



The Health Impacts of Ramadan Fasting

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ARTICLE INFO	ABSTRACT
<p><i>Article type:</i> Short Communication</p>	<p>Ramadan is the holy month of obligatory fasting for all the healthy Muslims who have reached puberty. In Ramadan, fasting individuals consume two meals per day, the first of which is before dawn to prepare for fasting (Sahur), and second meal is at sunset (Iftar). Fasting is a ritual and religious obligation with numerous beneficial health effects, especially in patients with diet-dependent diseases. Fasting could significantly reduce peptic and duodenal ulcers in combination with H2 blockers and improve the lipid profile, especially through the regulation of total cholesterol, high-density lipoprotein, and low-density lipoprotein, which may be involved in the incidence of heart failure. Furthermore, fasting could enhance the systolic and diastolic blood pressure more significantly compared to the use of drugs such as perindopril/indapamide. Evidence suggests that ischemic stroke and cancer could also be improved by intermitted fasting via multiple pathways and factors such as BDNF, bFGF, GRP78, Hsp70, tyrosine kinase receptor B (TrkB), fibroblast growth factor receptor 1 (FGFR1), and ketosis. The present study aimed to systematically review the published literature regarding the effects of Ramadan fasting on the mentioned diseases.</p>
<p><i>Article History:</i> Received: 20 May 2019 Accepted: 03 Jun 2019 Published: 15 Jul 2019</p>	
<p><i>Keywords:</i> Ramadan Fasting Iftar Ischemic Stroke Ketosis</p>	

► Please cite this paper as:

Hazafa A, Rehman KU, Jabeen Z. The Health Impacts of Ramadan Fasting. J Nutrition Fasting Health. 2019; 7(3): 116-120. DOI: 10.22038/jnfh.2019.40505.1197

Introduction

Ramadan is the ninth month in the Islamic lunar calendar and a holy month of obligatory fasting for 29-30 days. The word Ramadan is of the Arabic root *Ramida*, which means dryness [1]. Fasting is an Islamic obligation, which involves fasting for one month from sunrise to sunset. Duration of fasting in Ramadan varies depending on the geographical location of every country; however, the average duration is 10-19 hours per day [2, 3]. Fasting is obligatory for all the healthy Muslims who have reached puberty, and the exemptions of fasting include patients with chronic diseases (e.g., diabetes, cancer, and cardiac diseases), travelling individuals, and menstruating, lactating, and pregnant women [4].

Fasting is a ritual and religious obligation with numerous beneficial health effects against diet- and lifestyle-dependent diseases, as well as the disorders with challenging therapeutic treatment, including cardiac diseases,

osteoporosis, stroke, cancer, and hypertension [5]. Moreover, fasting has remarkable effects on basic homeostatic function. Previous findings have indicated that fasting could protect cells against oxidative stress, maintain the level of total cholesterol [6], significantly reduce systolic and diastolic blood pressure [7], improve peptic ulcers [8], protect the body against various cancers (especially breast cancer) [9], and improve ischemic stroke [10].

Physiology of Fasting

In healthy individuals, insulin secretion is stimulated by the dietary behaviors that enhance the storage of glucose in the muscles and liver as glycogen. Fasting leads to the decreased level of glucose, which in turn significantly reduces insulin, as well as the levels of catecholamines and glucagon [11]. In a study in this regard, Al Arouj et al. [2] claimed that after several hours of fasting, the levels of glycogen and circulating insulin decreased, thereby eliminating fatty acids from the adipocytes. As a result, the fatty acids

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were oxidized, producing ketone bodies that were used as fuel by various body organs, such as the liver, kidneys, cardiac and skeleton muscles, and adipose tissues.

A series of complex mechanisms are involved in the transition from the feeding state to prolonged fasting, which occurs in three stages, including the postabsorptive phase (6-24 hours), gluconeogenic phase (2-10 days), and protein conversion phase (after 10 days of fasting). A healthy individual uses approximately seven grams of glucose per hour in overnight fasting [2, 11].

Within the past two decades, several studies have been focused on the effects of Ramadan fasting on various diseases, proposing heterogeneous findings. However, fasting has been reported to positively influence some disorders, which have been discussed in the following section.

Benefit of Fasting for Patients with Peptic and Duodenal Ulcers

Ulcers occur due to the depletion of the upper thick layer of mucus, which protects the stomach against the acidic nature of digestive fluids, as a result of which the mucus layer becomes thin, and acidic fluids or foods could readily cross the tissues and ultimately form the ulcer [12]. Fasting is considered to be a common, yet underrated solution to this issue. Fasting contributes to the balance and in healing process of the body. According to a research in this regard, almost 15 days of regular fasting (12-14 hours) is required for the proper treatment of peptic ulcers [8, 13].

Two cohort studies confirmed the role of Ramadan fasting in the treatment of peptic and duodenal ulcers, and the findings were compared between fasting and non-fasting patients. Accordingly, during the treatment of peptic ulcer (PU), the fasting and non-fasting subjects were administered with H₂ blockers at Sahur and Iftar in Ramadan, and both groups were examined before and after Ramadan. After repeated examinations, a significant improvement was observed in the fasting group, while no changes occurred in the non-fasting group. Both of the mentioned studies also proposed findings regarding the treatment of erosive duodenitis (ED). According to the first study, approximately

43.75% of the fasting patients were recovered from ED, while in the second study, all the fasting patients were reported to be healthy after Ramadan [8]. With respect to the treatment of duodenal ulcer, both fasting and non-fasting subjects were administered with omeprazole (40 mg/day), which is a proton-pump inhibitor. Both cohort studies revealed that the fasting patients with duodenal ulcer significantly improved compared to the non-fasting subjects [14].

Fasting and Lipid Profile

Attarzadeh Hosseini et al. [15] and Langsted et al. [16] have reported that after Ramadan fasting, a significant improvement was observed in the levels of total cholesterol (TC) and high-density lipoprotein (HDL), which could be associated with the reduction of coronary heart disease. Additionally, another study in this regard indicated that the level of TC significantly reduced in fasting individuals during Ramadan, which resulted in the improvement of HDL [17, 18].

The study by Shehab et al. [19] was performed on 65 individuals, and the obtained results demonstrated a significant improvement in the HDL level of the subjects. On the other hand, the findings of another study confirmed the improvement of LDL in fasting individuals during Ramadan [7]. Further investigations are required to obtain more accurate results in this regard.

The role of Fasting on Blood Pressure

Rehman et al. [7] conducted a research on 20 fasting individuals during Ramadan, reporting the significant reduction of diastolic and systolic blood pressure. Similarly, Dewanti et al. [20] examined normotensive individuals, reporting the significant reduction of systolic and diastolic blood pressure in fasting individuals, while denoting the hypotensive effects of fasting. Samad et al. [21] conducted an experiment on 40 normotensive and non-smoker males aged 18-40 years, who were fasting in Ramadan. The researchers regularly assessed the patients one week before Ramadan, as well as on days seven, 14, and 21 of Ramadan before and after Iftar. Furthermore, they reported a significant reduction in the systolic blood pressure (approximately 7.61 mmHg) before (7.61

mmHg) and after Iftar (2.72 mmHg) ($P < 0.005$); the same reduction was observed in the diastolic blood pressure (approximately 3.19 mmHg).

In another study by Laurent (2003) [22], the correlation between fasting and low-dose administration of perindopril/indapamide was assessed, and the results indicated that after three weeks of fasting, blood pressure decreased by approximately 8/3 mmHg (mean: 9.4 ± 14.3 mmHg), while the intake of indapamide (0.625 mg; $P = 0.023$) and perindopril (2 mg; $P = 0.001$) was associated with the reduction of blood pressure by only 8.0 ± 16.5 mmHg within 12 weeks. It is notable that the mentioned study had some limitations, and the findings cannot be generalized to other patients with chronic diseases [21].

Treatment of Ischemic Stroke

A complex cascade is involved in ischemic stroke, which is stimulated spatially and temporally in the induction of damage to cerebrovascular tissues. The brain requires energy in the form of adenosine triphosphate (ATP) for proper function, and energy failure leads to ischemia and loss of ionic homeostatic, thereby activating the glutamate receptors, which play a key role in the cell death in ischemic stroke [9, 23]. Strong evidence suggests that intermittent fasting (IF) plays a pivotal role in the protection and improvement of neural survival from glutamate excitotoxicity in the rodent model of cerebral ischemia via multiple pathways through increasing neuroprotective proteins and factors such as *brain-derived neurotrophic factor* (BDNF), bFGF, GRP78, and Hsp70 [24]. BDNF and bFGF exert their effects when binding to tyrosine kinase receptor B (TrkB) and fibroblast growth factor receptor 1 (FGFR1), respectively, which activate various signaling pathways, including Akt (protein kinase B) and extracellular signal-regulated kinase, thereby resulting in the activation of the transcription factor cyclic AMP response element-binding protein (CREB). CREB

has been reported to exert neuroprotective effects during an ischemic stroke in animal models [9, 25].

Another study in this regard indicated that IF may be involved in the improvement of neural survival from oxidative stress in the rodent model of cerebral ischemia either by increasing the antioxidant effects or reducing the reactive oxygen species and providing mitochondrial protection in the brain [26]. Similarly, a study demonstrated that IF could also improve neural survival from inflammation in the rodent model of cerebral ischemia through multiple pathways either by the reduction of pro-inflammatory genes or eliminating inflammatory stimuli from the brain [27].

Treatment of Cancer by Fasting

Cancerous or normal cells utilize adequate energy in the form of ATP for their multiplication, while cancer cells use more energy, which is supplied by glucose through glycolysis and electron transport chain pathways. While fasting, the total availability of glucose decreases, and the requirement of cancer cells cannot be met, and these cells receive energy through ketosis-ketosis, which is a metabolic state of the body to acquire energy from ketone bodies. Ketosis often occurs during starvation or glucose shortage while fasting for approximately 10-17 hours per day. This process weakens the tumor cells due to the unavailability of nutrition and energy [9, 28].

A study conducted in 2009 reported that fasting is preferred after chemotherapy since the procedural complications could be improved by fasting during chemotherapy. DNA damage is considered to be the major complication caused by chemotherapy, which could lead to the development of secondary tumors. Therefore, fasting is an optimal method for the reduction of oxidative stress [29].

The effects of fasting on various diseases are presented in Table 1.

Table 1. Effects of Ramadan Fasting on Various Diseases

Disease	Number of Participants	Type of Fasting	Findings	References
Blood Pressure	40 Males	Regular Fasting (12-14h/day)	SBP before Ramadan: 124.55 mmHg SBP during Ramadan: 116.94 mmHg DBP Before Ramadan (78.8 mmHg) DBP During Ramadan (75.6 mmHg)	[21]
Peptic Ulcer	470 (Male and Female)	12-14 Hours of Complete Fasting/Day For 15 days	Higher Frequency of PUD and PPU One month after Ramadan compared to Ramadan ($P>0.05$ and $P= 0.008$, respectively)	[8]
Cholesterol	1,301 (Male and Female)	Regular Fasting (29-30 days)	Before Ramadan: 5.65 ± 0.80 ml/dl (Mean \pm SD) During Ramadan: 4.90 ± 1.07 ml/dl	[30]
Triglycerides	1,301 (Male and Female)	Regular Fasting (29-30 days)	Before Ramadan: 1.65 ± 0.81 ml/dl (Mean \pm SD) During Ramadan: 1.41 ± 0.62 ml/dl	[30]
HDL	1,301 (Male and Female)	Regular Fasting (29-30 days)	Before Ramadan: 1.42 ± 0.29 ml/dl (Mean \pm SD) During Ramadan: 1.34 ± 0.35 ml/dl	[30]
LDL	1,301 (Male and Female)	Regular Fasting (29-30 days)	Before Ramadan: 2.78 ± 0.99 ml/dl (Mean \pm SD) During Ramadan: 2.63 ± 0.76 ml/dl	[30]
Ischemic stroke	20 (young and middle- age mouse models)	IF	Significantly reduced the risk of Ischemic stroke via a several pathways (e.g. BDNF, bFGF, GRP78, and Hsp70)	[9]

SBP: systolic blood pressure; DBP: diastolic blood pressure; PUD: peptic ulcer disease; HDL: high-density lipoprotein; LDL: low-density lipoprotein; IF: intermittent fasting

Conclusion

Ramadan is a ritual and religious obligation with numerous beneficial health effects, especially on diet- and nutrition-dependent diseases. Fasting plays a pivotal role in the reduction of peptic and duodenal ulcers, improvement of TC, HDL, and LDL levels, improvement of systolic and diastolic blood pressure (8/3 mmHg; four-fold results compared to perindopril/indapamide), improvement of ischemic stroke via multiple pathways, and reduction of the risk of breast cancer by enhancing the effect of the growth hormone and ketosis. It is recommended that further investigations be conducted in this regard in order to achieve more accurate results.

Acknowledgements

Hereby, we extend our gratitude to Prof. Dr. Khalil-ur-Rehman and Dr. Zara Jabeen for

reviewing the article and providing helpful comments.

Conflicts of Interest

None declared.

Informed Consent

No informed consent was required for this research design.

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