

The Year in “Ramadan Fasting and Health” (2018): A Narrative Review

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Abstract

Introduction: There has been an increased interest in health implications of Ramadan fasting (RF). **Materials and Methods:** This is a narrative, nonsystematic review of the literature including all relevant full articles in English in three electronic databases (Scopus, PubMed, and Google Scholar). The search term “Ramadan fasting” was used to identify the relevant records to provide a readily comprehensible concise account of the contributions made to research and clinical practice in 1 year (2018). **Results:** The publications spanned basic, clinical, ethical, professional, and cultural and advocacy facets of the subject. The publications crossed the conventional disciplinary lines and geographical locations and appeared in journals with varying systems of access. Only full-text research articles in English were reviewed. Review articles, news, note items, and correspondence were not included. No formal bibliometric analysis is presented. Emerging concepts are presented under the relevant subheading depending on the available literature. Impact of RF on diabetes control, pregnancy outcome and fetal life, and sports and athletes’ well-being received somewhat more prominent coverage by research work published in 2018. Renovascular disease, and risk factors, posttransplant care, and some metabolic concerns for patients with hepatic, renal, and metabolic conditions were covered too. Patterns of use of emergency services during Ramadan and features of some specific medical emergencies were examined by some workers. Most interesting perhaps was the greater focus on documenting the perception, attitudes, and practices of both patients and healthcare professions regarding deciding and acting during Ramadan. Isolated research reports addressed subjects of wide nature from body composition and energy metabolism to smoking, law, music, and history. **Conclusions:** The volume of scholarly work on Ramadan fasting and health remains modest. Greater improvements in both quality and quantity of research on Ramadan are needed. Most studies indicate that Ramadan fasting is safe in mild and stable medical conditions under normal circumstances. High risk individuals must be identified, evaluated and managed on individual basis. Experiences from epidemiological, observational and experimental studies reviewed in this article should inform patients’ and physicians’ decisions.

Keywords: Bibliometric, diabetes, literature, patients’ perceptions, pregnancy, professional, Ramadan, research, sport medicine

INTRODUCTION

Ramadan fasting (RF) is practiced by adult Muslims during the 9th lunar month every year. It entails that they abstain from eating and drinking between dawn and sunset. Medical and religious scholars got closer in their approach to advice given to patients based on objective risk assessment.^[1] Muslim patients with acute or chronic medical conditions may be exempted from fasting; many do still choose to observe the fast sometimes against medical advice. This may adversely affect their health if not addressed properly by evidence-based recommendations.^[2]

There has been a tremendous recent interest in the health implications of RF. Keeping up with developments in this area may prove difficult, and hence, a narrative overview under a single cover may be particularly useful in presenting a digest of the research and expert opinion in the year.^[3] Our previous review of the literature published in 2017 was the most viewed

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article in this Journal having been viewed by over 4000 readers since its release less than a year ago.^[3]

This article aims to provide a thematic review of the global research work published in 2018. The review should give a concise bird's eye view of the literature and highlight the evidence base that may help direct clinical practice. It should be of value to practicing physicians providing good working knowledge to help them look after their fasting Muslim patients with full cultural competence. It should also help research workers in the identification of any unanswered questions and ambiguities of controversial issues.

MATERIALS AND METHODS

This is a narrative, nonsystematic review of the literature indexed in PubMed, Scopus, and Google Scholar in 1 calendar year (2018). The search term "Ramadan fasting" was used to identify the relevant records. For PubMed and Scopus, the only filter used was the date of publications, as specified above. However, for Google Scholar, further filters were used such as removal of patents, duplicates, citations, and any records other than scholarly publications. A total of 106, 93, and 82 records were found in Scopus, PubMed, and Google Scholar databases, respectively. The three sets are not mutually exclusive. The records were cleared from duplications and irrelevant articles and articles which were covered in previous narration.

SAB performed the literature searches retrieval and produced the initial draft. All authors further developed their assigned sections and reviewed the whole document for intellectual content using a single version loaded on Google Docs. All authors contributed to the revision of the manuscript. They all approved the final version of the manuscript before submission.

The publications spanned basic, clinical, ethical, professional, and cultural and advocacy facets of the subject. The publications crossed the conventional disciplinary lines and geographical locations and appeared in journals with varying systems of access. Only full-text research articles in English were reviewed. Review articles, news, note items, and correspondence were not included. Due to volume restriction and risk of duplication, no formal bibliometric analysis is presented. Emerging concepts are presented under the relevant subheading depending on the available literature. The research areas covered in 2018 included diabetes, impact of fasting on pregnancy, renovascular disease, attitudes, and healthcare professions' knowledge and attitudes. Limited research work addressed basic research questions.

THE LITERATURE NARRATION

Nutrition, body composition, and energy homeostasis

Mealtimes and feeding schedules during Ramadan may cause changes in body composition and energy metabolism and may interfere with the circadian system and sleep. Six articles were published in 2018 on the potential changes in healthy

adults and some medical conditions. These studies may help the understanding of the impact of intermittent fasting (IF), in general, and the management of certain conditions during RF, in particular.

Nutritional, body composition, and lifestyle changes during Ramadan with some correlations with metabolic parameters were explored by three groups. No significant changes in any of the body composition parameters before Ramadan (BR), during Ramadan, or after Ramadan (AR) in 44 healthy young adults were detected. Serum low-density lipoprotein (LDL) level decreased during Ramadan, compared to both BR and AR.^[4] Fasting blood glucose (FBG) and systolic blood pressure (BP) were slightly but significantly higher during Ramadan and even AR, though both of them were within normal levels. The food patterns, dietary diversity, and body weight changes in adolescents during Ramadan were studied in a prospective cohort study design with four measurement points was conducted in 366 adolescents in Junior High Schools in Ghana.^[5] Food pattern and diversity were assessed with a questionnaire and a 24-h dietary recall. Half of the pupils were female and the average age was 16 years. Pupils fasted for an average of 28 days for 14.3 h a day during Ramadan. The number and types of dishes taken at mealtimes differed substantially between Ramadan periods and outside Ramadan. Consumption of Vitamin A-rich fruits, other fruits, and milk and milk products increased markedly during Ramadan. However, fasting came with a reduction in consumption of foods from roots and tubers, legumes and nuts, and dark green leafy vegetables, while other food groups remained unchanged. Mean dietary diversity scores increased significantly during Ramadan while mean daily meal frequency decreased. There was significant body weight loss among adolescents. Weight loss was short-lived; weight was regained 1 month AR. Further, food intake, glucose homeostasis, lipid profiles, and body composition were determined before, during, and after RF in 160 healthy men.^[6] Anthropometric parameters such as body weight, body mass index (BMI), and body fat percentage as well as fasting blood sugar (FBS) and circulating triglycerides were all decreased significantly at the end of Ramadan compared with the same indices measured BR. At the end of Ramadan, homeostatic model assessment of insulin resistance (HOMA-IR) was significantly elevated. One month AR, these traits had all started to return to their pre-Ramadan levels but were still disrupted. Food intake of all food groups except carbohydrates decreased during Ramadan. Thus, a mixture of positive and negative health effects was seen in healthy adults. However, these effects were all transitory.

Three more articles were published concerning energy metabolism. Lessan *et al.*^[7] investigated the impact of RF on resting metabolic rate (RMR), activity, and total energy expenditure (TEE). Healthy nonobese volunteers ($n = 29$, 16 women) fasted during Ramadan. RMR was measured by indirect calorimetry. Activity ($n = 11$, 5 women) and TEE ($n = 10$, 5 women) in free-living conditions were measured with the use of accelerometers and the doubly labeled

water technique, respectively. Body composition was measured with the use of bioelectrical impedance. Measurements were repeated after a wash-out period of between 1 and 2 months AR. RF was associated with reduced activity and sleeping time but no significant change in RMR or TEE, suggesting that the weight changes seen with Ramadan are more likely to be due to differences in food intake. Akkoca *et al.*^[8] examined the effects of the energy and nutrients intake at RF on anthropometric measurements and metabolic and endocrine parameters. Their prospective study included a total of 80 healthy volunteers, aged 19–50 years, who were fasting during Ramadan. Anthropometric measurements and blood samples were taken, and nutritional intake was recorded for all participants at 5 days BR and on the 27th day at the end of Ramadan (AR). The anthropometric measurements, metabolic and endocrine parameters, and energy and nutrients BR and AR were compared generally. The authors observed that RF has positive effects on anthropometric measurements such as body weight, BMI, fat mass, and waist circumference, which are cardiovascular risk (CVR) factors, but no similar positive effect was seen on endocrine and metabolic parameters. Furthermore, Muhammad *et al.*^[9] examined the role of lifestyle and hormonal background on weight regain post-RF in overweight individuals in an observational study with a prospective cohort design. Subjects were overweight/obese men and women adults aged between 21 and 56 years. Bodyweight, percent fat, fat-free mass, and hip-waist circumference were measured before (week 0), 28 days after RF (week 4), and 2 weeks after the end of Ramadan (week 6). In addition, data on lifestyle factors such as dietary intake and physical activity were collected in those time points. Leptin was measured BR and at the end of RF period. Bodyweight was significantly reduced at the end of Ramadan and increased AR. Leptin was significantly reduced AR and leptin level at the end of Ramadan was associated with percent bodyweight reduction. They concluded that that dietary factor before fasting has a significant impact on overweight/obese individual.

Diabetes care in Ramadan

Diabetes management during Ramadan is widely accepted as the prime example of culturally-sensitive diabetes care in the context of Muslim population with diabetes.^[1] From experience, it was predictable that diabetes would have the lions share in the research productivity this year too.^[2] Several aspects of safety, efficacy, professional competence, patients' perceptions, and attitudes were addressed. Most of the work focused on adult populations. Studies related to the impact of diabetes on pregnancy are discussed separately.

General impact of fasting

A large cross-sectional study explored the impact of Ramadan on type 2 diabetes mellitus (T2DM) in 1246 patients.^[10] Sociodemographic features, lifestyle habits, BP measurements, serum lipid profiles, serum calcium, Vitamin D 25-hydroxy (25(OH)D), uric acid, and glycated hemoglobin (HbA1c) were examined before 4 weeks and after 12 weeks from Ramadan. The mean age was 50.4 years.

Males were marginally older than females. Significant differences were found in Vitamin D, blood glucose, HbA1c level, creatinine, bilirubin, albumin, total cholesterol, triglycerides, high-density lipoprotein-cholesterol (females), LDL-cholesterol (males), uric acid, and systolic and diastolic BP after and before the holy month of Ramadan. HbA1c, physical activity, hours of sleeping, BP, BMI, family history, and smoking were identified as significantly associated with RF as contributing factors. The authors concluded that RF has positive effects on T2DM patients as it reduces their BP, blood glucose, HbA1c, and BMI. The authors also claimed that there were improvements in the duration of sleep and physical activity. Tan *et al.*^[11] investigated the fasting pattern of 183 patients with diabetes (mean age = 57 years) in Brunei Darussalam. Fasting observance, and knowledge and practice in relation to diabetes control during Ramadan. A cross-sectional study that included 18 years and older, Muslim patients with DM who attended the main Diabetes Centre in Brunei. A self-administered questionnaire was designed, tested, and used to collect demographic information, fasting duration, knowledge and practice on diabetes control during fasting, and reasons for fasting. The prevalence of fasting during Ramadan was 93.4%, with an average number of days of fasting being 24.1 days. Those aged 55 and above had significantly higher prevalence of fasting than the younger group ($P = 0.010$). Only 49.1% of participants had consulted their healthcare professionals of their intentions to fast BR, and only 38.1% of participants monitored blood glucose levels throughout the month. The authors suggested that diabetes education and early treatment adjustment, especially BR and during the month of Ramadan, is essential to minimize hypoglycemic risks and frequency of diabetes complications.

Diabetes self-management education

Dwivedi *et al.*^[12] developed an educational module that would optimize the diabetic management of individuals observing Ramadan and evaluate the effectiveness of the module based on the special needs of fasting individuals. A needs assessment was conducted, and interdisciplinary team developed and implemented a comprehensive curriculum. The changes in skill level and knowledge were measured on a Likert scale. All residents and staff demonstrated a need for improved educational curriculum to address diabetes during Ramadan. For both residents and staff, self-reported confidence in their skillset improved on completing the curriculum. In addition, Lum *et al.*^[13] described the development and evaluation of a patient-centered epistemic tool to empower healthcare providers and patients in managing diabetes during Ramadan. A collaborative algorithm was developed with reference to the nominal group technique by a board-certified clinical pharmacist and discussed with endocrinologists, nurses, and family physicians. The empowerment component of the algorithm was developed based on the Basic Psychological Needs Theory. The algorithm was evaluated through a randomized controlled trial. HbA1c, fasting plasma glucose (FPG), and postprandial glucose (PPG) levels and safety profiles in terms

of hypoglycemic events were assessed. The algorithm was developed with four components: screening, education, dose modification by healthcare provider, and dose adjustment by a patient. A total of 62 individuals were recruited, with 30 and 32 randomized into the intervention and control groups, respectively. The mean age was 58.4 years, and two-thirds were females. There was a reduction in mean HbA1c ($P < 0.001$) in the intervention group but not in the control group ($P = 0.270$). FPG and PPG also improved significantly in the intervention group. There were no major hypoglycemic events and minor hypoglycemia comparable between both groups ($P = 0.465$). Healthcare professionals enrolled in pre-Ramadan education involving an endocrinologist, a diabetes specialized nurse, and a dietician were surveyed.^[14] Eighty-eight participants were surveyed for knowledge on fasting and safe practices of diabetes management during Ramadan. Participants had a racial distribution reflecting Malaysia and just over half were Muslims. Half practiced in primary care setting. The mean knowledge score was 81.1%; 84% would counsel people with diabetes for fasting, increasing to 96.7% after education. During the previous Ramadan, three quarters provided counseling or adjusted medication while half managed diabetes complications (63.8% predominantly hypoglycemia, 11.6% predominant hyperglycemia, and 24.6% only hypoglycemia).

The role of pharmacists in Australia in helping people observing Ramadan fast was evaluated.^[15] The perspective of patients with T2DM who undertake the fast of Ramadan, their experiences, health-related needs, and service preferences regarding diabetes management were studied using a qualitative, exploratory design. Semi-structured interviews were conducted using a standardized interview guide. Twenty-five semi-structured interviews (68% males) among a heterogeneous sample of fasting T2DM patients were conducted. Themes emerging from analysis included issues relating to sociocultural pressure for T2DM patients to fast; lack of awareness about the role of pharmacists; and, most importantly, the need to train pharmacists in cultural sensitivity and clinical implications thereof. In addition, the knowledge, attitude, and practice of 311 community pharmacists regarding the management of diabetes during Ramadan in Sudan were studied.^[16] The knowledge about medication regimen adjustment, diabetes risk stratification, and the condition in which the fasting diabetic patients have to stop their fast. This study showed that pharmacists had sufficient knowledge, positive attitude, and good practice about diabetes management during Ramadan.

Pharmacological management

Due to potential osmotic dehydration induced by the new class of antidiabetic agents, sodium-glucose co-transporter-2 inhibitors (SGLT2-I), some concern was expressed about the risk associated with their use in Ramadan. Two reports were published in 2018. Shao *et al.*^[17] investigated the effect of RF and continuing SGLT2-I use on ketonemia, BP, and renal function in Muslim patients with T2DM in a single-center prospective observational controlled cohort study. Muslim

patients aged 21–75 years with T2DM and estimated glomerular filtration rate (eGFR) ≥ 45 ml/min/1.73 m² were eligible if they had no contraindication to observe RF. Patients in the study group were on stable dose of SGLT2-I for at least 3 months before enrolment and continued during the study period, while patients in the control group were not on SGLT2-I before and during the study period. A total of 68 patients of similar baseline characteristics were (study: 35; control: 33) were included. During RF, patients from the study and control groups had similar change in weight, eGFR, sitting BP, and plasma β -hydroxybutyrate level. Fasting was associated with significant changes in weight, BP, and eGFR regardless of SGLT2-I treatment. Also, the continued use of SGLT2-I during Ramadan did neither increase ketonemia nor increase risk of eGFR deterioration or hypoglycemia. In another report, Bashier *et al.*^[18] provided real-life evidence about the safety of SGLT2-I during Ramadan. All patients over the age of 18 years on SGLT2-I BR 2016 who would be fasting during Ramadan were included. Demographic, clinical, and laboratory results were collected BR and AR. Phone interview to evaluate the frequency and severity of hypoglycemia and dehydration was conducted on a total of 417 patients. Of these, 27.0% experienced hypoglycemic events, and 82.3% checked their blood glucose using a glucometer. Confirmed hypoglycemia (<70 mg/dL) occurred in 78 (83.8%). The hypoglycemic events were significantly more frequent in the SGLT2-I plus insulin-treated patients than in those treated with SGLT2-I plus oral hypoglycemic agents ($P < 0.001$). Confirmed hypoglycemic events were more frequent in those using SGLT2-I plus intensive insulin compared to those using SGLT2-I plus basal insulin ($P = 0.020$). Symptoms of dehydration were seen in 39 (9.3%) of the total population. HbA1c and weight decreased by the end of Ramadan ($P < 0.001$). There were no significant changes in lipid profile and creatinine levels by the end of the study.

Hypoglycemia

Among the various metabolic changes in people with diabetes during Ramadan, hypoglycemia remains the most important complication in those on insulin therapy or hypoglycemic agents. Three studies addressed hypoglycemia during Ramadan. Elhadd *et al.*^[19] assessed the incidence of hypoglycemia in people with T2DM on three or more antidiabetic medications during Ramadan and studied people with T2DM on three or more glucose-lowering drugs during Ramadan, 2017. The dose of each drug was adjusted according to a prespecified protocol. The incidence of symptomatic or confirmed hypoglycemia was recorded in 181 participants who completed the study. Data on hypoglycemia were available in 172 subjects (115 males), the mean age was 53.6 years, and diabetes duration was 10 years. The incidence of hypoglycemia was 16.3% (28/172). Higher incidence of hypoglycemia occurs in people taking multiple glucose-lowering therapies during. They suggested that guidelines should emphasize increased associated with the increased complexity in antidiabetic regimens during RF. The modifications in antidiabetic medications during Ramadan

should carefully be individualized. Bashir *et al.*^[20] elaborated on patients on three or more antidiabetic medications for 2 weeks using flash glucose monitoring (FGM). The patients were classified as active (10) or sedentary (6) according to their daytime activity; there were 13 males and 3 females; the mean age was 53.4 years; the mean diabetes duration was 15 years, and the mean HbA1c was 7.9%. Over 2 weeks, there were 7.9 episodes of hypoglycemia recorded per patient, 50% of which were asymptomatic. There was no difference at baseline in age, BMI, HbA1c, diabetes duration, and antidiabetic medications between the active and sedentary groups. The active group had better glucose control and more episodes of hypoglycemia compared to the sedentary group. Patients with T2DM who are on three or more antidiabetic medications may benefit from FGM systems to fast safely during Ramadan by detecting asymptomatic hypoglycemia.^[21] Hypoglycemia was monitored in 25 adolescents (mean age 16 years) with T1DM during Ramadan using the FGM system. Percentage and total duration of hypoglycemia were extracted from the FGM downloads, and the differences were compared between different times of the day and night according to the eating pattern in Ramadan. The mean HbA1c was 8.6%, the mean glucose level was 200 mg/dL, and the overall time spent in hypoglycemia was 5.7%. The average daily time spent in hypoglycemia was 1.39 h per patient. Using the FGM, hypoglycemia is typically encountered during the hours preceding Iftar time indicating an overeffect of basal insulin.

Patients' experiences

Patients with uncontrolled T1DM are at high risk for RF and are exempt from fasting; however, most still insist on fasting. Glucose level fluctuations in those patients during RF were examined using a real-time continuous glucose monitoring system (RT-CGMS).^[22] The study involved adult patients with uncontrolled T1DM (HbA1c >7%) who insisted on fasting during Ramadan in 2014. A Medtronic RT-CGMS was used to monitor the participants' glucose levels for 3 consecutive days during fasting. The study included 22 patients (mean age 22 years, duration of diabetes 10.9 years, and HbA1c level 9.3). All participants were using the basal-bolus insulin regimen, except for one patient who was on an insulin pump. Sensor glucose (SG) profiles typically followed a pattern that was characterized by an exaggerated increase after *Iftar*, which was sustained overnight, and a second rapid rise after *Suhour*, with prolonged glucose decay over the daylight hours. The average SG was 199 mg/dL, which was lower during fasting 188 mg/dL than during the eating hours 213 mg/dL ($P=0.00$). There was a higher rate of hyperglycemia (48%) than hypoglycemia (10%). In conclusion, 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. The long-term effects for this finding are not known and warrant further investigation. The attitude and habits of 156 patients with T1DM during fasting Ramadan were examined in a prospective cohort of patients with T1DM who were on insulin pump (61) or

multiple daily insulin injections (MDI, 95) regimen.^[23] Patient questionnaires included the frequency of self-monitoring of blood glucose (SMBG), the need to make changes in insulin regimen by patients, timings of insulin administration, performing carbohydrate counting, and levels of physical activity. Patients on pump therapy performed SMBG more frequently than those on MDI regimen and were more likely to perform carbohydrate counting (32.7% and 8.4% of pump and MDI patients, respectively, $P < 0.001$). There was no difference in the percentage of patients who made changes in insulin doses (pump: 74.5%; MDI: 77.3%) or those who had any level of physical activity (pump: 12.5%; MDI: 21.1%). The timing of administering meal insulin in relation to sunset meal was variable with a preference to taking the injection immediately at sunset. There was no difference in glucose control between both groups as measured by fructosamine levels or the number of days that patients have to stop fasting. Also, the frequency and reasons for interruption of fasting during Ramadan were examined in 526 insulin-treated patients in an observational survey of diabetic patients during Ramadan of 2013 in Tunisia.^[24] T1DM represented 9.7% of the patients. The mean age was 36.8 and 58.3 years, the proportions of males were 62.8% and 57.5%, and the mean duration of diabetes was 11.0 and 14.4 years for T1DM and T2DM, respectively. During Ramadan, more than 55% of patients were treated with insulin analog and over one-third with premixed insulin. In this study population, fairly high proportion (71.5%) fasted without interruption. Furthermore, the average number of nonfasted days was low at 3 mainly due to hypoglycemia. The authors suggested that most patients with diabetes treated with insulin were able to fast without interruption during Ramadan.

There is limited experience regarding diabetes self-management, education, and support (DSMES) in refugee populations. Medecins Sans Frontieres undertook a DSMES survey in 292 diabetes patients seen in their primary health care program in Lebanon in 2015.^[25] Structured interviews were conducted with diabetes patients in three primary care clinics. Diabetes core knowledge in each patient (the DSMES score) was calculated. Awareness of long-term complications and educational preferences were also assessed. Patients with T2DM accounted for the majority (92%), and most (70%) had been diagnosed before the conflict. When asked about the previous Ramadan, 56% of the patients stated that they undertook a full fast, including patients with T1DM. Another cross-sectional study surveyed patients' diabetes-related knowledge over 4 months from one outpatient clinic in Saudi Arabia.^[26] Patients' group included 325 women and 152 men. Most patients (297, 62.3%) had type 2 diabetes. The patients' mean age was 39.7 years, and the mean duration of diabetes was 10.8 years. During the preceding Ramadan, 76% of patients reported fasting, whereas 58% said that they monitored their blood glucose levels once per day. Hypoglycemic episodes were reported in 60.3% of cases with type 2 diabetes and in 8.3% of cases with type 1 diabetes. Among those who had hypoglycemia, 2.8% of patients with type 1 diabetes and

17.8% with type 2 diabetes broke their fast. Finally, 54% of patients reported that their healthcare providers offered them instructions on diabetes management during Ramadan. They suggested that Ramadan health education in diabetes can encourage, improve, and guide patients to change their lifestyles during Ramadan while minimizing the risk of acute complications

Endocrine and metabolic effects of Ramadan

Beyond the most common metabolic disorder reported, i.e., diabetes, few studies addressed endocrine and other metabolic aspects such as insulin resistance, glucose homeostasis in overweight and obesity, thyroid hormone pharmacokinetics.^[27-31] Mushtaq *et al.*^[27] investigated the changes caused by RF on the body weight, glucose homeostasis, insulin resistance, and insulin sensitivity index in overweight, obese, and nonobese adult subjects of both the sexes in 110 adult volunteers (55 males, 55 females) aged between 20 and 40 years. Overweight and obese subjects of both sexes had a significant decrease in BMI as compared to normal weight subjects. FBG decreased significantly in pre- and post-overweight and obese males and females. Serum insulin levels in pre- and post-overweight males were significantly decreased. In the female group, serum insulin level reduced significantly in postoverweight, preobese, and postobese toward the end of the Ramadan. In addition, a significant improvement was also observed in insulin sensitivity of overweight and obese groups of both the genders. The authors suggested that RF in overweight and obese subjects as compared to nonobese has a beneficial effect on blood glucose homeostasis, serum insulin levels, as well as BMI and that the dietary and caloric control during Ramadan is helpful in promoting insulin sensitivity in obese people. Further, Prasetya and Sapwarobol^[28] determined the effect of fasting during Ramadan on the metabolic profile, anthropometry, and serum leptin and adiponectin concentrations. Anthropometry and blood samples were examined at two phases: baseline (within 3 days of the start of the Ramadan fast) and end line (in the last 3 days before the end of the Ramadan fast) in 27 healthy Muslim males who completed RF. Results demonstrate reductions in bodyweight, BMI, fat mass, muscle mass, and waist circumference followed by reductions in energy intake. Insulin sensitivity was improved. Serum insulin concentration and HOMA-IR decreased significantly. However, no significant change in FPG was observed. There was a significant correlation between the changes in bodyweight (%) and changes in serum leptin concentration. These results also demonstrate that IF during Ramadan leads to beneficial effects by improving insulin sensitivity. It also resulted in a beneficial effect on weight and fat loss. Many patients with hypothyroidism may be unable to comply with proper timings of levothyroxine (LT4) administration. Sheikh *et al.*^[29] determined the change in thyroid-stimulating hormone (TSH) level and quality of life (QOL) BR and AR in patients with primary hypothyroidism in a prospective cohort study of adults on stable doses of LT4 who fasted for at least 20 days during the month of

Ramadan (2016). Baseline characteristics and TSH levels were recorded on all consenting patients within 6 weeks BR. Post-Ramadan TSH was tested within 1–2 weeks after Ramadan. Sixty-four patients (58 females) were enrolled. The mean age was 44 years; the average daily dose of thyroxine was 95.3 µg. Patients fasted for 26.5 days and missed a dose of LT4 on 1.3 days. Mean TSH was 2.37 mIU/L and 4.69 pre- and post-Ramadan, respectively. Mean pre–post-Ramadan difference in TSH was 2.32 mIU/L ($P < 0.001$). However, the difference in TSH was not significantly different between those who were compliant with meals and LT4 interval (2.04 mIU/L) versus those who were not (3.15 mIU/L). Overall, an increase in QOL scores in the domains of physical health, psychological health, and social relationships was observed AR. Thus, there were some statistically significant changes in TSH concentrations AR fasting which was not affected by timing of LT4 intake and interval from meal. Chihoui *et al.*^[30] aimed to objectively evaluate the risk of hypoglycemia in patients with adrenal insufficiency (AI) and to determine the associated factors in a prospective case–crossover study on 30 patients (25 women and 5 men) aged 38.5 years. Patients underwent clinical examination and basic biochemical tests. A 24-h CGMS was performed for each patient during an RF day and then again during a nonfasting day. Interstitial glucose levels during the 24-h period, the fasting period, and the fasting period after exclusion of the five postprandial hours were significantly lower during the fasting day than on the nonfasting day. Hypoglycemia occurred in three patients (10%) during the fasting day but not during the nonfasting day ($P = 0.23$). Hypoglycemia was asymptomatic in two cases. Male sex was significantly associated with the occurrence of hypoglycemia. Although the interstitial glucose levels were lower during fasting in patients with AI, the risk for hypoglycemia was not increased. Finally, Varshney *et al.*^[31] reported a rare case of a 9-year-old male child having two genetic diseases, with an unclear association. An acute attack of acute intermittent porphyria is characterized by gastrointestinal (GI) symptoms and neuropsychiatric manifestations. The precipitating factor in the present case was prolonged fasting in Ramadan.

Impact on pregnancy and neonates

Despite being exempted from RF, many pregnant Muslim women fast during Ramadan. These studies investigated the impact of RF during the pregnancy on the pregnancy and neonatal outcomes and even long-term life outcomes in adulthood for children who were prenatally exposed to Ramadan. Interestingly, the coverage for pregnancy as a single subject was only second to diabetes in volume this year.

Epidemiological studies

A large epidemiological study assessed the impact of “Ramadan exposure *in utero*” on child mortality in Burkina Faso.^[32] The investigators analyzed data from 41,025 children born between 1993 and 2012, of whom 25,093 were born to Muslim mothers using a specific analysis to estimate the association between Ramadan exposure at different gestational

ages and mortality rate among children under 5 years of age. Mortality rate was 32 deaths per 1000/year. Mortality rate was 15% higher among Muslims than non-Muslims. The analysis revealed that the mortality rates of children born to Muslim mothers were 33%, 29%, and 22% higher when Ramadan occurred during conception, first trimester, and second trimester, respectively, compared with children of non-Muslim mothers born at the same time. Having a Muslim mother was not associated with higher mortality when the child was not exposed to Ramadan, born during Ramadan, or exposed during the third trimester. The study concluded that observance of Ramadan during early pregnancy can have detrimental consequences for the future health of the unborn child. The study stimulated two invited commentaries and a response from the authors.^[33-35] de Rooij was intrigued with how could the nutritional conditions in early life have such profound consequences for child mortality but he thought that the study is both astonishing and extremely relevant from a public health perspective.^[33] Also, Stein^[34] questioned how these behaviors might result in child mortality and he called for the findings to be replicated in other settings. The authors could not resist the opportunity for an elaborate response.^[35] Another large study was reported from Indonesia.^[36] The group examined the effects of prenatal exposure to Ramadan on stature during childhood and adolescence. They used data from the Indonesian family life survey consisting of 45,246 observations of 21,723 children born to 9771 mothers to examine the effects on stature (height-for-age Z-scores [HAZ], weight-for-age Z-scores, and body-mass-index-for-age Z-scores) from early childhood to late adolescence (0–19 years of age). Children were classified into three groups based on their mother's religion-religiosity: religious Muslims, less-religious Muslims, and non-Muslims. The authors claimed negative effects on stature for children born to religious Muslim mothers. These effects were age-dependent and timing-sensitive. For instance, children born to religious Muslim mothers were shorter in late adolescence (15–19 years of age) compared to their unexposed siblings if they were prenatally exposed in the first trimester of pregnancy (HAZ difference = -0.105 standard deviation). In addition, the authors found positive effects on stature for exposed less-religious Muslim children that peak in early adolescence (10–14 years of age) and negative effects on stature for exposed non-Muslim children that occur only in early childhood (0–4 years of age). Pradella and van Ewijk^[37] compared wheezing occurrence among adult Muslims who were exposed to RF as fetuses with those who did not. Wheezing prevalence was higher among adult Muslims who had been *in utero* during Ramadan, independent of the pregnancy phase in which the exposure to Ramadan occurred. This association tended to increase with age, being the strongest among those aged >44 years. This is in line with fetal programming theory, suggesting that impacts of *in utero* exposures often manifest only after reproductive age. Particularly, strong associations were detected for smokers. The respiratory system of prenatally exposed Muslims thus seems to perform worse in mitigating later *ex utero* harmful

influences, such as smoking. This study suggests that exposure to Ramadan during pregnancy may have lasting consequences for adult lung functionality.

Observational studies

Similar concepts were addressed in several smaller studies. Gul *et al.*^[38] compared the perinatal outcomes among fasting (100) and nonfasting (80) pregnant mothers who came for delivery in the labor suite being included. The analysis showed that perinatal outcomes, birth weight, head circumference, and midarm circumference were almost similar between the two groups. The authors concluded maternal fasting affects placental weight and the newborn length, with effect more pronounced in male babies. Abd Elbar *et al.*^[39] assessed the effect of fasting for a whole month during Ramadan on the fetal Doppler indices and amniotic fluid index. The umbilical artery resistance index (RI), middle cerebral artery (MCA) pulsatility index (PI), and amniotic fluid index (AFI) were measured at the beginning and the end of Ramadan. The study started with 240 healthy women in the third trimester of a normal singleton pregnancy. However, some were lost to follow-up. At the end of Ramadan, 228 women were assessed (152 fasting and 76 nonfasting). On initial assessment, there was no significant difference between fasting and nonfasting women regarding umbilical artery RI, MCA PI, and AFI. During reassessment at the end of Ramadan, there was no significant difference between the two groups regarding umbilical artery RI, MCA PI, and AFI, but there was a significant decrease of Doppler indices and AFI. However, all values were within the clinically accepted range suggesting that maternal fasting during Ramadan does not adversely affects fetal condition. In addition, Savitri *et al.*^[40] evaluated the association between fasting during pregnancy and the birth weight of newborns. A total of 139 women who had fasted for at least 1 day ($n = 110$) were classified as exposed to Ramadan. Birthweight of newborns who were exposed to Ramadan during pregnancy did not significantly differ from those who were not, both in the total and trimester-specific analysis. Women who fasted had significantly lower total energy, macronutrient, and water intake as compared with women who did not. Lifestyle changes that occur with Ramadan and fasting during pregnancy are associated with lower reported energy intake. The authors cannot conclude on the effect of fasting on birth weight due to low statistical power. Ahmed *et al.*^[41] evaluated the effects of RF on fetal development and outcomes of pregnancy in 240 healthy pregnant women. Fetal well-being ultrasonography was performed on all pregnant women in the beginning and the end of Ramadan. No significant difference was found between the two groups for the fetal age, maternal weight gain, estimated fetal weight gain, fetal biophysical profile, AFI, and umbilical artery systolic/diastolic ratio. The study observed a statistically significant increase in maternal weight in the second and third trimesters and a significant increase in the AFI in second trimester. They concluded that there was no difference in fetal outcome between fasting and nonfasting pregnant women.

Antenatal care during Ramadan

Masood *et al.*^[42] observed the pre-Ramadan health-seeking behavior, fasting trends, eating pattern, and sleep cycle in pregnant women in a cross-sectional observational study in Karachi. The tool used for data collection was interviewer-based closed-ended questionnaire. A total of 279 pregnant women who fasted were included in the study. One to ten days of fasting was observed by 85.7% of women. About 72.4% never consulted any doctor for pre-Ramadan advice on fasting. 81.7% believed that fasting would not cause any harm to their unborn child, while 42.7% of family members feared about the health of mother and unborn child. Three quarters of the respondents had reduced sleep cycle of about 3–4 h. The food items consumed at Suhoor and Iftar were rich in carbohydrates and fats. The authors concluded that pre-Ramadan medical consultation regarding safety of fasting during pregnancy should be structured and customized for women and their families. Gaps in knowledge identified in this study may help healthcare professionals to address these issues. Kalra *et al.*^[43] described a pragmatic, shared decision-making, based on patient-centered approach to this challenging clinical situation. It highlights simple, clinical and investigation-based clues which allow obstetric risk stratification of women in pregnancy or lactation. This clinical and laboratory-based assessment allows appropriate decision-making regarding fasting, while keeping fetomaternal safety paramount. Any patient worldwide seeks medical advice regarding safety of fasting during pregnancy. This issue lacks high-quality evidence, which makes giving medical advice challenging. To aid decision-making on this subject, Adler-Lazarovits and Weintraub^[44] performed an internet-mediated survey to determine the expert opinion on this issue. They examined the physicians' attitudes and views regarding religious fasting during pregnancy. The survey was answered by 108 obstetricians and gynecologists. The questions were aimed at the content of the medical advice given to Muslim pregnant patients on Ramadan. Most physicians recommended against fasting on the second or third trimester, while fasting on the first trimester was controversial. Differences were found between medical advice provided by physicians according to their demographic characteristics. Regarding Ramadan fast, senior specialists were more lenient about fasting than younger specialists (62% and 35%, respectively). A comprehensive literature review conducted revealing possible adverse maternal and fetal outcomes of fasting. However, the risk for long-term clinical complications is yet to be defined. The knowledge, attitudes, and practices of pregnant Thai-Muslim women during Ramadan was assessed in a study conducted between July 2016 and January 2017 on 619 pregnant women from six hospitals in Thailand.^[45] A questionnaire was used to collect data from pregnant women who had experienced pregnancy during Ramadan at least once in their lives. Logistic regression analysis demonstrated that their age ≥ 35 years and Islamic education increased the fasting during pregnancy. The main adversities from RF during pregnancy were weakness and fatigue. In conclusion, most pregnant women knew Islamic

law clear exemption from fasting during pregnancy; however, many pregnant women preferred fasting during Ramadan and they believed the fasting during pregnancy is not harmful to maternal health. Healthcare providers are required to understand the religious beliefs of Muslim pregnant women and design the standard guideline about managing lifestyle changes of RF during pregnancy. Despite understanding the risk of complications, especially hypoglycemia, Yahaya *et al.*^[46] suggested an insulin regimen for pregnant women with diabetes who wish to fast in Ramadan. The total daily dose of insulin requirement BR was divided into 3 parts; $\frac{2}{3}$ for Iftar (sunset meal) and $\frac{1}{3}$ for Suhoor (pre-dawn meal). For each timing, $\frac{2}{3}$ of the calculated dose was given as short-acting insulin and remaining $\frac{1}{3}$ as intermediate-acting insulin. All patients were reportedly able to fast without any hypoglycemic episode, both during the inpatient and outpatient periods. The suggested simple insulin regimen could help manage pregnant women with diabetes who insist on fasting do it safely with improvement of glycemic control and less reduced risk of hypoglycemia.

Respiratory function

During RF, both dietary and sleep patterns are adversely affected to cope with the rituals of Ramadan. Literature suggests that sleep deprivation and alteration of dietary pattern and nutritional impairment affect the pulmonary structure and function. Four papers reported on the impact of RF on spirometric parameter and inflammatory and hematological indices in healthy adults and in two patients with stable chronic obstructive pulmonary disease (COPD) and in two normal people. The effects of Ramadan on pulmonary function tests (PFTs) were investigated in a group of in healthy young males.^[47] Fifty sedentary nonsmoking healthy young Muslim male individuals of 20–25 years of age without any history of pulmonary or other major diseases were recruited by simple random sampling from different parts of Kolkata, India. Participants completed the American Thoracic Society questionnaire to record their personal demographic data, health status, and consent to participate in the study. Expirograph and peak flow meter were used to record the pulmonary function parameters (PFTs). PFTs were within normal range and did not show any significant variation during the Ramadan. Body height and body mass depicted significant correlation with PFTs. Tidal volume (TV), vital capacity, and peak expiratory flow rate (PEFR) had significant correlation with age. Simple and multiple regression equations were computed to predict PFTs in the studies. Thus, Ramada fasting did not affect the normal range of PFTs in young adults. Also, the immediate and delayed effects of RF on spirometric parameters in were evaluated in 50 apparently healthy young adults aged between 17 and 27 years.^[48] Spirometric recordings were done at three different time points. First: 5–10 days before the start of Ramadan (pre-Ramadan); second: Within 10 days of the beginning of RF (Ramadan); third: Within 7 days of the end of Ramadan (post-Ramadan). There were no statistically significant differences between the three phases with respect

to TV, inspiratory reserve volume, expiratory reserve volume, forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), FEV_1/FVC , PEF, and forced expiratory flow 25%–75%. To conclude, RF does not have any significant effect on PFTs as assessed by spirometry. Hence, the diagnosis and prognosis of a respiratory disorder made on spirometry findings are reliable and need no error correction if an individual is fasting. Furthermore, no previous study has raised the effects of RF on lung function data of COPD patients. Zouari *et al.*^[49] assessed the effects of RIF on spirometric data measured in male patients with 16 stable COPD patients (mean age: 64 years) who fasted during Ramadan. Three sessions (Before-R, End-R, and After-R) were selected for spirometry tests that were consistently performed 2.5–4.5 h before fasting break. Assessment sessions comprised FVC, FEV_1 , FEV_1/FVC , PEF, maximal mid-expiratory flow, and forced expiratory flow rate at the x% of FVC to be exhaled. Reversibility test was performed only during the BR session. Spirometric data were expressed in percentages of local reference values. Findings were analyzed by applying repeated measures analysis of variance. They demonstrated that fasting during Ramadan (2016) did not cause any significant changes in the spirometric data measured in the study in stable COPD male patients. Further, Rejeb *et al.*^[50] studied effects of Ramadan (2017) on inflammatory and hematological Indices of stable COPD in 15 male patients with a mean age of 71 years. Three sessions (BR, End-Ramadan, and AR) were selected. Spirometry tests and blood samples were consistently performed 2.5–4.5 h before the interruption of the fasting. Compared to the BR session, the End-Ramadan session values for hemoglobin, hematocrit, and red and white blood cells (RBC and WBC) were lower. Compared to the AR session, the End-Ramadan session values for hemoglobin and WBC were higher and lower, respectively. In conclusion, RF caused significant reduction in hemoglobin, hematocrit, RBC, and WBC. However, it did not induce any significant changes in the C-reactive protein and erythrocyte sedimentation rate indices.

Liver, kidney and post-transplant care

The effect of RF on liver functions and portal hemodynamics was assessed in patients with liver cirrhosis in comparison with healthy subjects.^[51] Participants were divided into three groups: 34 patients with liver cirrhosis who fasted during Ramadan, 8 patients with cirrhosis who did not fast, and 30 healthy volunteers who fasted. Portal hemodynamics were evaluated by portal vein diameter, congestion index (CI), and portal flow velocity. Laboratory investigations were determined BR, during Ramadan, and AR as an indicator of the changes in the liver functions. There were no dropouts during the study. Among the three groups, portal vein parameters showed statistically nonsignificant differences. Model for End stage Liver Disease (MELD) score and serum albumin levels showed a significant difference when the Group I and Group II compared separately to Group III ($P = 0.000$), while there were no differences between Group I and Group II ($P = 0.6$ and 0.57 , respectively). For portal vein CI,

there was a significant difference between the patients with cirrhosis (fasting – Group I and nonfasting – Group II) and healthy subjects (Group III) ($P = 0.000$), while the CI did not change significantly between the Groups I and II ($P = 0.54$). Therefore, patients with cirrhosis showed changes in their liver functions and portal hemodynamics, irrespective of their fasting status, and these differences were more pronounced in portal vein CI, MELD score, and serum albumin when compared with healthy subjects.

Nonalcoholic fatty liver disease (NAFLD) is the most frequent liver disease. Vaspin may modulate the inflammatory process, insulin resistance, and NAFLD. Omentin-1 is independently associated with hepatocyte ballooning. There was evidence of improvement in the adipokine level and histological hepatic steatosis following energy intake restriction and weight loss. Ebrahimi *et al.*^[52] evaluated the effects of RF on various circulating adipokines in NAFLD patients. This study included 83 NAFLD patients, of which 42 cases who fasted and 41 controls who did not fast during Ramadan. There is a potential for fasting in improving several anthropometric indices in NAFLD patients. In addition, fasting during Ramadan resulted in decreased levels of adipokines including vaspin and omentin-1. Studies with longer follow-up periods are required. In addition, Derbala *et al.*^[53] evaluated the safety and deleterious effect of fasting Ramadan in liver-transplant recipients. There were no significant differences between in tacrolimus levels between those who fasted and those who did not observe the fast. During Ramadan, there were significantly higher levels of albumin, total protein, cholesterol, hemoglobin level, platelet count, and serum creatinine compared to their values BR. However, no differences were detected between the groups. The authors concluded that patients with stable graft function in the absence of cirrhosis can fast safely.

Hassan *et al.*^[54] reported the first study of its kind to examine the impact of the RF on hydration status, plasma brain natriuretic peptide (BNP) levels, and kidney function in chronic kidney disease (CKD) patients. This prospective cohort study included two groups of patients with CKD grades 2–4: Thirty-one Muslim patients who fasted the month of Ramadan (fasting group) and 26 Muslim patients who did not fast (control group). One week BR fast, in the last week of the month of Ramadan (4 weeks), and 4 weeks after the end of the Ramadan month (8 weeks), hydration status and blood analysis of urea, creatinine, and BNP levels were measured. Among fasting patients, serum urea levels increased significantly ($P = 0.024$) during the last week of fasting and returned to basal levels at 4 weeks after the end of the Ramadan month, the eGFR did not change significantly at the end of fasting ($P = 0.411$), and the hydration status indices and plasma BNP levels were significantly decreased after fasting ($P \leq 0.021$) but returned to basal values 4 weeks thereafter. Patients with CKD grades 2–4 can fast throughout the month of Ramadan with no significant deterioration of renal functions and with a reasonable degree of safety. Fasting during the lunar month of Ramadan is mandatory to all healthy adult Muslims. Renal-transplant recipients are often worried

about the impact of fluid and electrolyte deprivation during fasting on the function of their allograft. Ibrahim *et al.*^[55] examined the effect of fasting Ramadan on the graft function in renal-transplant recipients in a retrospective cohort study, including patients who underwent kidney transplantation in our tertiary referral center. Baseline pre-Ramadan, eGFR, mean arterial pressure (MAP), and urinary protein excretion were compared to those during Ramadan and AR within and between the fasting and nonfasting groups. The study population included 280 kidney-transplant recipients who chose to fast during the Ramadan month (June–July 2014) and 285 recipients who did not fast. In the fasting group, baseline eGFR did not change from that during or post-Ramadan. Compared to baseline, there were no significant differences between the fasting and the nonfasting groups in terms of mean percent changes in eGFR, MAP, and urinary protein excretion. The authors concluded that fasting during the month of Ramadan did not have significant adverse effects on renal-allograft function. In addition, Ibrahim *et al.*^[56] examined the hydration status and liver function of young men before and during RF. The study design was a prospective cohort into 1st period (1 week before fasting) and 2nd period (the last 10 days of fasting). The subjects were 18 healthy young men (19–30 years old). Data on dietary intake were collected using food record 3 × 24 h, body composition were collected using bioelectrical impedance analyzer, and hydration status and liver function data were measured through urine and blood sample. They showed significant differences in bodyweight, fat body mass, BMI, body water, intake of energy, protein, fat, carbohydrate, and water, hydration status, and liver enzymes before and during RF ($P < 0.05$). There was significant correlation between fasting status and transaminase levels ($P < 0.05$). The study concluded that RF has a positive effect to control body weight and improve liver enzyme levels.

The impact of Ramadan in a prospective observational study on 54 patients with autosomal dominant polycystic kidney disease (ADPKD) who have normal to near-normal glomerular filtration rate.^[57] Comprehensive clinical and biochemical assessments were made in two groups (23 fasting versus 31 nonfasting). There were no significant differences between the two groups in terms of age, gender, ADPKD duration, and presence of hypertension. The authors concluded that a fasting duration of 17 h a day did not affect renal function negatively in patients with early-stage chronic kidney due to ADPKD. No significant changes occurred in acute renal markers.

Neurology and psychology

Razzak *et al.*^[58] aimed at examining the effect of baseline blood glucose levels on spatial ability, specifically verticality perception on the computerized rod and frame test (CRFT) in young healthy adults. 63 healthy male medical students (age range from 18 to 23 years), of whom 30 were nonfasting outside the month of Ramadan and 33 fasting during Ramadan of the year 2016, were recruited to create varying degrees of glycemia during which verticality perception was carried out. Baseline blood glucose reading was obtained before commencing the CRFT test. Blood glucose levels at

the time of testing decreased as the duration between the last meal and testing increased. A blood glucose range of 62–117 mg/dL was achieved among participants for this study. Linear regression analysis showed that blood glucose level at testing correlated positively with all alignment spatial error parameters, indicating a probable reduction of spatial perception ability with higher blood glucose levels. These results are consistent with other cognitive studies in older healthy humans and emphasize the critical impact of early glucose dyshomeostasis on cognitive function. They also indicate that elevated blood glucose may affect cognitive functioning outside of the usual complications of diabetes.

Dolu *et al.*^[59] investigated the effect of RF on plasma glucose levels and cognitive functions such as attention, memory, and decision-making. The study was carried out with 15 healthy adult participants. P300 recordings and plasma glucose levels were taken from all participants in fasting and subsequently nonfasting period as control group. The cancellation test was also administered to assess sustained attention in both periods. P300 was recorded using auditory oddball paradigm which consisted of 120 standard and 40 target stimuli. Latencies and amplitudes of P300 to target and standard stimuli were analyzed. P300 wave is an important component of auditory event-related potentials commonly used to examine cognitive function in decision-making processes. There was a significant difference between mean plasma glucose levels in fasting and nonfasting period. P300 amplitudes to target stimuli during fasting were significantly ($P < 0.05$) lower than those in the nonfasting period. P300 amplitudes to standard stimuli during fasting were also significantly lower than those in the nonfasting period. P300 latencies to standard stimuli during fasting were significantly longer than those in the nonfasting period. Cancellation test completion time in fasting was significantly ($P < 0.05$) longer than that in the nonfasting period. The authors suggest that RF may adversely affect cognitive functions such as perception, sustained attention, and decision-making. This is likely to be relevant clinically to those with a greater risk of cognitive dysfunction such as the elderly.

Erdem^[60] investigated the effect of RF on human psychology among healthy volunteer people. In this cross-sectional type study, the universe of the research is composed of healthy volunteer people who registered at a family health center in Diyarbakir and declared that they planned to fast at the month of Ramadan in 2017. A questionnaire form including a sociodemographic questionnaire and Turkish version of the Depression Anxiety Stress Scale-42 was formed. The online questionnaire technique was used to obtain the data via e-mail and smartphone. The survey conducted to the same healthy volunteer group 1 week BR and at the end of Ramadan (2017). Seventy-three healthy volunteer subjects with no known health problems and who were not in the risk groups in terms of mental and physical health were included in the statistical evaluation. Depression ($P = 0.001$), anxiety ($P = 0.01$), and stress ($P = 0.002$) scores were found to be lower at the end of Ramadan. When compared to the

pre-Ramadan scores of the samples and the post-Ramadan scores, anxiety ($P < 0.05$) prevalence was found to be lower at the end of Ramadan. The results of the study demonstrated that fasting in the month of Ramadan has been effective in diminishing stress, anxiety, and depression levels. Cay *et al.*^[61] evaluated the effect of fasting on ankle proprioception sense in 30 1st-year medical students (Inonu University, Turkey). The measurements were made 2 weeks BR started and 2 weeks AR started when the students were fasting. The authors proposed that fasting has an effect on proprioceptive sense, even though partly. Considering the difficulty of finding out the angles measured, associating the results with only fasting period is open to dispute. The clinical implications of the study remain unclear.

The impact of RF on circadian rhythm, sleep, and daytime sleepiness is an exciting topic where critically appraised.^[62] The authors suggested that larger studies are needed to control for potential confounding factors, such as environmental and cultural conditions (the delay in the start of work and school, light exposure, exercise, and meal composition), and to enable adequate assessment of the impact of diurnal RF on circadian rhythms, sleep, and daytime sleepiness. Therefore, the same group^[63] assessed the effects of fasting during Ramadan, on orexin, while controlling for lifestyle changes that may accompany Ramadan such as sleep duration, bedtime and wake time, energy expenditure, light exposure, and food. Eight young healthy volunteers reported to the laboratory BR (twice) and during Ramadan (once). Plasma levels of orexin-A were measured using an enzyme immunoassay five times. Caloric intake, light exposure, and sleep schedule were maintained during the participants' stays in the laboratory in the three study periods. Orexin-A levels increased in daytime during fasting and decreased at night compared to baseline. This finding supports the notion that fasting increases alertness.

The eyes in Ramadan

Changes in eating and sleeping habits during fasting, hunger, and thirst influence various ocular physiological parameters. Therefore, ophthalmologists have shown interest in the impact of fasting on the ocular system equipped with their sophisticated instruments capable of evaluating peripapillary retinal nerve fiber layer (RNFL) and choroidal thickness (CT) parameters during RF. Two studies of this kind were released in 2018. In the first study, 42 eyes of 21 fasting healthy volunteers were examined.^[64] RNFL and CT measurements were obtained using spectral-domain optical coherence tomography. Subfoveal and perifoveal CT were measured using enhanced depth imaging optic coherence tomography. Perifoveal CT was measured at a distance of 500, 1000, and 1500 μm nasally and temporally from the foveal center in each eye. There was no statistically significant difference between fasting and nonfasting RNFL thickness. Subfoveal and perifoveal CT values were significantly thinner in fasting than in nonfasting subjects. They speculated that it is possible that decreased choroidal vascular bed volume during fasting caused the reduction in CT. In the second study, the correlation between

variations of glucose and lipid biomarkers with the biometric properties and intraocular pressure changes associated with RF were examined in 89 healthy volunteers (51 males, mean age 36 years; 38 females, mean age 34 years).^[65] Right-eye ocular axial length and anterior-chamber depth were measured using the IOL Master. Afterward, the intraocular pressure of the right eye was measured using noncontact tonometer, and also, blood samples were obtained for fasting blood sugar, triglyceride, cholesterol, high-density lipoprotein, and LDL were measured. All the assessments were performed BR and AR. No significant correlations were observed between changes in axial length with variations of glucose and lipid biomarkers in the fasting individuals. Furthermore, only an insignificant correlation was denoted between the anterior-chamber depth and high-density lipoprotein changes during Ramadan. The findings also revealed only an insignificant association between intraocular pressure and cholesterol changes in healthy fasting individuals. The authors concluded that, according to the results, changes in the ocular parameters in RF are probably independent of the variation levels of glucose and lipid biomarkers. The literature on the impact of RF on the eyes warrants a careful critical appraisal.

Vascular disease and risk factors

The effect of RF on the symptoms of chronic heart failure with a reduced ejection fraction (HFrEF) was investigated prospectively in outpatients with HFrEF who observed RF at tertiary care cardiac center in Saudi Arabia in 2017.^[66] The investigators obtained information regarding the clinical assessment, diagnosis, emergency department (ED) visits, and hospitalization during and in the month preceding Ramadan. They enrolled 249 patients, of them 227 (91%) undertook the fast for the entire month. During Ramadan, 209 (92%) patients remained hemodynamically stable, whereas 18 (8%) developed instability. The mean New York Heart Association (NYHA) functional class was significantly lower in the stable than in the unstable group, although no intergroup differences were observed BR. Patients from the unstable versus the stable group showed significantly less adherence to medications and to diet and a lower likelihood of demonstrating ischemic cardiomyopathy as an underlying etiology of HFrEF. NYHA classification BR was significantly higher than during Ramadan. The group concluded that in most patients with chronic HFrEF, RF is considered safe. Nonadherence to medication and diet may be significantly associated with decompensated heart failure during Ramadan.

Heart rate variability (HRV) is an independent indicator of increased mortality in patients with myocardial infarction and congestive heart failure. Mzoughi *et al.*^[67] studied the effects of Ramadan fasting on hypertensive patients' HRV. They conducted a prospective study including 20 hypertensive patients (mean age, 55 years) with sinus rhythm. HRV was determined twice by ambulatory 24-h Holter recordings at fasting during Ramadan and AR. HRV parameters were found to be decreased in Ramadan. Thus, RF enhances the activity of the sympathetic system in hypertensive patients.

Bouida *et al.*^[68] assessed the effect of RF on aspirin resistance in 177 stable patients with two or more CVR factors and explored whether T2DM would influence this effect. All patients observed RF and were taking aspirin. Physical examination and standard biological tests including glycemia and serum lipids data were performed BR (Pre-R), at the last week of Ramadan (R), and 4 weeks after the end of Ramadan (Post-R). In the same visits, caloric intake was calculated and platelet reactivity to aspirin was assessed. In overall population, there was no significant change in absolute aspirin reaction unit (ARU) values and in metabolic parameters. In DM patients ($n = 127$), ARU change from Pre-R values was $+19.7$ ($P = 0.01$) and $+14.4$ ($P = 0.02$), respectively, at R and Post-R. During Ramadan, glycemia, triglycerides, and cholesterol levels increased significantly and returned to Pre-R values thereafter. These changes were not observed in non-DM patients. During RF, aspirin resistance increased only in DM patients. This effect persisted 1 month AR. Simultaneous alteration of glycemic control and increase of serum lipids levels could potentially be a favorable factor.

Alghamdi *et al.*^[69] evaluated the effect of RF on the international normalized ratio (INR) stability in patients using warfarin anticoagulation for mechanical prosthetic heart valves. Data were extracted retrospectively from a specialized anticoagulation clinic electronic database and were analyzed in a case-control manner, where Ramadan INR of each study subject was compared to his/her own pre-Ramadan INR level. Low-target and high-target therapeutic ranges represented 35% and 65%, respectively. Mean INR levels at baseline (2.81) and during Ramadan (2.75) were not significantly different. Achieving the desired target INR level BR was feasible in 62.5% and 64.8% of the low and high INR target groups, respectively. However, maintaining the desired INR level during Ramadan was feasible in 67.5% and 51.3% of the low- and high-target INR groups, respectively ($P = 0.07$). Duration of anticoagulation, warfarin, and adherence scale did not contribute significantly to the primary outcome. The authors suggested that RF and its associated lifestyle changes in the studied community may aggravate the INR fluctuations in warfarin-treated patients, requiring more careful attention and closer monitoring.

A retrospective cohort study included all patients admitted with acute ischemic stroke over 4 years.^[70] The association between stroke incidence and Ramadan month was evaluated adjusting for weekly temperature and seasonality. They compared the first versus the last Ramadan fortnight and performed an effect specificity analysis by assessing stroke incidence in population. The authors identified 4727 cases of ischemic stroke; 564 were Palestinian Arabs. Fifty-one cases occurred during Ramadan. Fasting was significantly associated with an increased risk for ischemic stroke, mainly during the first fortnight when compared with non-Ramadan periods. Mean weekly temperatures and the summer season were not associated with stroke incidence among the Palestinians. Such association was not observed in the Arab population.

The Ramadan month, particularly in its first 2 weeks, is an independent and ethnicity-specific risk factor for ischemic stroke hospitalizations among the fasting Palestinians.

Ramadan and sport

The optimal moment of the day for repeated-sprint training in the fasted state during Ramadan was evaluated by Aloui *et al.*^[71] Thirty amateur soccer players were randomly assigned 10 each to a morning training group, an evening training group, and a control group. Training sessions, conducted on alternate days, consisted of three sets of shuttle sprints with appropriate recovery time. The participants' performance was assessed BR and AR during both am and pm sessions by Countermovement Jump (CMJ), Repeated-Sprint Test (RST), and Yo-Yo Intermittent Recovery Test Level 1 (YYIRT1). They reported that AR, YYIRT1 performances were enhanced for both groups in the morning ($P < 0.05$) and in the evening ($P < 0.05$). Relative changes in YYIRT1 and RST at the specific time of training were similar for both groups. In addition, no differences were observed in CMJ performances BR and AR for any group. The authors recommended that morning or evening repeated-sprint training conducted in the fasted state during Ramadan enhanced soccer-specific endurance similarly.

During Ramadan, dehydration and disturbed sleep patterns are common, so accurate reliable methods for the assessment of hydration and sleep of athletes are necessary to maintain performance. Trabelsi *et al.*^[72] appraised the methodological and practical considerations: Monitoring athletes' hydration status and sleep patterns during Ramadan observance with view (1) to identify appropriate tools/methods for monitoring hydration status and sleep in sports people; (2) to discuss which of these tools/methods can be confidently used by sport scientists and trainers during Ramadan; and (3) to discuss the possible link that may exist between sleep and hydration status. Several markers of hydration status are currently used and include body mass, plasma/serum osmolality, dilution techniques, and neutron activation analysis. Used in an appropriate context, all can be indicative of the hydration status in the laboratory. In the field, monitoring hydration status in physically active individuals and athletes may be performed using a combination of body mass with some measures of urine concentration (e.g., urine osmolality, urine-specific gravity, and urine color) and sensation of thirst. During Ramadan, appropriate timing of sample collection and the use of reference methods in future studies are warranted. In the field, careful use of body mass in conjunction with urine indices may be used to monitor the hydration status of subjects practicing physical activity during Ramadan. There is a need for the use of polysomnography or actigraphy for sleep assessment during Ramadan in the future laboratory-based studies of athletes. However, in the field, monitoring sleep-wake patterns may be performed using actigraphy or the Pittsburgh Sleep Quality Index questionnaire.

Alkoot *et al.*^[73] assessed the Vitamin D status in 250 male athletes and its relationship with other variables such as body composition, lifestyle, and fasting during Ramadan

in a cross-sectional study. Blood tests, anthropometric measurements, and a lifestyle questionnaire were performed. Thirty-six percent of the samples were football players and the rest were players of 15 different sports. A prevalence of 83% of Vitamin D inadequacy (defined as serum 25(OH) D <75 nmol/L) was observed, of which 23% had severe deficiency (25(OH)D <25 nmol/L). This increased from 80% ($n = 130$) BR to 90% ($n = 79$) AR. Serum 25(OH) D concentrations correlated directly with Vitamin D intake and were significantly inversely associated with risk of injuries ($P = 0.008$) and with the concentrations of parathyroid hormone ($P = 0.029$). No significant associations between 25(OH) D concentrations and sun exposure, physical activity, or anthropometric levels were detected. The authors proposed that regular supplement intake and Vitamin D awareness campaigns for athletes are needed and more research to elaborate further the specific effects of Ramadan is also needed. It would have been interesting to show the difference between the football players (36%) and the rest of the participants! Furthermore, Tifrea and Cherkaoui^[74] highlighted differential use of body energy sources when practicing during daytime Ramadan. In prolonged exercise, the energy deficit leads the body into a “suffering” situation. In such a situation, it is difficult to get performance and cognitive focus without the necessary amount of energy. Exercising intense effort calls for other sources of energy, such as fats and proteins. The use of muscle proteins for energy purposes leads to changes in contractile fibers and weakens the muscle tissue. This risk is even greater if the hydration is not correct, a situation often associated with the absence of food intake. Associated dehydration increases the risk of tendon and muscle lesions (tendinopathy, elongation, and breakdown). During the Ramadan month, physical activities and sports performance are significantly reduced. Coaches have to take this into account. Scheduling competitions during this period is not compatible with high performance sports, as diet is a major component of sport performance. Furthermore, Boukhris *et al.*^[75] have shown that RF has no adverse effect on feelings, dietary intake, and short-term maximal performance. However, the Rating of Perceived Exertion Scale during repeated high-intensity short-term maximal exercise was reduced 20 days AR in comparison to the last 10 days of Ramadan. Brini *et al.*^[76] investigated the effects of a 4-week small-sided game (SSG) and repeated-sprint ability training during Ramadan and AR on aerobic and anaerobic capacities in senior basketball players. The results showed no significant differences in aerobic and anaerobic performances when compared with SSG and non-Ramadan in senior basketball players. They found no significant difference in mean HR ($P = 0.03$) between groups when comparing Ramadan and 1 month after Ramadan for small-sided games. This study indicated that RF combined with small-sided games and repeated-sprint ability training has no significant effect on most aerobic and anaerobic performances in male senior basketball players

Bataineh *et al.*^[77] examined the effects of carbohydrate mouth rinsing during RF on running time to exhaustion and on peak treadmill speed. The study concluded that carbohydrate mouth rinsing improves running time to exhaustion and peak treadmill speed under RF conditions. However, if this practice nullifies fasting from the religious viewpoint, the whole argument has no practical value. Finally, Chtourou *et al.*^[78] presented some challenges that could be observed in athletes during the training sessions or competition and present some practical recommendations to avoid GI disorders during Ramadan. Based on previous studies, the authors proposed that the prevalence of gut disorders will be more pronounced when athletes travel for international competitions during Ramadan. Besides, GI disorders are more frequent for athletes when there is a huge modification in the training load. Dehydration observed during Ramadan is one of the factors that may induce GI disorders. The latter could be exacerbated by sweat loss during training sessions. Carbohydrate is frequently used by athletes to improve performance and is associated with some GI disorders. Therefore, during Ramadan, coaches and athletes should be advised to maintain the same diet and a good hydration as before the fasting month and avoid air travel when preparing for competitions.

Medical emergencies during Ramadan

Recourse to EDs varies daily and changes considerably during holidays, posing challenges to resource allocation. It was noted in the past that Ramadan could represent a unique annual circumstance that predictably alters the pattern of arrivals at EDs in predominantly Muslim populations. In 2018, four reports addressed the ED workload and four specific clinical scenarios.^[79-84]

The activities of emergency services and patient characteristics were examined in two studies from the UAE and Lebanon. From an adult and pediatric ED in the UAE, the hourly arrivals, census, and visit characteristics were retrospectively compared for Ramadan versus non-Ramadan periods over 4 years (2010–2013) by Balhara *et al.*^[79] Hourly arrivals and census and differences in characteristics were examined. They detected a significant difference in the ED arrival pattern during Ramadan from non-Ramadan days, with sharp decreases after the fast was broken around sunset, followed by steep increases 2.5 h later. The median daily adult arrivals were similar, with slightly decreased length of stay (7%, $P < 0.001$) during Ramadan. The median daily pediatric arrivals were lower during Ramadan (43 vs. 57, $P < 0.001$), with decreased length of stay (20%, $P < 0.001$). Arrival pattern shifts led to significant census redistribution to evening hours. Patient characteristics were similar during both periods. In addition, Al Assaad *et al.*^[80] described the changes in ED visits and in frequencies of emergency conditions and impact on clinical outcomes during Ramadan in a tertiary care center in Beirut, Lebanon. Patients presenting to ED during Ramadan 1 month BR and 1 month AR over a 3-year period with specific conditions (acute coronary syndrome, stroke, seizure, diabetes, renal colic, headache, or hypertension) were examined. Clinical and sociodemographic

characteristics, ED volume, diagnoses, and outcomes were examined during two periods (Ramadan vs. non-Ramadan). A total of 3536 patients were included. The daily average ED volume was higher during non-Ramadan months (146 ± 22) compared with Ramadan (129 ± 15). The average ED length of stay was higher during Ramadan (5.4 vs. 4.0 h; $P = 0.006$). Frequencies and admission rates for the selected diseases were comparable during the two periods, except for patients with acute coronary syndrome or stroke who had lower admission rates during Ramadan. ED bounce-back rates and mortality at ED discharge were higher during Ramadan.

Emergency attendances necessitated by specific conditions were addressed by four reports.^[81-84] The characteristics of 186 patients with diabetes admitted during Ramadan compared with 216 admitted during a nonfasting lunar month (2016) in a retrospective cohort study medical record review at a busy general hospital in Benghazi, Libya.^[81] The authors compared differences in reasons for admission, length of stay, and in-hospital mortality between patients admitted in 2 months and between patients who were fasting at the time of admission during Ramadan and those who were not. No statistically significant differences in reasons for admission, length of hospital stay, or in-hospital mortality were detected between patients with diabetes admitted during Ramadan and non-Ramadan. However, only 59.1% were fasting on admission during Ramadan. Fasting patients admitted during Ramadan had a significantly higher proportion of the diseases of the circulatory system when compared with nonfasting patients (39.4% vs. 23.6%, $P = 0.028$) while in-hospital mortality was higher in nonfasting patients (29.2% vs. 8.7%, $P < 0.001$). There was no significant difference in length of stay between fasting and nonfasting patients. Although the sample is fairly small, the authors concluded that the frequency of admissions for most medical conditions is not different during Ramadan. Nonetheless, a greater frequency of acute coronary syndrome in those who were fasting on admission was observed. Appropriate modifications to allow adequate adherence to medications could be a contributing factor. On the other hand, a retrospective cross-sectional study using medical records of 237 patients admitted through ED with a diagnosis of renal colic secondary to urinary stones over a 10-year period in Riyadh, Saudi Arabia, was conducted.^[82] Patients fasting in Ramadan are two times more likely to present with a calculus of ureter as opposed to calculus in another location in the urinary tract, particularly when the holy month of Ramadan falls in summer season. There was no significant difference in the frequency of urinary stones between Ramadan and non-Ramadan months. Fasting in Ramadan did not increase the risk for developing urinary stones compared to nonfasting months. Furthermore, Drozdinsky *et al.*^[83] assessed whether acute pancreatitis (AP) is more common during Ramadan. The study compared the occurrence of AP in a fasting population and a nonfasting population during the Ramadan versus the rest of the year. Over the 10-year study period, 1167 patients were admitted to the ED with AP. Of these, 91.6% were

nonfasting and 8.4% were fasting. Of these, 17/98 (17.3%) fasting patients and 95/1069 (8.8%) nonfasting patients were admitted with AP during Ramadan. During Ramadan, the rate of AP out of referrals was 0.1% in fasting patients versus 0.004% in nonfasting individuals (odds ratio [OR]: 2.54, 95% confidence interval: 1.5–4.25). During the other months of the year, the rate of AP out of referrals was 0.009% (81/86,072) in fasting patients versus 0.008% (974/1,202,405) in nonfasting individuals (OR: 1.16, $P < 0.001$). The authors suggested that there is a higher risk of AP in the fasting population during Ramadan. Physicians should be aware of this link and suspect it for fasting patients presenting with epigastric pain during Ramadan. Salam *et al.*^[84] examined the effects of fasting in patients with acute heart failure (AHF) using data from a large multicenter heart failure registry (Gulf CARE). They included 4157 patients, of which 306 (7.4%) were hospitalized with AHF during Ramadan, while 3851 patients (92.6%) were hospitalized on other days. Patients admitted during Ramadan had significantly lower prevalence of symptoms and signs of volume overload compared to patients hospitalized in other months. Atrial arrhythmias were significantly less frequent and cholesterol levels were significantly lower in Ramadan. Hospitalization in Ramadan was not independently associated with increased immediate or 1-year mortality. The study represented the largest evaluation of the effects of fasting on AHF. It reported an improved volume status in fasting patients. There were also favorable effects on atrial arrhythmia and total cholesterol and no effects on immediate or long-term outcomes.

Emergency services might experience changes in volumes, time distribution, and length of stay and potentially worse outcomes of certain conditions during Ramadan. Changes in the frequencies of ED visits related to common conditions do not seem to happen. These findings should benefit EDs plan for efficient distribution of provider hours during Ramadan. Understanding the emergency needs posed by the specific medical conditions should come from careful examination of the interplay between the clinical condition, patient management and behavior, and the environmental changes during Ramadan.

Patients' and professionals' perspectives

Being a religious obligation entails that the decision to observe the fast remains a prerogative for the patient. It also entails that the medical profession should approach the issue of interface between medicine, religion, and culture very sensitively.^[1] Increased papers on professional competence, patients' knowledge, advocacy, and various cultural perspectives were published in 2018. We are cognizant of the nonmedical nature of some of these reports. However, they are still very important aspects of patients' care.

Patients' perspectives

Several articles addressed the patients' perspectives on fasting by asking research questions on patients' knowledge of religious rules, drivers to fast with, or against medical advice in different clinical situations such as diabetes,

pregnancy, and cancer. Some of the studies compared patients and healthcare professionals approaches. Al-Balhan *et al.*^[85] demonstrated that despite risks, about half (43%) with T1DM and most (86%) of those with T2DM fast during Ramadan. However, there is a dearth of information concerning the determinants that drive diabetic people to fast. A sample of 201 subjects volunteered to take part in this study. Mean age was 45 years. Most participants were female and married and had received at least primary education. They fasted for 23 days. Patients with complicated diabetes (32.8%) fasted for 21 days versus subjects with diabetes (67%), who fasted for 24 days ($P = 0.014$). Religious beliefs and practices influenced the number of fasting days in a statistically significant manner ($P = 0.004$). The attitudes of 295 patients with T2DM toward fasting Ramadan were assessed by face-to-face interviews conducted by the same investigator using a standardized questionnaire.^[86] The mean age was 47 years; 65.4% were females; nearly half were on insulin with or without oral antidiabetic drugs (OADs) and the rest on OAD alone. Two-thirds of the patients observed the fast and 70.7% consulted their doctors to fast BR. Of these, 46 (34.5%) were permitted fast, while 87 (65.5%) patients fasted against medical advice for a religious reason. The basic religious knowledge regarding the Islamic law, attitudes, and practices of RF during pregnancy in 619 pregnant Muslim women in a cross-sectional descriptive study.^[86] Most participants (85.5%) have knowledge regarding the Islamic law clear exemption from fasting for pregnant women and that the missed fasting days must be compensated later. However, 87.1% observed fasting during pregnancy since majority of pregnant women believed the fasting during pregnancy did no serious harm to maternal health. Mean fasting days was 24.6 days and 63.0% observed fasting between 21 and 30 days. Age over 35 years and having received Islamic education increased fasting during pregnancy. The main actual adversities from fasting during pregnancy were weakness and fatigue. In conclusion, healthcare providers are required to understand the religious beliefs of Muslim pregnant women and design the standard guideline about managing lifestyle changes of RF during pregnancy. Even though most Muslims do not believe that pregnant women are obligated to fast during Ramadan, fasting rates of up to 87% have been reported for pregnant women. The Mainz Study of Ramadan and Pregnancy surveyed pregnant Muslims and new Muslim mothers in Mainz between October 2016 and January 2017 and collected information on Ramadan adherence and behavior.^[87] The authors also collected data on personal characteristics and opinions, to identify determinants of fasting using statistical analysis. They found that 43% of pregnant Muslim women fasted at least 1 day during Ramadan 2016. Women who fasted were significantly younger and less educated. There was no significant difference in terms of country of origin between those women who fasted and those who did not. Only 49% of women who fasted and 38% of women who did not fast discussed the Ramadan with their doctor and less than 2% of women reported being proactively approached by their

doctor. Fasting practices among cancer patients and the opinions of healthcare professionals about fasting among cancer patients were assessed in a cross-sectional survey in Iran during Ramadan of 2013.^[88] Participants were 620 cancer patients and 187 healthcare professionals. Self-administered questionnaires and other data were collected. There were 428 (69%) women and 76 (13%) of patients fasted for at least a day during Ramadan and from which 41 (7%) had fasted whole months. Patients who did not observe the fast, did so because of lack of sufficient physical strength (65%) and excessive thirst (23%). Less than half of the patients (275, 44%) had consulted with their physician about fasting. More than 50% of physicians advised against fasting for patients following surgery, preoperation, recent hospitalization, and consumption of oral or intravenous chemotherapy. Most of the healthcare professionals (68%) believed that cancer survivors could not fast even if they have no signs or symptoms or side effects after the treatment. The authors called for development of guidelines for both healthcare professionals and cancer patients regarding RF. Finally, the impact of fasting on the psychological well-being of Muslim-graduate students was evaluated in a single-group pretest–posttest research design.^[89] Students responded to a psychological well-being scale and its subscales before and after the end of Ramadan. Fasting led to the promotion of overall psychological well-being, self-acceptance, autonomy, positive relations, environmental mastery, and personal growth among students who fasted Ramadan. Another interesting study suggested that while dietary restriction for health or appearance-related reasons is a known contributor to disordered eating (DE), dietary restriction for religious purposes, such as that observed during the practice of Ramadan, may not confer increased risk of DE symptoms.^[90]

Pre-Ramadan counseling

The health status of people with diabetes during Ramadan was explored by involving 15 patients in two focus group discussions.^[91] Most participants reported lack of knowledge regarding their own conditions and do not follow the medical advice of not fasting during Ramadan. Barriers facing the patients seeking healthcare BR and during Ramadan were the atmosphere, long distances to facilities, monthly appointments, and monthly prescribed medication. All respondents agreed on the importance of physical activity, but their opinions varied on how to conduct it. Regarding the services, most respondents were unsatisfied due to the lack of health services provided in addition to the shortage of essential medication or laboratory investigations. Others blamed primary healthcare center staff for the delay in laboratory investigation results and the unavailability of HbA1c. Respondents also claimed that self-check glucometer measurements are not as accurate as laboratory results. Doctors may be able to educate patients regarding the effects of fasting with diabetes, whereas religious leaders may influence individuals to follow doctors' advice. Furthermore, whether fasting diabetic patients ($N = 190$) received recommendations regarding fasting or they consulted

the physicians BR and during Ramadan of 2014 was investigated along with the effect of sociodemographic factors on RF.^[92] Sociodemographic characteristics, diabetes-related characteristics, recommendations of physicians, and behavioral patterns of fasting patients were captured. Overall 41.6% of diabetic patients fasted during Ramadan. 83.5% of them did not go to physician during Ramadan, 65.8% did not consult physicians before fasting, and 12.7% were informed by physicians regarding fasting and diabetes. Result of the study was that both physicians and patients were not well aware of the importance of pre-Ramadan education and close follow-up during fasting. Furthermore, the effect of pre-Ramadan education program on biochemical parameters and the risk of hypoglycemia was evaluated in 320 patients with T2DM in a prospective interventional controlled design.^[93] They were divided into two groups; the control group ($n = 200$) who received standard diabetic care and the intervention group ($n = 120$) who received focused individualized diabetic education sessions before Ramadan. The study was carried out on three phases (BR, during Ramadan, and AR). Posteducation change of hypoglycemia risk and biochemical parameters during Ramadan fasting were the primary outcomes. They found that FBG decreased significantly during Ramadan and AR in both groups ($P < 0.001$). Hypoglycemia during fasting occurred in 4.1% of patients in the intervention group versus 19.5% in the control group. Post-Ramadan reduction of HbA1c $< 7\%$ increased statistically significantly in the intervention group (from 20.8% of patients BR to 55.8% AR). LDL-cholesterol decreased in the intervention group ($P = 0.024$). The bodyweight of the patients did not significantly change in both groups. Therefore, they suggested that there was a significant impact of pre-Ramadan educational program on reduction of hypoglycemic risk and other acute complications, reduction of LDL cholesterol, and improvement of high-density lipoprotein cholesterol. Therefore, it is recommended for the fasting patients especially those with high and very high risk during Ramadan. The outcome for fasting patients with diabetes prepared with pre-Ramadan optimization through education and medication adjustment, tele-support, and intervention up to post-Ramadan was evaluated in a focused diabetes program for RF.^[94] It consisted of (a) a pre-Ramadan assessment and test fasting to optimize glycemic control, (b) education on diabetes management during fasting, (c) tele-monitoring from pre-Ramadan, and (d) a post-Ramadan review. Their metabolic profiles and diaries for meals, activities, and glucose monitoring were evaluated. Twenty-nine participants were enrolled, with a mean age of 58.4 years, 75.9% were females, 79.3% were Malays, and 93.1% had T2DM. A total of 92% needed medication adjustment and 93% fasted for at least 14 days. HbA1c and weight decreased. There were decreased complications of hypoglycemia and several-fold improvement in hyperglycemia during RF. The authors concluded that Muslims with diabetes were able to self-manage when fasting using tele-monitoring support and intervention, with decreased complications during Ramadan compared with pre-Ramadan.

Ramadan and smoking

Smoking is one of the personal habits which are not allowed while fasting during the day.^[1] Theoretically, Ramadan may therefore provide an opportunity to intervene in smokers who fast by promoting smoking reduction as an initial step to cessation. Many of the studies reported high smoking rates in Muslim communities. However, where available, data suggest that Muslim adults are the least likely to quit smoking compared to others. Opinions vary on the potential role for Ramadan as an opportunity to quit smoking or not. Two contrasting opinions are discussed below.^[95,96] Mughal and Kingstone^[95] reported that a Malay religiously sensitive behavioral smoking cessation intervention during Ramadan was effective in maintaining post-Ramadan smoking reduction. Such interventions have yet to be piloted within the United Kingdom. Community gatherings of fast opening, night prayers, and worship offer fasters who smoke ways of distraction and heighten internal strength to overcome cravings. In contrast, Alturki *et al.*^[96] presented a different approach. He suggested that healthcare professionals in primary care should ask briefly about smoking in fasting patients whom they consult. A short reminder of the opportunity to reduce smoking in Ramadan and adequate signposting to smoking cessation services and self-help guides, as well as advocating harm reduction techniques such as nicotine replacement therapy and e-cigarette use outside fasting times, may all help in facilitating smoking cessation in smokers during Ramadan and importantly post-Ramadan. Alturki, reminded the readers that the WHO Eastern Mediterranean Regional Office sometime in the past proposed “religiously inspired approach” to combat tobacco use. Alturki *et al.* examined two questions: (a) the need to identify the role Islamic beliefs and teachings plays in influencing individual motivation to quit smoking and (b) how best to gain support for public policies to reduce smoking. Ramadan and Hajj were taken as key points. These, it is argued, are times when Muslim religious motivation to abstain from smoking is strongest. Alturki *et al.* concluded that there is insufficient evidence base on which to adopt a religiously inspired approach. He argued that all of civil society, including religious Muslim authorities, should rather supplement the efforts of health professionals to encourage smoking cessation. He called for further research on developing culturally and religiously acceptable and feasible behavioral interventions to support smoking reduction and cessation BR, during Ramadan, and post-Ramadan.

History, music, and law

An interesting history of medicine tale was recalled recently.^[97] Opium addiction has been prevalent in Iran from the Safavid era (1501–1736). During this period, Hakim Imad al-Din Mahmud ibn-Mas’ud Shirazi (1515–1592 A.D) wrote one of the earliest books in the field of opium and addiction in history. In his book, he introduced two sustained release rectal (suppository) and oral (pill) dosage forms for Muslim addicts who fast in the month of Ramadan. He aimed to formulate them for these people so that they could keep fasting using the slow release drugs. In these formulations,

his innovation has important impacts in the history of both addiction and pharmaceutical sciences.^[97] Another interesting exploratory case study aimed to gain a better understanding of the experiences of tertiary-level woodwind players who practice, rehearse, and perform while fasting.^[98] Sixteen undergraduate woodwind players from two Malaysian university music faculties completed an 11-item questionnaire, as well as a 7-day food and playing diary, which formed the basis for a semi-structured interview. Their experiences were compared with previous studies of fasting athletes. Many participants stated that practicing from noon to 3:00 pm was difficult due to feeling thirsty, hungry, tired, and exhausted, with some experiencing a dry mouth and/or lips. By 3:00–6:00 pm, some had difficulty focusing and felt tired, dizzy, or lacked energy to practice. Many felt more comfortable playing after breaking the fast or after eating *Suhour*. The majority experienced positive impacts such as increased focus and efficiency while practicing. This study suggests that fasting woodwind players would benefit from practicing in the morning and after sunset, limiting their practice time in the afternoon, not skipping *Suhour*, and ensuring adequate hydration during sunset and sunrise. Finally, a novel discussion of the importance of addressing hypoglycemia during Ramadan, with specific reference to secular legal guidance on driving with diabetes in Europe and the United Kingdom was recently presented.^[99] They discussed religious rulings relating to fasting and driving in Islam. While there is no clear guidance or legal position on diabetes and driving for individuals who are fasting, Islamic law provides a logical framework to address this. They called upon healthcare professionals to raise and facilitate discussions on this often-overlooked topic with people with diabetes who are planning on fasting to minimize the potential for public harm. For some individuals, fasting perhaps should be avoided when driving and that this religiously compatible position would best be adopted when one is dependent on driving for livelihood. Ultimately, further research on glycemic control and management when fasting and driving, as well as a formal legal guidance on this topic, is required to safeguard healthcare professionals and the public from the potential risks from hypoglycemia-induced accidents.

Closing remarks

RF for the healthy adult is an article of faith that is not subject for much medical interest.^[1,2] However, we could still learn from studies in health how fasting may affect people in sickness or during certain stages of life such as the children, the elderly, or pregnancy or times of hardship such as traveling or adverse weather conditions with evidence rather than with consensus.^[2,100]

A narrative, nonsystematic review of the literature included all relevant full articles in English records found by search of records in the Scopus, PubMed, and Google Scholar databases. Impact of RF on diabetes control, pregnancy outcome and fetal life, sports and athletes' well-being received somewhat more prominent coverage by research work published in 2018. Renovascular disease, and risk factors, posttransplant care,

and some metabolic concerns in for patients with hepatic, renal, and metabolic conditions were covered too. Patterns of use of emergency services during Ramadan and features of some specific medical emergencies were examined by some workers. Most interesting perhaps was the greater focus on documenting the perception, attitudes, and practices of both patients and healthcare professions regarding deciding and acting during Ramadan. Isolated research reports addressed subjects of wide nature from body composition and energy metabolism to smoking, law, music, and history. Review of the literature revealed that in 2018, the research focused on diabetes, pregnancy, and athletes' well-being during sports and several professional competence and patients' perceptions and practices. The volume remains modest when the number of people involved is taken in consideration. Greater improvements in both quality and quantity of research on Ramadan are needed. The article should help both the busy clinicians; the starting researchers and even the established academic get a bird's eye view of research work productivity, changing perceptions and clinical practices relevant to fasting and feasting during Ramadan.

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Authors' contributions

All authors contributed to the conception of the study. SAB performed the literature searches and produced the initial draft. All authors developed further their assigned sections and reviewed the whole document for intellectual content. All authors contributed to the revision and finalization of this manuscript. They all approved the final version of the manuscript before submission.

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There are conflicts of interests.

Compliance with ethical principles

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