ABSTRACT

Ramadan, the ninth month of Islamic lunar calendar, is marked by religious ritual of fasting from early dawn till sunset by Muslims. Islam has allowed many categories of people to be exempt totally or temporarily from fasting. Patients with uncontrolled diabetes face possible major metabolic risks including hypoglycemia, hyperglycemia with or without the risk of impending ketosis, dehydration, and thrombosis. Diabetics can be stratified into four categories based on their level of risk associated with fasting. The recommended ruling for persons in categories 1 and 2 is that they are prohibited from fasting to prevent harming themselves based on the certainty or the preponderance of probability that harm will occur, whereas the recommended ruling for those in categories 3 and 4 is that they should fast. The strategies to ensure safety of diabetics who are planning to fast include Ramadan-focused patient education, pre-Ramadan medical assessment, following a healthy diet and physical activity pattern, physician-recommended modifications in medication protocol and therapeutic recommendations and checking blood glucose as and when required.

Key words: As-Saum, Diabetes Mellitus, exemption, Iftar, risk-stratification, safety strategies, suhur

INTRODUCTION

Ramadan, the ninth month of Islamic lunar Hijri Calendar, is marked by religious ritual of As-Saum (The Fasting), which is one of the five Pillars of Islam. Fasting starts from early dawn (Suhur/Sehri) till sunset (Iftar). During this period one has to abstain from eating or drinking. The Lunar Calendar is 11 days shorter than the Gregorian Christian solar calendar, and hence the starting of the month of Ramadan predates by 11 days its occurrence in the previous Gregorian calendar. Thus, the vagary of the changing of the day time and night time gradually gets assimilated uniformly in all parts of the world.

This ritual is compulsory for all mature followers of Islam, but exemptions are there to accommodate individuals who cannot fast for various reasons. These include, but are not limited to, very old/very young, the sick, the travelers, pregnant/lactating women, and women during their post-delivery and menstrual periods. Those people who fall into the above-specified categories and avail themselves of the provision of exemption should compensate for the missed/lost days of fasting of Ramadan by various means described in religion. Individuals who are permanently incapacitated are also given leverage to compensate accordingly.

THE PHYSIOLOGICAL STATES OF EATING, SATIETY, HUNGER AND FASTING

Under normal circumstances energy needs are met by the exogenous substrates derived from food. When caloric intake is greater than the immediate needs as occurs after the usual meals, the excess substrate is stored as glycogen, fat, and structural proteins—the anabolic phase of metabolism. This proceeds from intestines to liver, to utilization and storage sites. Insulin is the primary hormone mediating this phase during which counter regulatory hormone levels are suppressed. This phase lasts for about 4–5 hours.\textsuperscript{1,2}
At the end of 4–5 hours after a meal begins the catabolic phase of metabolism normally experienced during the overnight fasting state. Initially, the liver releases the glucose required for CNS metabolism almost exclusively from its stored glycogen, but soon this gets depleted as the liver stores on an average only about 70 g of glycogen. This gets hastened if there is any unusual physical exertion or any disease-related stress situation. At this stage, gluconeogenesis, especially in the liver, takes centre stage with the influx into the liver of lactate, pyruvate, and aminoacids primarily derived from the muscles, and glycerol released from adipose tissue consequent to lipolysis.[3]

Catabolic metabolism is initiated by a fall in plasma insulin circulation coupled with the secretion of the counter regulatory hormones glucagon, epinephrine, cortisol, and growth hormone. Of these, glucagon is the primary hormone for glucose maintenance, while other hormones play a secondary role. The hormone-sensitive lipoprotein lipase in the adipose tissues is activated and hydrolyzes stored triglyceride fat to long chain fatty acids and glycerol. Bulk of these fatty acids is utilized directly while the remainder (about 30%) is oxidized in the liver to ketones-acetoacetic acid and β hydroxyl butyric acid. Ketones act as the back-up for the brain, and also they are utilized as energy sources by other body tissues, but only minimally by the liver. Thus, the shift of most tissues to lipid metabolism and ketones in place of glucose further spares more glucose for utilization by the CNS.

Blood Glucose level Variations: In normal individuals, there is a slight fall in average blood glucose levels in the first few days of Ramadan fasting followed by normalization by about the 20th day, and a relatively slight increase subsequently, but all these variations are well within the normal physiological range.[4,5] In properly educated, well-informed and motivated persons with diabetes, under proper medical supervision, no significant aberrations in their blood glucose values were reported during Ramadan fasting. However, some of the diabetics who fasted during Ramadan experienced variations in their blood glucose values depending upon the type, composition, and quantity of food consumed, regularity in medicine taking, alterations in daily physical activities or occasional binge eating after the breaking of the fast.[6,7]

Body weight changes: In normal non-diabetic individuals, an average weight loss of 1.7–3.8 kg has been reported in different studies, the loss being greater in overweight persons.[8] In diabetics who fasted during Ramadan, some reports have shown no change, or a decrease, or even a slight increase in body weights perhaps due to the variations in the life style changes practiced by these persons especially in regard to quality and quantity of food intake and the level of physical activities.[9]

Other parameters of diabetic control during Ramadan fasting: In a large study, HbA1c, serum fructosamine level, insulin, and C-peptide levels did not show any significant changes during or soon after Ramadan fasting.[10]

Energy intake and serum lipid variations in fasting diabetics: In well-informed and motivated diabetics, total daily caloric intake showed a slight decrease during the Ramadan fasting[11] A slight increase/decrease in the total cholesterol levels, an increase in HDL-cholesterol, but no appreciable effects on triglycerides and LDL-cholesterol levels were observed.[10-14]

Other biological parameters during Ramadan fasting: Serum creatinine, uric acid, blood urea nitrogen, proteins—albumin and globulin, alanine-amino-transferase, and aspartate-amino-transferase values did not show significant changes in diabetics who were medically found fit to fast during Ramadan.[15]

Possible major metabolic risks associated with Ramadan fasting for people with uncontrolled diabetes include hypoglycemia, hyperglycemia with or without the risk of impending ketosis, dehydration, and thrombosis.[16-18] There have not been any published reports of increased hospitalizations due to thrombotic cardiac or cerebral conditions in fasting persons whose diabetes is reasonably well controlled.[19,20]

Hyperglycemia can occur in persons who are negligent about their medications and indulge in over-eating in the hours after or before the stipulated fasting period. Normally, the plasma glucose level fluctuates in a very narrow range. In the prandial state the plasma glucose level raises which is promptly sensed by the pancreas and results in an increase in insulin secretion, suppression of glucagon secretion, a decrease in hepatic glucose output, and an increase in the peripheral glucose utilization and its storage.

In diabetics, there is a loss of the first phase insulin secretion and an increase in the proinsulin and split proinsulin levels resulting in an increase in free fatty acids and triglyceride levels. Glucagon levels remain high and the hepatic glucose output is also not suppressed appropriately. All these result in post-prandial hyperglycemia. Even isolated post-prandial hyperglycemia is known to increase the risk of fatal cardiovascular disease.

Post-prandial hyperglycemia can be managed effectively
by following the time tested and well-established therapeutic measures:
- Diet rich in complex carbohydrates and fibers, which contain less fat and also have lower glycemic index.
- Alpha-glucosidase inhibitors, which delay the absorption of complex carbohydrates and sucrose. They are known to lower triglyceride levels to some extent.
- Metformin, as it effectively suppresses hepatic glucose output.
- Meglitinides—repaglinide and nateglinide, which target and reduce postprandial glycemic surges.

**Risk Stratification for Diabetics Planning Ramadan Fasting**

For the benefit of diabetics desirous of observing the ritualistic fasting of Ramadan, the Organization of the Islamic Conference, in its published recommendations under the head “Diabetes and Fasting in Ramadan: Summary of Recommendations of the Organization of Islamic Conference” has categorized such persons and issued rulings and recommendations as follows.[21,22]

**Category 1: Very high risk group**
- Severe hypoglycemia within the last 3 months prior to Ramadan
- History of recurrent hypoglycemia
- Hypoglycemia unawareness
- Sustained poor glycemic control
- Diabetic keto-acidosis within the previous 3 months
- Brittle type 1 diabetes mellitus
- Acute illnesses
- Hyperosmolar-hyperglycemic-state within the previous 3 months
- Performing intense physical labor
- Pregnant ladies
- On chronic dialysis

**Category 2: High risk group**
- Moderate hyperglycemia, 180–300 mg/dL (10.0–16.5 mmol/L), or HbA1c ≥10%
- Diabetic nephropathy and renal insufficiency
- Advanced diabetic retinopathy
- Advanced macro-vascular complications involving the heart, brain or peripheral vessels
- Patients living alone who necessarily are treated with insulin or sulphonylureas
- Living alone and afflicted with other co-morbid conditions that present additional risk factors
- Aged people with ill health
- Psychiatric states necessitating use of drugs that may affect cognitive state.

**Category 3: Moderate risk**
- Well controlled with short acting insulin secretagogues of meglitinide group of drugs.

**Category 4: Low risk**
- Well controlled with diet alone, metformin, or thiazolidinediones, and otherwise healthy.

The recommended ruling for persons in categories 1 and 2 is that they are prohibited from fasting to prevent harming themselves based on the certainty or the preponderance of probability that harm will occur to those who are in these two categories.

The ruling for those in categories 3 and 4 is that they should fast.

**Taking Option of not fasting**

The Holy Qur’an explicitly forbids acts that are harmful and injurious to one’s own self, and persons in the above category would be putting their health, safety and even life itself in jeopardy if they go against medical advice. “And let not your own hands throw you into destruction” and “do not destroy one another: for, behold, God is indeed a dispenser of grace unto you.”[23,24]

**Strategies to Ensure Safety of Diabetics Who Plan to Fast**

To quote Prof. Elliot Joslin: “The Patient who knows the most lives longest.” and, “Patient Education is not one of the treatments, it is the treatment.” This holds immense value and importance while dealing with diabetes.

**A. Ramadan focused Patient Education**
1. Focus on the causation, early recognition and emergency management of hypoglycemia, hyperglycemia, dehydration, renal colic, and impending DKA and HHS.
2. Self-monitoring of blood glucose at home especially for type--1 diabetics and those type2 diabetics who are taking insulin.
3. Urine testing to detect ketones.
4. Pulse, temperature and breathing rate calculations.
5. Meal planning and dietary advice, balanced diet with items of low glycemic index, less of fats, more of high fibers, fresh fruits, and vegetables.
6. Patient empowerment, increasing active participation and motivation to ensure total compliance not only in the month of fasting but all through the year.

**B. Pre-Ramadan Medical Assessment**
1. Preferably undertaken 1–2 months before the fasting month starts.
2. Physical status, weight, blood pressure, glycemic and lipid control, status of the eyes, heart, kidneys and the nervous system.
3. Individual risk stratification to identify those not fit to fast.

C. Diet and Nutrition in Ramadan
1. Limitation of sugary food items especially during the Suhur meal.
2. Inclusion of fruits, fresh vegetable salads without oily dressings, lentils, yoghurt, whole serial made food items, steam cooked or boiled vegetables with no or less of oils/fats, non-vegetarian items grilled or steam cooked instead of frying.
3. Delay the Suhur meals to the maximum permitted time limit, and hasten to break your fast at the beginning of the stipulated time.
4. At Iftar and there after encourage to drink sugar free drinks, fruit juices and water to quench thirst and to compensate for any water and electrolyte deficit that would have occurred in the day time.
5. Limit use of deep fried and oil rich food items like parothas, puris, pakodas, samosas, etc.
6. Moderation in eating is the key to good health. Avoid over-eating.

D. Medication Protocol and Therapeutic recommendations
1. Patients who are well under control on diet and lifestyle management do not need any changes in their daily physical activities. Avoid high calorie, high sugar, and deep fried oily food items especially after Iftar meals.
2. Metformin: Generally those on monotherapy with metformin do well and are able to fast safely. If on b.i.d dose, patients are usually advised to take their usual dose of metformin at the Iftar meals, but only half of the morning’s doze at Suhur time. Monitor blood sugar periodically before Iftar and Suhur. Emphasize on the need to take sufficient fluid intake to avoid risk of lactic acidosis.
3. Sulphonylureas: If on long acting types like glibencamide, it is better and safer to shift to the second-generation sulphonylureas like gliclazide, glipizide or glimepiride that are less associated with hypoglycemia. These could be taken at fast breaking time before the Iftar meals.
4. Meglitinides: Repaglinide and nateglinide of this category are considered particularly useful during fasting days because of their short duration of action, convenience of being taken while eating Iftar or Suhur in isolation, or at both times depending upon patient requirements and the prevailing glycemic control. The incidence of hypoglycemia is much less than that seen with sulphonylureas.
5. Incretins: The risk of hypoglycemia with incretins—both DPP IV inhibitors and GLP 1 analogues—is much less than that with sulphonylureas or even insulin, and this definitely provides benefits for type 2 diabetes people fasting in Ramadan.
6. Thiazolidinediones: These may be continued if they were found effective and well tolerated prior to the start of the fasting season.
7. Alpha-glucosidase inhibitors: These too, are safe, and their use does not necessitate any special precautions.
8. Insulin: Type 1 diabetics who depend on frequent doses of insulin, and experience extreme fluctuations in blood glucose values, or are afflicted with hypoglycemia unawareness, or advanced micro or macrovascular complications are medically advised not to fast. Those type1 diabetics who are in good health, and have satisfactory control can fast safely with basal-bolus insulin regime, where once or twice daily injections of intermediate or long acting insulin along with pre-meal short acting insulin are used. NPH for basal and regular insulin for bolus; and the insulin analogs detemir or glargine for basal combined with lispro, glulisine or aspart for bolus have shown almost similar good results. The newer analogues are equally effective as compared to traditional insulins, while causing much less hypoglycemia. Insulin pumps used in carefully selected educated type-1 diabetics could be very effective in enabling them to fast safely in Ramadan.
9. Insulin: Type 2 diabetics in good health, with reasonably good diabetic control and free from advanced complications, and requiring insulin alone or in combination with oral medications, may undertake Ramadan fasting. Generally speaking, long acting basal insulin is advised at Iftar times, and supplemented by short-acting insulin at Suhur times. Short-acting analog before meals instead of the regular insulin is reported to be associated with less hypoglycemia and smaller post-prandial glucose excursions in diabetics fasting in Ramadan. Persons who are doing well with b.i.d mixed insulin are advised to take the larger portion of the insulin dose at Iftar and the smaller portion at Suhur time.

E. Exercise and Physical Activity
1. Encourage usual daily physical activity, especially during non-fasting hours.
2. Regular light and moderate exercise is safe and beneficial in type-2 diabetes patients.
3. Avoid rigorous exercise during fasting hours particularly by persons on sulphonylureas or insulin.
4. Encourage participation in the pre-bed time congregational Travelh Salaath prayers observed in the month of Ramadan.

F. Checking Blood Glucose
Checking your blood glucose through finger prick does not invalidate fasting state. So encourage patients to check blood glucose periodically. If blood sugar levels are low and patient experiencing signs/symptoms of hypoglycemia, it is advisable that fast is broken immediately.

G. Dental Health: It needs mention because so often it is neglected by the patients. Severe periodontal disease often coexists with diabetes, and increases its severity and associated complications including nephropathy, neuropathy, CAD, MI, etc.[36] Proper control and treatment of chronic periodontal disease is essential for achieving long-term glycemic control,[37] and good diabetic control accelerates success in treatment of different presentation of periodontal disease like gingival disease, chronic periodontitis, aggressive periodontitis, necrotizing periodontitis, periodontal abscess, etc.[38,39]

CONCLUSION
Fasting in the month of Ramadan is ordained on the Muslim believers. Many categories of people who have temporary or passing afflictions and/or limitations like acute illnesses, pregnancy, lactation, menstrual periods, post-delivery incapacity, travelers, etc. are permitted to complete the lost days of Ramadan fasting by observing fast for equivalent number of days in other months.

Other persons with more or less permanent afflictions: the very old, the chronic and seriously or terminally ill; and some others like the diabetics with advanced and serious complications who by fasting might put themselves into grave and life-threatening situations are granted permission to provide provision to feed the poor and needy for the number of days they could not fast in Ramadan. Young children and those with unsound mental faculties are completely exempt from fasting and also exempt from compensating for the lost fasting days for as long as they remain in these states.

Ramadan focused patient education should focus on pre-Ramadan evaluation, risk stratification, and reminder about the generous religious exemptions available for deserving individuals. Those who are medically fit to fast need to be educated about the importance of balanced nutritious diet, moderate physical exercise, adherence to the advised drugs and medications, self-monitoring of their glycemic status, early recognition of dangerous situations, and the necessary remedial measures.

Review of available medical literature indicates that fasting in Ramadan is safe and probably beneficial with proper education and good management for the majority of persons suffering from diabetes. This is so especially for type 2 diabetics. Healthy, stable and well informed type-1 diabetics are also able to fast safely but need to be supervised and managed with greater care and strict attention to their diet, daily activities, glycemic control, and insulin dosage adjustments.

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