous glucose monitor (CGM; n = 37): This group included PWT1D who use an insulin pump and a CGM sensor that are not integrated (e.g., Medtronic pump with a first-generation Freestyle Libre sensor; an Omnipod Dash pump with a Dexcom sensor).
3. Pump + self-monitoring of blood glucose (SMBG; n = 8): This group included PWT1D who use an insulin pump and a blood glucose meter (no CGM).
4. Multiple daily injections (MDIs) + CGM (n = 155): This group included PWT1D who use basal and bolus insulin injections and a CGM sensor.
5. MDI + SMBG (n = 32): This group managed diabetes in the most traditional way, using basal or bolus insulin injections and a blood glucose meter.

None of our study participants were using a sensor-augmented pump in which the suspension-before-low or suspension-on-low feature is activated. Except for the AID users, all the other insulin pump users in our study were using the pump with either a CGM sensor that is not integrated with the pump (i.e., conventional open loop) or with a blood glucose meter (i.e., pump + SMBG). The study was approved by the Institutional Review Board at King Saud University and informed consent was obtained from all participants prior to enrollment in the study.

DATA COLLECTION

Data collection was performed over three phases. During phase 1, which was 2 months prior to Ramadan, participants were informed about the study during their routine clinic visits. Those who were interested in participating provided informed consent, verified their contact information, and confirmed with the study team that their pump and/or CGM accounts were linked to the clinics' accounts. During phase 2, at the end of Ramadan, an online survey was sent out to the study participants. The survey included multiple choice questions about their age, sex, socioeconomic status, level of education, employment and health insurance status, duration of diabetes, modality of diabetes treatment, as well as the number of days when their fasting was broken because of diabetes-related causes during Ramadan in 2022. And during phase 3, shortly after Ramadan, we retrieved the Ramadan and pre-Ramadan CGM data for the 149 participants who were using CGM (with either AID, conventional insulin pump, or MDI) and who had shared their CGM data with us through the cloud.

OUTCOMES AND COVARIATES

The self-reported number of days when fasting was broken because of diabetes-related causes during Ramadan was the end point for the main analysis. "Breaking the fast" in our study refers to consuming food or drink during the daytime in Ramadan and before Iftar, which is the designated meal for fast-breaking at sunset. There are several nondiabetes-related reasons for which Muslims are exempt from fasting and, therefore, they may break the fast during the daytime in Ramadan. These include traveling, illness, and menstruation for women. To focus our analysis on the impact of diabetes on fasting experience, we report the number of days during which fasting was broken because of a diabetes-related instead of reporting the number of days during which fasting

was completed. Moreover, we report the median number of days when fasting was broken because of each of the following: hypoglycemia, severe hypoglycemia (requiring help from a second person), hyperglycemia, DKA, or diabetes-related hospitalizations or ER visits.

Additional analyses of the CGM data were performed for the subcohort of 149 participants who were using CGM during and before Ramadan and who shared their data with us. The following CGM metrics were evaluated: glucose management indicator (GMI), time above range (TAR) >180 mg/dL (both high glucose level >180 mg/dL and very high glucose level >250 mg/dL), time in range (TIR; 70–180 mg/dL), time below range (TBR) <70 mg/dL (both low glucose level of 54–69 mg/dL and very low glucose level <54 mg/dL), coefficient of variation (CV), and glycemia risk index (GRI). The GRI is a new composite CGM metric that assigns higher weight to extreme hypoglycemia and hyperglycemia compared with other CGM metrics. It is presented as a single number from 0 to 100 that reflects the overall quality of glycemic control. The best GRI score is the quintile from the 0 to 20th percentile, whereas the worst is the quintile from the 81st to 100th percentile (14).

In addition, we explored a composite end point of a "double target": *1*) breaking fast ≤2 days only because of diabetes and *2*) maintaining TIR ≥70% during Ramadan. We compared the proportions of PWT1D who attained the double target during Ramadan across the different T1D treatment modalities. The double target composite end point was selected because of its high clinical relevance and importance to PWT1D and HCPs in the real-world setting. Data from CGM were included only if the participant used the CGM sensor for at least 10 days during Ramadan and 10 days during the month preceding Ramadan (15).

STATISTICAL ANALYSIS

All significant testing was two-tailed with α of 0.05, and data were analyzed using Stata Statistical Software (release 15). Categorical variables were examined using contingency table arrays, and the $\chi 2$ statistic and continuous variables were examined using Kruskal-Wallis test. When comparing the median number of days when fasting was broken because of a diabetes-related cause, *1*) data from all the participants who completed the online survey were included and *2*) the Kruskal-Wallis test was used to determine whether there was a statistically significant difference between the medians of the groups. When comparing CGM data across the three groups (AID, MDI + CGM, and conventional pump therapy), *1*) data from the 149 participants who had CGM data available during and before Ramadan were included; and *2*) Dunn's Kruskal-Wallis test of multiple comparisons was used to determine which groups were statistically significantly different from the other groups.

Logistic regression analysis was used to identify potential predictors of fasting most days of Ramadan (i.e., breaking fast ≤2 days only because of diabetes). The associations between the predictors and outcomes are presented as odds ratios (ORs) and 95% CIs. We present the ORs before and after adjusting for potential confounders, including age, sex, educational level, employment status, insurance status, diabetes duration, and modality of diabetes treatment during Ramadan (i.e., AID, conventional pump, pump + SMBG, MDI + CGM, and MDI + SMBG).

RESULTS

Patient Characteristics

Of the 294 study participants, 61% were women, 57% were students, and 38% had health insurance. A total of 62 participants (21%) were using AID systems, compared with 32 (11%) using MDI + SMBG, 8 (3%) using a pump + SMBG, 155 (52%) using MDI + CGM, and 37 (13%) using a conventional pump + CGM. The median age of the study participants was 22 years (interquartile range [IQR] = 15, 29). The AID group had the highest rates of health insurance (82%) compared with the other four groups (overall $P < 0.01$), and had patients with the youngest age at time of diagnosis of diabetes (median age at time of diagnosis, 9.5 years) compared with the other four groups (overall $P = 0.01$). The median diabetes duration for the five groups ranged from 7 years (IQR = 3.2, 13) for the MDI + CGM group to 15 years (IQR = 9, 19) for the pump + SMBG group (overall $P = 0.01$). Among the CGM users, the AID group had the best pre-Ramadan glycemic control compared with the conventional open loop and MDI + CGM groups. Otherwise, there were no significant differences noted in age, sex, employment status, or level of education when comparing the study participants by modality of diabetes treatment (for all, $P > 0.05$) (Table1).

Fasting Experience and Acute Complications During Ramadan

Users of AID had the lowest median number of days (n = 2; IQR = 0, 4) during which fasting was broken because of diabetes, compared with 5 days (IQR = 2, 8) for the conventional pump + CGM group; 3 days (IQR = 0, 6) for the MDI + CGM group; 3.5 days (IQR = 0.5, 4.5) for the pump + SMBG group; and 2.5 days (IQR = 1, 6) for the MDI + SMBG group (Table 2). The rates of acute complications of diabetes including severe hypoglycemia, severe hyperglycemia, DKA events, or ER visits were very low across the five groups with no statistically significant differences (for all, $P > 0.05$) (Table 2).

Glycemic Control and Insulin Doses During Ramadan

The impact of fasting on the glycemic profile of PWT1D during Ramadan differed significantly by the modality of treatment, as shown in Fig. 1*A* and *B*. Among the CGM users, those who were using AID had the best glycemic control during Ramadan, with the highest TIR of 73% and lowest TAR of 25%, TBR of 2%, and GRI of 30, compared with the MDI + CGM group, which had TIR of 52%, TAR of 45%, TBR of 3%, and GRI of 59; and the conventional pump + CGM group, which had TIR of 51%, TAR of 46%, TBR of 3%, and GRI of 57 *(*for all, $P < 0.05$).

More than half of the AID users (53%) attained the double target of fasting most days of Ramadan *(*i.e., breaking their fast ≤2 days because of diabetes) and maintaining TIR ≥70% during Ramadan, compared with only 3% of the conventional pump group and 44% of the MDI + CGM users (overall $P < 0.01$) (Fig. 1*C*).

Among the AID users, the average pre-Ramadan total daily dose of insulin was 42.8 units, compared with 41.3 units during Ramadan. The average pre-Ramadan basal insulin was 18.1 units/day compared with 17.1 units/day during Ramadan. The average pre-Ramadan bolus insulin was 24.7 units/day compared with 24.2 units/day during Ramadan. And the average pre-Ramadan autocorrection was

Table 1—Characteristics of study participants by modality of T1D treatment (*n* = 294)

	All (*N* = 294)	Pump + CGM (AID) (*n* = 62)	Pump + CGM (conventional open loop) (*n* = 37)	Pump + SMBG (*n* = 8)	MDI + CGM (*n* = 155)	MDI + SMBG (*n* = 32)	Overall *P* value*
Age, median (25th, 75th percentiles), years	22 (15, 29)	22 (16, 28)	21 (15, 29)	29 (22.5, 32.5)	21 (15, 27)	24 (17.5, 34)	0.17
Female sex (%)	61.22	64.52	59.46	87.50	58.06	65.62	0.47
Employment status (%)							0.13
Student	56.46	51.61	56.94	25	61.94	46.88	
Employed	31.63	38.71	29.73	50	29.03	28.12	
Other	11.9	9.68	13.51	25	9.03	25	
Educational level (%)							0.16
Elementary or middle school	28.23	27.42	35.14	0	29.03	25	
High school	26.19	19.35	13.51	25.00	30.32	34.38	
Bachelor's degree or higher	45.58	53.23	51.35	75.00	40.65	40.62	
Has health insurance (%)	38.10	82.26	40.54	62.5	21.29	25	<0.01
Diabetes duration, median (25th, 75th percentiles), years	9 (4, 15)	10 (6, 18)	11 (6, 15)	15 (9, 19)	7 (3.2, 13)	10 (5.5, 15.5)	0.01
Age at time of diagnosis, median (25th, 75th percentiles), years	12 (7, 16)	9.5 (5, 14)	10 (7, 14)	14.5 (10.5, 18)	12 (8, 18)	12.5 (7, 19)	0.01
Pre-Ramadan CGM metrics (*n* = 149)**							
GRI	49.5	32.3	55.3	N/A	56.2	N/A	<0.01
GMI, (%)	7.3	6.9	7.4	N/A	7.5	N/A	<0.01
TIR (70–180 mg/dL), (%)	59.3	71.7	54.5	N/A	54.5	N/A	<0.01
TBR (54–69 mg/dL) level 1, (%)	3.0	2.2	3.9	N/A	3.3	N/A	0.30
TBR (<54 mg/dL) level 2, (%)	0.7	0.5	0.7	N/A	0.7	N/A	0.88
TAR (181–250 mg/dL) level 1, (%)	22.3	19.3	26.2	N/A	23.2	N/A	0.01
TAR (>250 mg/dL) level 2, (%)	17.1	6.5	11.6	N/A	19.5	N/A	<0.01
CV (%)	36.7	35.4	38.7	N/A	37.0	N/A	0.24

N/A, not available. **P* values denote the overall comparison across the five groups by Kruskal-Wallis test for continuous variables and χ^2 for categorical variables. **Analysis of the CGM data from the month preceding Ramadan among the MDI + CGM users, open loop, and AID users.

6.8 units/day compared with 6.5 units/day during Ramadan.

Factors Predictive of Fasting Most Days of Ramadan

Being older than 20 years, having a bachelor's degree or a higher level of education, and being employed were all associated with higher odds of successfully fasting most days of Ramadan in the unadjusted model. Using an AID system during Ramadan increased the odds of successfully fasting most days of the month by more than two times compared with using MDI + CGM, after adjusting for age, sex, educational level, employment status, insurance status, and diabetes duration (OR 2.37; 95% CI 1.14–4.90) (Table 3).

Having better pre-Ramadan glycemic control (i.e., better CGM metrics) was predictive of both fasting most days during Ramadan (Supplementary Table 2) and attaining the double target during Ramadan (Supplementary Table 1). For instance, having a pre-Ramadan TIR of ≥70%, compared with having a pre-Ramadan TIR of <50%, increased the odds of fasting most days during Ramadan (i.e., breaking the fast ≤2 days only because of diabetes) by three times after adjusting for potential confounders (OR 3.05; 95% CI 1.18–7.88). Likewise, having a pre-Ramadan GRI of ≤20 and GRI of 21–40 increased the odds of fasting most days during Ramadan by 3.6 and 2.6 times, respectively, compared with having a pre-Ramadan GRI of >40 in the adjusted model (OR 3.62 [95% CI 1.11–11.75]; and 2.55 [95% CI 1.07–6.08], respectively) (Supplementary Table 2). In addition, those who were successful in attaining the double target during Ramadan, compared with those who were unable to attain the double target, were more likely to have health insurance and had significantly better glycemic control pre-Ramadan (i.e., higher pre-Ramadan TIR and lower GRI, GMI, TAR, and glucose CV) (for all, $P <$ 0.01) (Supplementary Table 1).

Table 2—Rates of acute complications of diabetes and days when fasting was broken during Ramadan for diabetes-related causes (*n* = 294)

	Pump + CGM (AID) (*n* = 62)	Pump + CGM (conventional open loop) (*n* = 37)	Pump + SMBG (*n* = 8)	MDI + CGM (*n* = 155)	MDI + SMBG (*n* = 32)	*P* value*
Patients who broke their fast because of diabetes for >2 days, *n* (%)	26 (41.9)	26 (70.3)	5 (62.5)	85 (54.8)	16 (50)	0.09
Days when fasting was broken because of a diabetes-related cause, median (25th, 75th percentiles), *n*	2 (0, 4)	5 (2, 8)	3.5 (0.5, 4.5)	3 (0, 6)	2.5 (1, 6)	*0.047*
Days when fasting was broken because of hypoglycemia, median (25th, 75th percentiles), *n*	2 (0, 3)	3 (1, 5)	1.5 (0.5, 3)	2 (0, 4)	1.5 (0, 4)	0.23
Days when fasting was broken because of hyperglycemia, median (25th, 75th percentiles), *n*	0 (0, 0)	0 (0, 3)	0.5 (0, 2)	0 (0, 1)	0 (0, 2)	0.18
DKA events during Ramadan, median (25th, 75th percentiles), events	0 (0, 0)	0 (0, 0)	0 (0, 0.5)	0 (0, 0)	0 (0, 0)	0.91
ER visits or hospitalization because of diabetes during Ramadan, median (25th, 75th percentiles), *n*	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.98
Severe hypoglycemia events during Ramadan, median (25th, 75th percentiles), *n*	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.94

**P* values denote the overall comparison across the five groups by Kruskal-Wallis test.

DISCUSSION

To our knowledge, this is the first and largest prospective, real-world study to examine and compare the effectiveness and safety of AID versus other modalities of T1D treatment during Ramadan intermittent fasting. We found that the use of AID technology was associated with fasting most days of Ramadan and having the best glycemic control during Ramadan. Users of AID were more than two times as likely to fast most days of Ramadan compared with users of MDI and CGM. Moreover, AID users were more likely to maintain their CGM metrics within the international CGM targets and had the greatest TIR, lowest TBR and TAR, and lowest GRI, compared with users of other modalities of treatment (15). In addition, PWT1D who attained the double target of *1*) fasting most days of Ramadan and *2*) maintaining TIR ≥70% were more likely to have better pre-Ramadan glycemic control (i.e., greater pre-Ramadan TIR and lower GRI, TBR, TAR, and CV values) than those who did not attain the double target.

The superiority of AID technology over other modalities of treatment during intermittent fasting is most likely attributed to the automation of insulin dosing in response to current and predicted glucose levels that this technology offers. Through this key feature, AID technology appears to mitigate the profound, abrupt, and often challenging lifestyle and behavioral changes that occur with Ramadan fasting. As a result, AID enabled PWT1D in our study to successfully complete their fasting as planned without compromising their glycemic control or increasing the risk of acute complications. This is relevant to a large proportion of PWT1D in the real world, especially those using MDI and SMBG who often maintain their glucose levels above target during the daytime in Ramadan to be able to complete the fasting and minimize daytime hypoglycemia. Although this approach may help PWT1D to fast more days of Ramadan, as seen in the MDI + SMBG group in our study, it carries a significant level of risk and can result in short- and long-term complications. Our findings support those from previous pilot studies and a case report that demonstrated the safety and effectiveness of AID during Ramadan, albeit with only a small number of PWT1D (16–18). Our results are also aligned with previous reports that AID technology can adapt to rapid changes in glucose and lifestyle, such as those seen with exercise (19, 20). Notably, most of the AID users in our study had private insurance compared with users of other treatment modalities of T1D. Despite advances in insulin delivery systems in recent years, the use of AID has been largely limited to PWT1D who have higher socioeconomic status and/or private insurance. Disparities in access to diabetes technology often affects PWT1D who are more vulnerable, including those with low socioeconomic status, no private insurance, or poor glycemic control. Addressing disparities in access to diabetes technology

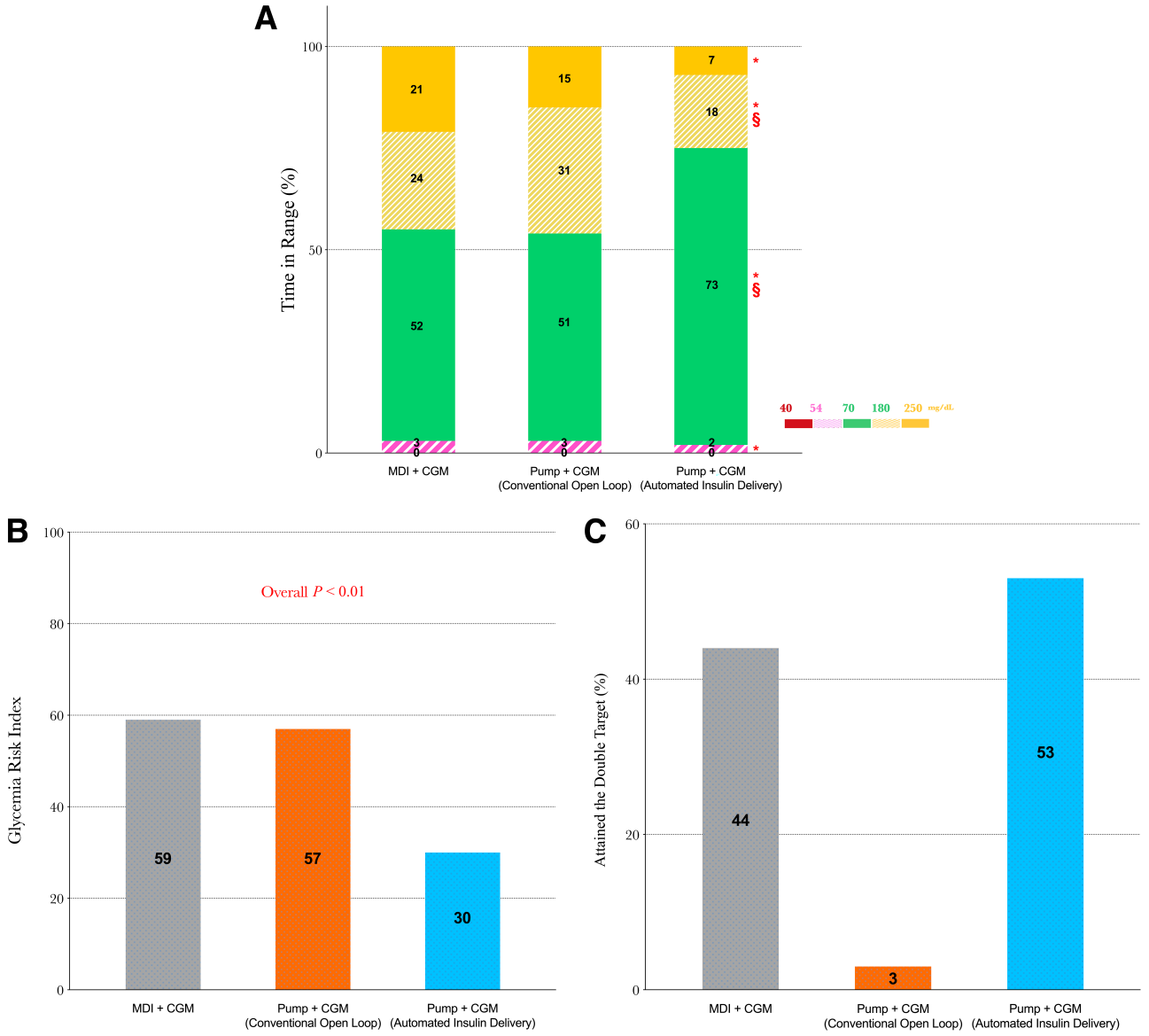

Figure 1—CGM metrics during the month of Ramadan (n = 149). *A*) TIR. *B*) GRI. *C*) Proportion of PWT1D who attained the double target of *1*) breaking fast ≤2 days and *2*) having TIR ≥70% during Ramadan. *$P < 0.05$ comparing the AID with MDI + CGM; §$P < 0.05$ comparing the AID with conventional open loop (this analysis was limited to CGM users).

has the potential to improve the clinical outcomes and mitigate the health and economic burdens of T1D in these vulnerable subgroups of PWT1D (21).

Our findings have important clinical and scientific implications because intermittent fasting is becoming popular among PWT1D for religious reasons (e.g., Ramadan, Yom Kippur, Lent) or health-related reasons (e.g., weight loss). Professional societies, such as the IDF-DAR and the American Diabetes Association, continue to recommend against fasting during Ramadan for most PWT1D (7,22,23). However, these recommendations are largely based on relatively old data showing an increased risk of hypoglycemia, hyperglycemia, and DKA in PWT1D who attempt to fast (1). These data are mostly from the era when CGM, AID technology, and structured pre-Ramadan education sessions were not available or used as often as they are nowadays (24). The latest IDF-DAR risk stratification calculator continues to assign the same moderate to high risk score to PWT1D, whether they use MDI or insulin pump therapy. Moreover, the IDF-DAR risk calculator assigns the same risk score to all pump users regardless of the type of the pump and whether AID technology is used (7). Nonetheless, many PWT1D, especially AID users and those living in Muslim-majority countries, continue to attempt to fast during Ramadan against the recommendations of professional societies and, many times, against the advice of their HCPs (9). Available data from those patients, albeit limited, show rates of acute complications that are much lower than previously reported, especially among users of CGM and/or insulin pump therapy (6,24–26). Therefore, considering these findings as well as the findings of our study, we believe it is now time to revise the current risk stratification calculator in the IDF-DAR practical guidelines to consider the type of insulin pump used by PWT1D and probably to assign a lower risk score to those who use AID technology (27).

The GRI gives higher weight to hypoglycemia compared with other CGM metrics

Table 3—Predictors of fasting most days of Ramadan (i.e., breaking fast ≤2 days because of diabetes) (*n* = 294)

	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)*	*P* value*
Age, years				
≤20	Reference		Reference	
>20	1.70 (1.07–2.71)	0.03	0.87 (0.36–2.10)	0.76
Female sex	0.93 (0.58–1.49)	0.76	0.91 (0.54–1.53)	0.72
Employment status				
Student	Reference		Reference	
Employed	1.92 (1.15–3.21)	0.01	1.45 (0.61–3.47)	0.41
Other	1.60 (0.77–3.34)	0.21	1.39 (0.53–3.62)	0.50
Level of education				
Elementary or middle school	Reference		Reference	
High school	1.40 (0.74–2.64)	0.31	1.56 (0.75–3.27)	0.24
Bachelor's degree or higher	2.30 (1.31–4.04)	<0.01	2.66 (1.02–6.99)	0.047
Has health insurance	0.95 (0.60–1.53)	0.85	0.62 (0.34–1.12)	0.11
Diabetes duration, years				
≤5	Reference		Reference	
>5–10	0.74 (0.40–1.37)	0.34	0.69 (0.36–1.34)	0.27
>10	0.91 (0.54–1.55)	0.74	0.56 (0.29–1.07)	0.08
Modality of therapy				
MDI + CGM	Reference		Reference	
Pump + CGM (AID)	1.68 (0.93–3.05)	0.09	2.37 (1.14–4.90)	0.02
Pump + CGM (conventional open loop)	0.51 (0.24–1.11)	0.09	0.59 (0.26–1.33)	0.20
Pump + SMBG	0.73 (0.17–3.16)	0.67	0.76 (0.16–3.50)	0.72
MDI + SMBG	1.21 (0.57–2.60)	0.62	1.32 (0.59–2.96)	0.50

*Adjusted for age, sex, educational level, employment status, insurance status, diabetes duration, and modality of diabetes treatment during Ramadan (AID, open loop, MDI + CGM, MDI + SMBG, or pump + SMBG).

(14). Considering that hypoglycemia is a major concern when PWT1D attempt to fast and is the most common cause of premature breaking of fasting during Ramadan, GRI may serve as a more relevant, sensitive, and predictive CGM metric in this context. In our study, pre-Ramadan GRI had a greater sensitivity in predicting PWT1D who are likely to fast most days of Ramadan compared with pre-Ramadan TIR. This is likely because GRI assigns greater weight to hypoglycemia than hyperglycemia, whereas TIR gives equal weight to hypoglycemia and hyperglycemia. Compared with PWT1D who had a pre-Ramadan GRI >40, those with GRI 21–40 were approximately two times as likely to fast most days of Ramadan, and those with GRI ≤20 were approximately three times as likely to fast most days during Ramadan. Moreover, the difference in GRI between PWT1D who attained the double target and those who did not was 31 points (23 vs. 54, respectively), compared with the smaller difference of 24 points noted in TIR between the same groups (80 vs. 56, respectively). Such disparity between GRI and TIR (despite both metrics being presented on a 100-point scale) suggests that GRI, compared with TIR, may have a greater dynamic range and potentially serve as a better predictor of who would be able to successfully fast during Ramadan. These findings are also aligned with the findings reported by Benhamou et al. (28), who found that GRI, compared with TIR, in a cohort of AID users also had a greater dynamic range and sensitivity to differences in the TBR. Therefore, pre-Ramadan GRI has the potential to serve as an additional, more sensitive predictor of successful fasting during Ramadan in conjunction with pre-Ramadan hemoglobin A_{1C} and/or TIR. Adding GRI to the risk stratification calculator in the IDF-DAR practical guidelines is worth considering.

Our study is unique in several aspects. To our knowledge, it is the first study to compare the safety and effectiveness of five treatment modalities of T1D during Ramadan, and it is the largest to examine the safety and effectiveness of AID during Ramadan intermittent fasting. Moreover, this is a real-world study in which the study participants were enrolled prospectively from the clinics without interventions in their routine clinical care. This type of studies minimizes the risk of performance bias, which can occur in clinical trials because of unequal care provided to the study groups. In addition, we used CGM-based data to comprehensively evaluate the glycemic control across the study groups, which allowed us to better assess the safety and effectiveness of the various treatment modalities.

The limitations of our study include the lack of glucose data and relatively small number of participants in the two SMBG groups (with MDI or pump therapy). Moreover, most of the MDI and open-pump users in our study were using intermittently scanned CGMs; few participants were using real-time CGMs. We also had no data about the level of income, physical activity, and dietary habits of the study participants nor the frequency of using the temporary target or exercise activity feature by the AID users, all of which may have affected the patients' glycemic control and their ability to complete fasting during Ramadan. In addition, the number of days during which fasting was broken was self-reported by the study participants, which carries the risk of recall bias. To minimize this risk, we collected the information about fasting immediately at the end of Ramadan. Furthermore, our

study participants were recruited from clinics that have endocrinologists, diabetes educators, and dietitians who are experienced in treating PWT1D, which may affect the generalizability of our findings to PWT1D who are cared for by less-experienced teams. Finally, whether our findings can be generalized to PWT1D living in parts of the world where fasting hours are longer than those in Saudi Arabia warrants additional studies.

Conclusions

Despite the challenges and presumed risks that PWT1D face as they attempt to fast during Ramadan, PWT1D who use AID technology can successfully fast most days of Ramadan while maintaining their glycemic control within the target range. The use of AID technology during Ramadan fasting is also safe, with no apparent increased risk of hypoglycemia, hyperglycemia, or acute complications of diabetes. Our study findings provide the first strong evidence of the safety, effectiveness, and superiority of AID technology relative to other treatment modalities of diabetes in PWT1D who plan to fast during the month of Ramadan, and we call for an update of the current guidelines and clinical practice. Assigning a lower risk score to PWT1D who use AID and would like to fast during Ramadan should be considered in these guidelines.

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Duality of Interest. M.E.A.-S. has served on an advisory panel for Medtronic, Insulet, Abbott, VitalAire, and Sanofi; has received honoraria for speaking from Abbott, Eli Lilly, Medtronic, Novo Nordisk, Sanofi, and VitalAire; and is a part-time diabetes consultant at Eli Lilly. N.A. has served on an advisory panel for Medtronic, Eli Lilly, and Sanofi and has received honoraria for speaking from AstraZeneca, Boehringer Ingelheim, Eli Lilly, Eva Pharma, Merck, Medtronic, Novo Nordisk, Vitalaire, and Sanofi. D.C.K. is a consultant with Better Therapeutics, EOFlow, Integrity, Lifecare, Nevro, Novo Nordisk, Rockley Photonics, and Thirdwayv. A.A. has served on an advisory panel for Medtronic, Novo Nordisk, Eli Lilly, Vital Air, and Sanofi; has received honoraria for speaking from AstraZeneca, Eli Lilly, Medtronic, Novo Nordisk, and Sanofi; has received research support from AstraZeneca and Novo Nordisk; and is a part-time diabetes consultant at Eli Lilly. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. M.E.A.-S. formulated the study idea and design, reviewed the literature, analyzed and interpreted the data, and wrote, reviewed, and edited the manuscript. S.A. reviewed the literature, collected part of the data, and wrote and reviewed the manuscript. S.A. collected part of the data and reviewed and edited the manuscript. N.A. helped with data collection and interpretation and reviewed and edited the manuscript. D.C.K. reviewed the data, contributed to discussion, and reviewed and edited the manuscript. A.A. helped with data collection and interpretation and reviewed and edited the manuscript. All authors approved the final version of the manuscript.

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