

RESEARCH IN ISLAMIC FASTING AND HEALTH

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Fasting during *Ramadan* is a religious duty for all healthy adult Muslims. *Ramadan* is the ninth month of the Islamic lunar calendar. Many of the world's great religions recommend a period of fasting or abstinence. The Islamic fast during the month of *Ramadan* during which a whole month is dedicated to fasting is particular to Islam, and is strictly observed by millions of Muslims worldwide. Since more than a billion people worldwide follow Islam, it is assumed that hundreds of millions of people observe the *Ramadan* fasting each year. The experience of fasting teaches Muslims self-discipline and self-restraint, and reminds them of the feelings of the impoverished. Fasting is not obligatory for children. Menstruating women as well as sick and travelling people are excused, and pregnant and lactating women are permitted to postpone the fasting during *Ramadan*, however, they should fast during another month of the year, when they have no reason for exemption.^{1,2}

During *Ramadan*, the majority of Muslims have two good-sized meals; one immediately after sunset and the other just before dawn. They are allowed to eat and drink between sunset and dawn but not after dawn. Since the Islamic calendar derives from a lunar cycle, the Islamic year contains 354 days. Therefore, the *Ramadan* month occurs 11 days earlier every year, and may occur in any of the four seasons, making the length of fasting hours variable from 11 to 18 hours in tropical countries. The month of *Ramadan* is either 29 or 30 days.

From the physiological standpoint, Islamic fasting provides a unique model of fasting. It is distinct from regular voluntary or experimental fasting by the fact that the observant of the fast does not drink during fasting hours. In addition, *Ramadan* fasting is not just disciplining the body to restrain from eating and drinking. The eyes, ears, tongue, and indeed the whole body, are equally obligated to be restrained. Therefore, one may assume that physiological changes occurring during Islamic fasting would be different from those noted during an experimental fast. This review discusses the findings of research conducted on various aspects of *Ramadan* fasting and its

impact on some disease processes. A comparison with the effects of experimental fasting is attempted whenever possible. The author conducted a *Medline* search, reviewed local journals in some of the Islamic countries, as well as some research findings from two international congresses on health and *Ramadan*.^{3,4}

Impact of *Ramadan* Fasting on Metabolism

Carbohydrate Metabolism

The effects of experimental short-term fasting on carbohydrate metabolism have been reviewed extensively.^{5,6} The post-absorptive period of fasting is defined as 8 to 16 hours after eating, a period of very early adaptation to starvation. The primary metabolic priority of this period is the provision of adequate glucose for the cells of the brain, red blood cells, peripheral nerves and renal medulla. A slight decrease in serum glucose to around 3.3-3.9 mmol/L (60-70 mg/d L) occurs a few hours after fasting in normal adults. However, the fall in serum glucose will cease due to a breakdown of glycogen and increased gluconeogenesis, as well as a decrease in both glycogen synthesis and glycolysis in the liver. These changes occur because of a fall in insulin and a rise in glucagon and sympathetic activity.⁵

In the early stage of the post-absorptive period, the fall in glucose is associated with depletion of glycogen stores of the liver. However, these stores are not limitless. There are only 1200 calories stored as carbohydrate in the liver and muscle glycogen, and skeletal muscle cells lack glucose-6 phosphatase and do not release glucose from stored glycogen directly into the circulation. Eventually, after about 24 hours of starvation, the glycogen stores become depleted and the only source of glucose remains to be gluconeogenesis.^{5,6} The substrates for gluconeogenesis are lactate (and pyruvate), glycerol and amino acids. Cortisol is the principal stimulus for the catabolism of muscle protein. These mechanisms will provide the daily glucose needs of the CNS (100-125 g) and RBC (45-50 g). Meanwhile, the decrease in circulating insulin and rise in catecholamine concentrations results in lipolysis in adipose tissue and a rise in the level of free fatty acids, which are then used as a fuel instead of glucose by other tissues of the body.⁶

Only a few studies have shown the effect of *Ramadan* fasting on serum glucose. One study showed a slight decrease in serum glucose in the first days of *Ramadan*,

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followed by normalization by the 20th day, and a slight rise by the 29th day.⁷ The lowest serum glucose level in this study was 63 mg/dL. Other studies have shown a mild increase^{8,9} or variation in serum glucose concentration.^{10,11} From these studies, one may assume that during fasting days which follow a rather large meal taken before dawn (*Sahur*), the stores of glycogen, along with some degrees of gluconeogenesis, maintain serum glucose within normal limits. However, slight changes in serum glucose may occur individually according to food habits and individual differences in mechanisms involved in metabolism and energy regulation.

Lipid Metabolism

Studies on the effect of *Ramadan* fasting on blood lipids have produced variable results. Serum cholesterol may decrease in the first days of fasting¹² and rise to pre-fasting values.^{12,13} Some studies¹⁴⁻¹⁶ have reported raised concentrations of cholesterol, which may be related to weight loss during *Ramadan* fasting. However, others have found no change,^{17,18} or only decreased levels of cholesterol during fasting.^{2,9,17-19} Recent evidence that a marked increase in plasma HDL cholesterol occurs after *Ramadan* fasting is promising.¹⁷⁻¹⁹ Increase in *Ramadan* and post-*Ramadan* Apo A-I concentrations in both normals and diabetics, with falls in Apo B levels have been reported.^{20,21} In all, changes in blood lipids seem to be variable and depend probably on the quality and quantity of food consumption and the degree of weight changes. These changes may also be related to consuming a large meal, as it has been shown that lipids increase in individuals taking one large meal every day,²² although, this was not confirmed in one study during fasting at *Ramadan*.¹⁸

Diabetes

There are no major problems encountered with type 2 diabetes and even controlled type 1 patients during *Ramadan* fasting.²³⁻²⁶ Most patients show no change in their glucose control. In some patients, serum glucose concentration may fall or rise, which may be due to the amount or type of food consumed, changes in body weight and exercise habits, regularity of taking medications, or engorging after the fast is broken. In most studies, HbA 1c values show little or no changes during *Ramadan*.²³⁻²⁹ The amount of fructosamine, insulin and C-peptide has been reported to have no significant change before and during *Ramadan* fasting.^{23,27,28}

Serum creatinine, uric acid, blood urea nitrogen, protein, albumin, alanine amino-transferase, and aspartate amino-transferase values do not show significant changes during the fasting period.^{27,30} The amount of energy (calorie) intake have been reported in some of the literature, indicating a decrease in energy intake. Most patients with diabetes type 2 and diabetes type 1 show no change or slight decrease in concentration of total cholesterol and

triglyceride.^{26,29} However, increase in total cholesterol levels during *Ramadan* seldom occurs.^{27,31}

It is recommended that the following patients should be advised against fasting: all brittle type 1 and poorly controlled type 1 diabetic patients; diabetic patients known to be non-compliant; those with serious complications such as unstable angina; patients with a history of diabetic ketoacidosis; pregnant diabetic patients; elderly patient with any degree of alertness problem; and patients with episodes of hypoglycemia and/or hyperglycemia during *Ramadan*.³²⁻³⁴ During *Ramadan* fasting, diabetics should avoid excessive gorging and should continue their usual exercise especially during non-fasting periods.³³ Many physicians recommend that type 1 patients should not fast. However, in mild forms of IDDM when the patient insists on observing the fast, it is feasible to give one dose of intermediate-acting insulin before *Sahur*, and if needed, another one before breaking fast (*Fatur*, *Iftar*). Glycemic control may improve and hypoglycemia reduced by using insulin lispro.³⁵ In patients with type 2 diabetes, the dose of short-acting sulfonylurea should be reduced to half during *Ramadan*, and given as either a single dose before *Iftar* or two doses before *Sahur* and *Iftar*.^{33,34} The authors of the largest series of patients treated with glibenclamide during *Ramadan* recommend to switch the morning dose (together with any mid-day dose) of this drug with that taken at sunset.²⁴

The Heart

Although bradycardia and hypotension may occur during prolonged fasting,³⁵ heart rate and blood pressure remain normal during the first few days of fasting. Changes in the electrocardiogram, including decreased altitude of QRS complex and T-wave and right axis deviation seen in prolonged fasting, are not seen in short fasts.³⁷ There seems to be no contraindication to observe fasting in patients with valvular problems or subjects with mild coronary artery disease. It is not known if mild dehydration and hemoconcentration may harm those with moderate to severe coronary artery disease. However, one study has speculated that *Ramadan* fasting does not increase acute coronary artery disease events.³⁸

The Lung

It has been shown that *Ramadan* fast does not exert a significant effect on pulmonary volume functions in healthy individuals.³⁹ Dehydration and dryness of respiratory tract mucosa may worsen bronchoconstriction in asthmatic patients. However, some workers have allowed asthmatic patients whose disease is stable to fast while using inhalers, slow-release drugs, and suppositories.⁴⁰

Gastrointestinal Tract

In experimental fasting, there is a fall in gastric secretion. Gastrointestinal tract movements occur every two

hours.⁴¹ It starts from the stomach and moves towards the duodenum, jejunum and ileum, evacuating all food debris, desquamated cells and GI secretions. The gallbladder empties less frequently than in the fed state, one to three times every 4 hours.⁴² GI function during *Ramadan* remains to be investigated.

Although complications of ulcers in fasting patients have been reported,⁴³ another study using proton pump inhibitor has found that patients with duodenal ulcer have equal rate of healing and no complications with or without fasting.⁴⁴ Therefore, patients with complicated peptic ulcer may be advised against fasting. However, asymptomatic patients may try fasting, and take cimetidine or ranitidine, or a small dose of proton pump inhibitors at *Iftar* and *Sahur*, if hyperacidity remains a problem. Since intestinal contractility decreases during fasting to approximately once every two hours,⁴¹ fasting may benefit patients with spastic colitis and some other intestinal motility disorders.

The Liver

A rise in serum bilirubin after 10 days of *Ramadan* fasting has been reported,⁷ however, another study from Riyadh did not show a similar result.¹² In experimental fasting, an increase in indirect bilirubin occurs 15 hours after fasting.^{45,46} Refeeding with a normal meal or carbohydrates only, but not with protein or fat diets, returns bilirubin concentration to normal values. In our observation, mean bilirubin was increased on days 10, 20 and 29 of *Ramadan*, however, the peak increase was on the 10th day, when blood glucose levels were the lowest. The fall in bilirubin observed in the last one-third of *Ramadan* was coincident with some rise in blood glucose concentration.⁷ This result may suggest that bilirubin concentrations during fasting may somehow be related to carbohydrate metabolism. No significant changes in serum SGOT, SGPT, protein and albumin concentrations occurred during *Ramadan*.^{7,12}

The Kidney

During *Ramadan*, urinary volume, osmolality pH, nitrogen, solute and electrolyte excretion remain normal.⁴⁷ Changes in serum urea and creatinine are usually small and not statistically significant.^{12,48} In prolonged fasting, serum uric acid increases to abnormal values.⁴⁹ This is probably due to decreases in glomerular filtration rate (GFR) and uric acid clearance. In Islamic fasting, however, there is only a slight increase in uric acid,^{12,50} due to the nature of fasting which is short-lasting and intermittent.

Ramadan fasting does not cause significant alterations in serum sodium and potassium.¹² In experimental prolonged fasting, urinary excretion of 25 meq potassium per day has been seen, however, serum potassium remains normal.⁵¹

Patients with chronic renal failure should be advised about the potential of having hyperkalemia, and if they

insist on fasting, their renal function and electrolytes should be monitored and they should stop fasting if any deterioration occurs.⁵² Subjects on hemodialysis may experience a rise in serum potassium, body weight and fluid overload between dialysis sessions, due to increased food consumption at night.⁵³ Renal transplant recipients on immunosuppressive therapy who have normal allograft function experience no harmful effects from fasting and their renal concentrating ability remains unchanged.⁵⁴ A study in frequency of urinary stone throughout the year in Saudi Arabia did not find significant increase in relation to *Ramadan* fasting.⁵⁵

Hematological Profile

No significant changes in hemoglobin, red blood cell indices, white blood cell count or the sedimentation rate have been noted.^{7,12} Decreased serum iron levels and total iron-binding capacity have been reported,¹² indicating that iron stores are not significantly disturbed.

Neuropsychiatric Function

No alteration in EEG has been reported, even in prolonged starvation.⁵⁶ One report has found that significantly fewer parasuicides occur during *Ramadan* in Jordan.⁵⁷ In experimental fasting, appetite is decreased after 1 to 4 days of fast,^{36,58} probably due to ketosis. Beta-endorphin may also play a role in diminishing appetite during fasting.⁵⁷ Significant decrease in the meal frequency occurs during *Ramadan* as compared to control period. Chronotype as evaluated by the Horn and Ostberg scale was changed significantly during *Ramadan*: an increase in the evening type and a decrease in the morning type of subjects was observed. Daytime sleepiness as evaluated by the Epworth Sleepiness Scale was significantly increased.⁶⁰ Oral temperature, subjective alertness and mood are decreased during daytime and increased at 23.00 h during *Ramadan* fasting.⁶¹ The stress encountered during this fasting period, as depicted in the platelet aggregation responses, is less than that encountered on an ordinary nonfasting day.⁶² Headaches were reported by 41% of the 91 persons who had fasted, as compared to 8% of those who did not fast. The headache was of the tension type in 78% of the cases. Headache frequency increased with the duration of fasting and affected mainly those prone to headaches, and the most important exogenous-associated factor was caffeine withdrawal.⁶³

Changes in Body Weight

Weight loss ranging from 1.7-3.8 kg has been reported in normal weight individuals after fasting in the month of *Ramadan*.^{7,64-66} In one study that was over-represented by females, no change in body weight was seen.¹⁵ It has also been reported that overweight subjects lose more weight than normal or underweight subjects.⁶⁶

Endocrine Glands

We have reported that no significant alterations in serum concentrations of T4, T3, TSH, and TSH response to intravenous injection of TRH occurs in males during *Ramadan*.⁵⁰ In women, total serum T4 and T3 may decrease in the last days of *Ramadan*; however, the fall is mainly due to TBG alterations, as free thyroid indices remain unchanged.^{66,67} A small but significant increase in serum T4 in the last days of *Ramadan* has been reported by some authors,¹⁴ but not substantiated by others.^{50,64,66-68} In experimental fast lasting more than 48 hours, many investigators have reported a fall in serum T3, along with a rise in serum rT3,⁶⁹⁻⁷¹ resulting from inactivation of 5'-monodeiodinase and decreased conversion of T4 to T3. TSH response to TRH has been reported to be decreased or unaltered. Refeeding with carbohydrates but not protein or fat causes an increase in serum T3.⁶⁹

In Islamic fasting, the length of fasting is not enough to cause any alteration in the pituitary-thyroid axis or peripheral conversion of T4. In prolonged fasting, serum testosterone and FSH may be unchanged⁷² or decreased.⁷³ Serum LH concentration and its response to GnRH injection remains unchanged, but FSH response to GnRH may be attenuated.⁷³ Serum prolactin is normal and its response to TRH injection may remain normal or diminished.⁷⁴ In Islamic fasting, no alterations in serum concentrations of testosterone, FSH, LH and prolactin and prolactin response to TRH has been detected in normal males.⁷³ Our unpublished observation showed no change in serum concentration of PTH during *Ramadan*. Mean serum concentrations of calcium may decrease slightly 10 day after the beginning of fasting, however, no subnormal values can be seen.⁷ In the last half of *Ramadan*, serum calcium remains normal, however, it may be slightly increased, as compared to pre-*Ramadan* values.^{7,12} Serum phosphorus does not change in *Ramadan*.^{7,8} In prolonged experimental fasting, normal serum phosphorus, normal or decreased serum calcium and increased urinary excretion of calcium and phosphorus, have been reported.^{5,6}

The shift in cortisol rhythm has been reported during *Ramadan*.⁷⁵ In a detailed study of *Ramadan* fasting subjects; the nocturnal peak of melatonin was diminished and delayed; there was a shift in the onset of cortisol and testosterone secretion; the evening peak of prolactin was enhanced; FSH and GH rhythmic patterns were affected little or not at all by the fasting, and only the serum TSH rhythm was blunted.⁷⁶

Pregnancy and Lactation

Acute starvation in pregnant women results in decreased blood glucose, however, after 20 hours of fasting, blood glucose remains within normal range, above 2.8 mmol/L (50 mg/dL).⁷⁷ Animal experiments also connote that even in long-term starvation, fetal energy is provided via compensatory mechanisms.⁷⁸ The outcome of pregnancy in

Gambian women who fasted during *Ramadan* was not satisfactory; however, no control group was employed.⁷⁹ A significant fall in glucose, insulin, lactate and carnitine and a rise in triglycerides and hydroxybutyrate was reported at the end of the fasting day in pregnant women,⁸⁰ however, the outcome of pregnancy was comparable to those who did not fast. *Ramadan* fast did not affect the birth weights of over 13,300 babies at delivery.⁸¹ Lactating mothers who fast may lose their body water and show changes in plasma osmolality, Na, and uric acid, and in lactose, sodium, and potassium content of the breast milk.⁸² The above-mentioned studies, along with the hypothesis that starvation of pregnant women may cause some alterations in later life,⁸³ indicate that until further studies are undertaken, pregnant women should avoid fasting in *Ramadan*.

Use of Medications during *Ramadan*

The administration of necessary medications via parenteral routes (IV or IM) or as suppositories and inhalers are allowed by some scholars during fasting. However, taking oral medications is not allowed,⁸⁴ and if there is no other alternative route for medications, the patient is exempted from fasting. The following guidelines are recommended:

1. Patients who must take their medications more than twice in 24 hours, should avoid fasting. Others may take their drugs at *Iftar* or *Sahur* (or both).
2. If possible, physicians should make every attempt to prescribe long-acting or slow-release drugs once or twice at night, and allow the patient to observe fasting.
3. Patients with epilepsy may experience convulsions if only 100 mg phenytoin is used at night,⁸⁵ however, one could control epilepsy with a single dose of 300 mg phenytoin daily,⁸⁶ allowing the epileptic patient to fast during *Ramadan*.⁸⁷
4. Elderly patients and those with underlying renal disease who take non-steroidal anti-inflammatory drugs should have frequent monitoring of renal function, since fasting may increase serum urea and sodium levels in such individuals.⁸⁸
5. Long-acting oral anticoagulant medications could be employed as a single night-time dose without affecting the incidence of thromboembolic events or hemorrhagic complications.⁸⁹

As perhaps 400 million people fast each year during the month of *Ramadan*, further scientific research on the medical aspects of the *Ramadan* fast on health and disease is needed. Physicians practicing in Muslim countries and those caring for Muslims in various parts of the world should be aware of the physiological alterations during *Ramadan*, the effect of Islamic fasting on various disease conditions and pharmacodynamics of different medications during the *Ramadan* fast.

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