

Physiology of Ramadan Fasting

Shokoufeh Bonakdaran*

Endocrine Research Center, Faculty of Medicine, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

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ABSTRACT

Considering the emphasis of Islam on the importance of fasting, Muslims attempt to fast from dawn until sunset during the holy month of Ramadan. Fasting is associated with several benefits for normal and healthy individuals. However, it could pose high risks to the health of diabetic patients due to certain physiological changes. This study aimed to compare the physiological changes associated with fasting in healthy individuals and diabetic patients during Ramadan. Furthermore, we reviewed the domestic articles published in this regard.

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Under normal circumstances, the primary compensatory mechanism in the feeding mode state (after eating) in response to high glycemic load is the increased level of insulin secreted by pancreatic beta cells. Elevated insulin level stimulates glucose storage in the liver and muscles in the form of glycogen. On the other hand, insulin inhibits gluconeogenesis and ketogenesis and preserves blood glucose at a normal level after eating. However, this process occurs in a reverse manner while fasting.

The initial defense mechanism in response to decreased glucose level is the reduction of insulin, which lowers the storage and peripheral uptake of glucose. If this mechanism is accompanied with longer durations of fasting, the processes of glycogenolysis-gluconeogenesis and ketogenesis are stimulated, causing the body to control the induced hypoglycemia (Figure 1).

The glycogen stored in the liver serves as an adequate source to supply the necessary glucose for approximately 12 hours in the fasting state. After this period, due to glycogen depletion, levels of fatty acids released from lipid cells are elevated, and these fatty acids participate in the process of gluconeogenesis.

Furthermore, these fatty acids increase the

level of ketone bodies, which are considered the alternative body fuel reserves in numerous cells. The remaining glucose is preserved for the metabolism of brain cells and erythrocytes, which perform by using the stored glucose.

Transition from the feeding state to fasting state encompasses several stages. In the postabsorptive stage (first few hours of fasting), 85% of glucose is supplied by the liver. In addition, 50-66% of the glucose in this state is produced through glycogenolysis, while the rest of the required glucose is provided through gluconeogenesis. After 48 hours, approximately 80% of the glucose is produced through gluconeogenesis, and 72 hours after fasting, gluconeogenesis becomes the only source of glucose supplementation.

In the holy month of Ramadan, duration of fasting is more than 12 hours per day in most of the regions and months of the year. Therefore, lack of sufficient stored glycogen around sunset (Iftar) stimulates ketogenesis. Comparison of the defense mechanisms within the early hours of fasting and after 12 hours of fasting is presented in Figure 2.

Reduced insulin level enhances glycogenolysis and prevents hypoglycemia. Moreover, this

* *Corresponding author:* Shokoufeh Bonakdaran, Endocrine Research Center, Faculty of Medicine, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran. Email: bonakdaransh@mums.ac.ir

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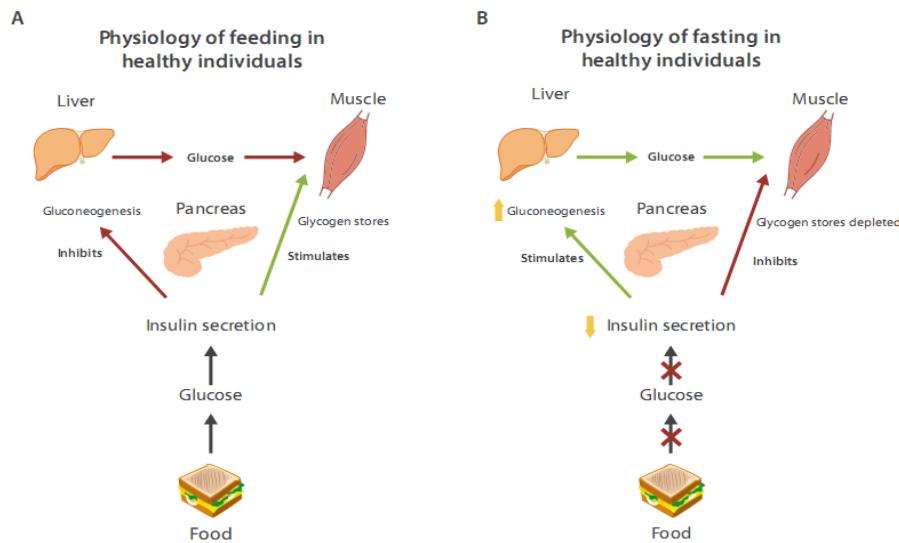


Figure 1. Normal physiology of feeding and fasting



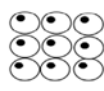
	Post absorptive period	Early starvation
Liver 	<i>Production of glucose by glycogenolysis</i> 5 g / h <i>Production of ketone bodies</i> 1 g / h	<i>Production of glucose by gluconeogenesis</i> 2 g / h 3 g / h
Muscle 	<i>Amino acid release</i>	
	1.5 g / h	2.5 g / h
Adipose tissue 	<i>Fatty acid release</i>	
	7 g / h	14 g / h

Figure 2. Transition phase in fasting state from post absorptive period to early starvation

process is followed by elevated levels of glucagon, growth hormone, and catecholamines, which are involved in the stimulation of gluconeogenesis and ketogenesis.

Evidence suggests that glucose level slightly drops at the time of Iftar in healthy fasting individuals and is maintained at 60-70. It is noteworthy that changes in the level of glucose depend on individual dietary habits and differences in metabolism.

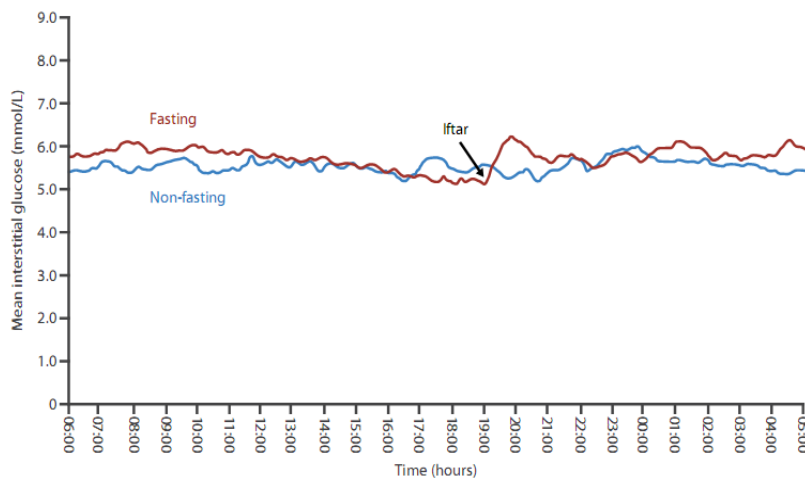
Evaluation of the changes of blood glucose in a healthy fasting individual during and before Ramadan is shown in Figure 3. As depicted in this figure, no significant difference is observed in the normal blood glucose of the healthy individual, which has been estimated using the continuous glucose monitoring system (CGMS),

before and after Ramadan.

This physiology is different in diabetic patients due to the pathophysiology of diabetes (i.e., insufficient insulin level in type I diabetes and insulin resistance in type II diabetes), as well as the type of medications used by these patients.

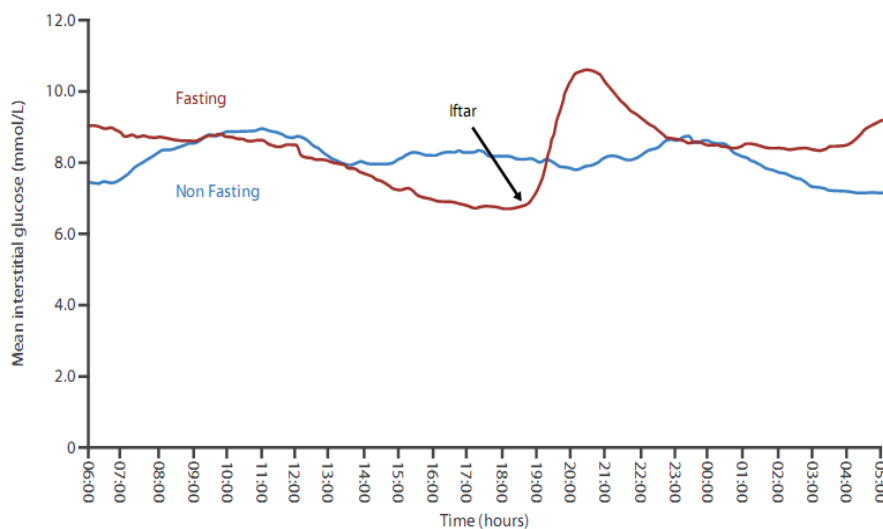
In diabetic patients, glycogenolysis accelerates due to insulin absence or resistance, and gluconeogenesis and ketogenesis are enhanced as well. Moreover, in the fasting state, decreased level of blood glucose in diabetic patients defense mechanism against hypoglycemia, which is induced by low glucagon level.

According to the literature, diabetic patients with autonomic neuropathy are likely to lose this defense mechanism due to decreased



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Figure 3. Mean continuous glucose monitoring (CGM) profiles of healthy subjects before and during Ramadan (remarkable stability of blood glucose during fasting hours, followed by a minimal rise in blood glucose at Iftar)



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Figure 4. Mean continuous glucose monitoring (CGM) profiles of diabetic patients before and during Ramadan (a rapid rise in blood glucose at Iftar)

catecholamine levels (1). Considering this physiological change, it seems that risk of hyperglycemia and hypoglycemia in the fasting state is higher in diabetic patients if they experience no changes in their drug and dietary regimen.

Changes in the blood glucose level of a diabetic patient as evaluated before and during Ramadan are shown in Figure 4. As depicted in this figure, changes in the blood glucose levels of diabetic patients are higher compared to healthy individuals. In addition, a significant reduction is

observed in the blood glucose before the meal at Iftar, followed by a sudden increase after this time.

Conflicting results have been proposed by previous studies conducted to assess blood glucose changes in fasting diabetic patients. Correspondingly, it seems that if diabetic patients with good conditions start fasting, no significant difference is observed in the blood glucose level of the majority of cases.

With respect to glycemic control in fasting individuals, previous studies have proposed

conflicting results; while some findings are indicative of the improvement of glycemic control during Ramadan, others denote the disturbed glycemic control in fasting individuals. Furthermore, levels of glycosylated hemoglobin during Ramadan have been reported differently in various studies; most of the findings in this regard have been indicative of no significant changes in the level of glycosylated hemoglobin, while only a few studies have denoted an increase in the level of glycosylated hemoglobin.

In the Epidemiology of Diabetes and Ramadan (EPIDIAR), which has been the largest study on fasting diabetic patients, it was reported that fasting in patients with type 1 diabetes significantly increased the risk of severe hypoglycemia (7.4 times) and hyperglycemia (3.2 times). Similarly, fasting in type 2 diabetic patients significantly increased the risk of severe hypoglycemia (7.5 times) and hyperglycemia (5 times) (2).

Considering the inconsistencies in the findings of the mentioned study regarding the effects of fasting on diabetic patients, we mostly reviewed local studies to investigate this issue. In a research by Yarahmadi et al. (3) conducted on 57 diabetic patients willing to fast, biochemical and clinical parameters of the subjects before Ramadan were compared with those performed on days 14 and 28 of the month. The results were indicative of no significant differences between the subjects in terms of blood pressure, fasting blood glucose, and fructosamine before and during Ramadan.

Moreover, it was reported that the body mass index of female participants increased, while it decreased in male subjects, and a significant reduction was observed in the insulin resistance of the subjects. Therefore, the researchers concluded that fasting leads to no significant changes in the glycemic control of diabetic individuals with proper modification of drug and dietary regimen.

In another study by Norouzi et al., (4) 88 diabetic patients with voluntary fasting during Ramadan were evaluated. Before and after Ramadan and one month after Ramadan, different tests were carried out to measure fasting blood glucose, glycosylated hemoglobin, and lipid profile. According to the findings, fasting deteriorated blood glucose and

glycosylated hemoglobin levels in diabetic patients, which was followed by the reduction of glycosylated hemoglobin one month after Ramadan.

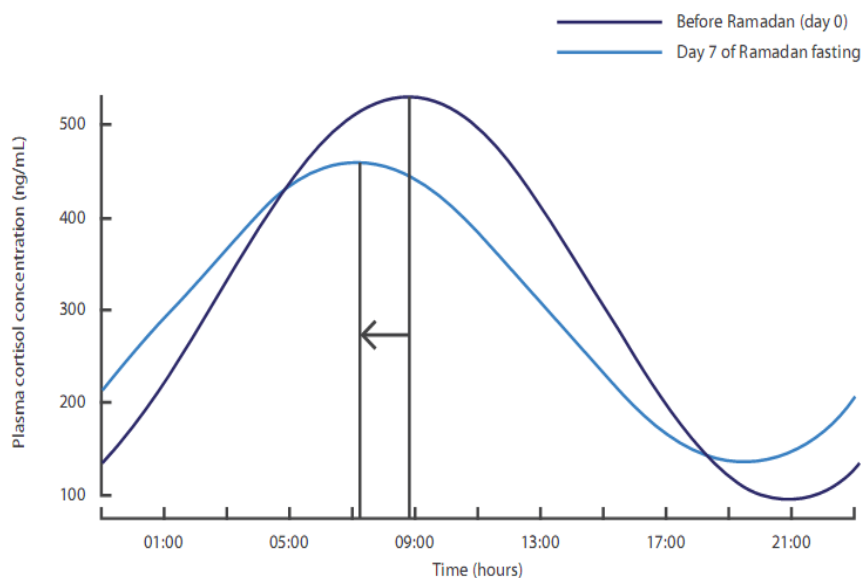
Authors of this paper conducted another study on 17 patients with type II diabetes at the Endocrine Research Center of Mashhad, Iran (5). Based on the guidelines of the American Diabetes Association (ADA), selected patients were classified as low- or medium-risk for fasting. All the patients underwent CGMS monitoring before Ramadan and were evaluated again in the second half of this month.

According to the findings, even well-controlled patients for fasting experienced fluctuations suggestive of hypoglycemia and hyperglycemia without clinical signs and symptoms before Ramadan. In the mentioned study, patients presented with an average of 1,047 minutes of hyperglycemia (blood glucose >180) during three days before Ramadan. However, duration of hyperglycemia significantly decreased while fasting (mean duration: 467 minutes). In addition, the patients were hypoglycemic for an average of 30 minutes during 72 hours before Ramadan, which increased to 67 minutes during Ramadan; however, the change in this regard was not statistically significant.

Samples in the mentioned study were divided into two groups of patients treated with metformin only or sulfonylureas. The results were indicative of a significant decrease in the blood glucose level of the second group compared to the first group. Considering the findings of local studies in this regard, no definite conclusion could be drawn about the effects of fasting on diabetic individuals.

Fasting is associated with changes in the sleep pattern (6). In general, fasting has been reported to reduce the length of sleep. In other words, although fasting individuals might sleep longer, duration of the rapid eye movement (REM) sleep phase decreases. Several studies have investigated the relationship between decreased length of sleep, increased insulin resistance, and impaired glucose tolerance. It seems that decreased sleep duration might be involved in the deterioration of glycemic control in Ramadan fasting.

Fasting has been shown to be associated with changes of the circadian rhythms of the body, which might bring about various



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Figure 5. Changes in cortisol circadian rhythm during Ramadan (a shift in cortisol profile on day 7 reverting to near-baseline [non-Ramadan] values by day 21)

hormonal consequences (7). One of the most important changes in this regard affects the concentration of cortisol.

Under normal circumstances, the highest level of cortisol is observed in the morning, while the lowest rate is observed at midnight. As depicted in Figure 5, the daily cortisol curve changes while fasting, and higher cortisol levels are detected at midnight, which is associated with changes in the blood glucose level.

Fasting is associated with other metabolic changes as well. The majority of studies have indicated that fasting could improve the lipid profile in healthy individuals. For instance, a meta-analysis was performed in 2014 reviewing 30 articles in this regard, and the results suggested no significant changes in the levels of high-density lipoprotein and triglyceride in the general study population. However, evaluation of the studied samples in terms of gender was indicative of a significant reduction in the triglyceride level of male subjects, as well as a significant increase in the high-density lipoprotein level of female subjects.

In addition, fasting was found to cause a significant decrease in the level of low-density lipoprotein cholesterol in both men and women (8). In this regard, only a few studies have been conducted on diabetic patients proposing conflicting results. In the study by Yarahmadi et

al (3), fasting was reported to significantly increase the level of low-density lipoprotein, while it adversely affected the lipid profile. By contrast, the results obtained by Noroozi et al. (4) were indicative of improved lipid profile in Ramadan.

A review was performed to evaluate the effects of fasting on the lipid profile. According to the results, while fasting enhanced lipid control in normal subjects, it aggravated this variable in diabetic patients (9)

Effects of fasting on body weight could also be associated with changes in the lipid and glucose metabolism. While there is lack of consistency between studies in terms of the body weight of fasting individuals, the findings of EPIDIAR suggested that fasting has no significant effect on this parameter (2).

In general, four main risk factors are associated with fasting in patients with diabetes, the most important of which are hypoglycemia and hyperglycemia (10). These risks factors could be minimized with the proper choice of patients for fasting, as well as comprehensive educational interventions within two or three months before Ramadan and changes in the drug regimen of these individuals.

Another major complication caused by fasting is the risk of diabetic ketoacidosis, which is mostly observed in patients who have

changed their insulin intake independently without proportionate calorie intake and insulin dose. Diabetic patients treated with insulin are considered a high-risk population for fasting compared to other individuals.

Finally, fasting has been associated with the risk of thrombosis in diabetic individuals. Long durations of fasting could lead to dehydration, which increases the level of coagulation factors and decreases fibrinolysis. These factors are highly associated with the risk of thrombosis. In a study conducted in Saudi Arabia, it was reported that the risk of retinal vein occlusion rises by 30% in Ramadan compared to the other months of the year (11).

In conclusion, despite the benefits of Ramadan fasting for healthy individuals (e.g., lipid profile and glycemic control), fasting diabetic patients might be at risk during this month. In order for the proper choice of fasting by diabetic patients, they must refer to physicians for changes in the drug regimen and receiving training on Ramadan fasting.

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