

Ramadan Fasting: Evidence or Expert Opinion? Results of Preliminary Studies

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ABSTRACT

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Each year, over a billion Muslims fast worldwide during the month of Ramadan. Through this religious practice, not only will one have spiritual growth, but can improve his/her diet, which is of pivotal importance in this month. Conversely, the available evidence regarding the health benefits of Ramadan fasting is scarce and highly contentious. Although Islam exempts patients from fasting, many of them fast conceivably and their clinical condition is prone to deteriorate. This is due to the persistent gap between current expert knowledge and conclusive, strong evidence regarding the pathophysiologic and metabolic alterations by fasting, and the consensus that healthcare professionals should reach, in order to manage various patient groups during this month. In this review, we summarize the results of our initial studies regarding the effects of Ramadan fasting on some clinical conditions including alterations of body composition. We also go through the important clinical results of patients who have had previous history of cardiovascular disease, type 2 diabetes, asthma and renal colic. Our studies have presented some evidence in favor of Ramadan fasting and encourage those with mentioned diseases to consult their physicians and follow medical and scientific recommendations. We attempt to present some relevant evidence clarify future scopes in this area of study, and provide suggestions for future investigations.

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Introduction

Ramadan is the ninth month in lunar Islamic year during which most adult Muslims fast worldwide, following a religious Islamic ritual, in an effort to achieve better spiritual reflection and to increase their devotion and sense of worship (1-2). This entitles refraining from food, drinks and smoking, as well as abstaining from participating in ill-natured or excessive

behaviors from sunrise (Sahar) to sunset (Iftar) (3-4). There is no restriction on the intake of food or fluids between Iftar and Sahar (5). Since the lunar calendar does not correspond to the Gregorian calendar, Ramadan moves back 11 days every year; therefore, the occurrence of Ramadan can vary from one season to another (6). Accordingly, the month of Ramadan covers a

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duration of 28 to 30 days, and the time from sunrise to sunset varies approximately between 10 and 20 hours, depending on the geographic location and the season in which Ramadan falls (1-2, 4, 7). Thus, this month provides valuable opportunity to investigate fasting.

Daily routines alter considerably during Ramadan (8), including changes in sleep-wake patterns and physical activities, as well as profound dietary alterations in eating schedules and the quality and amount of food and fluid ingestion (4, 9-10). As such, changes might be partly due the alterations in energy intake and dietary composition (8) with the common practice to consume more carbohydrates and fats (6, 11), mainly in the form of one large high caloric meal at sunset and one small low caloric meal just before sunrise (3). In some cultures, special festive foods that are richer in fat, protein and sugar may be consumed (12-13). Furthermore, it has been established that a given nutrient ingested at an unusual time can induce different metabolic effects (6).

These issues considerably affect the health and well-being of both patients and healthy individuals.

Generally, Ramadan fasting can't induce harmful effects on young healthy subjects (14); however, fasting is not meant to create excessive hardship. Hence, the Islamic practice exempts many people from fasting, including individuals with legitimate reasons (traveling, menstruation, pregnancy and breast feeding) who should compensate by fasting an equal number of days some other time (15), and also the sick individuals whose health conditions might be negatively affected by fasting (13). However, there is a lack of consensus on the definition of "the sick" (16), and little is known about metabolic and physiological changes and the safety of this practice during Ramadan fasting (4). Consequently, many Muslims do not consider themselves as "sick" and a large proportion of them fast without proper medical care that might result in various clinical complications (6, 16). These effects are extensively discussed in previous studies (8); however, the results lack conclusive evidence and the findings are still conflicting (4, 8). These mixed findings are, at least, partly due to variations in the daily fasting time, underlying

physical and demographic alterations, such as taking medications or smoking, heterogeneity in ethnic populations, and differences in dietary habits and cultural eating patterns (3-4, 8, 15). For example, the results of EPIDIAR multicenter international study of 12, 243 participants revealed that 79% of type 2 diabetic fasting patients fast during Ramadan; therefore, they are prone to hypo/ hyperglycemia (17). By contrast, Benaji and colleagues, in a review study, concluded that fasting does not affect glycemic control in well-controlled diabetic patients that regularly undertake glycemic control checks (14). On the other hand, the results of some studies indicated the significant effects of Ramadan fasting on the reduction of body fat and weight (18), whereas others reported no change (19-20) or increase (21) in body weight and composition during the same period. Interestingly, Bouguerra and colleagues reported that Ramadan fasting modifies glycemic control and lipoprotein levels in type 2 diabetic patients who had good metabolic control. On the other hand, these indices seemed to deteriorate in those with poor metabolic control (22).

Based on previous research, the available literature on the medical aspects of Ramadan fasting are scarce and inconclusive (9, 10, 20). Moreover, a large proportion of the classifications and recommendations are based on expert opinion rather than strong evidence, supported by scientific clinical studies (15, 23). Thus, we aimed to review our recent preliminary studies, carried out in Iran, to provide more conclusive data and enlighten the future scopes of Ramadan fasting in different patient populations for more extended investigations.

Medical aspects of Ramadan fasting and its effects on different diseases

Study 1 (24): Effects of Ramadan fasting on cardiovascular risk factors

This prospective observational study was carried out on 82 volunteers (38 males and 44 females) with at least one cardiovascular risk factor, including previous documented history of coronary artery disease (CAD), metabolic syndrome or cerebro-vascular disease in past 10 years. The volunteers were within the age range

of 29-70 years. Participants fasted for at least 10 days before the test, attended the metabolic unit, following at least 10 hours of fasting. Blood sample was obtained from all the patients. Lipid profile, plasma insulin, fasting blood sugar (FBS), homocysteine (Hcy), high-sensitivity C-reactive protein (hs-CRP), and complete blood count (CBC) were analyzed in all blood samples. Additionally, blood pressure and body mass index (BMI) were recorded for the participants. The results indicated a significant improvement in 10-year coronary heart disease risk. Also noteworthy was meaningful higher HDL-C, WBC, RBC and platelet count (PLT) in patients after Ramadan, whereas lower plasma cholesterol, triglycerides, LDL-C, VLDL-C, systolic blood pressure, BMI and waist circumference were recorded for them. Conversely, no difference was observed regarding changes in FBS, insulin, Homeostasis Model Assessment Insulin Resistance (HOMA-IR), Hcy, hs-CRP and diastolic blood pressure, before and after Ramadan.

To our knowledge, this study was the first to assess the effects of Ramadan fasting on patients with previous history of cardiovascular disease, based on Framingham risk score. Notwithstanding the restrictions of this single-center pilot study, the results demonstrated striking improvement in 10-year coronary heart disease risk score and other cardiovascular risk factors such as lipid profile, systolic blood pressure, BMI and waist circumference. Ramadan fasting signifies modifications in dietary habits and other lifestyle changes (24) that might contribute to reduction in resting heart rate (HR) and blood pressure (BP), an increase in HR diversity, and improvements in left ventricular functions, post-exercise recovery of both HR and BP, and flow-mediated vasodilation (4). Nevertheless, the available results are highly contentious. A reduction in cholesterol (25-26) and triglyceride levels (25, 27) during Ramadan fasting, and markers of cardiovascular and metabolic syndrome, following a 21-day Daniel fasting- a religious fasting tradition by Christians- has been reported in some studies (4). However, others reported no significant changes in cholesterol and triglycerides (28-29), and some even reported increased levels of cholesterol and triglyceride after Ramadan fasting (29). It should be noted that the majority of

previous studies regarding vascular events during Ramadan indicate that there is no increase in the rate of such events during Ramadan, either in patients with established vascular disease or in those with no previous history. Moreover, the annual period of fasting has no long-term effects on cardiovascular risks (30), these studies suffer from several confounding factors including restricted sample size, genetic diversity, daily activity alterations, heterogeneity in dietary patterns and food habits, diversity in the number of fasting days, period of daily fasting, and an increasing tendency to consume sweet foods and higher simple carbohydrates (4, 24) that might bias the presented data. Therefore, for these reasons controlled prospective trials are warranted to evaluate changes in cardiovascular disease risk factors during Ramadan fasting.

Study 2: Effects of Ramadan fasting on body composition and nutritional intake

This study was carried out on a random sample of 240 volunteers (158 males, 82 females) during Ramadan. Participants were recruited from six different districts of Mashhad by cluster sampling, and had fasted for at least 20 days. Anthropometric measurements including weight, height, waist, and hip circumferences were measured for all participants. Additionally, fat mass, fat-free mass, and the percentage of body fat were assessed by bioelectrical impedance. Measurements were taken two times, one week before and one after Ramadan. Energy and macronutrient intakes were assessed using a 3-day food frequency questionnaire on a sub-sample of subjects, before and during Ramadan. For the first time, in this study we have shown that Ramadan intermittent fasting resulted in weight loss and BMI reduction in almost all subjects, most strikingly in males ≤ 35 years ($P < 0.001$). Also noteworthy was that fat mass diminished in most subjects up to 4.3%, exempting females within the age range of 36-70 years. Hence, we observed that only young subjects and males lost body fat, whereas all subjects experienced a significant reduction in fat-free mass ($P < 0.001$).

Interestingly, the results of previous studies are highly debatable. Some of them revealed conflicting results regarding the variations of

age groups (31-32) and gender of participants (33), with studies that reported no significant change in the body composition, following a 21-day Daniel fasting (34). However, this remains to be investigated, since differences between sex and age may be the result of differences in nutrient oxidation, and changes in energy expenditure during the fasting period, as in former studies, this has been expressed to result in the reduction of diurnal energy expenditure (19) or absence of postprandial thermogenesis (35). Additionally, some arguments have been suggested for this phenomenon, such as the increased burden of meal preparation during Ramadan fasting for the female group (33), the increased rate of protein breakdown in relation to protein synthesis in the post absorptive state (36), and a decrease in protein consumption.

Since the effects of alterations in the body composition can be additive over long periods of fasting, which in turn contribute to diversity in the basal energy requirements, disregarding the dietary intake, and therefore more studies are required to determine the possible underlying responsible mechanisms such as variations in macronutrient oxidation.

Study 3: Effects of Ramadan fasting on asthmatic patients

In this prospective cohort pilot study, 29 well-controlled asthmatic patients (19 females and 10 males) with stable symptoms and pharmacotherapy, and the age range of 47 ± 12 years participated. The average duration of fasting was 26.5 days. Assessments of spirometric variables, daily peak expiratory flow, peak expiratory flow variability assessed by home peak expiratory flow monitoring, as well as clinical asthma symptoms including dyspnea, coughing, wheezing, and chest tightness were carried out. The results of this study not only showed no significant deterioration in the clinical symptoms of asthma including dyspnea, coughing, wheezing, and chest tightness, but also improvements in peak expiratory flow and variability were observed.

The results of previous studies by Siddiquie *et al* (37) and Berner *et al* (38) showed no significant changes in spirometric factors during Ramadan fasting in healthy and asthmatic patients, respectively. On the other hand, the results of studies by Subhan *et al* (39) and

Moosavi *et al* (40) indicated noticeable improvements in lung function of healthy subjects compared with pre-Ramadan baseline values. However, in contrast with these findings, a recent study demonstrated that there was an increase in the rate of emergency consultations for severe asthma exacerbations (41).

Our study was the first to examine the effect of Ramadan fasting on asthmatic patients, and our results declared that the effect of Ramadan fasting on the exacerbation of disease symptoms was not remarkable. One suggested mechanism to this phenomenon is the reduction in the proportion of released cytokines and mediators such as interleukin-6, TNF alpha, eotaxin, and the decline of anti-inflammatory adipokines, following the weight loss in obese subjects during Ramadan that conceivably reduces the air way inflammation.

However, the available literature regarding the effects of fasting on asthmatic patients is scarce and therefore, warrants more relevant data from large-controlled trials with regular spirometric measurements throughout Ramadan.

Study 4: Effects of Ramadan fasting on glycemic control in diabetic patients

This prospective cohort clinical trial on 88 patients with type 2 diabetes (45 males and 43 females, aged 51 ± 10 yrs), who opted to fast for at least 10 days during Ramadan, were recruited to evaluate the association between Ramadan fasting and glycemic control. Fasting blood samples were collected at the beginning and end of Ramadan, and also one month after Ramadan, to assess fasting blood glucose (FBG), fasting insulin, full blood count, glycated hemoglobin (HbA_{1c}) and fasting lipid profile. Insulin resistance was estimated, using the homeostatic model assessment. Anthropometrics and blood pressure were also measured. Data analysis showed a significant deterioration in FBG and HbA_{1c} ($P=0.002$ and $P \leq 0.001$, respectively), and substantial improvements in HDL-C, LDL-C and BMI after Ramadan ($P < 0.001$). One month after Ramadan, HbA_{1c} levels reduced by approximately 1% ($P < 0.001$). In this study, we showed that regardless of the small positive effects of Ramadan fasting on weight loss and lipid profile, it deteriorated the glycemic control in type 2 diabetic patients, which was more evident in patients using oral hypoglycemic medication

compared to diet-controlled patients. This might be related to the consumption of large proportions of food, especially high-carbohydrate foods in a short period of time. Also the diversity in dose and timing of taking oral hypoglycemic drugs (OHD), which potentially deteriorate the clinical condition of patients on OHDs, was worthwhile, as it was manifested by a study by Bouguerra *et al* (42). However, it should be emphasized that M'guil and colleagues (43), in a study on Moroccan patients showed that pre-Ramadan education, controlled dietary menu and re-scheduled OHD prescription, motivated patients with type 2 diabetes and controlled their glucose during Ramadan fasting, while some researchers indicated a good glycemic control during this month in fasting patients with type 2 diabetes, without any special pre-managements (23). Most recently, Peeters and colleagues in an observational study on Turkish migrants with diabetes, revealed that only slightly more than half (57%) of the fasting patients received recommendations regarding fasting and diabetes from their healthcare providers; hence, this finding suggests that health workers should pay more attention to raising the awareness of their Muslim diabetic patients about their dietary intake and medication use during Ramadan (44).

Fasting during Ramadan is associated with several risks which are greatly varied, such as , hypoglycemia, dehydration, hyperglycemia and diabetic ketoacidosis (16). Hence, fasting should be prohibited in all poorly-controlled and brittle type I diabetics, those who are not compliant with going on a diet, taking drugs and exercise advice, and those with poorly-controlled type II diabetes (30). As such, close monitoring and educational programs such as nutritional advice, exercise education, monitoring of glycemia and medication usage is highly mandatory for patients who are allowed to fast, especially in the matter of suggesting individualized oral hypoglycemic agents according to patients' specific circumstances (16).

Furthermore, In a recent trial by Al-Sifri *et al* (45), switching treatment to a sitagliptin-based regimen decreased the risk of hypoglycaemia, compared with remaining on a sulphonylurea-based regimen in fasting patients with type 2 diabetes. Additionally, the incidence of hypo-

glycaemia was lower with gliclazide, relative to the other sulphonylurea agents, and similar to that observed with sitagliptin. Both treatment regimens were generally well tolerated during the month of Ramadan.

In future investigations, performing continuous blood glucose monitoring on diurnal changes in blood glucose, considering short-term markers of glycemic control such as fructosamine, and treatment with certain anti-hyperglycaemic agents to assess the incidence of hypoglycaemia is encouraged to obtain more relevant data in patients with type 2 diabetes.

Study 5: Effects of Ramadan fasting on glycemic control in renal colic patients

This was a prospective observational study, carried out to compare the referrals to emergency wards due to symptoms of renal colic in fasting patients with previous history of renal colic in different stages. The study was divided into four intervals: two weeks prior to Ramadan (stage-1), during the first two weeks (stage-2), last two weeks of Ramadan (stage-3), and two weeks after Ramadan (stage-4). In this study, 610 subjects, with a male majority (72.3%), were admitted with renal colic during the four periods of study. We found a significantly higher proportion of admissions in fasting patients with renal colic during the first two weeks of Ramadan compared with the other periods ($P<0.05$). Nonetheless, the number of admissions followed a downward trend from the last two weeks until two weeks after Ramadan. One potential hypothesis for this finding might be the striking variations in the dietary habits and mundane lifestyles, particularly during the early days of fasting which might contribute to an increase in the onset of renal colic. Furthermore, what seems quite eminent is the importance of measurement and controlling the effects of environmental factors, such as humidity and temperature in different seasons in which Ramadan falls, as hot and humid climates have been shown to exacerbate the occurrence of renal colic in former studies (46-48).

Overall summary and conclusion

Our current preliminary observational studies showed beneficial effects of Ramadan fasting,

such as improvements in 10 years coronary heart disease risk score and other cardiovascular risk factors such as BMI and waist circumference in patients with a previous history of CVD after fasting during Ramadan. Additionally, Some of our results raised concerns for more attention to the management of glycaemic control in patients with type 2 diabetes, and to consider implementations to preserve the fat-free mass and improve alterations in body composition of healthy subjects.

This review sheds light on the potential different merits of Ramadan fasting as forms of dietary modification. It is our hope that the information provided within this review will initiate the design, and performance of future investigations focused on the health benefits of Ramadan fasting for healthcare providers.

Furthermore, different confounding variables such as variability in daily fasting time, differences in ethnicity and demographics of the participants, their smoking status, medication, cultural virtues and the diversity in dietary habits in these studies have made it difficult to make definitive conclusions about the safety of fasting for specific patient groups. For instance, the diversity of dietary habits, as mentioned before, led to the increase of energy intake of Saudi Muslims and the decrease in Indian Muslims during Ramadan; these discrepant findings are believed to be due to the differences in food choices between the groups (4). Hence, current information regarding the effects of Ramadan fasting on human health are heterogeneous findings based on expert opinions, rather than conclusive evidence, with subjects' variant dietary habits being the major cause of mixed findings.

Collectively, little consensus exists regarding the effects of Ramadan fasting on the majority of health-related outcomes. Therefore, making comparisons between available literature is not relevant, due to several underlying confounding variables. In future research attempts should be made to eliminate or minimize the effects of several confounders, as only through careful control within the research design will reliable results pertaining to the health effects of Ramadan fasting be obtained. High-quality prospective randomized controlled trials are

encouraged to support and modify expert evidence with indigenous and international conclusive evidence-based clinical practice for various fasting patients.

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