Ramadan Fasting and Diabetes (2020): The Year in Review

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Abstract

The literature on health aspects of Ramadan fasting (RF) is widely spread in many journals, making it not readily accessible to those interested in the subject. We aimed to provide a narrative overview of the global literature production in 1 year (2020) on diabetes and RF. This was a narrative, nonsystematic review of the international literature from a single major medical online database (i.e., PubMed) during the year 2020. The search term "Ramadan fasting AND Diabetes" was used, and the relevant literature was narrated in a concise thematic account. The publications spanned a vast array of topics related to RF, including assessments of safety and efficacy profiles of older and newer diabetes therapies, modes of insulin delivery, evaluating the role of utilizing advanced technology for the treatment, and monitoring of blood glucose during RF. Increased interest was evident in capturing patients' perspectives and healthcare professionals' perceptions, attitudes, and practices during Ramadan. Fasting by high-risk groups was studied. Not surprisingly, some reports covered COVID-19 and Ramadan and the role of telemedicine in ramadan. The current literature review presents this year's research data on the safety of fasting practices, care models, and patients' experiences and perspectives. It emphasizes the need for more comprehensive interventions for high-risk patients, promoting newer antidiabetic medicines, and advanced technology for safer fasting practices.

Keywords: Children and adolescents, diabetes, diabetic ketoacidosis, epidemiology, healthcare professionals, high-risk patients, hypoglycemia, literature, patients' perspectives, perceptions, Ramadan fasting, COVID-19, ethnic, muslims

INTRODUCTION

Ramadan fasting (RF) observed by adult Muslims entails abstinence from food, water, all oral substances, intravenous fluid therapy, and smoking between dawn and sunset during the 9th month of the Muslims' lunar calendar.[1] Ramadan's impact on health and disease stems from the biological effects of prolonged fasting during the daytime and possible overfeeding at night and its various social changes. The last three decades witnessed a rising interest in the research on RF in health and disease.[2] Diabetes has been the most extensively studied single medical condition in connection with RF.[3] Despite the increase in volume of the literature, concern has been voiced regarding the quality of publications on the subject.[4,5]

The literature on health aspects of Ramadan fasting (RF) is widely spread in many journals, making it not readily accessible to those interested in the subject. We therefore aimed to provide a thematic overview of the global research work conducted in the realm of RF during 2020 on the impact of RF in people with diabetes. We aimed to provide a concise bird's eye view of the literature published in a year and to identify the basis of evidence that may guide clinical practices for the years to come.

MATERIALS AND METHODS

This is a narrative, nonsystematic review of the literature retrieved from one online database over a full calendar year (2020). The PubMed search engine of the National Center for Biotechnology Information at the U.S. National Library of Medicine was used. The search term ("Ramadan Fasting" OR "Fast of Ramadan") AND diabetes, with time filters from January 1, 2020, to December 31, 2020, was used to identify the relevant records. Retrieved articles were examined for

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relevance, reviewed, and narrated thematically, similar to our previous reports.[6-8] The aim is to provide reasonably concise but adequately representative themes surrounding RF. One author drafted an initial manuscript, and all other authors contributed to the intellectual content using a single version loaded online using Google Docs. Full-text research articles in English were included. No statistical analysis was conducted on the data included in the original articles, and detailed numerical presentations were avoided. Original articles and systematic reviews were included, but guidelines, short narratives, and statements were excluded. The final product was refined through several multilateral rounds of discussion.

RESULTS

The various themes that emerged from the review of the literature are listed in Table 1. The results are presented in similar thematic flow.

Epidemiology of diabetes and Ramadan

The Diabetes and Ramadan—Middle East and North Africa (DAR-MENA) was a prospective, observational study of adults with type 1 diabetes (T1D) and type 2 diabetes (T2D) who did/did not intend to fast during Ramadan of 2016. Data were collected 6 weeks before Ramadan and within 1–2 months after Ramadan. Measurements included proportions of who fasted, reasons for fasting and/or not fasting, changes in diabetes treatment, rates of hypoglycemia, and the proportion with access to diabetes education. The T2D dataset was published in 2019, and the T1D subset was published in 2020.[9] In the analysis of the population with T1D of 136 participants, 76.9% fasted for at least 1 day, 72.3% fasted for at least 15 days, and 48.5% fasted for 30 days. The majority (63.0%) reported personal decisions as a reason to fast. The most common causes for not fasting were the fear of diabetes-related complications (58.6%) and previous complications related to fasting (48.3%). Diabetic medication regimens were adjusted for 84.6% of participants, and the treatment dose was changed for 72.8%. Confirmed and severe hypoglycemia was not different before and during Ramadan. Almost half of the

participants had access to diabetes education (45.6%). The DAR-MENA study found that despite the risks associated with fasting for people with T1D, almost half fasted for the entire month with no significant change in hypoglycemia events. Since the current International Diabetes Federation and Diabetes and Ramadan guidelines do not endorse fasting for people with T1D, it is crucial that those who insist on fasting work closely with their healthcare practitioner to avoid complications. Syed *et al.*[10] reported on glycemic control, physician counseling, and patient practices from a tertiary care hospital in Pakistan (DAR-GRACE study). They described patient practices and knowledge about RF. The group also assessed if and how physicians provided adequate counseling on RF and adjustment of medications accordingly. The work was conducted via a cross-sectional study in Islamabad, Pakistan, from June to August 2018 using a questionnaire to assess patients' knowledge, risk category, pre-Ramadan counseling, medication adjustment, lifestyle changes, pre- and post-Ramadan glycated hemoglobin levels, and complications during Ramadan. The mean number of fasting days observed was 22.0. Pre-Ramadan, 44.1% of the patients consulted their physicians regarding RF practices, of which 87.5% of them received appropriate counseling. Medications were adjusted in only 25% of cases. Overall, 15.1% of patients were in the high-risk fasting category, while 40.1% and 44.9% were in the moderate-risk and low-risk fasting categories, respectively. During the month of Ramadan, 6.25% were hospitalized due to diabetes-related complications. Glycated hemoglobin levels fell significantly ($P < 0.0001$). The study highlighted the need for Ramadan-focused physician and patient education.

Mansouri *et al.*[11] assessed the current practices of patients with diabetes to control blood glucose levels during Ramadan in a cross-sectional study. Data were collected through a structured and interview-based questionnaire to assess the association between self-monitoring of blood glucose (SMBG) and hypoglycemia. The questionnaire recorded information about demographics, duration of diabetes, treatment of diabetes, and hypoglycemia complications during Ramadan. The study's primary outcomes included frequency of SMBG during fasting in Ramadan and association of SMBG with hypoglycemia and break of fasting. The secondary outcomes included medications, glycemic control, and other influencing factors. The study showed that the majority of patients used a combination of metformin + sulfonylurea (23.02%), followed by metformin + insulin (20.86%), insulin alone (12.94%), and metformin alone (8.63%). The majority of the patients monitored their blood glucose level at pre-iftar (56.8%) following a hypoglycemic episode (30.2%), post-iftar (29.4%), and rarely monitored their blood glucose in the afternoon (3.5%). Only 10.1% monitored their blood glucose daily. Patients who experienced symptoms of hypoglycemia and had to break their fast at least once were 41% and 27.2%, respectively. There was a significant association between age and gender with symptoms of low blood sugar. Furthermore, a significant association between blood sugar monitoring and high blood

Table 1: Themes emerged from the review of the literature published on diabetes and Ramadan fasting during the year 2020

Epidemiology of diabetes in Ramadan: Observational studies documenting disease burden and patterns, patients' behavior, medical care, and outcomes in the community and clinic populations

Impact of diabetes on glycemic and metabolic control in general and on selected biomarkers

Education and lifestyle aspects of care

Pharmacological management: Clinical practice and research on safety and efficacy of various classes of antidiabetic medications

Use of technology in management (treatment and monitoring) of diabetes and its impact on reducing hypoglycemia

Professional perspectives and patients' advocacy

Patient's perspectives (including mental health, quality of life, etc.)

COVID-19 and Ramadan and role of telemedicine in Ramadan

sugar level was shown ($P = 0.041$), suggesting that daily blood sugar monitoring could increase blood sugar levels during Ramadan. The study helped provide a better understanding of SMBG level and risk of hypoglycemia. Furthermore, it emphasized the need for pre-Ramadan education on when to break the fast, along with the frequency and timing of recommended SMBG.

Impact of fasting on diabetes and metabolic metrics

Kovil and Shaikh[12] studied the alterations in biomarkers, viz., body weight (BW), body mass index (BMI), glycated hemoglobin A1c (HbA1c), and blood pressure (BP, systolic and diastole BP [SBP and DBP]) due to RF on 50 T2D patients of Western India. The biomarkers mentioned above were measured immediately before starting the fast and 45 days after Ramadan. The results showed a beneficial impact of intermittent fasting (IF) among T2D patients via reductions in BW, BMI, and serum HbA1c levels. Moreover, the authors advised that IF can be utilized as therapy with other pharmacological therapies for T2D.

To assess how physicians use the risk stratification tool for advising patients deemed at high risk for RF, Rashid *et al*.[13] conducted a systematic review. Their selection was limited to randomized controlled trials (RCTs) and prospective observational studies, between 2007 and March 2019, investigating the impact of Ramadan on patients with diabetes at high risk of fasting. The authors reported that the global dissemination and implementation of guidelines for the management of diabetes during Ramadan broke much of the previous inertia among healthcare providers. The concept of pre-Ramadan assessment for risk categorization, therapeutic dose modification together with SMBG has markedly reduced the risk and hospitalization during Ramadan. The authors acknowledge that there remains limited data on RF in high-risk patients with diabetes. In addition, there was minimal diversity in the published results. With education and self-titration, the complication rates during Ramadan were minimally higher than other times of the year in this group.

Abdullah *et al*.[14] investigated the effects of RF on adiponectin, leptin, leptin to adiponectin ratio (LAR), growth hormone (GH), human-sensitive C-reactive protein (hs-CRP), and diabetic and metabolic syndrome factors in patients with T2D, their first-degree relatives (FDRs), and healthy controls. The authors designed a cohort study involving 98 Yemeni male subjects aged 30–70 years old: 30 T2D, 37 FDRs of T2D patients, and 31 healthy control subjects. Subjects' BMI, waist circumference, and BP were measured, and venous blood samples were collected twice: The first samples were collected a couple of days before RF (baseline) and the second samples after 3 weeks of fasting. The authors found that Ramadan IF decreased adiponectin levels and increased leptin, LAR, insulin, and insulin resistance in both T2D and FDRs; decreased GH in both FDRs and healthy controls; and increased hs-CRP in healthy controls. Moreover, Ramadan IF neither worsened patients' glycemic parameters nor improved

it, except for a slight improvement in HbA1c in T2D, FDRs, and healthy controls.

Tahapary *et al*.[15] assessed the impact of RF on and metabolic profile and hypoglycemia events among T2D patients by a literature review of adult observational studies, which reported on glucose parameters, lipid profile, and hypoglycemia events among T2D patients during Ramadan. A total of 28 observational studies conducted in Middle Eastern, African, and Asian countries were included. The authors found decreases in fasting plasma glucose (FPG) level, total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride (TG). No studies reported fatal hypoglycemic events (HEs). The authors concluded that RF resulted in slight improvement of overall metabolic profile and anthropometry among T2D patients with a relatively low incidence of hypoglycemia.

Ramadan-focused education and outcomes

Four reports addressed the impact of Ramadan-focused education on patient outcomes.[16-19] Two were original studies,[16,17] and two were systematic reviews and meta-analysis.[18,19]

Shaltout *et al*.[16] evaluated the effect of a culturally-based pre-Ramadan education program (PREP) on glycemic control, weight, adherence to postsunset physical activity, perception of hypoglycemia, and antidiabetic medication dose adjustment during RF in T2D. A total of 1008 T2D patients were offered a culturally-based PREP in addition to the standard of care 2 months before Ramadan. A retrospective interview 1 month after Ramadan compared the fasting experience of PREP attendees (470 patients) with those who merely received standard of care (538 patients) (non-PREP). RF improved glycemic control with a significant correlation between HbA1c percent reduction and the number of fasting days. The authors concluded that RF was beneficial for people with T2D with reductions in HbA1c in correlation with the number of fasting days. PREP participants had better HbA1c and weight reduction even with an equal number of fasting days to nonparticipants. Further, PREP participants performed more Taraweeh night prayers with more decline of HbA1c and weight. Darko *et al*.[17] evaluated the implementation of a structured education program for safer Ramadan. A "Safer Ramadan" was a multifaceted exercise comprising self-management with community awareness program and healthcare professional (HCP) training. The program took place in two cities in the UK before Ramadan 2017. Uptake and attendance were evaluated, and qualitative interviews and focus groups were completed with people attending the program and various stakeholders involved in implementation and delivery. The success of the implementation varied, and engagement by primary care was limited. The interviews highlighted barriers and facilitators of the program implementation. These were the referral pathway, program content, and feedback on the delivery of the program. Provision of interventions that provide support and education for Muslims during Ramadan

were implemented in communities and valued by general practitioners and practice nurses. However, heavy workloads to support delivery made it difficult for practices to engage. Recommendations for future delivery of the program indicate that greater attention should be given to marketing and its supporting practices. Furthermore, training for practice nurses to support patients before Ramadan and provision of funding is required.

Gad *et al.*[18] assessed the effect of Ramadan-focused education on clinical and metabolic parameters in patients with T2D who fast during Ramadan. The literature search was done from 770 records; 430 full-text studies were assessed. After exclusions, the final quantitative analysis included 16 studies. Pre-Ramadan education was associated with a significant reduction in HbA1c and LDL, an increases in TG and weight, and no changes in HEs, BMI, TC, HDL, or BP ($P > 0.05$) during Ramadan. This systematic review and meta-analysis showed that Ramadan-focused diabetes education leads to a decrease in HbA1c and LDL but an increase in TG and weight during Ramadan. It also identified a lack of head-to-head studies and limited observational studies with adequately assessed endpoints. Furthermore, Tourkmani *et al.*[19] evaluated the impact of a Ramadan-focused diabetes education program on hypoglycemic risk and other clinical and metabolic parameters. A systematic literature search was performed to identify relevant studies meeting the inclusion criteria from inception. Seventeen studies were included in this systematic review; five of them met the criteria to compile for a meta-analysis. Significant reduction of hypoglycemia risk occurred (by 81%) for fasting patients in the intervention group who received Ramadan-focused education compared with patients receiving conventional care (odds ratio 0.19). In addition, HbA1c significantly improved among patients who received a Ramadan-focused diabetes education intervention, compared with those receiving conventional care. The authors concluded that Ramadan-focused diabetes education significantly impacted hypoglycemia and glycemic control, with no significant effect on BW, blood lipids, or BP.

Dietary practices during Ramadan
Three articles addressed the dietary and nutritional aspects of care during Ramadan.[20-22] Mohd Yusof *et al.*[20] evaluated the effect of structured Nutrition therapy (NT) program versus standard care (SC) in patients with T2D during Ramadan. The study was an 8-week, parallel, nonrandomized study with patients' preference involving 64 T2D patients. The participants chose their preferred group, i.e., structured Nutrition therapy (NT) (structured Ramadan NT [sRNT]) or SC. The participants in the site group received a Ramadan-focused nutrition plan throughout the study, whereas the patients in the SC group received standard nutrition care. Clinical outcomes and quality of life (QoL) inser was assessed. Nearly two-thirds, i.e., half of the participants (63%) chose sRNT as their preferred group. Both groups had comparable baseline characteristics. After 8 weeks of the respective intervention, participants in the sRNT group had lower levels of FPG, TG, and self-monitored glucose

levels at predawn and prebedtime ($P < 0.05$) than participants in the SC group. Although not different between groups, HbA1c levels decreased significantly in the sRNT but not in the SC group. QoL and satisfaction scores improved significantly in the sRNT group but not in the SC group. The structured NT regimen for Ramadan is a feasible and beneficial program for T2D patients observing RF as it showed an improvement in clinical outcomes and QoL.

Hsu *et al.*[21] explored the association between dietary knowledge, attitude, and practices during Ramadan among Muslim patients with T2D. A total of 401 patients with diabetes were recruited from public clinics in Indonesia. Patients were required to recall their food consumption frequencies of high-fiber food, deep-fried food, and high-sugar dessert and were assessed on relevant knowledge and attitudes. Vegetable consumption and preference were both high among patients. However, only 4.5% recognized that brown rice is rich in fiber, and 19% agreed that whole-grain foods were accessible. Deep-fried food consumption and availability at home were common, even though most thought it should be avoided. Patients with a lower preference for deep-fried foods were less likely to consume them during Ramadan. Knowledge of the health implication of glycemic index (GI) was associated with more high-fiber food consumption. Interestingly, knowing the potential risk of added sugar on blood glucose level was associated with high sugar dessert consumption. The authors concluded that the food environment is an essential factor influencing patients' dietary behavior, dietary knowledge and attitude.

Assaad Khalil *et al.*[22] determined the GI of a variety of meals containing dates in healthy subjects compared to patients with T2D and the effect of dates on the postprandial glucose excursions using a continuous glucose monitoring system (CGMS). Twenty patients with T2D and twenty healthy subjects matched for age, sex, and BW participated. Testing was applied on separate days (on three occasions) with 50 g of glucose and 50 g equivalent of available carbohydrates from 9 date meals. The GI was calculated as ratios of the total areas under the response curves for dates compared to glucose. The minimed 530G with-enlite system was used for continuous glucose monitoring. There was no significant difference between the mean GI of dates between both study groups. However, there was a significant difference in blood glucose peak among varieties of meals containing dates in those with T2D. The authors concluded that the varieties of dates included in the study have a low GI. However, CGMS was valued beyond GI calculation to study the postprandial glucose excursions among patients with T2D.

Pharmacological management of diabetes during Ramadan
Pharmacological therapies during Ramadan generated the most interest over the last year, with several new studies evaluating both oral and injectable diabetes therapies.[23-31] The studies included evaluations of individual drugs, targets, and professionals' perceptions [Table 2].

Table 2: Summary of the studies on pharmacological management of diabetes during Ramadan

First author [reference] (trials if any)	Study agent	Objectives	Outcomes
Sahay *et al.*[23] (LixiRam study)	Lixisenatide plus basal insulin	A *post hoc* analysis of the LixiRam trial	A combination of lixisenatide prandial+BI may be a suitable treatment option for people with T2D who fast Ramadan
Lum *et al.*[24]	Multiple medications	Efficacy and safety of use of the FAST during Ramadan: A prospective, multicenter, randomized controlled trial	The group emphasized the importance of efficacious, safe, and culturally tailored epistemic tools for diabetes management
Kalra *et al.*[25]	Premix insulins	A prospective validation survey of Indian physicians to assess usage of in management of diabetes	Premix insulins were preferred for insulin initiation. IDegAsp was preferred over other premixed insulins twice daily. premixed insulins were recommended for intensification
Hassanein *et al.*[26] (ORION study)	Insulin glargine 300 U/mL	Evaluate the safety and effectiveness of Gla-300 in insulin-treated people with T2D before, during and after Ramadan, in a real-world setting	People with T2D treated with GLA-300 who fasted during Ramadan had low risk of severe/symptomatic hypoglycemia and improved glycemic control
Hassanein *et al.*[27] (Dia-Ramadan)	Gliclazide MR (60 mg)	To explore the real-world safety and effectiveness of gliclazide MR in T2D during Ramadan	There is low risk of hypo, with maintenance of glycemic control and weight while fasting on gliclazide MR
Harbuwono *et al.*[30]	Multiple medications	Evaluate glucose variability in subjects with T2D on oral antidiabetic agents using CGMS during and after RF	Nutritional intake and energy expenditure during both periods were comparable. RF is not associated with increased glucose variability in this cohort
Ahmedani and Ghafoor[31]	Multiple medications	Evaluate the effect of keeping flexible glycemic targets during fasting and tighter targets during nonfasting hours in insulin-treated people during Ramadan	By keeping flexible glycemic targets during the day and tighter targets during the night, safe fasting was feasible with significant improvement in overall glycemic control without significant major complications

T2D: Type 2 diabetes, Hypo: Hypoglycemia, MR: Modified release, CGMS: Continuous glucose monitoring system, BI: Basal insulin, RF: Ramadan fasting, FAST: Fasting Algorithm for Singaporeans with T2D

LixiRam study was the first randomized trial comparing the safety and efficacy of lixisenatide + basal insulin (BI) versus sulfonylurea + BI in people with T2D who observed RF.[23] This *post hoc* analysis focused on the LixiRam study population from India. Adults with T2D insufficiently controlled with sulfonylurea + BI ± another oral antihyperglycemic drug, were randomized 1:1 to receive lixisenatide, (a Glucagon-Like Peptide-1 Receptor Agonist (GLP-1 RA)), + BI of continue sulfonylurea + BI treatment. In total, 150 participants were randomized. One participant with lixisenatide + BI versus 5 participants with sulfonylurea + BI experienced ≥one documented symptomatic HE during RF. The incidence of any hypoglycemia was numerically lower with lixisenatide + BI versus sulfonylurea + BI during RF (1.3% versus 14.7%, respectively). No new safety signals were identified. The combination of lixisenatide + BI may be a suitable treatment option for people with T2D who elect to observe RF.

Lum *et al.*[24] evaluated the efficacy and safety of using the Fasting Algorithm for Singaporeans with T2D (FAST) during Ramadan in a prospective, multicenter, RCT. Participants were randomized to use of FAST or control (usual care without FAST) groups. Efficacy outcomes were HbA1c level, fasting blood glucose, and postprandial glucose changes. The safety outcomes were major or minor hypoglycemia during RF. Glycemic variability and diabetes distress were also evaluated. A total of 97 participants were randomized (FAST = 46, control = 51). The HbA1c improvement during Ramadan was fourfold greater in the FAST group (−0.4%) than in the control group (−0.1%) ($P = 0.049$). The mean FPG level decreased in the intervention group (−3.6

mg/dL) and increased in the control group ($P = 0.034$). The mean postprandial glucose showed greater improvement in the intervention group (−16.4 mg/dL) than the control group (−2.3 mg/dL). There were more mild HEs based on SMBG readings in the control group (intervention: 4, control: 6; $P = 0.744$). Glycemic variability was not different between the two groups ($P = 0.284$). Diabetes distress scores were not different between groups ($P = 0.479$). The authors emphasized the importance of efficacious, safe, and culturally tailored epistemic tools for diabetes management.

To understand the pros and cons of premixed insulin in diabetes management during Ramadan, Kalra *et al.*[25] conducted a questionnaire-based survey to provide specific recommendations for appropriate management of T2D with premixed insulin. The respondents were requested to answer an electronic survey based on their clinical experiences with patients having diabetes. Overall, 1408 doctors participated in the survey. The majority of physicians preferred a premix insulin regimen for initiation. Short-term therapy with premix insulin in insulin-naive T2D patients with symptomatic hyperglycemia and/or glucotoxicity was strongly recommended by 40.7% of physicians. Initiation of insulin early in T2D was recommended by 58.7% of physicians in cases where noninsulin drugs did not achieve glycemic goals. Premix insulin analogs were preferred over human premix insulin by more than half of participating physicians (52.2%). Premix insulin analogs were preferred over BI by 49.8% of physicians. Nearly half (44.5%) of the physicians recommended initiating twice daily premix analogs over once-daily BI to achieve recommended glycemic targets. Around 42% of physicians strongly believed that

twice-daily/thrice daily premix insulin analogs provide comparable glycemic control and safety profiles to basal plus bolus regimens with the additional benefit of simplicity. During Ramadan, premix insulin analogs were recommended over human premix by 46.5% of physicians, giving improved safety and dosing flexibility. Therefore, it seems that the majority of Indian physicians concur with the recommendations of Indian 2017 guidelines. Premix insulins were preferred for insulin initiation. IDegAsp was preferred over other premixed insulins by the majority of physicians. Twice daily premixed insulins were recommended for intensification.

The ORION study evaluated the safety and effectiveness of GLA-300 during Ramadan in a real-world setting.[26] It was a prospective, observational study across 11 countries that included participants with T2D treated with GLA-300 before, during, and after Ramadan periods. The primary endpoint was the percentage of participants experiencing ≥one event of severe and/or symptomatic documented hypoglycemia with self-monitored glucose level of ≤70 mg/dL during Ramadan. Secondary endpoints included changes in HbA1c, insulin dosages, and adverse events (AEs). The percentages of those experiencing ≥one event of severe and/or symptomatic documented hypoglycemia were low in the pre-Ramadan (2.2%), Ramadan (2.6%), and post-Ramadan (0.2%) periods. No participants reported severe hypoglycemia during Ramadan or post-Ramadan; one participant reported severe hypoglycemia in pre-Ramadan. HbA1c fell from pre- to post-Ramadan, and GLA-300 daily dose was reduced from pre-Ramadan to Ramadan. The incidence of AEs was 5.5%. In ORION, people with T2D treated with GLA-300 who fasted during Ramadan had a low risk of severe/symptomatic hypoglycemia and improved glycemic control.

DIA-RAMADAN study explored the real-world safety and effectiveness of gliclazide modified-release (MR) in patients with T2D fasting during Ramadan.[27] DIA-RAMADAN was a prospective, international, observational study conducted in nine countries. Patients >18 years of age with T2D (N = 1244) were examined at an inclusion visit 6–8 weeks before the start of Ramadan. Patients were asked to record treatment changes, HEs, and other AEs. Gliclazide MR was taken once daily for 14–18 weeks. A second visit was conducted 4–6 weeks after the end of Ramadan. The primary endpoint was the proportion of patients reporting ≥one symptomatic HEs. Secondary endpoints included HbA1c, FPG, and BW were secondary endpoints. The proportion of patients reporting ≥one symptomatic HEs during Ramadan was low (2.2%) with no reported severe HEs. Significant changes in HbA1c (−0.3%), FPG (−9.7 mg/dL), BW (−0.5 kg), and BMI (−0.2 kg/m²) occurred between visits (P < 0.001). Therefore, the authors concluded that patients with T2D treated with gliclazide MR during Ramadan have a low risk of hypoglycemia, maintaining glycemic control, and weight while fasting.

Gad *et al*.[28] evaluated the safety and efficacy of the newer glucose-lowering treatments on glucose control, weight, BP, and hypoglycemia in patients with T2D during Ramadan. A literature search was done, and a total of 20 studies were included in the meta-analysis expressed as standardized mean difference (SMD). The authors found that dipeptidyl peptidase-4 inhibitors (DPP-4i) led to a significant reduction in HbA1c (SMD - 0.25) and a nonsignificant decrease in weight (SMD - 1.06) during Ramadan. Glucagon-like peptide-1 agonist therapy was associated with a significant decrease in HbA1c (SMD - 0.68) and a nonsignificant decrease in weight (SMD - 2.57) and SBP (SMD - 3.50) after Ramadan. Sodium-glucose co-transporter 2 inhibitor (SGLT-2i) therapy was associated with a significant decrease in HbA1c (SMD - 0.51) and a nonsignificant decrease in weight (SMD - 1.41), SBP (SMD - 1.10), and DBP (SMD - 2.08) after Ramadan. This meta-analysis confirmed the clinical benefits of these glucose-lowering medications in patients with T2D who fast during Ramadan.

Further evidence on the use of SGLT-2is during Ramadan was provided by Beshyah *et al*.[29] The authors followed up the evolving perceptions and practices regarding the use of SGLT-2is in Ramadan by comparing the results of three surveys published in 2015, 2017, and 2019. The results showed that senior doctors represented 43.5%–66.4%, and endocrinologists accounted for 38.1%–60.2% of respondents. There was a steady reduction in the proportions of respondents who did not know SGLT-2is at all, those who have just heard about the class, and those pretty familiar with the class but have not yet used any. While the proportions of those using the SGLT-2is class "occasionally only" were stable, those who used SGLT-2is "regularly" increased. Respondents who felt SGLT-2is are safe and may be used in all fasting diabetic patients increased. On the other hand, the view that SGLT-2is should not be used decreased progressively. The majority of the three surveys suggested that specific advice should be given if they allow SGLT-2is during Ramadan. More respondents recommended taking the medication with the first evening meal rather than before the last predawn meal and attending to their hydration status. One-third of respondents would resume SGLT-2is immediately after the end of Ramadan; 15% after 1–2 weeks, or prefer to wait till the following medical or educator's clinic visit.

RF is associated with changes in eating, physical activity, sleeping patterns, and medications, leading to considerable glucose variability (GV) in people with diabetes. However, limited studies have examined GV in subjects with T2D who fast in Ramadan. Thus, Harbuwono *et al*.[30] sought to evaluate GV in subjects with T2D on oral antidiabetic agents using a continuous glucose monitoring system (GCMS) during and after RF. The observational study was done in the Indonesian Medical Education and Research Institute, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia. Ten subjects with T2D who underwent RF in 2019 were recruited. The participants were free from cardiovascular, kidney, severe liver, chronic gastrointestinal, and autoimmune diseases. Insertion of GCMS for measuring interstitial glucose was performed after at least 2 weeks of RF and 4 weeks after the end of RF, with a minimum

of 3 days' observation. The mean amplitudes of glycemic excursion during and after Ramadan were similar ($P = 0.94$). In line with this, the average interstitial glucose ($P = 0.48$), the maximum interstitial glucose ($P = 0.35$), the minimum interstitial glucose ($P = 0.24$), and the duration of hypoglycemia ($P = 0.25$) were also similar in both periods. Overall, nutritional intake and energy expenditure during both periods were comparable. RF was not associated with increased GV in this cohort of subjects with T2D. Although the results were encouraging, the sample size was too small to be generalized to the wider T2D population.

Ahmedani and Ghafoor[31] proposed keeping flexible glycemic targets during fasting and tighter targets during nonfasting hours in insulin-treated people with T2D during Ramadan. They conducted a prospective study in Pakistan (2014). People with T2D on split mixed insulin therapy were recruited. The pre-Ramadan education was provided, and insulin doses were adjusted before Ramadan. A 24-h telephone helpline service was provided to achieve predetermined glycemic targets and minimize complications. A total of 54 people with T2D with a mean age of 55 years were recruited. Mean glucose levels achieved were 184 mg/dL and 179 mg/dL during the day and night, respectively. Mean HbA1c and serum creatinine significantly improved at the end of fasting. Only 0.6% of episodes of hypoglycemia, including one significant hypoglycemia and 30% of episodes of hyperglycemia, were recorded. No hospitalizations were needed. By adopting flexible glycemic targets in the day and tighter targets at night, safe fasting was feasible with significant improvement in overall glycemic control and no major complications.

Technology, hypoglycemia, and glucose variability

The use of technology has become an integral part of diabetes management, allowing patients to achieve better glycemic control and reduce the risk of hypoglycemia. In RF, this becomes even more pertinent to help patients achieve a safer Ramadan experience. Three studies evaluated the impact of technology in patients with diabetes during Ramadan.

Saadane *et al.*[32] assessed the effect of RF on several glucose metrics using flash glucose monitoring (FGM). Complete FGM data for 29–30 days before, during, and after Ramadan were available for 13 T1D and 27 insulin-treated T2D patients. Indicators of mean glucose, GV, and time in different glycemic ranges were analyzed. RF was associated with an increase in time in hyperglycemia ($P < 0.001$) and a decrease in time in hypoglycemia ($P = 0.003$) and time in the target range ($P < 0.001$). No significant differences in markers of GV occurred in RF; however, RF was associated with a significant reduction in GV during the day but not at night time with an increase in the ensuing nonfasting period. The authors concluded that RF was associated with an increase in hyperglycemia in insulin-treated patients, a reduced time in the target range, and a nocturnal increase in GV, indicating a need for more refined management algorithms.

The utility of the flash glucose monitoring system (FGMS) after adjusting the dose of insulin and sulfonylureas to mitigate the risk of hypoglycemia was evaluated in in patients with T2D who fast during Ramadan.[33] Patients with T2D on either BI or sulfonylureas and at least two other glucose-lowering agents received structured education and adjustment of insulin or sulfonylurea dose according to the PROFAST Ramadan protocol. GV and episodes of hypoglycemia were assessed (FreeStyle Libre [FSL]) before and during Ramadan. A total of 33 patients with T2D on sulfonylurea (SU+) ($n = 21$), on BI+ ($n = 12$) aged 51 years with a diabetes duration of 13.1 years were studied. The average sensor glucose was 154 mg/dL with 65.2% in the target range before Ramadan, while the average sensor glucose was 156 mg/dL with two-thirds in the target range during Ramadan. Hypoglycemia rates were in the whole group (2.9 vs. 2.9), in the SU+ (3.7 vs. 3.0), and in the BI+ (1.7 vs. 2.9) groups. Estimated HbA1c (eHbA1c), average glucose, and time in range did not change in the SU + and BI + groups before and during Ramadan. The authors concluded that a structured education with adjustment of the dose of glucose-lowering medication alongside the use of the FGMS could effectively mitigate the increased risk of hypoglycemia in patients with T2D on multiple glucose-lowering therapies who fast during Ramadan. The same group developed a machine-based algorithm from clinical and demographic data. Physical activity and GV were used to predict hyperglycemic and hypoglycemic excursions in patients with T2D on multiple glucose-lowering therapies who fast during Ramadan.[34] Thirteen patients (10 males and 3 females) with T2D on three or more antidiabetic medications were studied with a Fitbit-2 pedometer device and FSL (Abbott Diagnostics) 2 weeks before and 2 weeks during Ramadan. Several machine learning techniques were trained to predict blood glucose levels in a regression framework utilizing physical activity and contemporaneous blood glucose levels, comparing Ramadan to non-Ramadan days. The median age of the participants was 51 years, the median BMI was 33.2 kg/m^2, and the median HbA1c was 7.3%. Their model accurately estimated normal glucose levels in 95.2% and hyperglycemic events in 82.6% of the readings, but fewer hypoglycemic events (27.9%) were captured. The optimal XGBoost model prioritized age, gender, BMI, and HbA1c followed by glucose levels and physical activity. Interestingly, the blood glucose level prediction was influenced by the use of SGLT-2i. The authors concluded that XGBoost, a machine learning AI algorithm, achieves high predictive performance for normal and hyperglycemic excursions but has limited predictive value for hypoglycemia in patients on multiple therapies who fast during Ramadan.

Hybrid closed-loop automated insulin delivery systems have helped T1D users close the loop between glucose monitoring and insulin delivery, a significant step forward in simulating the glucose-responsive insulin secretory function of a healthy pancreas. Ahmed and Gallo[35] reported on a Do-It-Yourself Artificial Pancreas Systems (DIY APS) T1D user who was able to fast successfully on most days of Ramadan after adopting this system and the physician's perspective on these systems. DIY APS are forms of hybrid closed-loop systems that use open-source algorithms, which govern the delivery of insulin

in response to interstitial glucose and other variables that are personalized to an individual.

Professional perspectives and advocacy

A few reports addressed the professional perspectives [Table 3]. Alawadi *et al*.[36] assessed the impact of optimum care, which includes Ramadan-focused education, FGM, dietary advice, and treatment adjustment on the safety of RF in people with T1D. Thirty persons with T1D who insisted on observing RF were recruited into the study. At the pre-Ramadan visit, all patients received Ramadan-focused education and FSL sensor insertion and training. Patients used the sensor for 6 weeks (pre-Ramadan and during Ramadan). The physical and biological parameters were collected 2–4 weeks before and after Ramadan. Twenty-two patients on basal-bolus insulin and two on insulin pumps had FSL data. The average number of days fasted was 24. Learning benefits were reported by 95% of patients following the pre-Ramadan educational session. There were no clinically significant changes in physical and/or biological data between pre- and post-Ramadan. 63% reported making insulin dose adjustments in Ramadan. FGM data showed that 46.7% of patients had more than ten hypoglycemic episodes in the 2 weeks before Ramadan compared to 29.2% during Ramadan. However, none of the data were statistically significant apart from HbA1c, which decreased from 8.2% before Ramadan to 7.9% post-Ramadan ($P = 0.010$). There was one episode of diabetic ketoacidosis (DKA), reportedly due to missing insulin to avoid hypoglycemia. The optimal care of selective patients with T1D with low complication rates might allow RF to improve glycemic control and without an increase in hypoglycemic, biometric, or metabolic parameters. Larger, RCTs are required to generalize this as a recommendation.

Elamari *et al*.[37] assessed the impact of fasting on the glycemic control of patients with diabetes prepared for fasting as recommended by the American Diabetes Association (ADA) in 2010. They conducted a prospective cohort study in 2014, including diabetic patients wishing to fast during Ramadan, consenting to participate in this study. They excluded patients considered at very high risk according to the ADA classification. Patients included had a consultation before Ramadan (D0)

consisting of education and treatment adjustment. This was followed by a medical visit during Ramadan (D7), then at D30 and D60. The study included 34 patients, of whom 60% were women, with a mean age of 50.4 years, an average of 6.2-year diabetes history, and a mean BMI of 27.8 kg/m^2. Therapeutic adjustments (D0) were decreased dose of sulfonylurea (SH), gliptin adds in patients at risk of hypoglycemia, and a metformin dose distribution. During the 1st week (D7), two patients had lower hypoglycemia of 0.7 g/L before breaking the fast, and 38% of the sample showed hyperglycemia greater than 2 g/L after breaking the fast. They noted dietary errors in 15% of patients. Adjusting at D7 was to modify the dose of SH or to add a gliptin. No patient showed significant hyperglycemia, ketosis, or severe hypoglycemia. One patient presented with atrial fibrillation on a background of unknown ischemic cardiomyopathy with a cease of fasting. Three patients gave up fasting between D15 and D20 due to intense asthenia without hyperglycemia. Mean HbA1c in patients after fasting was 7.10% versus 6.8% before fasting ($P = 0.42$). Factors significantly associated with poor glycemic control were mainly HbA1c rate at admission ($P = 0.002$), absence of self-monitoring ($P = 0.01$), and diabetes duration ($P = 0.06$). This study allowed the authors to show that good evaluation of diabetic risk level, focused education, glycemic monitoring, and adjustment of treatment by implementing international recommendations allow Muslims with diabetes to fast with low risk of acute complications and metabolic derangements. During Ramadan (D7), a medical visit would allow for correction of the dietetic mistakes and adjustment of oral agents if necessary.

Catic and Jusufovic[38] evaluated the knowledge, practice, and attitudes of physicians treating diabetes in Bosnia and Herzegovina regarding the management of diabetes in fasting patients during Ramadan. A 32 questions' survey was developed, validated, and disseminated to physicians. The survey captured demographic characteristics, current practices and attitudes, and knowledge on diabetes management during Ramadan through online forms. All surveyed physicians dealt with patients who were fasting during Ramadan.

Table 3: Summary of studies on professional perspectives and advocacy

Authors	Study size and site	Intervention evaluated	Conclusions
Alawadi *et al*.[36]	*n*=30 UAE	Impact of optimum care: Ramadan-focused education, flash glucose monitoring, dietary advice, and treatment adjustment on the safety of RF in people with T1D	Optimal care of selective patients with T1D with low complication rates may allow RF with improvement in glycemic control and without an increase in hypoglycemia, biometric or metabolic parameters
Elamari *et al*.[37]	*n*=34 Morocco	Impact of RF on the glycemic control of patients with diabetes prepared for fasting according to the ADA 2010 guidelines	Good evaluation of diabetic risk level, focused education, glycemia monitoring, and treatment adjustment by implementing international guidelines enable fasting with a low risk of complications
Catic and Jusufovic[38]	*n*=27 Bosnia and Herzegovina	Knowledge, practice, and attitudes of physicians treating diabetes regarding the management of diabetes in fasting patients during Ramadan	There remains an opportunity for the additional introduction of specialized education and measures into the current practices to improve treatment outcomes and standards of care
Ulhaque *et al*.[39]	*n*=102 Pakistan	Role of a 24-h helpline service in diabetes management during RF	The intervention minimizes diabetic complications, facilitates timely treatment adjustments, and reduces hospital visits and admissions

ADA: American Diabetes Association, RF: Ramadan fasting, T1D: Type 1 diabetes

The majority of surveyed physicians (85.2%) proactively initiated discussions about planned fasting. More than 63.0% were primarily dependent on their experiences, with only 18.5% reported using the professional guidelines on diabetes management during Ramadan. Though not statistically significant, there were some differences in gender, place of work, and specialization of physicians when it came to specific knowledge related to treatment guidelines. Although physicians' knowledge of diabetes management during Ramadan was overall satisfying, the authors concluded that there remains an opportunity to introduce specialized education and measures into the current practices to improve treatment outcomes and standards of care.

The role of a 24-h helpline service in the management of diabetes was assessed during the month of Ramadan.[39] A prospective study was conducted in Pakistan (2017–2018). Patients with T1D and T2D who were planning to fast in Ramadan 2018 were included. Pre-Ramadan education on a one-to-one basis was given, and the 24-h helpline number was provided to each patient. Details of baseline characteristics, anthropometric measurements, and biochemical parameters (lipid profile, serum creatinine, urine protein, and HbA1c pre- and post-Ramadan) were noted. SMBG recording books were provided to each patient to record blood sugar levels during Ramadan. A total of 102 patients, 41 with T1D and 61 with T2D, were included. The mean age of patients with T1D was 17.0 years and that of patients with T2D was 49.5 years. Most of the patients were male in both groups. Using the 24-h helpline service, 912 calls were made to patients, 502 calls for T1D, and 410 calls for T2D. Mean HbA1c levels before and after Ramadan were 8.9% and 8.7% in patients with T1D and 8.6% and 7.7% in patients with T2D, respectively. In the last 10 days of Ramadan, decreasing trends of mean SMBG in patients with T1D were observed for the predawn meal (suhoor), presunset meal (iftar), and before sleeping, while a similar trend in T2D patients was found in the predawn meal (suhoor) and 2 h after iftar. Authors concluded that pre-Ramadan diabetes education and treatment adjustment using a station-based, 24-h helpline service during the holy month of Ramadan had a significant role in controlling blood sugar levels, thus minimizing the complications of diabetes, facilitating timely adjustments in treatment, and reducing unnecessary hospital visits and admissions.

Finally, Hussain *et al*.[40] challenged the widely held opinion that T1D should not observe fasting in Ramadan. They called to rethink classification of risk by taking into consideration the resources, types of medication, and availability of and access to technology and professional support.

Patients' perspectives

Koudstaal *et al*.[41] reported on Moroccan-Dutch migrant women's perceptions of health and lifestyle, focusing on Ramadan experiences using qualitative research integrating education and consultation. The context was that older Moroccan-Dutch migrant women exhibit high rates of diabetes, hypertension, overweight, and obesity, further compounded by their high risk of multimorbidity. HCPs' efforts to encourage this group to adopt a healthier lifestyle have had little success. The authors addressed whether the concepts used in health education and promotion relate to these women's experiences and beliefs. This explorative, qualitative research aimed to explore older Moroccan-Dutch women's perceptions of health and lifestyle and to analyze these in a broader context, related to other fundamental forms of identity such as gender, culture, and religion. The authors recruited women with Moroccan backgrounds. The author used (a) seven "natural" group discussions held (among women who regularly meet each other, aged between 22 and 69 years), and (b) Twelve in-depth interviews and an observation day (with women from 40 to 66 years). The transcripts were then analyzed using thematic content analysis. The study identified five major themes. Health was perceived in terms used in prevailing health promotion discourses in the Netherlands, but the lifestyle was interpreted in a much broader sense than the current health promotion debate allows; it is not seen as an individual responsibility or as something an individual could control on their own, and the social benefits of health behaviors appear to outweigh the health benefits themselves. Lifestyle was located in three social identities of the women: Moroccan, Muslim, and mother. Finally, Ramadan played a dominant role in the lifestyle experience of older Moroccan women and was central in this research. The finding that lifestyle is not seen as an individual responsibility but is located in social identities can be applied to other settings that older migrant-Dutch women occupy. Further research will clarify this.

Alsunni *et al*.[42] assessed the knowledge, attitude, and practice of T2D patients about fasting during Ramadan and identified the sociodemographic determinants of the knowledge, attitude, and practice. A total of 107 patients were interviewed at a diabetes clinic in Eastern Saudi Arabia. A questionnaire about RF was used to collect data. Data about age, gender, city of residence, nationality, level of education, and history of diabetes in the family were also collected. The mean total score for knowledge, attitude, and practice was 16.5/27. The individual scores for knowledge, attitude, and practice were 9.7/16, 4.1/6, and 2.8/5, respectively. Sex, education, and family history were significant independent determinants of the total score. Gender, family history of diabetes, and education were determinants of knowledge, attitude, and practice regarding RF in T2D patients. A significant knowledge practice gap was identified, which necessitates further strengthening of the pre-Ramadan education program for T2D patients.

Liao *et al*.[43] appraised the existing qualitative studies on RF in participants with diabetes and integrated valuable qualitative evidence for optimizing diabetes management. Twelve databases were searched to identify qualitative studies on experiences and perspectives of RF in participants with diabetes. Critical Appraisal Skills Program qualitative checklists were applied to appraise the included studies. A meta-synthesis approach was used to analyze the included

studies. The findings and quotations of the included studies were integrated into new themes and categories through inductive thematic synthesis and reciprocal interpretation. The authors concluded that insulin-dependent individuals call for particular concern during RF. There is a need for Ramadan-focused education needs to be developed and generalized, and existing guidelines should be improved to optimize the management of diabetes. Professional HCPs contribute to weighing the patients' health risks and mental satisfaction, partly to balance health and religion.

Alfahadi *et al.*[44] evaluated the effect of fasting during Ramadan on cognitive functions and fatigue severity in T2D patients using the Cambridge Neuropsychological Test Automated Battery (CANTAB). Participants included 43 controls and 39 T2D patients. The standardized fatigue severity scale and tests from CANTAB, including the Motor Screening Task, Spatial Span (SSP), and Intra-Extra Dimensional Set Shift, were recorded during the 3rd week of Ramadan and 2–3 weeks after Ramadan under controlled environmental conditions. Neurocognitive functions were recorded through CANTAB. The authors found that patients with T2D had impaired cognitive functions, including poor motor performance, low flexibility of attention, and insufficient working memory capacity than healthy control subjects during and in the post-Ramadan period. Nonetheless, there is no clear statistical evidence that the cognitive functions (except for SSP span length (SL) scores) and fatigue severity of T2D subjects differ between Ramadan and after Ramadan in both T2D and controls.

Physical activity, sleep duration, and sleep time are all susceptible to significant alterations in Ramadan due to changes in timing and frequency of meals. Alghamdi *et al.*[45] compared physical activity and sleep patterns of individuals with T2D during and after Ramadan using the international physical activity questionnaire (IPAQ) and a Fitbit Flex 2 accelerometer. The study included Saudi individuals ($n = 36$) with T2D using a self-reported questionnaire and wore a Fitbit device for 7 consecutive days during and after Ramadan. Fitbit generated weekly step counts, activity intensities, sedentary time, and sleep durations and times. IPAQ was used to estimate the physical activity and sitting time of participants in each period. Sleep patterns were assessed in each period by a self-reported questionnaire. Both Fitbit and IPAQ indicated a high prevalence of low physical activity among the participants with nonsignificant variances between during and after Ramadan periods. Further, significantly shorter total daily sleeping hours and daily night-time sleeping hours were seen during the Ramadan period. The duration of night-time sleep was observed to be low in each period. This was the first study to use a Fitbit device to monitor individuals with T2D who fast during Ramadan. The study showed a high prevalence of low physical activity among Saudi individuals with T2D in each period and short sleep duration during the Ramadan period compared to after Ramadan.

Yousuf *et al.*[46] explored the association of RF with symptoms of depression, anxiety, and stress in people with diabetes by conducting an observational study at the Baqai Institute of Diabetology and Endocrinology in 2017. The Depression, Anxiety and Stress Scale (DASS-21) was used to assess depression, anxiety, and stress symptoms both pre- and post-Ramadan. A total of 150 people with diabetes participated in this study. One hundred people were in the fasting group, and 50 were in the nonfasting group. In the fasting group, symptoms of pre-Ramadan depression, anxiety, and stress were present in 45%, 45%, and 49% of people, respectively. This improved to 23%, 26%, and 35% post-Ramadan ($P < 0.0001$, $P < 0.0001$, $P = 0.001$), respectively. In the nonfasting group, pre-Ramadan, depression and anxiety symptoms were present in 34% and 50% of people, respectively, and improved to 30% and 40% post-Ramadan though non-significantly ($P = 0.625$, $P = 0.227$), respectively. No improvement was observed in stress symptoms. The authors concluded a significant improvement in symptoms of depression, anxiety, and stress in people with diabetes post-RF.

Ramadan, diabetes, and COVID-19

The coronavirus disease 2019 (COVID-19) pandemic brought forth new challenges for patients with diabetes. Having no prior experience with anything on the scale of the current pandemic, HCPs looking after patients with diabetes struggled to provide optimum care in the absence of specific guidelines. Several independent groups and diabetes organizations did propose guidelines to help HCPs manage people with diabetes who opted to fast during the COVID-19 pandemic summaries in Table 4.[47-53] Early reports addressed RF during the COVID-19 pandemic by invoking first principles and reconciling them with the impact of COVID-19 on diabetes and applying these on the scene during Ramadan.[47-49]

More formally, the South Asian Health Foundation of the UK provided structured guidelines for managing diabetes during Ramadan.[50] These were developed to help physicians mitigate the complications associated with RF. The role of focused pre-Ramadan risk stratification and counseling by HCPs, the need for advice on adequate dietary and fluid intake, glucose monitoring, and awareness of when to break the fast were highlighted. They reviewed the current literature and provided clinically relevant recommendations on lifestyle modifications and glucose-lowering therapies such as metformin, sulfonylureas, DPP-4i, SGLT-2i, thiazolidinediones, GLP-1 RAs, and insulin. They emphasized an individualized patient-centric treatment plan to achieve optimal glycemic outcomes to enable them to observe a risk-free month of fasting. An updated report from the same group sheds light on Muslims' challenges during Ramadan 2020.[51] The latter not only represented one of the longest fasting months experienced in the UK, approximating 18 h in length, but it also occurred at the height of a global pandemic. Reports show that diabetes appears to be a risk factor for more severe diseases with COVID-19. In addition, the UK experience has shown diabetes and COVID-19 to be associated

Table 4: Summary of publications on the impact of COVID-19 era on Ramadan fasting and its management

Authors [reference]	Settings	Context	Outcome/conclusions
Chowdhury *et al.*[47]	UK	Review/opinion	They addressed "RF during the COVID-19 pandemic" by invoking first principles and reconciling them with the impact of COVID-19 on DM and applying these on the scene during Ramadan
Tootee *et al.*[48]	Iran	Review/opinion	
Tootee and Larijani[49]			
Hanif *et al.*[50]	UK	Position statement*	
Hanif *et al.*[51]			
Hassanein *et al.*[52]	Multinational; 13 countries	Electronic patient survey - T1D; 1483 participants	COVID-19 pandemic had a minor impact on the decision to fast Ramadan in the cohort (71.1% fasted). Some regional differences were observed
Khan *et al.*[53]	Tower Hamlets, London, UK	Telephone patient survey - T2D; 829 participants	COVID-19 had an impact on people with T2D and their fasting intentions. Most people who were advised not to fast did not fast. There were few adverse outcomes from fasting. COVID-19 was not more common among people who observed the fast
Al-Sofiani *et al.*[54]	Saudi Arabia	Diabetes telemedicine clinic; 210 patients and 14 HCP; virtual clinic and virtual education session	Patients: 97% thought telemedicine was essential in maintaining reasonable control, 88% recommending continuing the educational activity HCPs: 93% thought the clinic protocol was simple
Zabeen *et al.*[55]	Bangladesh	Phone support. 90 T1D patients using an insulin pump	Most of the patients to fast>20 days; no severe hypoglycemia or DKA. Mild hyper and hypoglycemia were common

*South Asian Health Foundation of the UK. HCP: Healthcare professionals, T1D: Type 1 diabetes, T2D: Type 2 diabetes, DKA: Diabetic ketoacidosis, DM: Diabetes mellitus

with dehydration, starvation ketosis, diabetic ketoacidosis, and hyperosmolar hyperglycemic state. This makes fasting in Ramadan particularly challenging for Muslims with diabetes.

Two surveys evaluated the impact of COVID-19 on patients' perceptions, experiences, and outcomes during Ramadan in T1D and T2D.[52,53] The DaR Global survey included Muslim T1D patients from 13 countries shortly after Ramadan (2020), using a simple questionnaire. Of the 1483 participants with T1D, 71.1% fasted during Ramadan. Concerns about COVID-19 were higher in individuals ≥18 years ($P = 0.002$). The number of participants who decided not to fast plus those who received Ramadan-focused education was significantly higher in the ≥18-year group ($P < 0.05$). Hypoglycemia (60.7%) and hyperglycemia (44.8%) were significant fasting complications during Ramadan in both groups, irrespective of age. COVID-19 pandemic had a minor impact on the decision to fast Ramadan in the T1D cohort. This was notably higher in the ≥18 years of age group compared to those <18 years. Only regional differences were noted for fasting attitude and behavior among T1D groups. Furthermore, Khan *et al.* examined the experiences of patients with T2D during Ramadan 2020. A telephone survey of Muslim patients with T2D in Tower Hamlets, London, was conducted. Patients were surveyed on the effects of COVID-19 on their fast, any discussions with a HCP before Ramadan, whether they followed their HCP advice, the number of fasts undertaken, medication changes, and AEs. A total of 829 participated. 40.2% discussed fasting with an HCP; 59.3% were advised not to fast; 86.3% elected not to fast. 1.4% were admitted to the hospital during Ramadan – one fasting-related severe hypoglycemia, one nonfasting cerebrovascular accident, and 10 (4 fasting and 6 nonfasting) with COVID-19 symptoms. 8.2% of patients in the fasting group developed COVID-19 symptoms before or during Ramadan and 7.2% in the nonfasting cohort. 37.5% of patients reported that COVID-19 had significantly influenced their decision not to fast. Compared to Ramadan 2016, in Ramadan 2020, fewer people fasted, fewer people discussed fasting with an HCP, more patients who discussed fasting with their HCP were advised not to fast, and fewer patients fasted against medical advice. The two surveys highlighted the need for Ramadan-focused diabetes education for people with T1D to improve glucose control and prevent complications during fasting. Further, COVID-19 had an impact on people with T2D and their fasting intentions during Ramadan 2020. Most people who were advised not to fast did not fast; there were few adverse outcomes from fasting. COVID-19 was not more common among people who observed the fast.

Telemedicine, COVID-19, and Ramadan

Telemedicine emerged as an effective mode of managing various needs of individuals with medical conditions and was particularly useful for people with diabetes. In 2020, two reports presented telemedicine experiences in two countries with different logistical and socioeconomic profiles: Saudi Arabia and Bangladesh.[54,55]

Al-Sofiani *et al.*[54] described a simplified protocol for a diabetes telemedicine clinic that utilizes resources available to most clinicians and people with diabetes worldwide. They reported the satisfaction of most patients and HCPs who participated in the virtual clinic and patients who attended the virtual educational sessions about "Diabetes and Ramadan". The majority of patients (97%) agreed or strongly agreed that telemedicine was essential in maintaining reasonable glucose control during the pandemic and that they would use the clinic again in the future (86%). Further, patients who attended the "Diabetes and Ramadan" virtual educational session reported a similar high satisfaction rate, with 88% recommending continuing this activity virtually every year.

The majority of the HCPs (93%) thought that the clinic protocol was straightforward and did not require a dedicated orientation session before implementation. The authors were also able to successfully reduce the number of patients, HCPs, and staff physically present in clinics during the COVID-19 pandemic without negatively impacting the patients' or HCPs' satisfaction with the visits. Zabeen *et al.*[55] reported on the telemedicine experience of a more focused group (T1D patients using insulin pumps) who fasted Ramadan 2020 during the COVID-19 pandemic. Routine diabetes outpatient care was closed due to lockdown measures in Bangladesh. The diabetes team contacted nine patients who wished to observe RF over the phone. This simple intervention allowed most of the patients to fast >20 days. Hyperglycemia and mild hypoglycemia were common complications during fasting. There was no severe hypoglycemia or DKA, and none of the patients required admission.

These studies confirmed the feasibility of remote care and patient's favorable experiences. The simplicity of their clinic protocol and the high satisfaction rates reported by patients and HCPs made it a suitable model to be adopted by clinics during pandemics or disasters in resource-limited settings. This model can be quickly implemented and does not require technological tools other than those widely available to most people with diabetes in Saudi Arabia. Furthermore, patients with T1D using insulin pumps could fast safely in Ramadan during the COVID-19 crisis in Bangladesh, with the support of the telemedicine services.

Conclusions

The impact of RF on the management of diabetes, continued to receive interest in 2020. Particular interest was in epidemiology, patients' perspectives, pharmacological management, professional competency, and patients' adequacy. The unprecedented circumstances of a global viral pandemic added to the challenge of providing optimum care for people with diabetes, especially in Ramadan, and warranted some studies of different nature. We are cognizant that some of the literature could have been missed if authors published it in non-PubMed–indexed emerging journals in the MENA region. Perhaps future reviews should attempt to include them, although the magnitude of work increases. The volume, however, remains modest and below expectations, and the quality and depth can be expanded.

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