

## High-Risk Patients Observing Ramadan Fasting: More Data and More Insights!

Over the last two decades, academic and clinical interest in the impact of Ramadan fasting on health has progressively increased. The global literature production was quantified recently using fundamental bibliometric analysis using different databases and search strategies.<sup>[1-3]</sup> Research and publication expanded in quantity and improved in quality relatively well. Nonetheless, it was notably less than other, perhaps, “equally important and relevant matters.” Diabetes care, kidney function, and cardiac disease have been the focal point of interest of research workers and key opinion leaders.<sup>[1]</sup> Also, a move from the consensus-based to more evidence-based guidelines was witnessed.<sup>[4-6]</sup> More experimental studies have been published, and better quality recommendations have been developed based on critical appraisal and even grading of the evidence rather than opinion based on limited personal experiences.<sup>[1-3]</sup>

On the other hand, the collaboration resulted in a harmony between physicians and religious scholars that made the “*imam*” and doctors speak the same language.<sup>[7]</sup> This collaboration resulted in moving from talking about fasting using a medical jargon being relatively contraindicated and absolutely contraindicated<sup>[8-10]</sup> to graded risk stratification of 3 or 4 strata with more unmistakable implications in unified religious and medical terms and recommendations.<sup>[4-6]</sup>

Many of the early studies were conducted on normal healthy volunteers, perhaps for safety and convenience. Because fasting is a religious obligation ordained on all healthy adult Muslims, research conducted on healthy adults lacked any direct translation into clinical practice. However, such studies helped the interpretation of changes that may affect people with various chronic conditions. It has been well established that many patients with chronic medical conditions such as diabetes do observe the fast.<sup>[11,12]</sup> This may happen either

without seeking the appropriate advice or even against medical advice.<sup>[13,14]</sup> Consequently, recent studies focused on the high and very high end of the risk scale. In the current issue of *Ibnosina Journal of Medicine and Biomedical Sciences*, Elbarsha *et al.* from Benghazi, Libya, compare the impact of fasting during Ramadan in a prospective observational study on the low and high-risk groups.<sup>[15]</sup> This study enriches the literature from several studies that have addressed the same theme and warrants highlighting the recent developments as they were not discussed in detail in the manuscript. Among the participants, 83 high-risk patients were categorized as “high/very high-risk” and 65 low-risk patients were categorized as “moderate/low risk”.<sup>[4]</sup> Full-month fasting was possible in 100% in the low-risk group and 79% in the high-risk group. Hypoglycemia occurred in 20.9% of the high-risk group and no one from the low-risk group. Furthermore, severe hyperglycemia occurred in 13.5% in the high-risk group. The study supported the notion that patients in the high-risk category were significantly more likely to break the fasting during Ramadan than those in the low-risk category. Hypoglycemia was significantly higher in the high-risk group. Severe hyperglycemia, hospitalization, and presumed mortality were not significantly higher in the high-risk group. Being treated with insulin was the most significant risk factor for breaking the fast in this study.

Alawadi *et al.* from the Diabetes Research Group at Dubai Hospital, Dubai, UAE explored the risk of hypoglycemia during Ramadan fasting by the use of continuous glucose monitoring (CGM) and observed the glycemic control and renal functions in patients with diabetes and chronic kidney disease Stage 3 (CKD3).<sup>[16]</sup> The study involved 25 patients with Type 2 diabetes mellitus (T2DM) and CKD3 who intended to fast during Ramadan. Although fasting was not associated with worsening glycated hemoglobin (HbA1c) and renal function, patients

had significantly more frequent and prolonged hypoglycemic episodes during Ramadan. Malek *et al.*<sup>[17]</sup> described a prospective multicentric study conducted in 26 counties before and after Ramadan involving 836 patients with T2DM and 65 patients with Type 1 diabetes mellitus (T1DM). Many patients insist on fasting, regardless of their doctors' warnings. The main consequences were hyperglycemia and hypoglycemia and, surprisingly, self-monitoring of blood glucose (SMBG) was less checked during Ramadan. Ba-Essa *et al.*<sup>[18]</sup> described the attitude of patients with T2DM and the rates of hypoglycemia during Ramadan according to the type of treatment. In a 2-year, prospective, nonrandomized study, a total of 360 participants with T2DM attending a diabetes center in Saudi Arabia with a mean HbA1c of 8.9 were studied. The majority (>80%) were categorized in the high-risk group. Nevertheless, they all fasted despite medical advice. Approximately one-quarter of the people with T2DM in the cohort experienced hypoglycemia, which was directly related to their fasting risk level. A sizable proportion continued the fast despite being hypoglycemic. Before Ramadan, insulin therapy with or without oral agents and previous hypoglycemia episodes before Ramadan predicted hypoglycemia risk. HbA1c and weight showed some clinical improvements in post-Ramadan fasting.

Hassanein *et al.* also from Dubai Hospital Diabetes Group assessed the value of optimized care in diabetes management during Ramadan on the metabolic parameters of high-risk patients with diabetes. The authors intended to assess and understand the safety of fasting in this group in a prospective interventional study.<sup>[19]</sup> Patients with high-risk diabetes insisted on fasting were included in the study. High-risk patients were defined as those on insulin, those with gestational diabetes, those with Stage 3 kidney disease, or those with a history of ischemic heart disease. The assessment was made through the use of FreeStyle Libre flash-CGM (FSL-CGM). There was a remarkable improvement in glycemic control, a negligible change in serum creatinine with some worsening in total cholesterol. Another study by the same group evaluated the safety of fasting in CHD

patients with diabetes, insisting on fasting Ramadan under optimal care.<sup>[20]</sup> In this prospective study, 21 patients with T2DM with stable known CHD who fasted for 3 months before the study, although advised against it, were included. All patients received CGM with the FSL-CGMS during and outside the Ramadan period. Diabetes mellitus or cardiovascular disease-related emergency visits or hospitalization were recorded. In addition, changes in weight, systolic and diastolic blood pressure, lipid profile, estimated glomerular filtration rate, HbA1c, and hypoglycemia frequency during Ramadan fasting and nonfasting periods were documented. The authors could not associate any adverse cardiovascular effects with Ramadan fasting in stable CHD patients under optimal diabetes care. FSL-CGMS data showed higher frequency of hypoglycemia during Ramadan fasting. Studies with a larger sample size are needed for further validation of these findings. Abdelgadir *et al.*<sup>[21]</sup> conducted a prospective interventional study on high-risk diabetes patients who insisted on fasting. All patients were treated with insulin ± sodium/glucose cotransporter-2 inhibitors and received an FSL-CGMS and Ramadan-focused education. All patients attended the clinics before and after Ramadan, where they were advised on treatment modification and biometric and biochemical measurements. There were minimal interruption of fasting, significant improvement in glycemic control, and no significant kidney function change after Ramadan.

On the other hand, new data were published and new opinions were expressed regarding fasting of patients with T1DM. People with T1DM who choose to fast during Ramadan are conventionally considered at a high risk of acute diabetes complications, including hypoglycemia and remarkable hyperglycemia.<sup>[4-6]</sup> Hence, they are exempt from fasting; however, many still insist on fasting. Alfadhli<sup>[22]</sup> examined glucose-level fluctuations in those patients during Ramadan fasting using a real-time continuous glucose monitoring system (RT-GCMS), which involved adult patients with uncontrolled T1DM (HbA1c >7%) who insisted on fasting during Ramadan. A real time

continuous glucose monitorings system (RT-CGMS) was used to monitor the participants' glucose levels for 3 consecutive days during fasting. The patients with uncontrolled T1DM who fasted during Ramadan experienced a wide fluctuation of glucose levels between fasting and eating hours, exhibiting a greater tendency toward hyperglycemia. However, in the past few decades, several advances have allowed people with T2DM to live near-normal lives and participate in activities, previously considered to be of high risk. These advances include providing structured education and analog insulins and technologies including constant subcutaneous insulin infusion (CSII), CGMS, and automated insulin delivery or artificial pancreas systems. These advances were not considered in guidance for T1DM patients, who may wish to fast if they are supported adequately. Recently, Al-Ozairi *et al.*<sup>[23]</sup> proposed that people with uncomplicated T1DM would be able to fast safely during Ramadan following structured education and daily advanced glucose monitoring. People with stable and uncomplicated T1DM on multiple daily injections or CSII who chose to fast during Ramadan were recruited. The participants received Dose Adjustment for Normal Eating (DAFNE), a structured education training program, and basal insulin was reduced in a controlled fashion. The authors concluded that people with uncomplicated T1DM could safely participate in intermittent fasting, similar to Ramadan fasting, if equipped with structured education and advanced glucose monitoring systems. A recent comment proposed a revised risk stratification tool to support people with T1DM, considering fasting during Ramadan, and help health-care professionals categorize them according to the availability of technical and professional support.<sup>[24]</sup>

In conclusion, there are currently a dynamic environment of active clinical research, evolving expert opinion, and changing perceptions of practicing clinicians regarding the definition of high-risk patients observing Ramadan fasting. More data are being collected, and more insights are being gained that may impact clinical practice. Although one should be open to the new suggestions of a lower

risk when patients have access to professional and technical support, there should be no complacency when high risk cannot be excluded.

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#### Conflicts of interest

There are no conflicts of interest.

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