

## Ramadan Fasting and Risk of Covid-19

### Abstract

Almost all religions recommend periods of fasting. Many adult Muslims fast during the holy month of Ramadan each year. Ramadan fasting as a type of intermittent fasting is a non-pharmacological intervention refining the overall health. This year, Ramadan is coincided with coronavirus disease 2019 (COVID-19) outbreak making it one of the most challenging fasting periods for Muslims in the world. There is no solid direct evidence to suggest any adverse effect of Ramadan fasting during the COVID-19 pandemic in healthy individuals. However, there are exemptions in Ramadan Fasting and those at risk of health issues should not fast. COVID-19 is a new disease and there is limited studies concerning its risk factors. The purpose of this review was shedding more light on the potential mechanisms involved in influence of practice of fasting in all forms, including Ramadan fasting on the vulnerability to infection.

**Keywords:** COVID-19, pandemic, Ramadan fasting

### Introduction

Muslims fast from sunrise to sunset during the month of Ramadan is a compulsory act for all healthy Muslim adults. While fasting is an important part of Ramadan, it is also a time of self-reflection and a wonderful opportunity to quit harmful habits for Muslims.

Ramadan is the 9<sup>th</sup> lunar month migrates throughout the seasons. The 2020 Ramadan coincides with the coronavirus disease 2019 (COVID-19) outbreak, making it one of the most challenging fasting periods for Muslims in the world.

In recent years, the effect of intermittent fasting (IF) as a way of calorie restriction (CR) on health outcome has been considered in many studies. Indeed a lessening in caloric intake without malnutrition, has frequently been found to improve health in a variety of species,<sup>[1]</sup> including non-human primates.<sup>[2]</sup>

In medical terms, Ramadan fasting (RF) can be considered a unique model of IF with periods of food, drink and smoking abstinence daily for 1 month. Knowledge about the effects of Ramadan fasting on the viral respiratory disease is poor, mainly because of a scarcity of scientific research in this area. So we focus on the

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association of Ramadan fasting/IF and potential preventive/susceptive mechanisms on viral disease. IF influences several body systems, including the immune system, and metabolic state which plays a critical role in regulating and maintaining body response to pathogens. The pandemics caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) raised growing interest concerning the effect of RF on COVID-19.<sup>[3]</sup> The purpose of this review was shedding more light on the potential mechanisms involved in influence of Ramadan fasting on the vulnerability to infection.

### Fasting and Metabolic Changes

Fasting is associated with shifting the primary energy source of the body from glucose to free fatty acid (FFA). In a fed human, glucose is used for energy and fat is stored in adipose tissue as triglycerides. During fasting, the liver converts fatty acids derived from triglycerides to ketone bodies to supply new source of energy for many tissues.<sup>[4]</sup> This states are associated with altered immune cell function in the body.<sup>[5]</sup> In a fast human, ketone bodies levels increase within 8 to 12 hours after the beginning of fasting and could reach to 6-8 mm after prolonged fasting.<sup>[6,7]</sup>

The brain relies on the ketone bodies  $\beta$ -hydroxybutyrate and acetoacetate as fuel, besides glucose, in fasting.<sup>[8]</sup>

**How to cite this article:** Javanmard SH, Otraj Z. Ramadan fasting and risk of Covid-19. *Int J Prev Med* 2020;11:60.

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#### Access this article online

**Website:** [www.ijpvmjournal.net/www.ijpvm.ir](http://www.ijpvmjournal.net/www.ijpvm.ir)

**DOI:** 10.4103/ijpvm.IJPVM\_236\_20

#### Quick Response Code:



$\beta$ -hydroxybutyrate can inhibit innate immune responses, sparing ATP for the functioning of ketone-dependent organs such as the brain and heart.

Ketone bodies are effective signaling molecules acting on several cell and organ functions.<sup>[9]</sup> They have major effects on body metabolic state through peroxisome proliferator-activated receptor  $\gamma$  coactivator 1 $\alpha$  (PGC-1 $\alpha$ ), poly (adenosine diphosphate [ADP]-ribose) polymerase 1 (PARP1), and ADP ribosyl cyclase pathways.<sup>[10]</sup>

Fasting also has significant effect on metabolic hormones concentration and function including insulin, IGF-I, adiponectin, and ghrelin. It also has a robust role in tissue homeostasis by suppressing cell growth, and enhancing apoptosis of damaged cells.<sup>[11]</sup>

IF also arise adaptive stress response that leads to increased expression of several defenses mechanisms including DNA repair, protein quality control, autophagy, oxidative stress response pathways

### **Fasting and Respiratory System Function**

Several studies reported no significant change in the lung function parameters during Ramadan as compared to the pre-Ramadan period. However, some groups reported significant increase of vital capacity and mean/peak expiratory flow rate it seems that RF did not affect expiratory flow rates in healthy subjects. FVC was decreased significantly in the post-Ramadan period compared to Ramadan.

Poor hydration and inadequate water intake is one of the concerns raised around susceptibility to COVID-19 infection by Ramadan fasting. There is no evidence for association of RF with severe water deprivation and negative water balance in healthy subjects.<sup>[12]</sup> It has been shown that total body water remained within the normal range of 30-46 kg.<sup>[13]</sup> In addition, although fasting causes some changes in urinary volume and metabolites concentration, there is no significant change in maximum urinary concentration.<sup>[14]</sup>

The adverse effects of dehydration on mucociliary function as a key defense mechanisms against infection is previously known.<sup>[15]</sup> Indeed, RF research denies the harmful effect of fasting on mucociliary clearance. In a study conducted to evaluate the difference in a mucociliary clearance among volunteers who underwent RF, there was no significant difference in the mucociliary clearance time between the RF and control.<sup>[16]</sup>

### **Fasting and Immune System**

Several studies highlighted the mild inflammatory state associated with obesity and metabolic syndrome. RF have been shown to significantly damp down the inflammation of the body by suppressing pro-inflammatory cytokine expression. Indeed, intermittent fasting modulates the levels

of visceral fat and several additional adipokines, including leptin, IL-6, TNF- $\alpha$  and IGF-1.<sup>[17,18]</sup>

Since, leptin raises neutrophil chemotaxis and macrophage phagocytosis, and triggers the maturation and function of T-cells, some changes of immune functions during fasting could be in part the result of a drop in the plasma leptin.<sup>[19,20]</sup>

The number of total leukocytes, granulocytes, lymphocytes and monocytes were significantly decreased during Ramadan in comparison to pre-Ramadan in some reports,<sup>[17]</sup> while in infected patients RF was associated with increasing the numbers of macrophages. It has been shown that fasting could activate a regenerative switch in stem cells, leading to the generation of new immune cells.<sup>[21]</sup>

Interestingly, in Muslim fasting HIV patients, the change of twice-daily dose of antivirals to once-daily dosed had no significant changes on CD4 cell counts, viral load, or disease state in comparison with the twice-daily dose therapy for non-fasting patients.<sup>[22]</sup>

The results of a comprehensive systematic review showed that fasting during Ramadan was associated with mild transient changes in the immune system, which return to the basal pre-Ramadan status shortly afterward.<sup>[23]</sup>

Fasting also has some effects on pathogen defense mechanisms and adaptive/innate immune responses. Since immune cells also rely on glucose to sustain their function and proliferation reduced glucose availability as well as hypoinsulinemia during fasting may have negative effect on immune defense mechanisms. However, their function can be restored after re-feeding.<sup>[24]</sup>

On the other hand, it has been shown that innate immunity response for intracellular infection factors during RF was not decreased. In fact, it increased, indicating the beneficial effect of fasting to protect against bacterial infection.<sup>[23]</sup>

### **Conclusion**

In conclusion, scientific evidence indicates that all types of IF including RF has several health benefits in healthy people without malnutrition. In addition, RF might not be harmful for many patients with controlled and stable disease.<sup>[25]</sup> However, undernourishment could be dangerous in acute viral diseases.<sup>[26]</sup> We couldn't find any evidence of adverse effect of metabolic changes associated with RF on the immune and respiratory system related to COVID-19.

Although Ramadan fasting is safe for all healthy individuals, the Qur'an exempts ill patients and those at risk of various diseases from fasting. COVID-19 is a novel disease and there is not enough information about its risk factors. However, older people (more than 65 years) and those who have serious comorbidity such as cardiovascular disease, diabetes, cancer and chronic lung and kidney

disease might be at higher risk for severe illness from COVID-19.<sup>[27]</sup>

It has been shown that Muslims aware of their religious exemption from fasting decide not to take that exemption and fast.<sup>[28]</sup> In respect of patient-centered care, it seems that risk assessment, organized education and choice of appropriate medication can reduce the possible hazards associated with fasting among at risk people.

Stress of RF could lead to a transient increased level of cortisol and potentially prolonged the viral shedding duration in COVID-19 patients,<sup>[29,30]</sup> so national health authorities should be considered the regulations and advice regarding physical distancing and other public health measures related to COVID-19 during Ramadan.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

**Received:** 02 May 2020 **Accepted:** 02 May 2020

**Published:** 25 May 20

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