Consensus on Insulin Dose Modification During Fasting in Type 2 Diabetes

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Abstract
Introduction: Fasting for patients with type 2 diabetes mellitus (T2DM) carries a risk of an assortment of complications. The decision of T2DM patient to fast should be made after sufficient discussion with physician regarding the risks involved. The current consensus is developed to help physicians manage T2DM patients during fasting.

Objective: To provide simple and easily implementable guidelines on insulin dose modification during fasting in T2DM patients.

Methods: The expert group committee discussed and proposed six recommendations for the use of insulin regimens during fasting. The recommendations were proposed on diet, exercise and categorization of risks during fast, breaking fast, dose modification of basal insulins, premix insulins and prandial insulins. All these recommendations were based on established guidelines and published scientific literature. These evidences were then factored into the national context based on the expert committee representative's patient-physician experience in their clinical practice and common therapeutic practices followed in India to successfully achieve optimal glucose control. The final consensus-based recommendations were proposed and collectively recorded for each insulin regimen.

Results: Recommendations based on insulin dose modification during fasting in T2DM patients has been developed. Patients with diabetes, who fast are recommended to keep themselves hydrated, consume low glycaemic and high fibre food but, avoid sugary and caffeinated drinks along with fried foods. The main goal of insulin therapy during fasting is to provide adequate insulin to prevent post meal hyperglycaemia and prevent hypoglycaemia during fast.

Conclusion: We hope that the consensus based recommendations mentioned in this paper will be a useful reference tool for health care practitioners to initiate and intensify insulin therapy in T2DM patients in order to successfully complete fasting without much complication.

Introduction
The prevalence of diabetes is increasing worldwide with approximately 415 million people in 2015, which is expected to increase by 55% and could rise to 642 million by 2040. Diabetes lead to around 5 million deaths in 2015.¹ India is amongst the 3 top countries with highest diabetes burden and the number is estimated to increase from 69.2 million (2015) to 123.5 million by 2040. Moreover, a recent ICMR study reported poor level of glycaemic control in Indian patients with self-reported Diabetes.²

Fasting is a willing abstinence from food, drink, or both for a period of time. It is a religious cultural practice, which causes profound changes in dietary habits and lifestyle. Various types of fasts have been evident in Indian culture since long period of time (Figure 1). Based on their frequency of occurrence and duration of fasting, the fasts have been categorised as infrequent short duration fasts (12-15 hours; for eg. Karva Chauth, Hoi Ashtami, etc), frequent short duration fasts (12-24 hours; for eg. Ekadashi, Purnima, Pradosha etc), and annual/semi-annual long duration fasts (Figure 2) (at least 7 days; eg. Ramadan, Navarathri, Paryushan, Buddhist lent, Parsi fast, etc.).³⁵

During fasting, there is a lower level of circulating glucose, which leads to declined secretion of insulin and augmentation of gluconeogenesis and ketogenesis processes. There is an increase in the levels of adrenaline (epinephrine), noradrenaline (norepinephrine), cortisol during the fasting period, which enhances the release of glucose into the bloodstream. Elevated levels of these hormones, gluconeogenesis and ketoacidosis, may result in various major risks in patients with diabetes, including hypoglycaemia, hyperglycaemia, diabetic ketoacidosis, dehydration and thrombosis.⁶ Other associated features include increased heartbeat, blood pressure, enlarged eye pupil, etc. Various studies have reported a positive correlation between hyperglycaemia and macro- and microvascular complications.⁷⁸ Due to restricted fluid intake, there are high chances of dehydration, which further deteriorates with hot and

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humid climatic conditions, excessive sweating and excessive physical labour. It may also lead to increased blood viscosity, which may enhance the chances of thrombosis.

Published evidence have shown higher rates of hypoglycaemia in Type 2 diabetes mellitus (T2DM) patients on fasting.\textsuperscript{9,10} A survey of medical records of 90 patients from Saudi Arabia reported a statistically significant increased incidence of retinal vein occlusion during the months of Ramadan (29.5%) when compared with other months of the Gregorian year.\textsuperscript{11} Two multinational studies (‘Multi-country retrospective observational study of the management and outcomes of patients with Type 2 diabetes during Ramadan in 2010’ CREED Study and Epidemiology of Diabetes and Ramadan [EPIDAR]) reported complications of neuropathy (19.8% and 27.8%), retinopathy (12.4% and 19.7%), and nephropathy (11.1% and 12.1%) in patients with T2DM. Furthermore, both studies also reported higher prevalence of hypertension (62.1% and 48.8%) and dyslipidaemia (56.6% and 32.5%) in these patients.\textsuperscript{9,10} Therefore, patients with diabetes, should seek medical advice before deciding to proceed with fasting.

Currently there is no existing comprehensive consensus on most appropriate insulin type & regimen during fasting for T2DM. Thus there is a need to develop guidelines in the national context with increasing treatment options in insulin therapy. The proposed consensus plans to provide simple & easily implementable guidelines to health care physicians treating T2DM.

The objectives of this meeting were:

- Evaluate the available dosing regimens & titration algorithms for currently available insulins
- Examine the existing evidence for dosing & titration of currently available insulins
- Evolve consensus statement of recommendations on the topic

**Methods**

A group of experts came together in Delhi on 20 August 2016 for the consensus meeting on “Insulin dose modification during fasting in type 2 diabetes”. The expert group committee discussed the following insulin regimens and proposed six recommendations for 1) Diet and exercise during fast; 2) Risk categorization for patients

**Fig. 1: Various fasts followed in Indian culture**

- Guru Purnima
- Karva Chauth
- Hoi Ashtami
- Navarathni
- Paryushan
- Purnima
- Pradosha
- Ayambil/Oli
- Buddha lent
- Ramadan
- Ekadashi
- Paryushan
- Pradosha
- Karva Chauth, Guru Purnima, Hoi Ashtami (12 - 15 hours)
- Ekadashi, Purnima, Pradosha (12 - 24 hours)
- Navarathni, Paryushan, Ramadan, Buddhist lent, Ayambil/Oli, Parsi fast, Maas Khaman, Varshitap, Christian lent (At least 7 days)
Insulin dose in fasting

**General considerations**

- Insulin dose in fasting
- Risk stratification
- Diet and exercise
- Breaking fast
- Consensus Recommendations

**Dose modifications in type 2 diabetes**

- Basal insulins
- Premix insulins
- Prandial insulins

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**Fig. 3: Consensus on fasting in Type 2 Diabetes Mellitus patients**

who fast; 3) Breaking fast; 4) Dose modification of basal insulins; 5) Dose modification of premix insulins; and 6) Dose modification of prandial insulins (Figure 3).

Each insulin regimen was presented and evaluated based on established guidelines (American Diabetes Association: Recommendations for Management of Diabetes During Ramadan [written hence forth as ADA, 2010]), International Diabetes Federation (IDF) Diabetes and Ramadan Practical Guidelines (written hence forth as IDF-DAR, 2016) and South Asian Consensus Guideline: Use of insulin in diabetes during Ramadan [written hence forth as SAFES-2016] and published scientific literature. These evaluations were then factored into the national context based on the expert committee representative’s, patient-physician experience in their clinical practice and common therapeutic practices followed in India. The evaluations were debated and discussed within the expert group committee. The final consensus-based recommendations were proposed and collectively recorded for each insulin regimen in easily implementable steps, without any bias and in an unambiguous language.

**Consensus 1: Diet and Exercise During Fast**

**Current Place in Guidelines**

IDF-DAR 2016 provided Ramadan Nutrition Plan (RNP) (a mobile and web based application) for physicians to help patients to develop daily caloric target and avoiding risks associated with fasting in diabetes. RNP recommends to take adequate amount of total daily calories; meals should be balanced preferring carbohydrates with low glycaemic index (e.g. Whole grains, legumes, green salads, vegetables) - 45-50%; proteins (dairy, nuts, seeds, legumes) around 20-30%; and fat (mono and polyunsaturated fat preferred) comprising <35% of the meal. Saturated fat should be limited to <10% of the total daily caloric intake with adequate hydration. Carbohydrates, particularly high in fibres should be encouraged. Carbohydrates from sugar and highly processed grains should be avoided. Non-sweetened beverages should be encouraged at or between the two main meals (diet beverages may be consumed). Consumption of caffeinated drinks should also be minimised as they are diuretics. In morning meal, adequate amount of protein and fat are recommended and lower level of carbohydrate should be taken. Evening meal should begin with plenty of water and 1-2 dried or fresh dates to raise blood glucose levels.

ADA guidelines recommends to maintain normal physical activity but, avoid higher level of physical activity which may lead to higher risk of hypoglycaemia, particularly during the few hours before the sunset meal. Similarly, common practice of ingesting large amounts of foods rich in carbohydrates and fats, especially at the time of breaking fast should be avoided. It is also recommended that fluid intake should be increased during non-fasting hours.

SAFES 2012 recommends that diet and meal plan should be changed as per individual’s customs and habits. One should consume liquid diet during non-fasting hours so as to avoid the possibility of dehydration and electrolyte imbalance.

**Published Scientific Literature**

In a time-course prospective study, the daily recordings of quality and quantity of food intake was noted for seven days; before and after Ramadan in 46 healthy volunteers. The carbohydrate intake was found to be slightly higher in females as compared to males in the second week (24% Vs.22%) of fasting. The levels of low density lipoproteins (LDL) decreased in females and males by 20% and 55% post-Ramadan compared to pre-Ramadan. The study reported 1.4 fold increases in high density lipoprotein (HDL) at day 28 of Ramadan.

Furthermore, a prospective cohort study on 88 patients with mean age of 51±10 years reported that fasting during Ramadan weakened the glycaemic control in T2DM patients. The study reported decline in fasting blood glucose (FBG) and glycosylated haemoglobin (HbAlc) control; but, observed significant improvements in HDL, LDL cholesterol and body mass index after Ramadan.

**NIS 2016 Consensus on insulin dose modification during fasting in T2DM**

**Consensus 1: Diet and exercise during fast**

- Calorie intake needs to be divided between eating periods with addition of snacks
- Avoid fried foods and replace it with boiled and baked food.
- Include high fibre and low glycaemic index foods with enough fruits, vegetables and salads facilitating slow energy release before and after fasting
- Avoid high saturated fats, high sugary desserts, caffeinated and sweetened drinks
Consensus 2: Risk Categorization for Patients who Fast

Current Place in Guidelines

IDF-DAR-2016 recommends avoiding fast if the probability of impairment is high. The new IDF-DAR risk stratification approach defines three risk categories-1) “very high” 2) “high” and 3) “moderate/low” (Table 1).

As per ADA 2010 recommendations, patients who insist on fasting need to be aware of the associated risks of the fasting and techniques to decrease this risk. Patients may be at a higher or lower risk of fasting related complications depending on the number and extent of their risk factors. Patients are classified to have “very high risk”, “high risk,” “moderate risk,” and “low risk” (Table 1).6

As per SAFES guidelines, patients were categorized into 4 risk groups: “very high risk”, “high risk”, ”moderate risk”, and “low risk” (Table 1).12

Published Scientific Literature

A correlation between hyperglycaemia and microvascular complications and possibly macrovascular complications is reported in two landmark trials.8,16 In the EPIDIR study, higher rates of severe hyperglycaemia were recorded in people with T1DM and T2DM during Ramadan compared with before Ramadan (4.7-fold or 7.5-fold increases, respectively). The rate of severe hyperglycaemia increased by 5.0-fold in T2DM patients during Ramadan.9

Consensus 3: Breaking fast

Current Place in Guidelines

IDF-DAR emphasises the need to educate the patients in identifying the symptoms of hypoglycaemia and hyperglycaemia. It is recommended to frequently monitor the blood sugars and break the fast if blood glucose is <70 mg/dL (3.9 mmol/L) or >300 mg/dL (16.6 mmol/L).12

As per ADA 2010, it is recommended to break the fast if blood glucose is <60 mg/dL [3.3 mmol/L], or it reaches <70 mg/dL (3.9 mmol/L). Delaying this treatment may drop their blood glucose further. Similarly, fast should be broken if blood glucose exceeds 300 mg/dL (16.7 mmol/L) and in ‘sick days’.6

SAFES guideline recommends T2DM patients to start their fasting plan at least 3 months prior to fasting, facilitating certain factors to be assessed by the physician including glycemic status. This guideline recommends to avoid fasting, if HbA1c > 10% or in the presence of frequent hypoglycemia, hyperglycemic unawareness, and high fluctuation of blood glucose profile. Complications and other comorbid conditions, which may be aggravated by prolonged fasting should be assessed.13

Published Scientific Literature

An observational study based on 493 consecutive patients with diabetes at Benghazi Diabetes and Endocrine Centre reported that 30% of T2DM patients have to break their fasts due to complications like hypoglycemia (43.40%) hyperglycemia (27%) hypertension (10%) and infection (5.6%).17 Another study group reported hypoglycemia followed by hyperglycemia as the two most common complications contributing for breaking the fast during Ramadan.9

Consensus 4: Dose Modification of Basal Insulins

The judicious use of intermediate or long-acting basal insulin preparations can provide adequate coverage in patients during fasting as long as the dosage is appropriately individualized.

Current Place in Guidelines

IDF-DAR recommended to administer 15-30% reduced daily dose in evening, if a patient is on NPH/insulin detemir (IDet)/insulin glargine (IGlar)/ insulin degludec (IDeg) once daily (OD). However, if a patient is on NPH/IDet/IGlar
Table 1: Comparisons of Risk categorization for patients who fast by present guidelines:

<table>
<thead>
<tr>
<th>ADA 2010</th>
<th>SAFES 2012</th>
<th>IDF-DAR 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Very High Risk</strong></td>
<td>• Severe hypoglycemia within the last 3 months prior to Ramadan</td>
<td>• One or more of the following:</td>
</tr>
<tr>
<td>• A history of recurrent hypoglycemia</td>
<td>• Patients with a history of recurrent hypoglycemia</td>
<td>• Severe hyperglycaemia within the 3 months prior to Ramadan</td>
</tr>
<tr>
<td>• Hypoglycemia unawareness</td>
<td>• Patients with hypoglycaemia unawareness</td>
<td>• Diabetic ketoacidosis within the 3 months prior to Ramadan</td>
</tr>
<tr>
<td>• Sustained poor glycemic control</td>
<td>• Patients with sustained poor glycemic control</td>
<td>• Hyperosmolar hyperglycemic coma within the 3 months prior to Ramadan</td>
</tr>
<tr>
<td>• Ketoacidosis within the 3 months prior to Ramadan</td>
<td>• Ketoacidosis within the last 3 months prior to Ramadan</td>
<td>• History of recurrent hypoglycemia</td>
</tr>
<tr>
<td>• Type 1 diabetes mellitus</td>
<td>• Hyperosmolar hyperglycemic coma within the last 3 months prior to Ramadan</td>
<td>• History of hypoglycemia unawareness</td>
</tr>
<tr>
<td>• Acute illness</td>
<td>• Patients on dialysis</td>
<td>• Poorly controlled type 1 diabetes mellitus</td>
</tr>
<tr>
<td>• Hyperosmolar hyperglycemic coma within the previous 3 months</td>
<td>• One or more of the following:</td>
<td>• Acute illness</td>
</tr>
<tr>
<td>• Performing intense physical labor</td>
<td>• Type 2 diabetes with sustained poor glycaemic control</td>
<td>• Pregnancy in pre-existing diabetes, or gestational diabetes mellitus</td>
</tr>
<tr>
<td>• Pregnancy</td>
<td>• Well-controlled type 1 diabetes</td>
<td>• treated with insulin or sulfonylureas</td>
</tr>
<tr>
<td>• Chronic dialysis</td>
<td>• Well-controlled type 2 diabetes on multiple dose insulin or mixed insulin</td>
<td>• Chronic dialysis or chronic kidney disease stage 4 &amp; 5</td>
</tr>
<tr>
<td><strong>High Risk</strong></td>
<td>• Patients with renal insufficiency</td>
<td>• Advanced macrovascular complications</td>
</tr>
<tr>
<td>• Moderate hyperglycemia (average blood glucose 150–300 mg/dl or HbA1C</td>
<td>• Patients with advanced macrovascular complications – coronary, cerebrovascular and severe retinopathy</td>
<td>• Old age with ill health</td>
</tr>
<tr>
<td>7.5–9.0%)</td>
<td>• Autonomic neuropathy – gastroparesis and postural hypotension</td>
<td>• One or more of the following:</td>
</tr>
<tr>
<td>• Renal insufficiency</td>
<td>• People living alone and are treated with multiple insulin injection or sulfonylureas</td>
<td>• Type 2 diabetes with sustained poor glycemic control</td>
</tr>
<tr>
<td>• Advanced macrovascular complications</td>
<td>• Old age with ill health</td>
<td>• Well-controlled type 1 diabetes</td>
</tr>
<tr>
<td>• Living alone and treated with insulin or sulfonylureas</td>
<td>• Treatment with drugs that may affect mentation</td>
<td>• Well-controlled type 2 diabetes on multiple dose insulin or mixed insulin</td>
</tr>
<tr>
<td>• Patients with comorbid conditions that present additional risk factors</td>
<td></td>
<td>• Pregnant type 2 diabetes or gestational diabetes mellitus controlled by diet only or metformin</td>
</tr>
<tr>
<td>• Old age with ill health</td>
<td></td>
<td>• Chronic kidney disease stage 3</td>
</tr>
<tr>
<td>• Treatment with drugs that may affect mentation</td>
<td></td>
<td>• Stable macrovascular complications</td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td></td>
<td>• Patients with comorbid conditions that present additional risk factors</td>
</tr>
<tr>
<td>Well-controlled diabetes treated with short-acting insulin secretagogues</td>
<td></td>
<td>• People with diabetes performing intense physical labour</td>
</tr>
<tr>
<td><strong>Low Risk</strong></td>
<td>Well-controlled patients treated with short-acting insulin secretagogues such as repaglinide or nateglinide</td>
<td>• Treatment with drugs that may affect cognitive function</td>
</tr>
<tr>
<td>Well-controlled diabetes treated with lifestyle therapy, metformin, acarbose, thiazolidinediones, and/or incretin based therapies in otherwise healthy patients</td>
<td>Well-controlled patients treated with diet alone, metformin, or a thiazolidinedione who are otherwise healthy.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Well-controlled T2DM treated with one or more of the following:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Lifestyle therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Metformin</td>
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<tr>
<td></td>
<td>• Acarbose</td>
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<tr>
<td></td>
<td>• Thiazolidinediones</td>
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<td></td>
<td>• Second-generation SUs</td>
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<td></td>
<td>• Incretin-based therapy</td>
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<tr>
<td></td>
<td>• Sodium glucose transporter 2 (SGLT2) inhibitors</td>
<td></td>
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<tr>
<td></td>
<td>• Basal insulin</td>
<td></td>
</tr>
</tbody>
</table>

twice daily (BD), administer the usual morning dose at sunset meal and reduce evening dose by 50% and administer before morning meal. SAFES guidelines recommends that in case of basal-bolus insulin therapy, 50% of basal dose should be administered in morning if the patient is on NPH and the same dose should be taken at bedtime if patient is on basal analogue.¹²

**Published Scientific Literature**

Two observational trials reported IGlar to be safe for use during Ramadan with no significant increase
in hypoglycaemia when compared to non-fasting diabetes or those taking oral anti-diabetic drugs (OADs). In the first trial the effect of regaplinide (thrice daily) + single dose IGLar was evaluated in low risk T2DM during Ramadan fasting. None of the patient reported major or minor hypoglycaemia event. In the second trial IGLar was compared with regaplinide and glimepiride during fasting. There was no significant difference in proportion of patients having hypoglycaemia and glycaemic control.18,19

Evidence from open label, multicentre, randomised study on insulin treated T2DM patients receiving IDet dosed at sunrise and biphasic insulin aspart 70 (NovoMix 70) dosed before dinner during Ramadan indicated lower adverse events in IDet and NovoMix 70 compared to standard treatment. Further the hypoglycaemia rates were significantly lower in the intervention group (0.00 (SD 0.01) vs. 0.01 (SD 0.03) p ≤ 0.001).20

Safety and efficacy study on insulin IGLar and glimepiride in 349 patients with T2DM during before and after Ramadan reported single episode of severe hypoglycaemia in each time period. Improvement in fasting blood glucose (FBG) and glycated hemoglobin during the titration period was noted, which remained constant for rest of the study period. The study concluded that glimepiride at the time of breaking the fast and basal insulin (IGLar) titration to achieve FBG > 6.7 mmol/L may be used during Ramadan.21

A recent review by Kalra et al (2015) recommended reducing the dosage of basal insulin to 2/3rd for patients previously on NPH/IDet/IGlar and no change for patients on IDeg who wish to have brief fasts like Karva Chauth. Similarly, for patients on weekly fasting, insulin with higher flexibility (IDeg) is preferred with comparable reduction of morning dose to 2/3 on day of fast.4

### Consensus 5: Dose Modification of Premix Insulins

Premixed insulin can be initiated OD before evening meal and then if needed can be upgraded to BD (Before morning and evening meal) to reach target glycaemic control in majority of patients without significant risk of hypoglycaemia.

### Current Place in Guidelines

IDF-DAR recommends that, in patients on OD dosing, the normal dose should be taken before evening meal. For BD dosing, the normal dose should be taken before evening meal and morning dose to be reduced by 25–50%. For TID dosing, afternoon dose be omitted and evening and morning doses are to be adjusted based on the glucose levels. If FBG is <70 mg/dL (3.9 mmol/L), then premixed insulin dose to be reduced by 4U, if FBG is 70-90 mg/dL (3.9-5.0 mmol/L), dose to be reduced by 2U, for FBG 90-126 mg/dL (5.0-7.0 mmol/L), no change is required, if 126-200 mg/dL (7.0-11 mmol/L) and >200 mg/dL (11.1 mmol/L), dose to be increased by 2U and 4U respectively.12

For patients on premixed insulin, ADA recommends to change the regimen to long- or intermediate acting insulin in the evening and add short acting insulins before meals.6

SAFES recommend the usual morning dose at evening and half of the evening dose at morning. In case of biphasic insulin + Metformin use, insulin should be taken with the evening meal and metformin before morning meal. There may be no requirement of insulin before morning meal. If the mid-day blood sugar control is not good, then insulin should be taken at 50% of the evening dose before morning meal.13

### Published Scientific Literature

The flexibility and convenience of premixed insulin owing to fewer injections finds this treatment regimen more suitable for T2DM patients. Person on 50:50 premixed insulin may benefit from 30:70 transition of premixed insulin. The published literature recommended to avoid 50:50 premixed insulin ratio and prefer 30:70 or 25:704. In an open label, multicentre randomised crossover study on 151 patients, biphasic insulin lispro (LisproMix) was associated with significantly lower pre-meal FBG, daily blood glucose concentration and 2hour postprandial glucose (PPG) excursion following the main evening meal than identical doses of biphasic human insulin (BHI) 30/70. However, there was no difference in the number of hypoglycaemic episodes between treatments.22 A
randomised study. The new regimen
of insulin LisproMix50 in the
evening meal was assessed in another
60% was given as NovoMix 70 before
given as IDet at the morning and
40% of the daily insulin dose was
incidence of hypoglycaemic
LisproMix50 significantly improved
glycaemic control without increasing
weight or risk of hypoglycaemia.24

A new regimen in which
the incidence of hypoglycaemic
events.23 A new regimen in which

\[
\begin{array}{|c|c|c|}
\hline
& \text{Once daily premix insulin} & \text{Twice daily premix insulin} \\
\hline
\text{Infrequent short duration} & \text{No dose modification, but to} & \text{No dose modification, but to} \\
& \text{be dosed when fast is broken} & \text{be dosed when fast is broken} \\
& \text{To be taken as once daily dose} & \text{To be taken as once daily dose} \\
& \text{on the day of fast & dosed} & \text{on the day of fast & dosed} \\
& \text{when fast is broken} & \text{when fast is broken} \\
\hline
\text{Frequent short duration} & \text{No dose modification but to} & \text{No dose modification but to} \\
& \text{be taken when fast is broken} & \text{be taken when fast is broken} \\
& \text{in the evening} & \text{in the evening} \\
& \text{Take usual pre-dinner dose at} & \text{Take usual pre-dinner dose at} \\
& \text{night meal & reduce morning} & \text{night meal & reduce morning} \\
& \text{dose by 25-50%} & \text{dose by 25-50%} \\
\hline
\text{Annual/semi-annual long} & \text{No dose modification but to} & \text{No dose modification but to} \\
\text{term (Dawn to dusk)} & \text{be taken when fast is broken} & \text{be taken when fast is broken} \\
& \text{in the evening} & \text{in the evening} \\
& \text{Take usual morning dose &} & \text{Take usual morning dose &} \\
& \text{reduce evening dose by 50%} & \text{reduce evening dose by 50%} \\
\hline
\end{array}
\]

regimen of insulin LisproMix50 in the
evening and regular human insulin
with NPH (30:70) in the morning
was compared with regular human
insulin with NPH (30:70) given
twice daily during Ramadan in a
small observational study. Switching
the evening meal dose to insulin
LisproMix50 significantly improved
glycaemic control without increasing
the incidence of hypoglycaemic
events.23 A new regimen in which
40% of the daily insulin dose was
given as IDet at the morning and
60% was given as NovoMix 70 before
evening meal was assessed in another
randomised study. The new regimen
was found to be non-inferior to
standard care with a significantly
lower hypoglycaemic event rate.20 A
prospective observational study in
Indonesia found that biphasic insulin
aspart (BIAsp) 30 significantly
reduced all glycaemic indices in
Ramadan without an increase in body
weight or risk of hypoglycaemia.24

**Consensus 6: Dose
Modification of Prandial
Insulins**

**Current Place in Guidelines**

IDF recommends a normal dose
before evening meal, omit lunch time
dose and reduce morning dose by
25- 50%. If fasting/ pre-meal blood
glucose is <70 mg/dL (3.9 mmol/L)
and is 70–90 mg/dL, (3.9–5.0 mmol/L)
morning/ evening dose before
meal to be reduced by 4U and 2U
respectively. Further, the guidelines
recommend no dose change if fasting/
pre-meal blood glucose is 90–130 mg/
dL (5.0–7.2 mmol/L). However, if
fasting/ pre-meal blood glucose is 130–200 mg/dL (7.2–11.1 mmol/L) or
>200 mg/dL (11.1 mmol/L) increase
dose by 2U and 4 U respectively.12

ADA recommends administration
of short or rapid-acting insulin in
combination with the basal insulin
at meals, particularly at the evening
meal, as an effective strategy under
fasting condition. Rapid-acting
insulin analogue are associated with
less hypoglycaemia and smaller
postprandial glucose excursions as
compared to regular human insulin
before meal in patients with T2DM
who fast during Ramadan.6

SAFEES postulated that the risk of
hypoglycaemia, particularly amongst
elderly patients, and postprandial
glucose excursions can be prevented
by using rapid-acting or short acting
insulin analogues such as aspart
(IAsp), lispro, or glulisine. Short
acting insulin along with basal
insulin analogues have lesser risk of
hypoglycaemia and offer meal time
flexibility. SAFES guidelines also
emphasised that rapid-acting insulin
analogues are safe to use in patients
with renal and hepatic impairment
and in pregnancy (IAsp, lispro)
with good glycaemic control (SAFEES
2012). Adjustments in dosage of short
acting insulin before morning meal
should be done by monitoring blood
glucose 2 hours after morning meal.13

**Published Scientific Literature**

Few published studies have
shown that insulin treatments give
a better control of PPG after the meal
to break the fast.22,25 It is preferable
to use analogue insulin and reduce
the morning dose by half 4.

An open-label, randomized,
cross-over study based on 70 outpatients
assessed the rate of hypoglycaemic
episodes and PPG values, after the
main meal, between insulin lispro and soluble human insulin in T2DM patients during Ramadan. This study reported that lispro is associated with significantly lower rates of hypoglycaemic episodes and better PPG control than soluble human insulin in T2DM, who fast during Ramadan (Hypoglycaemia:1.3±0.1 Vs.2.6±0.2, p<0.002, PPG: 3.0±/0.4 mmol/L Vs. 4.3±/0.4 mmol/L p<0.01).25

**Conclusion**

Safe religious fasting in patients with T2DM is possible with vigilant planning. Most T2DM patients can be managed during fasting with proper patient education and appropriate adjustment of insulin doses. Hyperglycaemia and hypoglycaemia are major risks in T2DM patients and treatment regimen need to be adjusted to decrease the risk of hypo- and hyperglycaemia. The present consensus has been made keeping safety of patients in mind. The key recommendations provided in present consensus are:

- Diabetes patients, who fast are recommended to keep themselves hydrated during fast, consume foods with low glycaemic index and high fibre content and avoid sugary, caffeinated drinks and fried foods.
- The key factor for insulin therapy during Ramadan is to provide adequate insulin to prevent the post meal hyperglycaemia and also prevent hypoglycaemia during the period of fast.
- Individual risk factors should be identified and patients at high risk are recommended to avoid fasting.
- Key recommendation is to maintain the same evening/ post-fast dose of insulin and reduce the morning/ pre-fast dose of insulin.

The strength of the current consensus is that it has been developed with due considerations to national context based on experience and common therapy practices in India while drawing on recommendations from globally acceptable guidelines and relevant clinically published evidence. The final proposed consensus-based recommendations were collectively recorded for each insulin regimen in easily implementable steps, without any bias and in an as much possible unambiguous language.

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