Diabetes management in Ramadan

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Muslims wait to break their fast on the 21st day of the holy month of Ramadan at Jama Masjid on June 6, 2018, in New Delhi, India. | Burhaan Kinu/Hindustan Times via Getty Images

O believers! Fasting is prescribed for you—as it was for those before you¹—so perhaps you will become mindful 'of Allah'

[']Fast a['] prescribed number of days.¹ But whoever of you is ill or on a journey, then 'let them fast' an equal number of days 'after Ramadân'. For those who can only fast with extreme difficulty,² compensation can be made by feeding a needy person 'for every day not fasted'....

Objectives: to answer the following

Patient

- 1. Does everyone have to fast? Is it okay for me to fast with diabetes?
- 2. What risks should I be aware of?
- 3. Is fasting harmful when a woman is expecting a baby?
- 4. Do I stop taking diabetes medications during Ramadan?

Educators/Docs:

- 1. Contraindications to fasting?
- 2. Which non-insulin medications or insulin's are safe?
- 3. Which regimen is better? Insulin and non insulin agents.
- 4. What dose adjustments need to be made?
- 5. When to start educating patients regarding Diabetes management in relation to Ramadan?

Prevalence of Diabetes among Individuals aged 20-79 years, Europe, North America, Oceania, 2010



+ Standardized to the global population.

Source: Public Health Agency of Canada (2011); adapted from Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diab Res Clin Pract* 2010;87:4-14.

Diabetes in Canada: Prevalence of Diagnosed Diabetes by Age and Sex

Prevalence of diagnosed diabetes among individuals aged ≥ 1 year, by age group and sex, 2008/09



Prevalence increased with age. The sharpest increase occurred after age 40 years. The highest prevalence was in the 75-79 year age group.

Public Health Agency of Canada. Diabetes in Canada: Facts and figures from a public health perspective. Ottawa, 2011.

Prevalence Rates in Canada



*Estimated diabetes statistics in Canada are generated by the Canadian Diabetes Cost Model.



Benefits of Fasting!

- Lower blood sugars
- Lower LDL, TG and higher HDL
- Lower BP and lower resting HR
- Boosts working and verbal memory
- Weight loss
- Protection against cancer and neurodegenerative disorders
- Minimizes inflammation

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- Fasting from water and food from sunrise to sunset
- 2 meals:
 - Suhoor small meal before sunrise
 - Iftar Large meal at sunset

Normal physiology when we fast

- Circulating glucose levels fall \rightarrow decreased secretion of insulin
- Glucagon and adrenalin levels rise \rightarrow breakdown of glycogen
- As fasting state prolongs, low insulin levels cause increase in fatty acids to be released from fat cells
- Oxidation of fatty acids \rightarrow ketones

Risks of fasting in diabetes

- Hypoglycemia
- Hyperglycemia
- Diabetic Ketoacidosis (DKA)
- Dehydration and/or Thrombosis

Muslims with diabetes are exempt from fasting. However, many will still choose to fast

Risk Assessment

- Categorize patient into either very high, high, moderate, or low risk
- This should happen 1-2 months before Ramadan

What do the Canadian Guidelines say?

- Who MUST not fast? very high risk
- Who SHOULD not fast? high risk
- Who can fast? low-moderate risk

Who MUST not fast? – VERY HIGH RISK

- Poorly controlled T1 Diabetes A1c >9%
- Pregnancy with type 1 diabetes
- Severe recurrent hypoglycemia
- Hypoglycemic unawareness
- Ketoacidosis in the last 3 months
- Acute Illness (in diabetes or outside diabetes)
- Hyperosmolar Hyperglycemic coma in last 3 months
- Advanced macrovascular disease (especially if recent)
- Kidney disease (on dialysis, or stage 4 or 5)
- Uncontrolled epilepsy
- Cognitive dysfunction / dementia
- Insulin treated type 2 and gestational diabetes

Who SHOULD not fast? – HIGH RISK

- Type 2 diabetes with poor control (A1c >9%)
- Well controlled diabetes on 3-4 daily insulin doses
- Pregnant type 2 or Gestational diabetes controlled on diet only treatment or metformin alone
- Stage 3 kidney disease
- Stable macrovascular complications
- Anyone performing intense physical labour
- Well controlled type1 diabetes

Who CAN fast but with medical advice? – Moderate / Low risk

- Patients with well controlled type 2 diabetes who:
 - Are on lifestyle and diet treatments only
 - Are treated with any non insulin agents
 - Are on basal insulin only or on basal insulin + other non insulin agents
- Patients with pre-diabetes

Risk stratificatio	n for fasting during Ramadan for people living with diabetes
Classification Ris of Risk	sk Factors
Very High Risk MUST NOT FAST	 Poorly controlled T1DM (defined as a pre-Ramadan A1C >9% Severe hypoglycemia within 3 months, recurrent hypoglycemia, and/or unawareness of hypoglycemia Ketoacidosis within 3 months Hyperosmolar hyperglycemic coma within 3 months Acute illness Advanced macrovascular complications, renal disease (on dialysis, stage IV or V), cognitive dysfunction, or uncontrolled epilepsy Pregnancy in diabetes or GDM - treated with insulin
High Risk SHOULD NOT FAST	 T2DM with sustained poor glycemic control* Well-controlled T2DM on MDI or mixed insulin Pregnant T2DM or GDM controlled by diet only CKD stage 3 or stable macrovascular complications Performing intense physical labour Well-controlled T1DM
Moderate/Low Risk CAN FAST WITH MEDICAL ADVICE	 Well-controlled diabetes Treated with lifestyle alone, or with: metformin, acarbose, incretin-therapies (DPP-4 inhibitors or GLP-1 RA), second generation SU, SGLT2 inhibitors, TZD or basal insulin in otherwise healthy individuals

CKD, chronic kidney disease; DPP-4, dipeptidyl peptidase; GDM, gestational diabetes mellitus; GLP-1 RA, glucagon-like peptide-1 receptor agonist; MDI, multiple daily injections; SGLT2, sodium glucose transporter-2; SU, sulfonylurea; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; TZD, Thiazolidinedione *The level of glycemic control is to be agreed upon between the health-care provider and the person living with diabetes. Reproduced with permission from Hassanein et al. [8].

Table 1



Pregnancy

• Fasting is exempted when pregnant

- However, some patients still choose to fast
- Risks involved may be weight loss \rightarrow impact on fetus
- Higher ketones \rightarrow unknown risk to fetal brain development
- If on insulin, discuss insulin timing and blood glucose testing schedule with patient
- If managed through diet and exercise, may see blood sugar being measured before and 2 hr after the 2 meals eaten

 Reference Tith RM, Bilodeau-Bertrand M, Lee GE, Healy-Profitos J, Auger N. Fasting during Ramadan Increases Risk of Very Preterm Birth among Arabic-Speaking Women. *The Journal of Nutrition*, Volume 149, Issue 10, October 2019, Pages 1826– 1832, <u>https://doi.org/10.1093/jn/nxz126</u>

Conclusions

- With growing Muslim communities in Western countries, it could be important to consider religious and cultural practices in the care of pregnant women.
- Community-based public health campaigns guided by Muslim health care providers, including physicians, nurses, and religious and community leaders, could help to disseminate these findings to pregnant women. Pregnant women should be advised against fasting in the second trimester to reduce the risk of preterm birth.

Type 1 Diabetes in Pregnancy – Do not fast

	Type 1 Diabetes
1 st Trimester	VERY HIGH RISK* – DO NOT FAST
2 nd Trimester	VERY HIGH RISK* – DO NOT FAST
3 rd Trimester	VERY HIGH RISK* – DO NOT FAST

* Very High risk of hypoglycemia, hyperglycemia, ketoacidosis and fetal demise, maternal coma/seizures from low sugars, larger or smaller fetal size depending on full profile

****SUMMARY SLIDE**

Type 2 Diabetes in pregnancy – Do not fast

	Type 2 or pre- diabetes – DIET controlled	Type 2 Metformin	Type 2 basal insulin alone or with metformin	Type 2– multiple Insulin doses
1 st Trimester	Moderate to high risk	Moderate to high risk	Moderate to high risk	Very High risk of low sugars
2 nd Trimester	High Risk of pre- term labour	High Risk of pre- term labour	High Risk of pre- term labour	High Risk of pre- term labour -Very High Risk of low sugars
3 rd Trimester	Moderate to high risk	Moderate to high risk	Moderate to high risk	Very High Risk of low sugars

****SUMMARY SLIDE**

Gestational Diabetes – GDM – Do Not Fast

	GDM – diet controlled	GDM – Metformin	GDM – Basal insulin alone or with metformin	GDM – multiple 3-4 daily injections
1 st Trimester				
2 nd Trimester	High risk of preterm labour	High risk of preterm labour	High risk of preterm labour	High risk of preterm labour
3 rd Trimester	Moderate to high risk	Moderate to high risk	Moderate to high risk	Very high risk

Pregnancy – no diabetes

	No Diabetes
1 st Trimester	Low-Moderate risk*
2 nd Trimester	High risk of pre-term labour
3 rd Trimester	Low-moderate risk*

* low-moderate risk of having dehydration, ketone production which has an unknown effect on fetal brain development

What do I do with my diabetes medications?

Classes of Medications

Class of Medication	How/What	Site/Location
α -glucosidase inhibitors	Glucose absorption	Gut
Biguanide (metformin) TZDs	Peripheral glucose uptake and utilization Glucose production	Adipose Muscle Liver
Sulphonylureas, Meglitinides Incretins – GLP1a and DPP4i	Insulin secretion (Insulin replacement)	Pancreas
SGLT2 inhibitors	Glucose reabsorption	Kidney

Metformin

 Table 2 Noninsulin and insulin pharmacotherapy for type 2 diabetes: Recommendations for changes and adjustments 1 to 3 months prior to Ramadan

Medications considered safe during Ramadan		
Drug class	Dosage	Recommendation
Biguanides		
Metformin	500–850 to 1,000 mg BID	No change
Metformin XR	500 to 2,000 mg OD	No change

DPP-4 Inhibitors

DPP-4 inhibitors		
Sitagliptin	25–50 to 100 mg OD	No change
Saxagliptin	2.5 to 5 mg OD	No change
Linagliptin	5 mg OD	No change
DPP-4 inhibitor/metformin combination		
Sitagliptin/metformin	50/500, 850 or 1,000 mg BID	No change

Alpha-Glucosidase Inhibitors and TZDs

Alpha-glucosidase inhibitors		
Acarbose	25–50 to 100 mg TID	No change
Thiazolidinediones		
Pioglitazone	15–30 to 45 mg OD	No change

SGLT2 inhibitors			
Canagliflozin	100–300 mg OD	 Reduce dose or hold temporarily prior to fasting for those with high risk for dehydration (>75 years of age, eGFR <60 mL/min/1.73 m², loop divretic) 	
Dapagliflozin	5–10 mg OD		
Empagliflozin	10–25 mg OD	 Do not hold dose for those with clinical cardiovascular disease Do not initiate within 4 weeks prior to or during Ramadan Hold for vomiting, diarrhea or orthostasis 	

SGLT2 inhibitor/metformin combination

Canagliflozin/metformin	50 or 150/500, 850 or 1,000 mg BID	 Reduce dos prior to fasti for dehvdrat
Dapagliflozin/metformin	5/850 or 1,000 mg BID	eGFR <60 m diuretic) 2. Do not hold
Empagliflozin/metformin	5 or 12.5/500, 850 or 1,000 mg BID	 Do not not a clinical cardi Do not initiat or during Ra Hold for vom orthostasis

- Reduce dose or hold temporarily prior to fasting for those with high risk for dehydration (>75 years of age, eGFR <60 mL/min/1.73 m², loop diuretic)
- 2. Do not hold dose for those with clinical cardiovascular disease
- **3.** Do not initiate within 4 weeks prior to or during Ramadan
- **4.** Hold for vomiting, diarrhea or orthostasis



GLP-1

Incretins



GLP-1 Agonists

GLP-1 receptor agonists

Liraglutide	0.6–1.2 to 1.8 mg OD
Exenatide	0.6–1.2 to 1.8 mg OD
Exenatide extended release	2 mg qweekly
Dulaglutide	0.75–1.5 mg qweekly
Lixisenatide	10–20 mg OD
Semaglutide	0.25–0.5 to 1 mg qweekly

- No change if tolerating prior to Ramadan
- 2. Do not initiate within 4 weeks prior to or during Ramadan
- **3.** Reduce dose or hold for nausea, vomiting, diarrhea or orthostasis
- 4. Exenatide should be taken before 2 meals
- 5. Lixisenatide should be taken before sunset meal
- 6. Longer-acting agents can be taken any time

Scretagogues

Secretagogue	Dosage	Recommendation
Glimepiride	1–2–3 to 4 mg OD	 Consider switching to an alternative drug class with lower risk for hypoglycemia If continuing, consider switching to a safer agent within a class with lower risk for hypoglycemia and reducing dase by 25% to 50%
Glyburide	2.5–5 to 10 mg BID	
Gliclazide MR	30–60 to 120 mg OD	
Repaglinide	0.5–1–2 to 4 mg AC meals	 3. Repaglinide may be safest in class; adjust according to alteration of meal times and sizes during Ramadan

types of insulin



Inhaled insulin

Rapid-acting insulin (insulin aspart, insulin lispro, insulin glulisine)





Pharmacodynamic Action Profiles of Long-Acting Insulins

Source: Mathieu, Chantal; Gillard, Pieter; Benhalima, Katrien. Insulin analogues in type 1 diabetes mellitus: getting better all the time. Nature Reviews Endocrinology 2017/04/21/online http://dx.doi.org/10.1038/nrendo.2017.39 (Used with permission)

Basal Insulin

Insulin type	Recommendation	
Basal		
Degludec, detemir, glargine U100, glargine U300	 Preferred options; consider reducing dose by 15% to 30% 	
Neutral protamine Hagedorn (NPH)	 Consider switching to longer acting basal analogs or reduce dose by 25% to 50% 	

Short acting insulin

Short-acting	
Aspart/faster aspart, glulisine, lispro	 Preferred options. Take usual evening meal dose at sunset meal, reduce predawn meal dose by 25% to 50%, omit lunchtime dose
Human regular insulin	 Consider switching from human regular insulin to rapid-acting insulin analogs

Medications that are safe to use and do not require dose adjustments

- Metformin
- DPP-4 inhibitors Combination medications of any of these 2 classes
- Acarbose
- Pioglitazone
- GLP1 agonist --- as long as without combined insulin therapy

Medications that need to be adjusted in fasting

- SGLT2Is need to decrease the dose
- Combination pill of Metformin plus SGLT2I need to separate the 2 medicines and decrease the SGLT2I dose
- Insulin secretagogues decrease by possibly 50% and use rapid acting ones as these are safer from a hypoglycemia perspective
- Basal slow insulin decrease by 15-50% (depending on which kind)
- Bolus rapid insulin decrease by 25-50% and skip breakfast and lunch doses.
- If taking GLP1 with insulin then expect that the insulin dose might need an even larger decrease in dose to avoid low sugars

General Tips

- Drink lots of water during non fasting hours
- Check your sugars as often as needed:
 - If not feeling well
 - Before meals
 - 2 hours after meals
- Often, people find that the first few days of fasting set the stage and are important in determining what the plan will be for the rest of the month.
- It is not uncommon to need to break fast in the first few days until things are sorted with insulin doses / insulin secretagogue doses

Take home points

- Individualization of plan for fasting is key
- Take a patient centered approach to engage the patient and ensure that they feel heard and are satisfied given the huge spiritual value of Ramadan
- Be creative and consider fasting a few days, alternating days expecting that the first few days are always tough
- There are many ways to recognize and celebrate the sacred month other than fasting

- 61 yo male with T2DM for 15 years, A1c 7.2%, on :
 - Metformin 1000 mg BID
 - Gliclazide MR 120 mg QD
 - Jardiance 25 mg QD
 - Ozempic 1 mg q1 week
 - Basaglar 12 units qhs
- Fast or not fast?
- Plan for Ramadan:
 - Metformin 1000 mg Iftar, 1000 mg Suhoor
 - Gliclazide MR 60 mg Iftar
 - Jardiance 10 mg Iftar
 - Ozempic 1 mg weekly
 - Basaglar 8-10 units at night

- 55 yo female with T2DM x 10 years, A1c 7.6%, on:
 - Metformin 1000 mg BID
 - Repaglinide 5 mg TID meals
 - Januvia 100 mg daily
 - Tresiba 15 units QHS
- Fast or not fast?
- Plan for Ramadan:
 - Metformin 1000 mg Iftar, 1000 mg Suhoor
 - Repaglinide 5 mg with Iftar, 1 mg at suhoor (or more depending of what they plan to eat!)
 - Januvia 100 mg at Iftar
 - Tresiba 10 units at night (start 2-3 days before Ramadan starts)

- 42 yo female with T2DM x 6 years, BMI 32, A1c 11.5%, on:
 - Metformin 1000 mg BID
 - Gliclazide MR 120mg daily
 - Invokana 300 mg daily
 - Basaglar 10 units qhs
 - Wants to start Ozempic
- Fast or no fast?
- Insists that she will fast, what do you tell her?
- Plan for Ramadan:
 - Metformin 1000 mg Iftar, 1000 mg Suhoor
 - Gliclazide MR 120 mg at Iftar
 - Invokana 100 mg at iftar
 - Basaglar 15-20 units at night
 - Do not start Ozempic yet until after Ramadan

- 62yo male with T2DM for 16 years, A1c 7.5%, on:
 - Intolerant to metformin
 - Novolin NPH 12 units am, 25 units qhs
 - Novolin Toronto 7 units with meals
- Fast or no fast?
- Insists on fasting.. Plan for Ramadan :
 - Ideally switch to Tresiba/Basaglar and Rapid insulin if not possible:
 - NPH none to 5 units at Suhoor, 12 units at night
 - Toronto (ideally NR or Humalog) 7 units with Iftar, 1-2 at suboor possibly depending on what they are eating)



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Source: Mathieu, Chantal; Gillard, Pieter; Benhalima, Katrien. Insulin analogues in type 1 diabetes mellitus: getting better all the time. Nature Reviews Endocrinology 2017/04/21/online http://dx.doi.org/10.1038/nrendo.2017.39 (Used with permission)

