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 9th lunar month and 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 outcomes 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, including non-human primates.

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 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. The purpose of this review was shedding more light on the potential mechanisms involved in influence of fasting in all forms, including 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. This states are associated with altered immune cell function in the body. 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.

The brain relies on the ketone bodies β-hydroxybutyrate and acetoacetate as fuel, besides glucose, in fasting.

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α-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.[9] They have major effects on body metabolic state through peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α), poly (adenosine diphos­hate [ADP]–ribose) polymerase 1 (PARP1), and ADP ribosyl cyclase pathways.[10]

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.[11]

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.[12] It has been shown that total body water remained within the normal range of 30-46 kg.[13] In addition, although fasting causes some changes in urinary volume and metabolites concentration, there is no significant change in maximum urinary concentration.[14]

The adverse effects of dehydration on mucociliary function as a key defense mechanisms against infection is previously known.[15] 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.[16]

**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-α and IGF-1.[17,18]

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.[19,20]

The number of total leukocytes, granulocytes, lymphocytes and monocytes were significantly decreased during Ramadan in comparison to pre-Ramadan in some reports,[17] 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.[21]

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.[22]

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.[23]

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.[24]

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.[25]

**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.[25] However, undernourishment could be dangerous in acute viral diseases.[26] 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.\cite{29}

It has been shown that Muslims aware of their religious exemption from fasting decide not to take that exemption and fast.\cite{30} 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,\cite{29,30} 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.

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**References**

1. Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG, et al. Flipping the metabolic switch: Understanding and applying the health benefits of fasting. Obesity (Spring) 2018;26:254-68.

2. Colman RJ, Anderson RM, Johnson SC, Kastman EK, Kosmatka KJ, Beasley TM, et al. Caloric restriction delays disease onset and mortality in rhesus monkeys. Science 2009;325:201-4.

3. Paraskevis D, Kostaki EG, Magiorkinis G, Panayiotakopoulos G, Souvinos G, Tsiodras S. Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. Infect Genet Evol 2020;79:104212.

4. de Cabo R, Mattson MP. Effects of intermittent fasting on health, aging, and disease. N Engl J Med 2019;381:2541-51.

5. Youm YH, Nguyen KY, Grant RW, Goldberg EL, Bodogai M, Kim D, et al. The ketone metabolite beta-hydroxybutyrate blocks NLRP3 inflammasome-mediated inflammatory disease. Nat Med 2015;21:263-9.

6. Cahill GF Jr. Starvation in man. N Engl J Med 1970;282:668-75.

7. Newman JC, Verdin E. Ketone bodies as signaling metabolites. Trends Endocrinol Metab 2014;25:42-52.

8. Harvie MN, Pegington M, Mattson MP, Frystyk J, Dillon B, Evans G, et al. The effects of intermittent or continuous energy restriction on weight loss and metabolic disease risk markers: A randomized trial in young overweight women. Int J Obes (Lond) 2011;35:714-27.

9. Newman JC, Verdin E. β-Hydroxybutyrate: A signaling metabolite. Annu Rev Nutr 2017;37:51-76.

10. Puchalska P, Crawford PA. Multi-dimensional roles of ketone bodies in fuel metabolism, signaling, and therapeutics. Cell Metab 2017;25:262-84.

11. LongoVD, Mattson MP. Fasting: Molecular mechanisms and clinical applications. Cell Metab 2014;19:181-92.

12. Leiper JB, Molla AM, Molla AM. Effects on health of fluid restriction during fasting in Ramadan. Eur J Clin Nutr 2003;57(Suppl 2):S30-8.

13. Chumlea WC, Guo SS, Zeller CM, Reo NV, Siervoel GM. Total body water data for white adults 18 to 64 years of age: The Fels Longitudinal Study. Kidney Int 1999;56:244-52.

14. Shirreffs SM. Markers of hydration status. Eur J Clin Nutr 2003;57(Suppl 2):S6-9.

15. Lewis BW, Patial S, Saini Y. Immunopathology of airway surface liquid dehydration disease. J Immunol Res 2019;2019:2180409.

16. Develioglu ON, Sirazi S, Topak M, Purisa S, Kulecki M. Differences in mucociliary activity of volunteers undergoing Ramadan versus Nineveh fasting. Eur Arch Otorhinolaryngol 2013;270:1655-9.

17. Faris MA, Kacimi S, Al-Kurd RA, Fararjeh YK, Mohammad MK, et al. Intermittent fasting during Ramadan attenuates proinflammatory cytokines and immune cells in healthy subjects. Nutr Rev 2012;70:947-55.

18. Davies AR, Ethimioiu E. Curing type 2 diabetes mellitus with bariatric surgery - Reality or delusion? Br J Diabetes Vasc Dis 2012;12:173-6.

19. La Cava A, Matarrese G. The weight of leptin in immunity. Nat Rev Immunol 2004;4:371-9.

20. Xu DL, Wang DH. Fasting suppresses T cell-mediated immunity in female Mongolian gerbils (Meriones unguiculatus). Comp Biochem Physiol A Mol Integr Physiol 2010;155:25-33.

21. Mihaylova MM, Cheng CW, Cao AQ, Tripathi S, Mana MD, Bauer-Rowe KE, et al. Fasting activates fatty acid oxidation to enhance intestinal stem cell function during homeostasis and aging. Cell Stem Cell 2018;22:769-78.e4.

22. Yakasai AM, Muhammad H, Babashani M, Jumare J, Abdulmuminu M, Habib AG. Once-daily antiretroviral therapy among treatment-experienced Muslim patients fasting for the month of Ramadan. Trop Doct 2011;41:233-5.

23. Adawi M, Watad A, Brown S, Aazza K, Aazza H, Zouhir M, et al. Ramadan fasting exerts immunomodulatory effects: Insights from a systematic review. Front Immunol 2017;8:1144.

24. Walrand S, Moreau K, Caldefie F, Tridon A, Chassagne J, Portefaix G, et al. Specific and nonspecific immune responses to fasting and relfeeding differ in healthy young adult and elderly persons. Am J Clin Nutr 2001;74:670-8.

25. Bragazzi NL, Briki W, Khabbache H, Rammouz I, Mnadla S, et al. Ramadan versus Nineveh fasting. Eur Arch Otorhinolaryngol 2011;268:233-8.

26. Li Y, Song Z, Mo Q, Li N, Zhang J, et al. Differences in mucociliary activity of volunteers undergoing Ramadan versus Nineveh fasting. Eur Arch Otorhinolaryngol 2013;270:1655-9.

27. Faris MA, Kacimi S, Al-Kurd RA, Fararjeh YK, Mohammad MK, et al. Intermittent fasting during Ramadan attenuates proinflammatory cytokines and immune cells in healthy subjects. Nutr Rev 2012;70:947-55.

28. Amin MEK, Abdelmageed A. Clinicians’ perspectives on caring for Muslim patients considering fasting during Ramadan. J Relig Health 2019. doi: 10.1007/s10943-019-00820-y.

29. Roky R, Houti I, Moussamih S, Qotbi S, Aadil N. Physiological measures related to COVID‑19 during Ramadan. Intern Med J 2020;50:694-706.

30. Janicki‑Deverts D, Cohen S, Turner RB, Doyle WJ. Basal salivary cortisol secretion and susceptibility to upper respiratory infection. Brain Behav Immun 2016;53:255-61.