

Diabetes during Ramadan – PRE-approach model: Presentation, Risk stratification, Education

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Abstract. – OBJECTIVE: Fasting (Sawm) during Ramadan is one of the five pillars of Islam and mandatory for all Muslim healthy adults. Most of the Muslim diabetic patients insist on fasting in Ramadan despite their exemption. Due to paucity of literature, diabetes during Ramadan is underestimated and the statistics are not reflecting the actual reality. The aim of this study is to highlight the demographics in diabetic Muslim population and emphasize its ramifications on Ramadan fasting.

METHODS: In this study, we developed a 3 step PRE-approach model based on Presentation, Risk stratification, Education in diabetics who fast during Ramadan. For the establishment of this model we identified 40 published studies in database searches including ISI-web of science and pub-med. We searched the related literature by using the key words including diabetes mellitus, Ramadan fasting. All studies in which diabetes and fasting in Ramadan was investigated were included. There was no limitation on publication status, design or language. Finally, we included 35 publications and remaining 5 were excluded from the study.

RESULTS: The diabetic patients who fast are at risk of severe hypoglycemia, hyperglycemia, diabetic ketoacidosis, dehydration, thrombosis, strokes and retinal artery occlusion. Lack of education, poor healthcare and no structured guidance cause adverse health consequences.

CONCLUSIONS: It is vital to empower the healthcare workers and the patients in the frontlines with appropriate information. To preempt and minimize the problems faced by the diabetic patients who fast, available resources should be mobilized to efficiently and effectively reach out these patients. Diabetic patient educational guidelines about Ramadan fasting should be disseminated and translated into major regional languages to minimize the complications. Diabetic patients who are stable, free of deteriorating complications and able to manage can be allowed to fast.

Key Words:

Diabetes mellitus, Fasting, Ramadan.

Introduction

Muslim world covers a vast geographic area, comprising of 57 countries with 1.72 billion people¹. The Muslim Majority Countries (MMC) are 62% in the Asia-Pacific, 20% in Middle East and North Africa, 16% in Sub-Saharan Africa and around 2% in Europe and the America (Butler 2006)². Most recent reports indicate that 382 million people worldwide have diabetes mellitus and the number is set to rise beyond 592 million in coming two decades^{3,4}. Today's emerging diabetes hotspot countries are in Middle East, Western Pacific, sub-Saharan Africa and South-East Asia where one in ten adults in the region have the disease. In terms of the prevalence of adults with diabetes, Middle East and North Africa region has the highest 10.9%⁴. Looking into this pandemic 90% of the world's Muslim population is located in these regions Figure 1. These countries are facing a firestorm of ill health with inadequate resources to protect their population. Global health spending to treat and manage the diabetes totaled at least US\$ 548 billion in 2013. 20% of global health expenditure on diabetes was made in low and middle-income countries, where 80% of people with diabetes live. About 43% patients with type 1 diabetes and 79% with type 2 diabetes fast during Ramadan⁵ lead to the estimation that 40-50 million people with diabetes worldwide fast during Ramadan. Few Muslim states are privileged enough to involve health care professionals who are aware of the fasting practice, adjustments to their therapeutic regimens and provision of Ramadan-specific diabetes education⁶. In contrast, patients in poor countries and remote communities face huge challenges related to the adequacy of and access to health care and availability of medications. This is in addition to lack of education and difficulties in providing the necessary Ramadan-focused diabetes education. Keeping all these facts

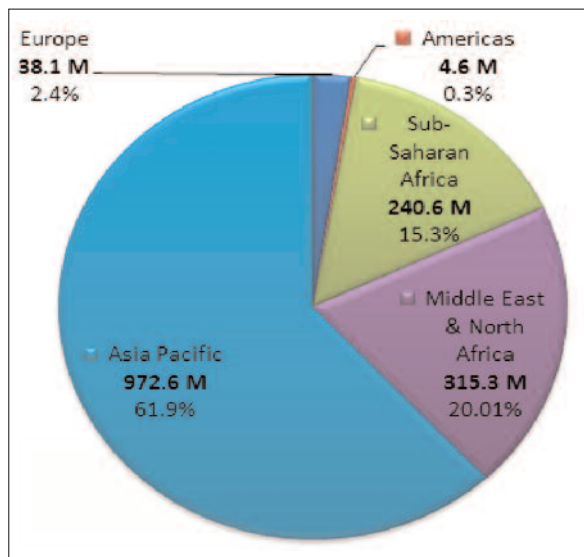


Figure 1. Distribution of Muslim population in various continents of the globe.

in mind, this study aimed to highlight the confounding demographics in the diabetic Muslim population and emphasize its ramifications on fasting during Ramadan.

Methods

The present study was conducted in the University Diabetes Centre, College of Medicine, King Saud University, Riyadh, Saudi Arabia.

Selection of Studies

In this study, we developed a 3 step PRE-approach model (**P**resentation, **R**isk stratification, **E**ducation) in diabetics who fast during Ramadan. This model concerns the Ramadan fasting patients, and is based on risk stratification factors and the role of diabetes educators. For the establishment of this model, we identified 40 research documents published on Ramadan fasting, epidemiology, risk factors, complication and diabetes educators' role, available in ISI-Web of Science and Pub-med. We searched the related literature by using the keywords including diabetes mellitus, Ramadan, fasting, education and risk factors. In addition, we also entered the keywords in the google scholar search engine and after getting any related article, we re-entered the title of that article in the ISI-Web of Science and Pub-Med.

The title and abstract of the studies were evaluated to determine eligibility for the documents.

All studies in which diabetes mellitus, Ramadan, fasting was discussed were considered eligible for inclusion. No limitations on publication status, study design or language of publication were obligatory. We reviewed 40 papers, finally we included 35 studies and remaining 5 studies were excluded from the study.

Ethics Statement

In this study we reviewed the data base literature on diabetes mellitus and Ramadan fasting, hence, we did not require the ethical approval.

Data Analysis

The extracted findings for diabetes mellitus and Ramadan fasting were entered into the computer program, SPSS Version 20 (SPSS Inc., Chicago, IL USA), and findings were analyzed descriptively.

Results

Figure 1 shows the distribution of Muslim population and their percentage. The maximum percentage of Muslim population is in Asia Pacific 972.6 million (61.9%), Middle East and North Africa 315.3 million (20.01%), Sub Sahran Africa 240.6 million (15.3%), Europe 38.1 million (2.4%), America 4.6 million (0.3%).

Figure 2 shows the clinical care pathway for diabetic patients planning to fast during Ramadan. We found that there are multiple risk factors in patients who fast during Ramadan. These factors are low, moderate and high risk factors. Considering the significance of Ramadan focused education, a clinical care pathway for diabetic patients who are planning to fast is proposed (Figure 2). It combines both the assessment and management aspects and consists of three steps termed as ***PRE approach** (**P**resentation, **R**isk stratification, **E**ducation: Ramadan focused approach).

In the first step the patient is instructed to contact the physicians and / or health care provider two months prior to Ramadan . The physician must get the detailed clinical history and order lab investigations. Based on the clinical history, lab investigations and overall health status, patients are categorized under the risk stratification of diabetic patient who wish to fast during Ramadan.

Diabetic patients whose fasting blood sugar and HbA1c is well controlled, on diet alone, on metformin, Dpp4 inhibitor, or TZD who are otherwise healthy are categorized as low risk⁷. Well

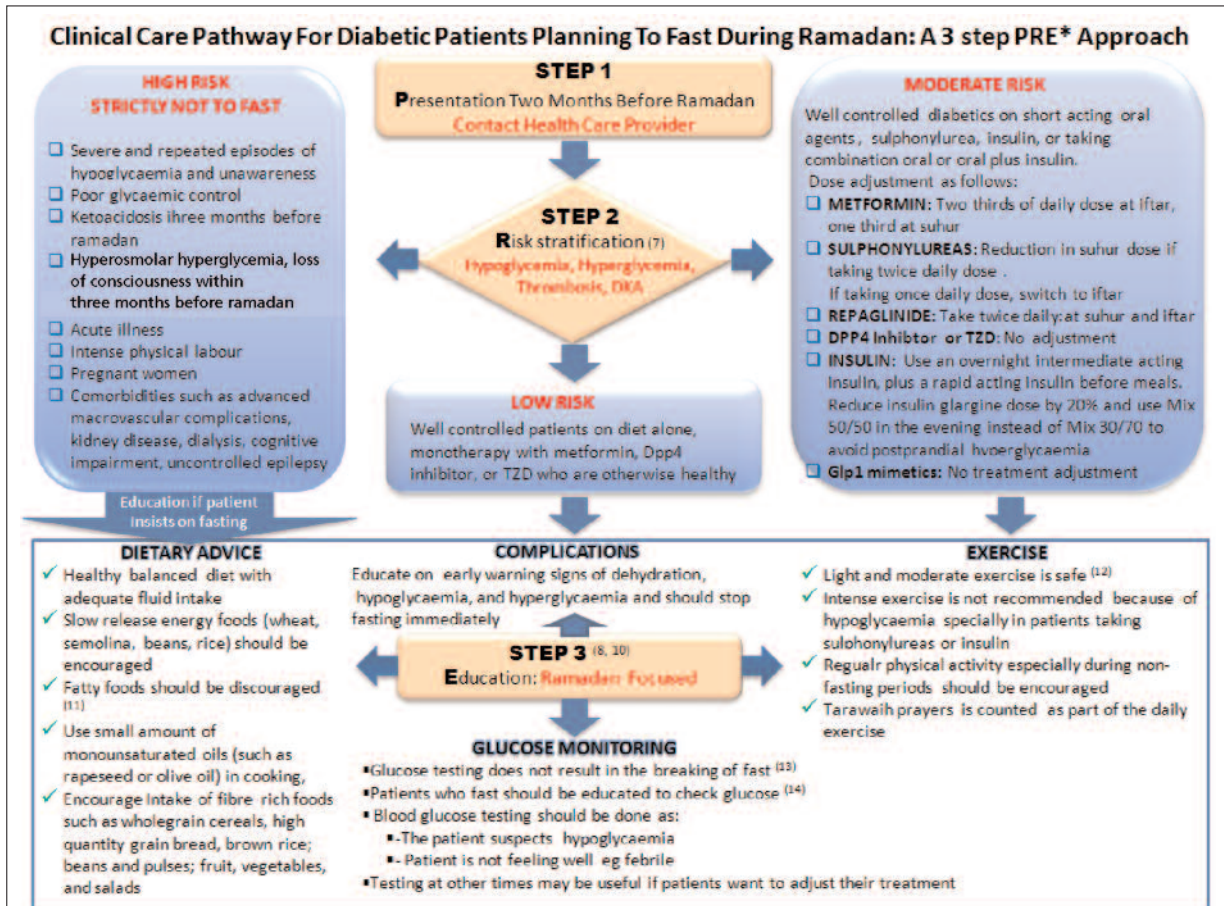


Figure 2. A 3step PRE- approach model (Presentation, Risk stratification, Education) for diabetic patients planning to fast during Ramadan.

controlled patients on short acting secretagogue, sulphonylurea, insulin, or taking combination oral or oral plus insulin are categorized as moderate risk⁷. History of severe and recurrent episodes of hypoglycaemia and unawareness, poor glycaemic control, ketoacidosis in the three months before Ramadan, hyperosmolar hyperglycaemic coma, unconsciousness within the three months before Ramadan, acute illness, intense physical labour, pregnant women, comorbidities such as advanced macro-vascular complications, renal disease on dialysis, cognitive dysfunction, uncontrolled epilepsy must be categorized as severe risk⁷. Patient education concerning fasting during the Ramadan is essential, and physicians/diabetic educators must play a role of a mentor.

Discussion

Fasting during Ramadan is one of the five pillars of Islamic practices, mandatory for all Mus-

lim healthy adults. Most of the Muslim diabetic patients insist on fasting in Ramadan despite their exemption in the religion. The holy book of Muslims, Quran specifically exempts the sick from the fasting (Holy Quran, Al-Bakarah, 183-185). Patients with diabetes fall under this category because their chronic metabolic disorder may place them at high risk for various complications. This exemption represents more than a simple permission not to fast; the Prophet Mohammad (PBUH) said, “God likes his permission to be fulfilled, as he likes his will to be executed”. However majority of diabetic Muslims insist on fasting.

Ramadan is a lunar-based month, and its duration varies between 29 and 30 days and moreover the fasting month is brought forward by about 10 days in a year, it means over time the season in which Ramadan falls changes. In fasting, there is periodic food and water deprivation during daylight hours with free access during the night for the duration of one lunar month. Depending on

the geographical setting and season, the duration of the daily fast may range from 12 to 20 h.

In the current study, we established a 3 step approach model called PRE approach model (Presentation, Risk stratification, Education):

- **Presentation:** In the first step the patient must contact the physicians and / or health care provider two months prior to Ramadan. The physicians must get the detailed clinical history, laboratory investigation including CBC, fasting blood sugar, HbA1c, liver and renal functions and electrolytes, etc. Based on the clinical history, lab investigations and overall health status, patients must be categorized under the risk stratification of diabetic patient who wish to fast during Ramadan.
- **Risk Stratification:**

Low risk factors: Diabetic patients whose fasting blood sugar and HbA1c is well controlled and patients on diet alone with metformin, Dpp4 inhibitor, or TZD who are otherwise healthy are categorized under low risk⁷.

Moderate risk factors: Well controlled patients on short acting secretagogue, sulphonylurea, insulin, or taking combination oral or oral plus insulin are categorized as moderate risk⁷.

Severe Risk factors: Severe and recurrent episodes of hypoglycaemia and unawareness poor glycaemic control, ketoacidosis in the three months before Ramadan, hyperosmolar hyperglycemia, unconsciousness within the three months before Ramadan, acute illness, intense physical labour, pregnant women, comorbidities such as advanced macro-vascular complications, renal disease on dialysis, cognitive dysfunction, uncontrolled epilepsy must be categorized as severe risk⁷.
- **Education:** Patient education concerning fasting during the holy month of Ramadan is essential, and physicians / diabetic educators must play a key role of a mentor. Physicians must inform the patient about the complications of diabetes during fasting, and based on the clinical history, lab reports, and overall status of diabetic patients, counsel the patient either to fast or not. Here the significance of education of patients is vital and is the cornerstone of safe fasting⁸. But access to appropriate diabetes education is severely limited in many low and middle-income countries, and non-existent in rural parts of the developing world⁹.

Physician must guide the patient about nutrition as in Ramadan there is a major change in dietary patterns. Because of the delay in digestion and absorption, ingestion of foods containing “complex” carbohydrates may be advisable at the predawn meal, while foods with more simple carbohydrates may be more appropriate at the sunset meal. It is also suggested that intake of fluid must be increased during non fasting hours and that the predawn meal may be taken as late as possible before the start of the daily fast.

In a large observational study¹⁰, patients who fasted during Ramadan without attending a structured educational session had a fourfold increase in hypoglycaemic events, whereas those who attended an education program focusing on Ramadan had a significant decrease in hypoglycaemic events.

The role of physician is vital in guiding the patient for other aspects such as exercise and termination of the fast. Strenuous physical activity may result in excessive hypoglycemia hence it should be avoided, particularly during the 2-3 hours before the sunset meal. Tarawaih prayer should be considered as part of the daily exercise. It should be kept in mind that patients should understand that they must always and immediately terminate their fast if hypoglycemia (blood glucose of < 60 mg/dl [3.3 mmol/l]) occurs. Fast may also be abandoned if blood sugar exceeds 300 mg/dl (16.7 mmol/l)⁷.

During Ramadan the number of meals reduces to two, one large meal at sunset and one light meal before dawn. Along with changes in number, timing and calorie content of the meals the composition of the meal is disturbed as well. During Ramadan, there is more consumption of fried foods and carbohydrates in the form of dates, juices and specially sweet foods. Activity generally reduces during the daytime because of fasting, however, during the night especially for people who perform Taraweeh (prayer) there is increased activity.

In normal people during fasting, in entire body the circulating blood glucose levels fall, which can cause decrease secretion of insulin, however, the level of glucagon and catecholamines rise, causing breakdown of glycogen and increase gluconeogenesis. In diabetic patients this mechanism is disturbed due the underlying pathophysiology and the effects of pharmacological agents. The risks of fasting include severe hypoglycaemia, hyperglycaemia, ketoacidosis, dehydration, thrombosis, stroke and retinal artery occlusion⁵.

Hypoglycemia

The EPIDIAR study⁵ found that the change in eating patterns during Ramadan increased the risk of severe hypoglycaemia 4.7-fold in type 1 diabetes and 7.5-fold in type 2 diabetes. Severe hypoglycemia is more frequent in patients whom the dosage of oral hypoglycemic agents or insulin were changed and in those who reported a significant change in their lifestyle⁵. In another observational study, the incidence of hypoglycemia was 20% in sulfonylurea-treated patients who were fasting for Ramadan¹⁵. And in another study the authors reported an increase in symptomatic hypoglycaemia¹⁶, but other studies have not found a significant increase during Ramadan in patients treated with oral hypoglycaemic medications or insulin^{16,17}. The point worthy to be discussed is that, incidence of hypoglycaemia vary according to the season and the year of study performed.

Hyperglycemia

In EPIDIAR study, authors also demonstrated a fivefold increase in the incidence of severe hyperglycemia during Ramadan in patients with type 2 diabetes and an approximate threefold increase in the occurrence of severe hyperglycemia with or without ketoacidosis in type 1 diabetic patients⁵.

Diabetic Ketoacidosis

Patients with diabetes, especially type 1 diabetes, are at increased risk for development of diabetic ketoacidosis, particularly if they are grossly hyperglycemic before Ramadan⁵. In addition, the risk for diabetic ketoacidosis may be further increased due to excessive reduction of insulin dosages based on the assumption that food intake is reduced during the month.

Dehydration and Thrombosis

Limitation of fluid intake during the fast, especially if prolonged, is a cause of dehydration. This may become severe in hot and humid climates and among individuals who perform hard physical effort. In addition, hyperglycemia can result in osmotic diuresis and contribute to volume depletion. Intravascular space contraction can contribute to a hypercoagulable state due to an increase in clotting factors, decrease in endogenous anticoagulants and impaired fibrinolysis¹⁸. Increased blood viscosity secondary to dehydration may enhance the risk of thrombosis, stroke and retinal vein occlusion¹⁹.

Patients Taking Oral Hypoglycaemic Agents

In general, agents that act by increasing insulin sensitivity are associated with a significantly lower risk of hypoglycemia than compounds that act by increasing insulin secretion. It seems that hypoglycaemic events are more frequent in patients taking full doses. Thus, it could, be recommended that type 2 diabetic patients reduce their morning OHA doses especially the aged patients. Levels of risk for hypoglycaemia among people taking metformin who are not fasting range from 0-21%²⁰. Expert consensus suggests that the dose of metformin must be split, two thirds of the dose is taken at iftar and one third at suhur. For patients on extended-release metformin preparation, the dose should be taken once at Iftar. A randomized double blind study showed that the risk of hypoglycaemia is low with acarbose taken with meals and it is acceptable to continue²¹.

A multicentre study showed that repaglinide, contributed to improved glycaemic control with a lower number of hypoglycaemic events among fasting patients during Ramadan when compared with glibenclamide²². Hypoglycaemia was documented in only one patient who took glimepiride during Ramadan²³. The evidence cited suggests that rapid acting insulin secretagogues taken at suhur and iftar are a safer alternative than glibenclamide for patients who fast. Sulphonylureas are believed to be unsuitable for use during fasting because of the inherent risk of hypoglycemia. Newer members of the sulfonylurea family (gliclazide MR or glimepiride) have been shown to be effective, resulting in a lower risk of hypoglycemia²⁴. In a study from Turkey the authors concluded that use of repaglinide might be safer than sulfonylureas²³. On the basis of the prospective study²⁵ it is recommend that during Ramadan clinicians change the timing of the once daily dose of sulphonylurea from the usual morning dose to the evening. With regard to gliclazide, it is recommended that patients take a larger dose at iftar than at suhur and clinicians consider reducing the prescribed dose for suhur if the patient's glycaemic control before Ramadan is stable.

A randomized controlled trial that compared pioglitazone 30 mg once daily with placebo in patients already taking other oral hypoglycaemic agents only, there was no increase in hypoglycaemia during Ramadan fasting²⁶. Continuing with thiazolidenediones during fasting is considered safe.

A retrospective audit of patients with type 2 diabetes showed that adding vildagliptin to metformin treatment was associated with a reduced incidence of hypoglycaemic events and improved glucose control compared with patients treated with gliclazide and metformin during Ramadan²⁷. This low grade evidence suggests that it may be safer to combine dipeptidyl peptidase-4 inhibitors, rather than sulphonylureas, with metformin in patients who are not well controlled when taking metformin alone and are planning to fast during Ramadan.

In non-Ramadan studies, hypoglycaemic events associated with glucagon-like peptide-1 mimetics occurred primarily in patients taking a sulphonylurea²⁸. The findings of an audit suggested that its dosage does not need to be adjusted during Ramadan but that other agents, such as sulphonylureas, may need dose reductions when used as a combination treatment²⁹.

Patients on Insulin

Single Basal Insulin and Oral Combined Treatment

A multicentre, prospective, observational study compared fasting patients taking metformin combined with glimepiride, repaglinide, or glargine¹⁷. Although, the rate of hypoglycaemia was higher in the glimepiride group than in the repaglinide and glargine groups, the increased rate was not significant. In a small prospective non-randomised study of type 2 diabetes, who were at low risk of diabetic complications, and had a pre-Ramadan HbA1c concentration of < 8%, neither fasting nor non-fasting patients who were taking repaglinide three times a day and glargine experienced hypoglycaemic events and both groups maintained stable glycaemic control¹⁶. It is advised that, patients who take long acting basal insulin, such as glargine to decrease the dose by 20% to avoid hypoglycaemia. Patients taking repaglinide and single dose glargine may continue taking the same doses of repaglinide but to be safer should consider reducing glargine by 20%.

Premixed Insulins

A randomized, open labelled study comparing Humalog Mix25 (25% short acting insulin lispro and 75% intermediate acting neutral lispro protamine) and Humulin M3 (human insulin 30% soluble, 70% isophane) given in identical doses

showed that the former offered better control of postprandial blood glucose after iftar and a lower occurrence of hypoglycaemic events³⁰. However, the findings of an observational study suggested that using Humalog Mix50 at iftar instead of Mix30 reduced postprandial glucose excursions and reduced hypoglycaemia³¹. It is suggested that patients taking twice daily insulin should reduce the suhur dose by 30% if they are well controlled, and consider switching to a Mix 50 preparation if their postprandial glucose remains raised.

Fasting in Pregnant Women with Diabetes

While pregnant women are exempt from fasting during Ramadan, some with known diabetes insist on fasting. These women constitute a high-risk group and their management requires intensive care³². Preconception counseling for diabetic women must include education about the substantial risks associated with poor glycaemic control to help dissuade them from trying to fast.

Patients with Type 1 Diabetes

In general, patients with type 1 diabetes, especially if “brittle” or poorly controlled, are at maximum risk of developing severe complications and should be strongly advised not to fast during Ramadan. Furthermore, patients who are unwilling or unable to monitor their blood are at high risk and should be advised not to fast. A small sample size study examined the use of glargine and insulin lispro or aspart, in nine patients with type 1 diabetes³³.

None of the patients had any episodes of severe hypoglycaemia or diabetic ketoacidosis requiring admission to hospital and the patients’ HbA1c remained stable at the end of Ramadan. As the insulin requirement in this study group decreased by 28% from baseline ($p = 0.002$), the authors suggested a reduced dose (70% of a patient’s usual dose) during the fast. An open label, comparative, crossover study of 64 patients with type 1 diabetes found significantly lower ($p = 0.026$) two hour, postprandial glucose concentrations after iftar and fewer hypoglycaemic events with insulin lispro than with regular human insulin³⁴. One option would be to use once daily injection of the long-acting insulin analog glargine or twice-daily injections of the insulin analog detemir along with premeal rapid-acting insulin analogs. Results of a study using insulin glargine in 15 relatively well-controlled patients with type

1 diabetes who fasted for 18 h showed that the mean plasma glucose declined from a value of 125 to 93 mg/dl during the fast³⁵. It is suggested that patients with type 1 diabetes who are on a basal bolus regimen four times daily should be discouraged from fasting owing to the risks of poor glycaemic control. If patients choose to fast despite medical advice, it will help if they are familiar with carbohydrate counting. It is advised to reduce the background insulin by 20% and omit the midday rapid acting insulin if their capillary blood glucose concentration is ≤ 7 mmol/l. If their blood glucose concentration is > 7 mmol/l, patients will need to calculate their insulin correction dose as determined by their specialists.

Conclusions

It is vital to empower the healthcare workers and the patients in the frontlines with the appropriate information. In the short term to mitigate and preempt the problems faced by the patients, available resources should be mobilized to reach out these patients efficiently and effectively. To bring about uniformity and avoid any misinformation consistent patient education should be disseminated and translated into the major regional languages i.e. Arabic, Persian, Urdu, Turkish, Bengali, Hindi, Malay, English and French which should be kept simple and relevant. Not only is it important what information to provide but how. In underprivileged communities, public places including schools, colleges, universities, mosques, public gathering places can be used for education and the role of both print and electronic media will be very useful. In order to assess the actual burden, to improve the precision of the estimates, and contribute to an evidence base that is fundamental for future strategy, the need for high-quality clinical trials and studies in this field cannot be overemphasized. As a long term strategy more robust guidelines and recommendations should be formulated. Such an apparently huge challenge of fasting in Ramadan should be part of universal agenda which then transcends into regional, national, provincial and local strategies so that it eventually reaches the patients. The future development agenda needs to respond to a new epidemiological, demographic and political reality, and a paradigm shift is needed if progress is to be made. Fact remains that a significant majority of Muslims live in underprivileged soci-

eties with primitive or poorly structured health care and limited access and resources. Ramadan fast represents a challenge to people with DM who wish to fast.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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