Recommendations for management of diabetes during Ramadan: update 2020, applying the principles of the ADA/EASD consensus

Mahmoud Ibrahim ¹, Melanie J Davies,² Ehtasham Ahmad,³ Firas A Annabi,⁴ Robert H Eckel,⁵ Ebtesam M Ba-Essa,⁶ Nuha Ali El Sayed,⁷ Amy Hess Fischl,⁸ Pamela Houeiss,⁹ Hinde Iraqi,¹⁰ Ines Khohtali,¹¹ Kamlesh Khunti,² Shabeen Naz Masood,¹² Safia Mimouni-Zerguini,¹³ Samad Shera,¹⁴ Jaakko Tuomilehto,^{15,16} Guillermo E Umpierrez ¹⁷

To cite: Ibrahim M, Davies MJ, Ahmad E, *et al.* Recommendations for management of diabetes during Ramadan: update 2020, applying the principles of the ADA/EASD consensus. *BMJ Open Diab Res Care* 2020;**8**:e001248. doi:10.1136/bmjdr-2020-001248

Received 5 February 2020
Revised 31 March 2020
Accepted 6 April 2020

© Author(s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to
Dr Mahmoud Ibrahim;
mahmoud@arab-diabetes.com

ABSTRACT

Fasting the Holy month of Ramadan constitutes one of the five pillars of the Muslim faith. Although there is some evidence that intermittent fasting during Ramadan may be of benefit in losing weight and cardiometabolic risk factors, there is no strong evidence these benefits apply to people with diabetes. The American Diabetes Association/European Association for the Study of Diabetes consensus recommendations emphasize the importance of patient factors and comorbidities when choosing diabetes medications including the presence of comorbidities, atherosclerotic cardiovascular disease, heart failure, chronic kidney disease, hypoglycemia risk, weight issues and costs. Structured education and pre-Ramadan counseling are key components to successful management of patients with diabetes. These should cover important aspects like glycemic targets, self-monitoring of blood glucose, diet, physical activity including Taraweeh prayers, medication and dose adjustment, side effects and when to break the fast. The decision cycle adapted for the specific situation of Ramadan provides an aid for such an assessment. Children with type 1 diabetes should strongly be advised not to fast due to the high risk of acute complications such as hypoglycemia and probably diabetic ketoacidosis (DKA), although there is very little evidence that DKA is increased in Ramadan. Pregnant women with diabetes or gestational diabetes should be advised to avoid fasting because of possible negative maternal and fetal outcomes. Hypoglycemia is a common concern during Ramadan fasting. To prevent hypoglycemic and hyperglycemic events, we recommend the adoption of diabetes self-management education and support principles. The use of the emerging technology and continuous glucose monitoring during Ramadan could help to recognize hypoglycemic and hyperglycemic complications related to omission and/or medication adjustment during fasting; however, the cost represents a significant barrier.

INTRODUCTION

Fasting the Holy month of Ramadan may be challenging for the people with diabetes

and their care providers due to potentially increased risk of acute complications such as hypoglycemia, hyperglycemia, dehydration and probably diabetic ketoacidosis (DKA), although there is very little evidence that DKA is increased during Ramadan.¹ Hence, in 2005, the first statement for management of diabetes during Ramadan was published as an American Diabetes Association (ADA) working group report²; after receiving multiple inquiries asking for regular updates addressing the most important issues not covered in the initial document, the authors decided to do regular 5 yearly updates.^{3,4} In this 2020 update, we aimed to apply the principles of ADA/European Association for the Study of Diabetes (EASD) type 2 diabetes management guidelines to Ramadan. New sections on the management of children with type 1 diabetes and pregnancy are included. We have carefully reviewed the literature and published data on medical nutrition therapy (MNT) and the use of glucose-lowering medications during Ramadan.²

It is estimated that the total Muslim population worldwide approached 1.9 billion as of 2019, which includes about 24.4% of the world population.⁵ Based on the recent International Diabetes Federation Atlas Ninth Edition 2019 report on the prevalence of diabetes of 463 million or 9.1% worldwide,⁶ one can estimate that almost 112 million people with diabetes worldwide may choose to fast during Ramadan.

Fasting the Holy month of Ramadan constitutes one of the five pillars of the Muslim faith, it is obligatory for all adult Muslims. Although, illness constitutes exemption from fasting,⁷ a vast majority of Muslims with diabetes do not

consider themselves unwell and exempted and choose to fast. This should be respected, and such patients should be supported to help them fast.

Ramadan fasting may have a positive effect on increased self-esteem, promoted psychological stress, decreased anxiety and stress, self-control and the ability to sympathize with others,⁸ however very few studies have looked at the emotional consequences of short-term Ramadan fasting in healthy people versus people with diabetes, this could be an interesting future research point where the directional hypothesis needs to focus on mood changes, irritability, feeling of reward, fear of punishment and self-restrain and control and sexual behavior will be few interesting avenues with larger and diverse sample size via a robust statistical testing.

INTERMITTENT FASTING

Intermittent fasting is an eating pattern where you cycle between periods of eating and fasting and is increasing in popularity as a mean of losing weight and controlling chronic illness.⁹ It could be for religious reasons or non-religious reasons like losing weight. The Ramadan fast is a form of intermittent fasting where the normal eating pattern shifts to exclusive nocturnal eating. Based on the current available evidence and knowledge, intermittent fasting can be safe in people with diabetes when done under medical supervision and may reduce body weight, central adiposity and glycated hemoglobin (HbA1c). There is also evidence that intermittent fasting improves insulin sensitivity and cardiovascular disease (CVD) markers.¹⁰ It should be noted that unlike most forms of intermittent fasting, Ramadan fasting involves no intake of water/fluids. Also, intermittent fasting has the potential for hypoglycemia in patients receiving antidiabetic medications associated with hypoglycemia such as sulfonylureas (SU) and insulin therapy.¹¹

APPLYING THE PRINCIPLES OF THE ADA/EASD CONSENSUS

The ADA/EASD consensus report 2018 and its recent update provides comprehensive recommendations on the management of hyperglycemia in patients with type 2 diabetes incorporating the evidence from the outcomes of new trials into decision making.^{12–14} The report considers major aspects of type 2 diabetes management including the presence of comorbidities such as atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), chronic kidney disease (CKD), hypoglycemia risk and weight management. It gives recognition to patient-centred care, optimization of quality of life and reducing burden of complications. This consensus recommendation applies to most scenarios encountered in the Holy Month of Ramadan observed by Muslim patients with type 2 diabetes. The ADA/EASD consensus does not address the management of type 1 diabetes for which relevant guidance is available.^{4,15}

Applying the principles of decision cycle in the management of patients with type 2 diabetes who observe Ramadan fasting

The key to successful diabetes management in Ramadan should be no different and the general aim is control of symptoms, prevent deterioration in glycemic control and prevention of acute complications.

The decision cycle for patient-centred glycemic management in type 2 diabetes provides an aid for healthcare professionals (HCPs) while proposing and making management decisions for Muslim patients with type 2 diabetes who are planning to fast during Ramadan (figure 1). This has been adopted and modified specifically for Ramadan based on the ADA/EASD consensus recommendations 2018.

Pre-Ramadan assessment including assessment of key patient characteristics, treatment choice and shared decision making

Pre-Ramadan counseling and clinical assessment is essential component of managing patients with type 2 diabetes during Ramadan. This should comprise assessment of areas highlighted in decision cycle, including key patient characteristics like age, frailty, lifestyle, cultural and socio-economic factors and presence of comorbidities with risk stratification as highlighted in box 1.^{3,4}

Diabetes management plan during Ramadan

Review management plan and adjusting treatment regimen is required during Ramadan to avoid hypoglycemic and hyperglycemic events. Suboptimal adherence to medication, fear of hypoglycemia, medication adverse effects and lack of access to medication should be identified and addressed prior to Ramadan fasting.

It is important to inform patients that blood glucose testing during Ramadan does not break the fast; a common misconception in some parts of the world. Blood glucose should be regularly monitored during fasting, especially those on insulin or insulin secretagogues.

All patients should be educated about the symptoms of hypoglycemia, and to stop the fast in case of symptoms of hypoglycemia, hyperglycemia, dehydration or acute illness occur and blood glucose level of <3.9 mmol/L (<70 mg/dL) or >16.6 mmol/L (>300 mg/dL).¹⁶

Use of self-monitoring of blood glucose (SMBG) should be individualized during Ramadan with need for more frequent monitoring in those at higher risk of hypoglycemia, especially in regions with longer fasting hours or warmer climate.

The use of novel technologies such as continuous glucose monitoring (CGM) is currently not routinely recommended for patients with type 2 diabetes.¹⁷

Structured education for patients planning fasting

The role of a structured education in patients with type 2 diabetes is well established,^{18–25} and this benefit is also

Figure 1 Decision cycle for patient-centred glycaemic management in Muslim patients during Ramadan. Modified and adopted from Davies *et al.*¹³ ASCVD, atherosclerotic cardiovascular disease; BD, twice a day; CKD, chronic kidney disease; DKA, diabetic ketoacidosis; HF, heart failure; HHS, hyperosmolar hyperglycemic state; MNT, medical nutrition therapy; OD, once a day; SMBG, self-monitoring of blood glucose.

proven in Muslims with diabetes practicing Ramadan.^{26–32} In a retrospective study, patients receiving pre-Ramadan education experienced less hypoglycemia.²⁶ It is important that the structured education is implemented and ideally it should incorporate community awareness package, HCP training and patient self-management course like ‘A Safer Ramadan’.³³

The therapeutic options for fasting patients with type 2 diabetes during Ramadan including lifestyle, weight management and medications

Lifestyle management

Medical nutrition therapy and dietary patterns for Ramadan

Medical nutrition therapy should be provided by a registered dietitian or nutrition professional³⁴ and should include principles of healthy eating behaviors, preventive methods for hypoglycemia, proper portion intake.³⁵ Since foods consumed during Ramadan tend to be higher in carbohydrate, strategies should include portion control as well as the possible incorporation of physical activity after meal. The DAR International Alliance has developed the Ramadan Nutrition Plan, a web-based tool designed to help HCPs in delivering patient-specific nutrition education for Ramadan.³⁶

A frequently ignored aspect is food consumption during Eid, which is the 3-day festival after Ramadan involving high consumptions of calories and carbohydrates with family and friends.

Dates consumption

Daily consumption of dates is a deeply rooted tradition among Muslims, especially during Ramadan. The habitual eating patterns have changed recently; however, consumption of dates remains in most countries. The highest consumption of dates was found among Arab Gulf populations,^{37–40} with a daily date intake in these countries between 68 and 164g.⁴⁰ It is actually recommended to break the fast on dates, as Prophet Mohammad (peace and blessings be on him) used to do. Dates have a low glycemic index (GI) provided it is consumed in a small amount. Therefore, up to two to three dates can be eaten safely when breaking fast.⁴¹

Physical activity and Taraweeh prayers

Although increased physical activity should generally be encouraged in all patients with type 2 diabetes, but during Ramadan it warrants caution. The Taraweeh prayer during Ramadan after Iftaar meal involves repeated cycles of rising, kneeling and bowing and should be considered as

Box 1 Categories of risk in patients with type 2 diabetes who fast during Ramadan

Very high risk: fasting not recommended

- ▶ Severe hypoglycemia within the 3 months prior to Ramadan.
- ▶ Severe hyperglycemia with average fasting or premeal plasma glucose >16.7 mmol/L (300 mg/dL) or glycated hemoglobin (HbA1c) >86 mmol/mol (10%).
- ▶ A history of recurrent hypoglycemia or hypoglycemia unawareness.
- ▶ Diabetic ketoacidosis/hyperosmolar hyperglycemic state within the 3 months prior to Ramadan.
- ▶ Acute illness.
- ▶ Performing intense physical labor.
- ▶ Pregnancy.
- ▶ Chronic dialysis.
- ▶ Patients with significant dementia or cognitive deficits.

High risk: may choose not to fast

- ▶ Moderate hyperglycemia (average blood glucose 8.3–16.7 mmol/L (150–300 mg/dL) or HbA1c 64–86 mmol/mol (8%–10%).
- ▶ Significant microvascular or macrovascular complications.
- ▶ Living alone and treated with insulin or sulfonylureas.
- ▶ Patients with comorbid conditions that present additional risk factors like heart failure, stroke, malignancy, renal impairment.
- ▶ Elderly >75 years of age.

Moderate risk: may choose to fast with caution

- ▶ People with type 2 diabetes with no complications and HbA1c <64 mmol/mol (8%) treated with lifestyle intervention, metformin, thiazolidinedione (TZD), incretin-based therapies, sodium-glucose cotransporter-2 inhibitors* and/or short-acting insulin secretagogues.

Low risk: may choose to fast

- ▶ People with type 2 diabetes with no complications and HbA1c <53 mmol/mol (7%) treated with lifestyle intervention, metformin, TZD and/or incretin-based therapies.

*With encouragement on adequate hydration during permissible hours to reduce risk of dehydration and postural hypotension, especially in hot humid environments.

Adopted and modified from Al-Arouj *et al*² and Ibrahim *et al*.⁴

part of daily exercise.⁴ Physical activity should be encouraged for people with diabetes and normal levels may be maintained during the month of Ramadan. However, excessive physical activity may lead to a higher risk of hypoglycemia and should be avoided, especially before the sunset meal, in those with high risk of hypoglycemia and those on insulin or insulin secretagogues.³

Glucose-lowering medications

Summary of the recent ADA/EASD update 2019 to the ADA/EASD consensus 2018

It is recommended that decision to start a new glucose-lowering medication should be made in advance of start of Ramadan and dose adjustments or medication reviews are done accordingly, especially if hypoglycemia or tolerability becomes a concern during fasting. The ADA/EASD 2018 consensus^{12 13} and its recent update¹⁴ recognize presence or absence of ASCVD, HF and CKD an important early step in treatment selection (figure 2).

This is based on the outcomes of various Cardiovascular Outcome Trials mainly involving glucagon-like peptide-1 receptor agonists (GLP-1RA) and sodium-glucose cotransporter-2 inhibitors (SGLT2i).^{42–52}

A key new recommendation in the ADA/EASD consensus update is initial combination therapy including metformin in newly diagnosed patients with type 2 diabetes based on the outcome of VERIFY (Vildagliptin Efficacy in combination with metformin For early treatment of type 2 diabetes) trial.⁵³

Glucose-lowering medications and Ramadan

1. *Metformin*: Metformin has a long history of safety and efficacy and remains the first-line medication for management of type 2 diabetes^{12 13} either alone or in combination.¹⁴ Usually, no dose change is advised during Ramadan, but timings need to be reviewed for Ramadan.
2. *Sodium-glucose cotransporter-2 inhibitor (SGLT2i)*: Since the last Ramadan update in 2015,⁴ several studies have shown the safety of the SGLT2i class during Ramadan including lower risk of hypoglycemia and renal safety.^{54–57} However, careful pre-Ramadan assessment and education is important including advice on hydration and potential risk of volume contraction and postural hypotension, especially in warm climates with long fasting hours and risk of diabetic ketoacidosis (DKA). Testing for ketones when unwell is required for all patients who chose to fast and are using SGLT2i.¹⁵ Patients should be encouraged to drink extra fluids during permissible hours and should have clear instructions when to break fasting, especially if vomiting or positive ketones even with normal blood glucose levels. We generally recommend not starting SGLT2i as a new medication during or immediately prior to Ramadan and patients should be well established on these drugs prior to start of Ramadan. Elderly patients, those with renal impairment, hypotensive patients or those on diuretics if they are planning to fast for Ramadan, should proceed with caution and consider stopping¹⁶ or reducing the dose of SGLT2i.
3. *Glucagon-like peptide-1 receptor agonist (GLP-1RA)*: GLP-1RA agents are effective in improving glycemic control with low risk of hypoglycemia or weight gain (figure 2). GLP-1RA constitute a very desirable option for fasting patients with weight concerns, high-risk factors for ASCVD or established ASCVD. Randomized controlled trial has reported on the efficacy and safety of treatment with liraglutide in combination with metformin compared with SU during Ramadan.⁵⁸ Two further studies have also demonstrated the safety and efficacy of liraglutide during Ramadan.^{59 60} Depending on the formulation used, the GLP-1RA may need to be injected daily or once-weekly. Weekly preparations are an attractive option for fasting patients who prefer a simplified regimen. The most common adverse events of GLP-1RA are GI effects including nausea and vomiting, increasing the risk of dehydration. Thus, it is

Figure 2 Glucose-lowering medications use before and during Ramadan. Modified and adopted from Davies *et al.*¹³ *For intensification beyond dual therapy, choose option with lower risk of hypoglycemia. **Consider sulfonylurea (SU) or basal insulin with lower risk of hypoglycemia. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; DKA, diabetic ketoacidosis; DPP4, dipeptidyl peptidase-4; GLP-1RA, glucagon-like peptide-1 receptor agonists; HbA1c, glycated hemoglobin; HF, heart failure; HHS, hyperosmolar hyperglycemic state; SGLT2i, sodium-glucose cotransporter-2 inhibitors; SMBG, self-monitoring of blood glucose; TZD, thiazolidinedione.

recommended that GLP-1RA should be started at least 4–8 weeks prior to fasting with titration to tolerated dose before the start of Ramadan.

4. *Dipeptidyl peptidase-4 inhibitor (DPP4 inhibitors)*: the ADA/EASD consensus recommends DPP4 inhibitors as an add-on option to metformin where there is a compelling need to minimize hypoglycemia (figure 2). DPP4 inhibitors are weight neutral and have a low risk of hypoglycemia but when combined with SU, the risk of hypoglycemia is increased by 50%.⁶¹ Generally, no change in the dose of DPP4 inhibitor is required either as monotherapy or combination therapy during Ramadan. Several trials have reported similar efficacy but significant reduction in hypoglycemic events with the use of DPP4 inhibitors compared with SU treatment during Ramadan in patients with type 2 diabetes.^{62–64}
5. *Thiazolidinediones (TZD)*: TZD use is not associated with hypoglycemia and is recommended as one of the add-on options to metformin in fasting patients during Ra-

madan, especially when hypoglycemia is a major risk (figure 2). Additionally, TZD is an attractive option in lower middle-income countries where cost consideration is a major issue. TZD should be avoided in patients with history of HF.

6. *Sulfonylurea (SU)*: SUs have widespread availability but are known to increase the risk of hypoglycemia, which is of great concern during Ramadan. The newer generation SU like glipizide, glimepiride and gliclazide have a lower risk of hypoglycemia compared with older and longer-acting agents.⁶⁵ This has also been shown in patients observing fasting during Ramadan.⁶⁶ The Cardiovascular Outcome Study of Linagliptin vs Glimepiride in Type 2 Diabetes (CAROLINA) trial which compared linagliptin and glimepiride, reported similar cardiovascular safety profile, but higher risk of hypoglycemia in glimepiride-treated patients.⁶⁷ We recommend either substituting or stopping or reducing the dose of SU in patients at high risk of hypoglycemia.

Table 1 gives a summary of recommendations in terms of dose adjustment during Ramadan for non-insulin glucose-lowering therapies.

7. *Other glucose-lowering agents:* The meglitinides like repaglinide are shorter-acting insulin secretagogues with lower risk of hypoglycemia compared with SUs but require twice-daily or thrice-daily doses with main meals. One study showed no difference in the incidence of hypoglycemia between groups taking repaglinide and glimepiride.⁶⁸ Alpha-glucosidase inhibitors are useful for patients with type 2 diabetes who have a tendency for hypoglycemia and therefore a very suitable option during Ramadan.⁶⁹ The rest of the oral glucose-lowering options like colesevelam, bromocriptine and pramlintide are not discussed due to lack of major new scientific information on these medications and the fact that they are not widely available during Ramadan.
8. *Managing injectable therapies including insulin during Ramadan (figure 3):* The ADA/EASD 2018 consensus^{12 13} recommends use of GLP-1RA prior to insulin as a first-line injectable therapy if HbA1c is above target despite dual or triple oral therapy. In addition, the consensus recommends initial combination of GLP-1RA plus insulin if HbA1c >86 mmol/mol (10%) and/or >23 mmol/mol (2%) above target. The efficacy and safety of insulin is dependent on its appropriate use

during Ramadan including patient training and education, diet and activity, dose titration, timing (Suhoor and Iftaar) and type of insulin used. It is very important that patients requiring injectable therapy (either GLP-1RA or insulin) are well established on stable injectable therapy preferably for at least 4 weeks prior to start of Ramadan.

- I. **Basal insulin:** Basal insulin is the preferred initial insulin regimen in patients with type 2 diabetes (figure 3). Providers should consider insulin preparations associated with less risk of hypoglycemia and to adjust the established dose during Ramadan. In a study comparing use of insulin degludec and glargine in patient with type 2 diabetes, prespecified adjudicated severe hypoglycemia occurred in 4.9% patients in the degludec group and in 6.6% patients in the glargine group, for an absolute difference of 1.7% over 2 years.⁷⁰ A concern with insulin use, especially in those who require large doses of insulin, is weight gain. In such situations, GLP-1RA therapy combined with basal insulin may result in improved weight, HbA1c and lower risk of hypoglycemia.^{71–74} Such a combination therapy, however, should be planned well in advance of Ramadan and patients should be on stable doses of insulin and GLP-1RA before the start of Ramadan. Similarly, studies combining

Table 1 Recommended medical therapy changes during Ramadan for patients with type 2 diabetes

Prior to Ramadan	During Ramadan
Metformin	No change in total daily dose.
Once a day	Usual dose at Iftaar meal.
Twice a day	Usual dose at Iftaar and Suhoor.
Three times a day	Combine the lunch time dose with Iftaar meal and take the morning dose at Suhoor.
Slow release formulation	Take at Iftaar.
SGLT2i	<ul style="list-style-type: none"> ▶ No dose change is usually required but patients should be well established on these prior to start of Ramadan. ▶ Ensure adequate hydration and take usual dose with Iftaar meal. ▶ We do not recommend starting it as a new medication immediately prior to or during Ramadan.
GLP-1RA	<ul style="list-style-type: none"> ▶ No dose change is usually required but patients should be established on a stable tolerated dose a few weeks prior to start of Ramadan. ▶ If not tolerated, either reduce the dose or stop the GLP-1RA, especially if nausea or vomiting.
DPP4 inhibitor	No dose change is usually required but consider reducing the dose of concomitant SU or stopping SU.
TZD	<ul style="list-style-type: none"> ▶ No dose change is usually required. ▶ Taken with either Iftaar or Suhoor, preferably with the larger meal, which is usually Iftaar meal. ▶ It will take 10–12 weeks for maximal effect, therefore consider starting a few weeks prior to start of Ramadan. ▶ Reduce the dose or stop SU if concomitant use.
SU	Consider either substituting, stopping or reducing the dose.
Once a day	Take the usual dose at Iftaar meal.
Twice a day	Usual dose at Iftaar meal and 50% of the usual dose with Suhoor meal.

DPP4, dipeptidyl peptidase-4 ; GLP-1RA, glucagon-like peptide-1 receptor agonists; SGLT2i, sodium-glucose cotransporter-2 inhibitors; SU, sulfonylureas; TZD, thiazolidinedione.

Figure 3 Managing injectable therapy before and during Ramadan. Modified and adopted from Davies *et al.*¹³ Consider basal insulin with lower risk of hypoglycemia (degludec/glargine 300<glargine 100/detemir<NPH). BD, twice a day; GLP-1RA, glucagon-like peptide-1 receptor agonists; HbA1c, glycated hemoglobin; NPH, Neutral Protamine Hagedorn; OD, once a day; TDS, three times a day.

SGLT2i and insulin have shown to be a safe and efficient combination in non-fasting patients with type 2 diabetes.^{75–77} However, the use of insulin in combination with SGLT2i may increase the risk of hypoglycemia during fasting.⁵⁶ In addition, we recommend reducing the dose or preferably stopping SU therapy when commencing insulin therapy for patients planning to fast during Ramadan.

- II. Other insulin formulations including short-acting insulins and premixed insulins: based on ADA/EASD consensus, we recommend when blood glucose is not adequately controlled with basal insulin, to start short-acting insulins with the two main meals (Iftar and Suhoor) during Ramadan¹⁵ (figure 3). Various premixed insulin combinations are commercially available. Al-Arouj *et al* recommend switching premixed or intermediate-acting insulin twice daily to long-acting or intermediate-acting insulin in the evening and rapid-acting insulin with meals; with usual dose at Iftar meal and half usual dose at Suhoor.³ Premixed insulins remain frequently prescribed option in many Muslim countries because of cost and availability issues and if required we recommend usual dose

for Iftar meal and 50% of the usual dose for Suhoor if on twice-daily regimen.

Table 2 gives a summary of the recommended changes to different insulin regimens for Ramadan.

Hassanein *et al*⁷⁸ advocate dose adjustment to premixed insulin dose depending on the blood glucose and we recommend following algorithm for self-titration of premixed insulin during Ramadan (table 3).

Generally, it is recommended to consider stopping or reducing the dose of any glucose-lowering medication with risk of hypoglycemia for Ramadan, particularly if the HbA1c is <48 mmol/mol (6.5%) or if there is a recent history of hypoglycemia.

HYPOGLYCEMIA

Hypoglycemia is by far the most common concern for people with diabetes observing Ramadan fasting, as described previously. The Epidemiology of Diabetes and Ramadan (EPIDAR) study showed significant increase in all forms of hypoglycemia among people with diabetes during Ramadan fasting.⁷⁹ Diabetes self-management education and support (DSMES) for prevention and treatment could serve as a good tool to minimize the

Table 2 Recommended changes for insulin therapy for patients with type 2 diabetes during Ramadan

Prior to Ramadan	During Ramadan
If taking insulin with sulfonylureas (SU)	Consider stopping SU.
For any insulin	Try to titrate and establish dose to achieve adequate glycemic control prior to start of Ramadan and then adjust dose during Ramadan accordingly.
Basal insulin	
Once a day	Take with Iftaar meal, but consider a 20% reduction from usual dose.
Twice a day	Take the usual morning dose with Iftaar meal and 50% of the usual evening dose for Suhoor meal.
Rapid-acting analogues	Take the usual morning dose with Iftaar meal, skip the usual lunch time dose and take 50% of the usual evening dose for Suhoor meal if required.
Premixed insulins	Take the usual morning dose with Iftaar meal and 50% of the usual evening dose for Suhoor meal. Skip the usual lunch time dose if on three times a day regimen.

hypoglycemic episodes during Ramadan fasting. The US National Standards are designed to define quality DSMES and assist those who provide DSMES services to implement evidence-based DSMES.⁸⁰

EMERGING TECHNOLOGY USE IN DIABETES

There is an increasing recognition of use of technology in diabetes. Blood glucose monitoring, exercise time, medication dosages and energy ingestion can all be digitalized

Table 3 Algorithm for premixed insulin titration during Ramadan

Fasting/Premeal blood glucose	Recommended action
>16.6 mmol/L (300 mg/dL)	Break the fast. Increase daily insulin dose by 20%.
>10 mmol/L (180 mg/dL)	Increase insulin daily dose by 10%.
5.5–10 mmol/L (100–180 mg/dL)	No change.
<3.9 mmol/L (70 mg/dL)	Break the fast. Reduce insulin daily dose by 20%.
<2.8 mmol/L (50 mg/dL)	Break the fast. Stop Insulin. Or reduce insulin daily dose by 30%–40%.

and accessed remotely. Pattern recognition in software is also available to help clinicians make complex decisions. Remote technologies like texts, emails and video-links can improve communication. All this can be used where available to improve care and support for people with diabetes who are fasting during Ramadan. The use of CGM has illustrated the wide variability in glucose levels during fasting and feast.^{81 82} This information can be a valuable tool, whether used intermittently or continuously, to aid in adjusting medications as well as composition of meals for optimal blood glucose control.^{83 84}

A clinical observational study in Ajman (UAE) examined glucose variability using CGM during Ramadan fasting in patients with type 2 diabetes without insulin treatment.⁸¹ They found that patients on SU and on more than two glucose-lowering medications showed early significant increase in mean amplitude of glycemic excursions. They concluded that except for an initial increase in glucose variability, fasting during Ramadan for patients with non-insulin-treated type 2 diabetes did not cause any significant changes in metabolic control, glucose fluctuation or time in hypoglycemia during CGM recording days compared with the non-fasting pre-Ramadan period and pre-Ramadan and early Ramadan patient education and follow-up of high-risk patients may help avoid initial significant glucose variability in patients with non-insulin-treated type 2 diabetes.⁸¹

CHILDREN WITH TYPE 1 DIABETES

Management of children and adolescents with type 1 diabetes during Ramadan is highly variable in Arab countries⁸⁵ and hypoglycemia during daytime fasting remains a major concern. Although the use of CGM may reduce risk of hypoglycemia during Ramadan,⁸⁶ the fear of hypoglycemia persists. A recent retrospective analysis of children and adolescents with type 1 diabetes during ~3 weeks of fasting showed that approximately 54% of them were on multiple daily insulin injections (MDI) and 46% on insulin pump therapy.⁸⁷ Although there were no differences between the two groups in breaking days of fasting, patients with HbA1c ≥69 mmol/mol (8.5%) experienced more frequent hypoglycemic attacks than patients with HbA1c <69 mmol/mol (8.5%). A more extensive meta-analysis of observational studies of young adults with type 1 diabetes revealed similar findings.⁸⁸ However, despite a lower level of HbA1c before fasting, the insulin pump group had lower rates of severe hypoglycemia than patients treated with MDI.

Defects in epinephrine responsiveness to hypoglycemia have been demonstrated in children and adolescents with type 1 diabetes,^{89 90} and defects in cortisol particularly at night have also been seen.⁹¹ Children with type 1 diabetes should strongly be advised not to fast. Children and adolescents with type 1 diabetes and their families need careful education and management of their insulin regimen and CGM to reduce the risk of hypoglycemia during Ramadan,⁸⁷ if planning to fast.

PREGNANT WOMEN WITH DIABETES OR GESTATIONAL DIABETES

Most guidelines have advised against fasting for pregnant women with diabetes during Ramadan.^{4 16} Despite the clear religious and clinical guidance, alarming reports of 59%–90% show that pregnant and lactating Muslim women fast during Ramadan.^{92 93}

Maternal outcomes

Research looking into the effect of maternal diet restriction during Ramadan fast on maternal and perinatal outcomes and/or metabolic changes has resulted in conflicting and insufficient result.⁹⁴

A small study in rural West Africa in lactating and pregnant women with diabetes showed metabolic derangements in late pregnancy that were suspected to be due to accelerated starvation that may occur in late pregnancy.⁹² Similar metabolic derangements in those with and without diabetes during pregnancy were reported by other authors.^{95 96} A study in Emirati pregnant women without diabetes found a significantly higher 1 hour post-prandial glycemia in pregnant women as compared with their non-fasting controls during Ramadan fast.⁹⁷ Based on 36628 readings by the CGM device and 408 readings by glucose meters the study found that all hypoglycemic episodes occurred between 16:00 and 19:00 hours in both approaches and only 38 readings (9%) of SMBG readings were done in the same time frame indicating that the timing of SMBG missed such hypoglycemic episodes. The rate of hyperglycemia was 5.7% and 14.2% and hypoglycemia was 4.4% and 1.5% using CGM and glucose meters, respectively.

Hyperglycemia in pregnancy is associated with adverse pregnancy outcomes⁹⁸ and early strict glycemic control during pregnancy is critical to prevent higher risk of hypoglycemia.^{99 100} Adding the burden of fasting to the complicated state of health in pregnant women with diabetes is not prudent or recommended due to increased risk of hypoglycemia and hyperglycemia.

Fetal outcomes

Studies looking at the effects of fasting on fetal outcomes varied in design and have shown conflicting outcomes. One prospective study in the Netherlands using self-reported data in 130 Muslim pregnant women on adherence to Ramadan fasting during pregnancy reported that 50% of women were adherent to fasting.¹⁰¹ Among them, the birth weight of newborns did not show a statistically significant difference, but it tended to be lower than that of newborns of non-fasting mothers. A meta-analysis pooled data from 22 studies and included 31 374 pregnancies of whom 18920 were exposed to Ramadan fasting.⁹⁴ This study's primary outcome, preterm delivery, was not impacted by fasting during Ramadan and one of the secondary outcomes, birth weight, was not affected by maternal fasting. However, placental weight was significantly lower in fasting mothers, putting in consideration

that this observation was dominated by a single large study.¹⁰²

The possible effect of nutritional restriction and how it can impact the development of the placental enzyme required to convert cortisol to its inactive form may result in a state of prolonged elevation of hypothalamic-pituitary-adrenal axis function which is detrimental and is linked to long-term health consequences such as type 2 diabetes, hypertension and cognitive impairment.^{103 104}

Another study found that the incidence of GDM was significantly higher in the fasting group compared with control group. Furthermore, there was a high rate of induction of labor ~16%, cesarean section as well as higher admissions to the special care baby unit in the fasted group as compared with control group.¹⁰⁵

Pregnant women with diabetes or GDM are at high risk of negative maternal and fetal outcome, they should be advised to avoid fasting.

REGIONAL PECULIARITIES OF DIABETES DURING RAMADAN

Egypt

Egypt ranks among the top 10 countries for the number of adult people with diabetes.⁶ The cultural norm for Egyptian Muslims with diabetes is to fast during Ramadan. Unlike those from the Arab Gulf and North African nations, the majority of Egyptian Muslims break their fast by consuming the main meal (Iftaar) immediately after sunset. In contrast to traditional Muslim teachings of moderation in food intake, this main meal is seen as an opportunity to feast.

Saudi Arabia

Ramadan is a month of nocturnal life in Saudi Arabia. Ramadan fasting in the Kingdom of Saudi Arabia, unlike other Muslim and Arab countries, is associated with profound changes in sleeping and feeding patterns, with an almost complete reversal of the rest/sleep versus wake cycle and restriction of food intake to night-time only.¹⁰⁶ Working hours for school and offices are reduced to 6 hours during working days for people to rest before and after Suhoor and Iftaar.

According to a recent study, Saudis fasting during Ramadan stay up at night and sleep through much of the day, mimicking the patterns of shift workers.¹⁰⁷ In a cross-sectional study in Riyadh, it was observed that most patients with diabetes (76%) were able to fast during Ramadan.³⁰ Hypoglycemic episodes were reported in 60% in people with type 1 diabetes and in 8% in those with type 2 diabetes. It was concluded that over half of the patients with diabetes who fast during Ramadan may alter their medicines schedule without seeking medical advice.¹⁰⁸

Pakistan

A study regarding baseline knowledge of family physicians across the country found that almost one-third of physicians had incorrect perceptions and misbeliefs regarding management of diabetes during Ramadan

fasting.¹⁰⁹ Another study reported that skin prick for SMBG would make the fast void; as a consequence, 40% of participants who were taking insulin never checked their blood glucose levels during fasting.¹¹⁰

The recommendations given by Ramadan Prospective Diabetes Study Group is to reduce the pre-Suhoor dose of oral glucose-lowering medications or insulin to 75% of the total dose, especially when the drug has to be given within 12 hours.¹¹¹

The dietary habits with consumption of high carbohydrates, fats and sweets are common in Pakistan.¹¹²

Lebanon, Jordan and Palestine

In Lebanon, people with diabetes continue their daily work, but with less physical activity and less sleep. Usually, they consume two large meals between sunset and dawn. Studies in the Middle East where Lebanon took part reported that SMBG and glucose-lowering drugs are safe to be used during Ramadan. In the Lira Ramadan and VIRTUE studies, the liraglutide and vildagliptin groups had a lower rate of hypoglycemic events, better glycemic and weight control compared with the SU groups.^{60 113} In Canagliflozin in Ramadan Tolerance Observational Study, patients with type 2 diabetes receiving canagliflozin had an increased risk of volume depletion events.⁵⁵ Among patients treated with insulin, the insulin degludec/aspart group had a lower risk of hypoglycemia than the biphasic insulin aspart 30 group.¹¹⁴ Also, switching from SU to lixisenatide in patients on basal insulin was found to be safe in the LixiRam study.¹¹⁵ GLP-1RAs (liraglutide or dulaglutide), metformin, DPP4 inhibitors (vildagliptin, linagliptin, sitagliptin, alogliptin, saxagliptin), SGLT2i (empagliflozin, dapagliflozin, canagliflozin, ertugliflozin) and TZD (pioglitazone) are usually acceptable treatment options when adjusted to respond to patients' habits in Ramadan. The incidence of hypoglycemia in the Middle East is higher during Ramadan.¹¹⁶

A prospective, observational, open-label study conducted in Jordan to assess the safety of a protocol involving dose adjustments to four different glucose-lowering drug regimens in patients with type 2 diabetes who chose to fast during Ramadan concluded that no cases were reported of DKA or hyperosmolar state among different regimens and hypoglycemia occurred at a lower rate than pre-Ramadan values, especially in those who were treated with premixed 70/30 insulin, insulin glargine and regular insulin.¹¹⁷ Another in Palestine found that Ramadan fasting is tolerable by hemodialysis patients. However, the potential risk of fluid overload and hyperkalemia must be closely monitored.¹¹⁸

North Africa

In Algeria, patients with both type 1 diabetes and type 2 diabetes fast despite their physicians' recommendations. Iftaar is usually a very heavy meal that consists of many courses with no breaks in between, unlike people in other Muslim cultures in North Africa who rest in between courses. Once the meal is done, Algerian people

spend the evening around coffee, tea and different kinds of pastries. During the evening, men and few women usually go to the mosque for the Taraweeh prayer.¹¹⁹ During Ramadan SMBG is rarely checked.¹²⁰ As in other Muslim countries, severe hypoglycemia is the main reason for hospitalization in Algeria during the Holy month. Ketoacidosis, dehydration, orthostatic hypotension and thrombosis are some of the other complications that people with diabetes are exposed to during fasting.^{121 122}

In Tunisia, the majority of people with type 1 and type 2 diabetes fast during Ramadan while receiving insulin. In a Tunisian observational study in patients with diabetes treated with insulin during the month of Ramadan, 10% had type 1 diabetes.¹²³ In this study population, 72% reported having fasted without insulin interruption during the month of Ramadan. The average number of non-fasted days was 3 days, mainly due to hypoglycemic episodes. Another study looked at patients with ≥ 2 cardiovascular risk factors to evaluate metabolic effects of fasting during Ramadan month.¹²⁴ There was a significant decrease in HbA1c after Ramadan (75 mmol/mol (9.0%) to 60 mmol/mol (7.6%)). No acute metabolic incidents were reported during the study period.

CONCLUSION

Fasting the Holy month of Ramadan constitutes one of the five pillars of the Muslim faith. Illness such as diabetes constitutes an exemption from fasting. Although there is some evidence that intermittent fasting may be of benefit in losing weight and some cardiometabolic benefits, yet, there is little evidence that this may be applicable on people with diabetes.

The ADA/EASD consensus recommendations for diabetes management emphasize the need to consider patient factors including comorbidities when deciding on medication selections. The general principles included in the decision cycle in the ADA/EASD consensus applies to Ramadan taking into consideration the presence of comorbidities like ASCVD, HF and CKD, risk of hypoglycemia, weight issues and cost-effectiveness. Care should be individualized with shared decision making between the provider and the patient. Structured education and pre-Ramadan counseling are key components to successful management of diabetes for patients during Ramadan. These should cover all important aspects like glycemic targets during Ramadan, SMBG, diet, physical activity including Taraweeh prayers, glucose-lowering medication dose adjustments and side effects and decision when to break the fast. The decision cycle in [figure 1](#) adapted for the specific situation of Ramadan provides an aid for such an assessment.

People with type 2 diabetes and multiple serious comorbidities and diabetic complications, as well as patients with type 1 diabetes should strongly be advised not to fast considering the very high risk of developing complications. Pregnant women with diabetes or GDM

should also be advised to skip fasting because of the possible negative maternal and fetal outcomes.

The use of the emerging technologies and CGM during Ramadan could optimize the outcome, although the cost is a significant barrier. Ongoing support and monitoring remain integral to a successful outcome and a proper management plan is required. Ramadan guidance for patients with diabetes should be reviewed periodically in the light of new emerging evidence and technology.

Author affiliations

- ¹EDC Center for Diabetes Education, McDonough, Georgia, USA
- ²Diabetes Research Centre, University of Leicester, Leicester, UK
- ³Diabetes Research Centre, University of Leicester and Leicester General Hospital, Leicester, UK
- ⁴Islamic Hospital Amman, Amman, Jordan
- ⁵Division of Endocrinology, Metabolism & Diabetes Division of Cardiology, University of Colorado Denver Anschutz Medical Campus Official Bookstore, Denver, Colorado, USA
- ⁶Dammam Medical Complex, Dammam, Saudi Arabia
- ⁷Adult Diabetes, Joslin Diabetes Center, Boston, Massachusetts, USA
- ⁸Section of Adult and Pediatric Endocrinology, Diabetes and Metabolism, University of Chicago Medicine, Chicago, Illinois, USA
- ⁹Division of Endocrinology, American University, Beirut, Lebanon
- ¹⁰Faculty of Medicine and Pharmacy, Mohamed V University, Rabat, Morocco
- ¹¹Department of Endocrinology and Internal Medicine, University of Tunisia, Monstair, Tunisia
- ¹²Obstetrics & Gynecology, ISRA Medical University, Karachi, Sindh, Pakistan
- ¹³Pierre & Marie Curie Center, University of Algiers, Algiers, Algeria
- ¹⁴Diabetic Association of Pakistan, Karachi, Pakistan
- ¹⁵Chronic Disease Prevention Unit, National Institute for Health and Welfare, Helsinki, Finland
- ¹⁶Dasman Diabetes Institute, Kuwait City, Kuwait
- ¹⁷Medicine, Emory University, Atlanta, Georgia, USA

Contributors MI determined the manuscript strategy, wrote the first draft, he also wrote a section about Egypt and fixed the coauthors' comments on each version; MJD, EA and KK wrote a section about the ADA/EASD consensus and the related figures; FAA wrote a section about Jordan; RHE wrote a section about children with type 1 diabetes; EMB-E wrote sections about intermittent fasting and also section about Saudi Arabia along with dates consumption; NAES wrote a section about pregnancy; AHF wrote a section about nutrition and hypoglycemia; PH wrote a section about Lebanon; HI, IK and SM-Z wrote a section about north Africa; SNM and SS wrote a section about Pakistan; JT and GEU provided intellectual content in interpreting data and critically reviewed the manuscript. All authors revised and approved the final version of the manuscript.

Funding This research was supported by the National Institute for Health Research (NIHR) Leicester Biomedical Research Centre (BRC), the NIHR Leicester Clinical Research Facility (CRF) and the NIHR Applied Research Collaboration East Midlands (ARC-EM).

Disclaimer The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article. De-identified participant data.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Mahmoud Ibrahim <http://orcid.org/0000-0003-4460-9849>

Guillermo E Umpierrez <http://orcid.org/0000-0002-3252-5026>

REFERENCES

- 1 Beshyah SA, Chowdhury TA, Ghouri N, *et al*. Risk of diabetic ketoacidosis during Ramadan fasting: a critical reappraisal. *Diabetes Res Clin Pract* 2019;151:290–8.
- 2 Al-Arouj M, Bouguerra R, Buse J, *et al*. Recommendations for management of diabetes during Ramadan. *Diabetes Care* 2005;28:2305–11.
- 3 Al-Arouj M, Assaad-Khalil S, Buse J, *et al*. Recommendations for management of diabetes during Ramadan: update 2010. *Diabetes Care* 2010;33:1895–902.
- 4 Ibrahim M, Abu Al Magd M, Annabi FA, *et al*. Recommendations for management of diabetes during Ramadan: update 2015. *BMJ Open Diabetes Res Care* 2015;3:e000108.
- 5 Available: https://en.wikipedia.org/wiki/Muslim_world
- 6 International Diabetes Federation. *IDF diabetes atlas*. 9th edition. Brussels, 2019. <http://www.diabetesatlas.org>
- 7 The Holy Qur'an. Sura 2:v.183–185.
- 8 Nikfarjam M, Noormohammadi M-R, Mardanpour-Shahrekordi E. The effect of fasting on emotional intelligence. *National Journal of Laboratory Medicine* 2015;4:67–71.
- 9 Grajower MM, Horne BD. Clinical management of intermittent fasting in patients with diabetes mellitus. *Nutrients* 2019;11:E873.
- 10 Shubrook J, Katuna J. A physician's introduction to therapeutic fasting. When a patient asks about intermittent fasting, what information would be helpful for the physician? Intermittent fasting and type 2 diabetes | diabetes.medicinematters.com, 2019. Available: <https://diabetes.medicinematters.com/diet/type-2-diabetes/intermittent-fas-10-01-2019> | Diet | Case study | Article
- 11 Chaudhury A, Duvoor C, Reddy Dendi VS, *et al*. Clinical review of antidiabetic drugs: implications for type 2 diabetes mellitus management. *Front Endocrinol* 2017;8 <https://doi.org/>
- 12 Davies MJ, D'Alessio DA, Fradkin J, *et al*. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American diabetes association (ADA) and the European association for the study of diabetes (EASD). *Diabetes Care* 2018;41:2669–701.
- 13 Davies MJ, D'Alessio DA, Fradkin J, *et al*. Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American diabetes association (ADA) and the European association for the study of diabetes (EASD). *Diabetologia* 2018;61:2461–98.
- 14 Buse JB, Wexler DJ, Tsapas A, *et al*. Brief update to the 2018 consensus report by the American diabetes association (ADA) and the European association for the study of diabetes (EASD) on the management of hyperglycaemia in type 2 diabetes. update to 2018 ADA-EASD consensus report. *Diabetes Care/Diabetologia in press* 2019.
- 15 Ali S, Davies MJ, Brady EM, *et al*. Guidelines for managing diabetes in Ramadan. *Diabet Med* 2016;33:1315–29.
- 16 Hassanein M, Al-Arouj M, Hamdy O, *et al*. International diabetes Federation (IDF), in collaboration with the diabetes and Ramadan (Dar) International alliance. diabetes and Ramadan: practical guideline. review. *Diabetes Res Clin Pract* 2017;126:303–16.
- 17 Available: https://www.diabetes.org.uk/about_us/news/flash-on-nhs
- 18 Steinsbekk A, Rygg Lisbeth Ø, Lisulo M, *et al*. Group based diabetes self-management education compared to routine treatment for people with type 2 diabetes mellitus. A systematic review with meta-analysis. *BMC Health Serv Res* 2012;12:213.
- 19 Powers MA, Bardsley J, Cypress M, *et al*. Diabetes self-management education and support in type 2 diabetes: a joint position statement of the American diabetes association, the American association of diabetes educators, and the Academy of nutrition and dietetics. *Diabetes Care* 2015;38:1372–82.
- 20 Chvala CA, Sherr D, Lipman RD. Diabetes self-management education for adults with type 2 diabetes mellitus: a systematic review of the effect on glycemic control. *Patient Educ Couns* 2016;99:926–43.
- 21 Zhao F-F, Suhonen R, Koskinen S, *et al*. Theory-based self-management educational interventions on patients with type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. *J Adv Nurs* 2017;73:812–33.
- 22 Odgers-Jewell K, Ball LE, Kelly JT, *et al*. Effectiveness of group-based self-management education for individuals with type 2 diabetes: a systematic review with meta-analyses and meta-regression. *Diabet Med* 2017;34:1027–39.

- 23 He X, Li J, Wang B, *et al.* Diabetes self-management education reduces risk of all-cause mortality in type 2 diabetes patients: a systematic review and meta-analysis. *Endocrine* 2017;55:712–31.
- 24 Chatterjee S, Davies MJ, Heller S, *et al.* Diabetes structured self-management education programmes: a narrative review and current innovations. *Lancet Diabetes Endocrinol* 2018;6:130–42.
- 25 Yorke E, Atiase Y. Impact of structured education on glucose control and hypoglycaemia in type-2 diabetes: a systematic review of randomized controlled trials. *Ghana Med J* 2018;52:41–60.
- 26 Bravis V, Hui E, Salih S, *et al.* Ramadan education and awareness in diabetes (read) programme for Muslims with type 2 diabetes who fast during Ramadan. *Diabet Med* 2010;27:327–31.
- 27 Mohamed OMI, Hassanein M, Syeed A, *et al.* Impact of Pre-Ramadan Intervention Program on Diabetic Patients (PRINTED 1): A Randomised Controlled Trial in a Family Medicine Clinic - Abu Dhabi. *World Family Medicine* 2019;17:10–22.
- 28 McEwen LN, Ibrahim M, Ali NM, *et al.* Impact of an individualized type 2 diabetes education program on clinical outcomes during Ramadan. *BMJ Open Diab Res Care* 2015;3:e000111.
- 29 Yan L, Zainudin SB, Ling C, *et al.* The effect of structured education and intervention for diabetes patients during fasting in Ramadan. 18th Asean Federation of endocrine societies Congress 2015.
- 30 Almalki MH, Hussien I, Khan SA, *et al.* Assessment of Ramadan education and knowledge among diabetic patients. *Clin Med Insights Endocrinol Diabetes* 2018;11:117955141775161.
- 31 Ahmedani MY, Ahsan S, Haque MSU. Role of Ramadan specific diabetes education (RSDE); a prospective study. *Pak J Med Sci* 2017;33:586–93.
- 32 Hossein JM, Jalali MH, Mahmoud F, *et al.* Impact of structured education on diabetes management during Ramadan. International diabetes Federation 2017 Congress 2017.
- 33 Daly H, Byrne J, Martin-Stacey L, *et al.* 'A Safer Ramadan': developing an integrated approach to support safer fasting and feasting for people with type 2 diabetes. *Practical Diabetes* 2014;31:292–7.
- 34 Mnt versus nutrition education. Available: www.eatrightpro.org/payment/coding-and-billing/mnt-vs-nutrition-education [Accessed 22 Dec 2019].
- 35 Shadman Z, Akhoundan M, Poorsoltan N, *et al.* Nutritional education needs in relation to Ramadan fasting and its complications in Tehran, Iran. *Iran Red Crescent Med J* 2016;18:e26130.
- 36 Handy O, Yusof BNM, Reda WH, *et al.* Chapter 7: the Ramadan nutrition plan (RNP) for patients with diabetes, 2016. Available: <http://www.daralliance.org/daralliance/>
- 37 Al-Mssallem MQ. Consumption of dates among Saudi adults and its association with the prevalence of type 2 diabetes. *Asian J. Clin. Nutr* 2018;10:58–64.
- 38 Aleid SM, Al-Khayri JM, Al-Bahrany AM. Date Palm Status and Perspective in Saudi Arabia. In: Al-Khayri JM, Jain SM, Johnson DV, eds. *Date palm genetic resources and utilization, volume 1*. Ed. Netherlands: Springer, 2015: 49–95.
- 39 Qazaq HS, Al Adeeb NZ. The consumption pattern of dates and its related food habits among UAE citizens in Al-Ain City, UAE: a pilot study. *Acta Hort* 2010;882:1083–9.
- 40 Ismail B, Henry J, Haffar I, *et al.* Date consumption and dietary significance in the United Arab Emirates. *J Sci Food Agric* 2006;86:1196–201.
- 41 Alkaabi JM, Al-Dabbagh B, Ahmad S, *et al.* Glycemic indices of five varieties of dates in healthy and diabetic subjects. *Nutr J* 2011;10:59.
- 42 Marso SP, Daniels GH, Brown-Frandsen K, *et al.* Leader Steering Committee; leader trial Investigators. liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2016;375:311–22.
- 43 Marso SP, Bain SC, Consoli A, *et al.* Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2016;375:1834–44.
- 44 Holman RR, Bethel MA, Mentz RJ, *et al.* Effects of once-weekly exenatide on cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2017;377:1228–39.
- 45 Zinman B, Wanner C, Lachin JM, *et al.* EMPA-REG outcome Investigators. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med* 2015;373:2117–28.
- 46 Figtree GA, Rådholm K, Barrett TD, *et al.* Effects of canagliflozin on heart failure outcomes associated with preserved and reduced ejection fraction in type 2 diabetes mellitus. *Circulation* 2019;139:2591–3.
- 47 Gerstein HC, Colhoun HM, Dagenais GR, *et al.* Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. *Lancet* 2019;394:121–30.
- 48 Wiviott SD, Raz I, Bonaca MP, *et al.* Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2019;380:347–57.
- 49 Kato ET, Silverman MG, Mosenzon O, *et al.* Effect of dapagliflozin on heart failure and mortality in type 2 diabetes mellitus. *Circulation* 2019;139:2528–36.
- 50 Perkovic V, Jardine MJ, Neal B, *et al.* CREDENCE trial Investigators. canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med* 2019;380:2295–306.
- 51 McMurray JJV, Solomon SD, Inzucchi SE, *et al.* Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med* 2019;381:1995–2008.
- 52 Husain M, Birkenfeld AL, Donsmark M, *et al.* Oral Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2019;381:841–51.
- 53 Matthews DR, Paldanius PM, Proot P, *et al.* Glycaemic durability of an early combination therapy with vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (verify): a 5-year, multicentre, randomised, double-blind trial. *Lancet* 2019;394:1519–29.
- 54 Wan Seman WJ, Kori N, Rajoo S, *et al.* Switching from sulphonylurea to a sodium-glucose cotransporter2 inhibitor in the fasting month of Ramadan is associated with a reduction in hypoglycaemia. *Diabetes Obes Metab* 2016;18:628–32.
- 55 Hassanein M, Ehtay A, Hassoun A, *et al.* Tolerability of canagliflozin in patients with type 2 diabetes mellitus fasting during Ramadan: results of the canagliflozin in Ramadan tolerance observational study (CRATOS). *Int J Clin Pract* 2017;71:e12991.
- 56 Bashier A, Khalifa AA, Abdelgadir EI, *et al.* Safety of sodium-glucose cotransporter 2 inhibitors (SGLT2-i) during the month of Ramadan in Muslim patients with type 2 diabetes. *Oman Med J* 2018;33:104–10.
- 57 Shao Y, Lim GJ, Chua CL, *et al.* The effect of Ramadan fasting and continuing sodium-glucose co-transporter-2 (SGLT2) inhibitor use on ketonemia, blood pressure and renal function in Muslim patients with type 2 diabetes. *Diabetes Res Clin Pract* 2018;142:85–91.
- 58 Brady EM, Davies MJ, Gray LJ, *et al.* A randomized controlled trial comparing the GLP-1 receptor agonist liraglutide to a sulphonylurea as add on to metformin in patients with established type 2 diabetes during Ramadan: the treat 4 Ramadan trial. *Diabetes Obes Metab* 2014;16:527–36.
- 59 Khalifa AA, Alaaeldin MK AOER, Rashid AOE. Safety and efficacy of liraglutide as an add-on therapy to pre-existing anti-diabetic regimens during Ramadan, a prospective observational trial. *J Diabetes Metab* 2015;06.
- 60 Azar ST, Ehtay A, Wan Bebakar WM, *et al.* Efficacy and safety of liraglutide compared to sulphonylurea during Ramadan in patients with type 2 diabetes (LIRA-Ramadan): a randomized trial. *Diabetes Obes Metab* 2016;18:1025–33.
- 61 Salvo F, Moore N, Arnaud M, *et al.* Addition of dipeptidyl peptidase-4 inhibitors to sulphonylureas and risk of hypoglycaemia: systematic review and meta-analysis. *BMJ* 2016;353:i2231.
- 62 Hassanein M, Hanif W, Malik W, *et al.* Comparison of the dipeptidyl peptidase-4 inhibitor vildagliptin and the sulphonylurea gliclazide in combination with metformin, in Muslim patients with type 2 diabetes mellitus fasting during Ramadan: results of the vector study. *Curr Med Res Opin* 2011;27:1367–74.
- 63 Al-Arouj M, Hassoun AAK, Medlej R, *et al.* The effect of vildagliptin relative to sulphonylureas in Muslim patients with type 2 diabetes fasting during Ramadan: the virtue study. *Int J Clin Pract* 2013;67:957–63.
- 64 Hassanein M, Abdallah K, Schweizer A. A double-blind, randomized trial, including frequent patient-physician contacts and Ramadan-focused advice, assessing vildagliptin and gliclazide in patients with type 2 diabetes fasting during Ramadan: the STEADFAST study. *Vasc Health Risk Manag* 2014;10:319–26.
- 65 Khunti K, Chatterjee S, Gerstein HC, *et al.* Do sulphonylureas still have a place in clinical practice? *Lancet Diabetes Endocrinol* 2018;6:821–32.
- 66 Aravind SR, Al Tayeb K, Ismail SB, *et al.* Hypoglycaemia in sulphonylurea-treated subjects with type 2 diabetes undergoing Ramadan fasting: a five-country observational study. *Curr Med Res Opin* 2011;27:1237–42.
- 67 Rosenstock J, Kahn SE, Johansen OE, *et al.* Effect of linagliptin vs glimepiride on major adverse cardiovascular outcomes in patients with type 2 diabetes: the Carolina randomized clinical trial. *JAMA* 2019;322:1155–66 <https://doi.org/>
- 68 Anwar A, Azmi K, Hamidon B, *et al.* An open label comparative study of glimepiride versus repaglinide in type 2 diabetes mellitus Muslim subjects during the month of Ramadan. *Med J Malaysia* 2006;61:28–35.

- 69 Van de Laar FA, Lucassen PL, Akkermans RP, *et al.* Alpha-Glucosidase inhibitors for type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2005;18:CD003639 <https://doi.org/>
- 70 Marso SP, McGuire DK, Zinman B, *et al.* DEVOTE Study Group (2017) efficacy and safety of Degludec versus Glargine in type 2 diabetes. *N Engl J Med* 2017;377:723–32 <https://doi.org/>
- 71 Eng C, Kramer CK, Zinman B, *et al.* Glucagon-Like peptide-1 receptor agonist and basal insulin combination treatment for the management of type 2 diabetes: a systematic review and meta-analysis. *The Lancet* 2014;384:2228–34 <https://doi.org/>
- 72 Aroda VR, Bailey TS, Cariou B, *et al.* Effect of adding insulin degludec to treatment in patients with type 2 diabetes inadequately controlled with metformin and liraglutide: a double-blind randomized controlled trial (begin: add to GLP-1 study). *Diabetes Obes Metab* 2016;18:663–70 <https://doi.org/>
- 73 Maiorino MI, Chiodini P, Bellastella G, *et al.* Insulin and glucagon-like peptide 1 receptor agonist combination therapy in type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Care* 2017;40:614–24 <https://doi.org/>
- 74 Wysham CH, Lin J, Kuritzky L. Safety and efficacy of a glucagon-like peptide-1 receptor agonist added to basal insulin therapy versus basal insulin with or without a rapid-acting insulin in patients with type 2 diabetes: results of a meta-analysis. *Postgrad Med* 2017;129:436–45 <https://doi.org/>
- 75 Tang H, Cui W, Li D, *et al.* Sodium-Glucose co-transporter 2 inhibitors in addition to insulin therapy for management of type 2 diabetes mellitus: a meta-analysis of randomized controlled trials. *Diabetes Obes Metab* 2017;19:142–7 <https://doi.org/>
- 76 Rosenstock J, Jelaska A, Zeller C, *et al.* Impact of empagliflozin added on to basal insulin in type 2 diabetes inadequately controlled on basal insulin: a 78-week randomized, double-blind, placebo-controlled trial. *Diabetes Obes Metab* 2015;17:936–48 <https://doi.org/>
- 77 Rosenstock J, Jelaska A, Frappin G, *et al.* Improved glucose control with weight loss, lower insulin doses, and no increased hypoglycemia with Empagliflozin added to titrated multiple daily injections of insulin in obese inadequately controlled type 2 diabetes. *Diabetes Care* 2014;37:1815–23 <https://doi.org/>
- 78 Hassanein M, Belhadj M, Abdallah K, *et al.* Management of type 2 diabetes in Ramadan: Low-ratio premix insulin Working group practical advice. *Indian J Endocrinol Metab* 2014;18:794–9 <https://doi.org/>
- 79 Salti I, Bénard E, Detournay B, *et al.* A population-based study of diabetes and its characteristics during the fasting month of Ramadan in 13 countries: results of the epidemiology of diabetes and Ramadan 1422/2001 (EPIDIAR) study. *Diabetes Care* 2004;27:2306–11 <https://doi.org/>
- 80 Beck J, Greenwood DA, Blanton L, *et al.* 2017 national standards for diabetes self-management education and support. *Diabetes Care* 2017;40:1409–19 <https://doi.org/>
- 81 Aldawi N, Darwiche G, Abusnana S, *et al.* Initial increase in glucose variability during Ramadan fasting in non-insulin-treated patients with diabetes type 2 using continuous glucose monitoring. *Libyan Journal of Medicine* 2019;14:1535747 <https://doi.org/>
- 82 Lessan N, Hannoun Z, Hasan H, *et al.* Glucose excursions and glycaemic control during Ramadan fasting in diabetic patients: insights from continuous glucose monitoring (CGM). *Diabetes Metab* 2015;41:28–36 <https://doi.org/>
- 83 Afandi B, Kaplan W, Majid L, *et al.* Rate, timing, and severity of hypoglycemia in adolescents with type 1 diabetes during Ramadan fasting: a study with freestyle libre flash glucose monitoring system. *Ibnosina J Med Biomed Sci* 2018;10:9–11 <https://doi.org/>
- 84 Beshyah S, Haddad M. Impact of Socializing, Fasting and Feasting on Day to Day Blood Glucose Profiles in Diabetes Elucidated by the FreeStyle® Libre™ System. *Ibnosina J Med Biomed Sci* 2016;8:114–9 <https://doi.org/>
- 85 Elbarbary N, Deeb A, Habeb A, *et al.* Management of diabetes during Ramadan fasting in children and adolescents: A survey of physicians' perceptions and practices in the Arab Society for Paediatric Endocrinology and Diabetes (ASPED) countries. *Diabetes Res Clin Pract* 2019;150:274–81 <https://doi.org/>
- 86 Al-Agha A, Kafi S, Zain Aldeen A, *et al.* Flash glucose monitoring system may benefit children and adolescents with type 1 diabetes during fasting at Ramadan. *Saudi Med J* 2017;38:366–71 <https://doi.org/>
- 87 Mohamed K, Al-Abdulrazzaq D, Fayed A, *et al.* Fasting during the Holy month of Ramadan among older children and adolescents with type 1 diabetes in Kuwait. *J Pediatr Endocrinol Metab* 2019;32:843–9 <https://doi.org/>
- 88 Loh HH, Lim Lee-Ling, Loh HS, *et al.* Safety of Ramadan fasting in young patients with type 1 diabetes: A systematic review and meta-analysis. *J Diabetes Investig* 2019;10:1490–501 <https://doi.org/>
- 89 BJØRGAAS M, AASARØD K. Circulatory responses to hypoglycaemia in diabetic and non-diabetic children. *Scand J Clin Lab Invest* 2003;63:233–8 <https://doi.org/>
- 90 Tsilikian E, Tamborlane W, *et al.* Diabetes Research in Children Network (DirecNet) Study Group. Blunted counterregulatory hormone responses to hypoglycemia in young children and adolescents with well-controlled type 1 diabetes. *Diabetes care* 2009;32:1954–9 <https://doi.org/>
- 91 Fredheim S, Foli-Andersen P, Laerkholm G, *et al.* Adrenaline and cortisol levels are lower during nighttime than daytime hypoglycaemia in children with type 1 diabetes. *Acta Paediatr* 2018;107:1759–65 <https://doi.org/>
- 92 Prentice AM, Prentice A, Lamb WH, *et al.* Metabolic consequences of fasting during Ramadan in pregnant and lactating women. *Hum Nutr Clin Nutr* 1983;37:283–94.
- 93 Afandi B, Kaplan W, Al Kuwaiti F, *et al.* Ramadan challenges: fasting against medical advice. *J Fasting Health* 2017;5:133–7 <https://doi.org/>
- 94 Glazier JD, Hayes DJL, Hussain S, *et al.* The effect of Ramadan fasting during pregnancy on perinatal outcomes: a systematic review and meta-analysis. *BMC Pregnancy Childbirth* 2018;18 <https://doi.org/>
- 95 Malhotra A, Scott PH, Scott J, *et al.* Metabolic changes in Asian Muslim pregnant mothers observing the Ramadan fast in Britain. *Br J Nutr* 1989;61:663–72 <https://doi.org/>
- 96 Metzger BE, Ravnkar V, Vileis RA, *et al.* "Accelerated starvation" and the skipped breakfast in late normal pregnancy. *Lancet* 1982;1:588–92.
- 97 Baynouna Al Ketbi LM, Niglekerke NJD, Zein Al Deen SM, *et al.* Diet restriction in Ramadan and the effect of fasting on glucose levels in pregnancy. *BMC Res Notes* 2014;7:392 <https://doi.org/>
- 98 Yogev, Chen Het *al.* Hyperglycemia and adverse pregnancy outcome (HAPO) study cooperative Research Group. hyperglycemia and adverse pregnancy outcome (HAPO) study: preeclampsia. *Am J Obstet Gynecol* 2010;202:255.e1–7 <https://doi.org/>
- 99 Maher N, McAuliffe F, Foley M. The benefit of early treatment without rescreening in women with a history of gestational diabetes. *The Journal of Maternal-Fetal & Neonatal Medicine* 2013;26:318–20 <https://doi.org/>
- 100 Nielsen LR, Pedersen-Bjergaard U, Thorsteinsson B, *et al.* Hypoglycemia in pregnant women with type 1 diabetes. *Diabetes Care* Jan 2008;31:9–14.
- 101 Savitri AI, Yadegari N, Bakker J, *et al.* Ramadan fasting and newborn's birth weight in pregnant Muslim women in the Netherlands. *Br J Nutr* 2014;112:1503–9.
- 102 Alwasel SH, Abotalib Z, Aljarallah JS, *et al.* Secular increase in placental weight in Saudi Arabia. *Placenta* 2011;32:391–4.
- 103 Kapoor A, Dunn E, Kostaki A, *et al.* Fetal programming of hypothalamo-pituitary-adrenal function: prenatal stress and glucocorticoids. *J Physiol* 2006;572:31–44.
- 104 Seckl JR, Holmes MC. Mechanisms of disease: glucocorticoids, their placental metabolism and fetal 'programming' of adult pathophysiology. *Nat Clin Pract Endocrinol Metab* 2007;3:479–88.
- 105 Mirghani HM, Hamud OA. The effect of maternal diet restriction on pregnancy outcome. *Am J Perinatol* 2006;23:021–4.
- 106 Ajabnoor GM, Bahijri S, Borai A, *et al.* Health impact of fasting in Saudi Arabia during Ramadan: association with disturbed circadian rhythm and metabolic and sleeping patterns. *PLoS One* 2014;9:e96500.
- 107 Ajabnoor GMA, Bahijri S, Shaik NA, *et al.* Ramadan fasting in Saudi Arabia is associated with altered expression of clock, DUSP and IL-1alpha genes, as well as changes in cardiometabolic risk factors. *PLoS One* 2017;12:e0174342.
- 108 Al Hejji R, Al Ghamdi M, Al Haqbani D, *et al.* Safety and Efficacy of Gliflozin Group Among Patients with Type 2 Diabetes Including Patient's Satisfaction in Saudi Arabia 2019.
- 109 Ahmedani MY, Hashmi BZ, Ulhaque MS. Ramadan and diabetes - knowledge, attitude and practices of general practitioners; a cross-sectional study. *Pak J Med Sci* 2016;32:846–50.
- 110 Masood SN, Sheikh MA, Masood Y, *et al.* Beliefs of people with diabetes about skin prick during Ramadan fasting. *Diabetes Care* 2014;37:e68–9.
- 111 Ahmedani MY, Haque MS, Basit A, *et al.* Ramadan prospective diabetes study: the role of drug dosage and timing alteration, active glucose monitoring and patient education. *Diabet Med* 2012;29:709–15.
- 112 Masood SN, Saeed S, Lakho N, *et al.* Pre-Ramadan health seeking behavior, fasting trends, eating pattern and sleep cycle in pregnant

- women at a tertiary care institution of Pakistan. *Pak J Med Sci* 2018;34:1326–31.
- 113 Hassoun AA, Pathan MF, Medlej RC, *et al.* Effects of vildagliptin relative to sulfonylureas in Muslim patients with type 2 diabetes fasting during Ramadan: influence of age and treatment with/without metformin in the virtue study. *Diabetes Metab Syndr Obes* 2016;9:225–32.
 - 114 Hassanein M, Ehtay AS, Malek R, *et al.* Original paper: efficacy and safety analysis of insulin degludec/insulin aspart compared with biphasic insulin aspart 30: a phase 3, multicentre, international, open-label, randomised, treat-to-target trial in patients with type 2 diabetes fasting during Ramadan. *Diabetes Res Clin Pract* 2018;135:218–26.
 - 115 Hassanein MM, Sahay R, Hafidh K, *et al.* Safety of lixisenatide versus sulfonylurea added to basal insulin treatment in people with type 2 diabetes mellitus who elect to fast during Ramadan (LixiRam): an international, randomized, open-label trial. *Diabetes Res Clin Pract* 2019;150:331–41 <https://doi.org/>
 - 116 Alsairafi ZK, Taylor KMG, Smith FJ, *et al.* Patients' management of type 2 diabetes in middle Eastern countries: review of studies. *Patient Prefer Adherence* 2016;10:1051–62.
 - 117 Beano AM, Zmaili MA, Gheith ZH, *et al.* Predetermined anti-diabetic drug regimen adjustments during Ramadan fasting: an observational study of safety. *Endocrinol Metab* 2017;32:265–73.
 - 118 Khazneh E, Qaddumi J, Hamdan Z, *et al.* The effects of Ramadan fasting on clinical and biochemical markers among hemodialysis patients: a prospective cohort study. *PLoS One* 2019;14:e0218745.
 - 119 Bencharif M, Fenaghra A, Boudaoud C, *et al.* Impact of Ramadan fasting on energy intake and anthropometry of type 2 diabetics – study in 2 regions of the central highlands and southeastern Algeria. *Journal of nutrition fasting & health* 2017;5:31–7.
 - 120 Malek R, Hannat S, Nechadi A, *et al.* Diabetes and Ramadan: a multicenter study in Algerian population. *Diabetes Res Clin Pract* 2019;150:322–30.
 - 121 Bencharif M, Sersar I, Bentaleb M, *et al.* Highlighted of Ramadan fasting on Diabetes-Study of complications, biochemical aspects and anthropometry. *Romanian J of Diabetes, Nutrition Metabolic diseases* 2019;26:227–34.
 - 122 Chentli F, Azzoug S, Amani MEA, *et al.* Diabetes mellitus and Ramadan in Algeria. *Indian J Endocrinol Metab* 2013;17:295–8 <https://doi.org/>
 - 123 Abid M, Hsairi M, Elleuch M, *et al.* Survey on diabetic patients treated with insulin during the fasting month of Ramadan. *Int J Gen Med* 2018;11:33–40 <https://www.ncbi.nlm.nih.gov/pubmed/29416371>
 - 124 Beltaief K, Bouida W, Trabelsi I, *et al.* Metabolic effects of Ramadan fasting in patients at high risk of cardiovascular diseases. *Int J Gen Med* 2019;12:247–54 <https://doi.org/>