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Ramadan Fasting and Risk of Coronavirus Disease 2019 (Covid-19) in Healthy People: A Review

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Abstract

Fasting the month of Ramadan is one of five obligatory pillars of the Islamic creed, observed strictly by hundreds of millions of Muslims every year. The fasting process includes absolute abstinence from eating and drinking for an average of around 15 hours daily for one month. As the coronavirus disease 2019 (COVID-19) pandemic has been ongoing during the month of fasting, there are public concerns that fasting may increase the susceptibility for infection of COVID-19. According to Islamic jurisdiction, if adequate scientific evidence of harm on health is available, fasting is discouraged and should not be practiced. Such concern is not only relevant to the Muslim population but is becoming increasingly relevant to other populations due to the practice of intermittent fasting which is a popular current health trend worldwide. There is no direct evidence of any disadvantage effect of Ramadan fasting during the COVID-19 pandemic on healthy people, for this purpose, we performed a systematic review of 37 articles published between 2005 and April 2020 which investigated the effect of fasting on markers of the respiratory system function and immune response. Our main findings from this analysis show that there is no evidence that fasting the month of Ramadan have a negative impact on the respiratory function and the immune system of healthy individuals.

Key words: Ramadan fasting; COVID-19; Immunity, Respiratory system function

Introduction

Ramadan requires healthy Muslim adults to strictly abstain from eating and drinking from sunrise to sunset^{1, 2, 3}. The duration of fasting can range from 12 to 22 hours/day depending on the geographical area and season^{4,5}. Fasting in Ramadan is obligatory with some valid exemptions for children, pregnant, breastfeeding, and menstruating women, elderly, and sick individuals^{6,7,8}.

Ramadan is the 9th lunar month migrates throughout the seasons. During Ramadan 2020 as the COVID-19 has been spreading globally, people were more concerned about their immunity and the possibility that fasting may

increase their vulnerability to acquiring this infection.

COVID-19 belongs to a large family of viruses, the coronaviruses when transmitted to humans, they can result in a variable clinical course ranging from asymptomatic carrier status, mild flu-like symptoms, pneumonia, and up to an aggressive systemic infection that require hospitalization and intensive care. Infection is transmitted by droplets through direct contact or at the community level by aerosol transmission based on different reports^{9, 10, 11,12}.

With the rapidly pandemic of COVID-19, the high growing interest of individuals in potential preventive, dietary, change lifestyle, and remedies that may enhance the immunity against covid-19. a growing debate rose toward the expected impact of Ramadan fasting on the body's immunity and respiratory system functions.

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As a first step to investigate this hypothesis, we performed a systematic review of studies that evaluated the effect of Ramadan fasting on intermediate markers that can indicate susceptibility to such infection. The main intermediate markers searched included the respiratory function parameters and markers of the immune system. Other relevant markers such as dehydration and inflammation were also included. Our aim was to collect the current evidence regarding the effect of Ramadan fasting on the immune system, respiratory function and vulnerability to COVID-19 infection in healthy subjects.

Methods

In this article, we reviewed recently conducted studies on the impact of Ramadan fasting on the immune system, dehydration, infection, and respiratory system function. MEDLINE (<http://www.pubmed.com>) was searched by using "Ramadan" as keyword and the most recent articles in mentioned topics since 2005 until April 2020 were selected.

A systematic review of the following databases was used: Institute for Scientific Information ISI/ Web of Science (WoS), Scopus, PubMed/MEDLINE, Google Scholar, Directory of Open Access Journals (DOAJ), EbscoHOST, Scirus, Science Direct, the Cochrane Library, and ProQuest.

The search was carried out using a string made up of a combination of keywords including "Islam," "Ramadan," "Fasting," "Immunity," "Immune system", "Respiratory system", "Pulmonary function" and "Inflammatory".

Review articles relevant to the aim of this systematic review were scanned in order to improve the chances of finding potentially relevant studies, the aim of this review was excluded, while all other research articles and each reference of the potentially relevant articles were manually consulted and screened in an iterative way until no new references were found.

Results

After removing duplicates and not pertinent Articles, A total of 37 studies were included in the current systematic review, Twenty-three studies focused on the impact of fasting on the immune system

and inflammatory in healthy individuals in Healthy individuals while fourteen focused on the impact of fasting on respiratory system structure and function.

The impact of Ramadan fasting on the immune system and inflammatory in healthy people

Maliji et al., 2006¹⁵ investigated the effects of Ramadan fasting on key parameters of the immune system including complement components of C3 and C4. Researchers applied SRID and CH50 test on two different occasions during the fourth week of Ramadan and one month later. Fifty healthy male and female volunteer students, aged 20-25, were included in that study. The study concluded that Ramadan fasting had no negative effect on markers of innate immunity including complement components. In the study of Latifynia et al., 2007¹³, the effect of fasting on circulating immune complex (CIC) level and immune system was investigated. The serum levels of CIC of 28 healthy adult male students were compared before and after Ramadan by using the polyethylene glycol method. The blood samples were examined using quantitation chemiluminescence and circulating immune techniques, based on the results, no significant difference between the CIC level before and after Ramadan and fasting in Ramadan does not have a bad effect on the immune system in healthy people. In another research by Latifynia et al., 2007¹⁶ the Neutrophil Respiratory Burst (Innate Immunity) in 24 healthy male adults from Tehran aged 18-35 years were measured and compared before and after Ramadan, using the chemiluminescence method, this study has shown the fasting in Ramadan does not effect on blood neutrophil respiratory burst function and has no critical effect on the immunity of the healthy individuals. The same group, Latifynia et al., 2008¹⁴ has studied the effects of Ramadan fasting on neutrophil's respiratory burst (as markers of innate immunity) and circulating immune complex (CIC), in 21 young fasting individuals using standardized chemiluminescence and polyethylene glycol methods respectively. Their findings showed that 11 (52%) of the study participants had normal chemiluminescence (CL) activity, and CIC levels before and after Ramadan fasting, despite an insignificant decrease or increase in CL activity or CIC level. Therefore, the changes in the immunological parameters were not significant, and the levels remained in the range of normal.

In study of Latifynia et al., 2009¹⁸, the Blood samples were tested, neutrophil phagocytosis, serum opsonization power, and NBT reduction for thirteen healthy males, aged between 28-54 years, to investigate the effect of Ramadan fasting on opsonization, phagocytosis, and nitroblue tetrazolium (NBT) reduction by leucocytes, they found a decrease in the neutrophil phagocytic index and serum opsonization index, while the neutrophils participating were increased in phagocytosis Ramadan. Although there was a decrease in the opsonization of the serum, the increased percentage of opsonization compensated for this defect. The result demonstrates the beneficial effect of fasting during Ramadan on neutrophil phagocytic function in healthy people.

The study of Chennaoui 2009³⁵ was included, 40 healthy fasting males and females volunteers (20 females aged 20–38 years and 20 males aged between 23–39 years) with normal weight, they were compared with 28 healthy non-fasting volunteers (14 males, and 14 females). The biochemical parameters were investigated including C-reactive protein (CRP), IL-6, and homocysteine or hcy levels. The levels of the inflammatory markers (IL-6, CRP, and hcy) were shown to be significantly decreased as a result of Ramadan fasting in both genders compared to their primary basal values.

Mohammed & Mahmood, 2010²¹ performed a study on the effect of Ramadan fasting on immune cytokines, by evaluating the level of IL-1 α , IL-2, IL-6, and IL-8 in 30 healthy fasting individuals compared with 30 healthy non-fasting individuals. Interleukin 1 α , interleukin 2, IL-6, and interleukin were shown to be decreased although not reaching a significant level, which seems to suggest that fasting in Ramadan is safe and causes immunomodulation for healthy people. A study by Trepanowski & Bloomer, 2010²⁴, on fifty healthy fasters, were reported measurements of pro-inflammatory cytokines IL-1 β , IL-6, and TNF- α , was conducted in three phases (7 days before the fasting, 21 days after fasting, and 1 month after Ramadan fasting). Significant reductions in cytokines IL-1 β , IL-6, and TNF- α levels compared to baseline (78%, 57%, and 71%, respectively) were noted. IL-6 levels remained significantly low one month after the end of Ramadan fasting, implying a potential long-term beneficial role of Ramadan fasting on inflammatory profile and fasting can

be a time of a great improvement of the health. Faris et al., 2012¹⁷, designed A cross-sectional study to investigate the advantage of Ramadan intermittent prolonged fasting RIF on selected inflammatory cytokines and immune biomarkers in Fifty (21 men and 29 women) healthy volunteers who practiced Ramadan fasting for 8-24 hours during the hours between dusk and dawn, they were recruited for the investigation of circulating pro-inflammatory cytokines “interleukin [IL]-1 β , IL-6, and tumor necrosis factor α ” immune cells “total leukocytes, granulocytes, monocytes, lymphocyte”, and anthropometric with dietary assessments. The researchers found that the Immune cells significantly decreased during the month of Ramadan, and still within the ranges. The results showed that RIF attenuates the inflammatory status of the body by suppressing pro-inflammatory cytokine expression and decreasing body fat and circulating levels of white blood cells (WBC).

In a study by Lahdimawan et al., 2013³⁰ Blood sampling was drawn for the examination of IFN-gamma, TNF-alpha, iNOS and SOD level from Twenty-seven healthy volunteers males aged 18–22 years who were fasting in Ramadan, Blood sampling was conducted before 7 days of Ramadan, 7th day of Ramadan, and 21st day of Ramadan. The authors suggest that Ramadan fasting induce classically activated, inflammation, decrease the oxidative stress on macrophage, altered activated macrophage regulation-signaling and induces macrophage function.

In Develioglu et al., 2013³¹ study, blood, and saliva samples were collected from 35 healthy men one week before Ramadan and during the last week of Ramadan to determine the Albumin, total lymphocyte count, electrolytes, IgG and IgM concentrations, and IgA concentrations. The results showed that although IgG concentration was decreased after-Ramadan in comparison to before-Ramadan, it was not out of the normal range. The reduction in the concentration of salivary IgA was also observed, while the lymphocyte number was elevated. The results show that Ramadan fasting has no severe effect on the immune system. Mohajeri et al. 2013³² determined the levels of biochemical parameters for 58 healthy fasting subjects, aged 20–40 years, chemokine (C–X–C motif) ligand 1 (CXCL1), chemokine (C–X–C motif) ligand 10 (CXCL10) and chemokine (C–X–C motif) ligand 12

(CXCL12) chemokines levels using enzyme-linked immunosorbent assay (ELISA). The results showed a significant decrease in the pro-inflammatory chemokines (CXCL1, CXCL10) and the constitutive chemokine (CXCL12).

Lahdimawan et al., 2014¹⁹ took blood samples from thirty healthy volunteers males seven days before Ramadan and on the seventh and 21st day of Ramadan to determine whether fasting in Ramadan change the ability of serum, peripheral blood mononuclear cells (PBMC), and macrophages kill *Mycobacterium tuberculosis*. Blood sample were measured by ELISA: Complement C3, inducible nitric oxide synthase (iNOS), superoxide dismutase (SOD) levels in serum, PBMC, and the killing ability of immune components determined by measuring colony-forming units (CFUs). They found that CFU in PBMC infected with *M. tb* (PIM), and macrophages infected with *M. tb* (MIM) decreased, the CFUs in serum infected with *M. tb* (SIM) increased, and CFUs in MIM decreased compared with that before Ramadan fasting. The levels of iNOS in serum and the CFUs in MIM decreased and the CFUs in SIM and PIM increased and the levels of iNOS in PBMC significantly increased on the 7th and 21st days of Ramadan compared with before Ramadan fasting. The study suggested that Ramadan fasting has a beneficial effect on host defense against *M. tb* and decreases the risk of tuberculosis (TB) infection in healthy people.

In another study of Siadat et al., 2014²⁶. The pre-Lymphocytic subpopulations analysis was conducted using flow cytometry for 38 healthy peoples (9 females and 29 males), age range 17-51 years, were assessed before Ramadan and one day before the end of Ramadan. The results showed that the percentage of the total lymphocytes was 25.82% and 26.23% in the pre and late-Ramadan, respectively, therefore, the results seem Ramadan fasting does not affect the lymphocyte count, percentage ratio, and the main lymphocyte subpopulations of healthy individuals.

Feizollahzadeh et al., 2014³³ studied the effect of the Ramadan fasting on serum levels of adiponectin and tumor necrosis factor- α (TNF- α) as two inter-related peptides involved in cells sensitivity to insulin and glucose metabolism for seventy healthy men, with age range equal or greater than 30. The results

showed that the Ramadan fasting resulted in augmented adiponectin levels which may help in improving metabolic stress induced by insulin resistance in people with predisposing factors of type2 DM. In Gorjipour et al., 2015²⁰ Study, the Plasma granulysin levels as a biomarker of the immune system were investigated in 44 healthy male volunteers with a mean age of 41.15 \pm 13.6 years. Blood samples were obtained on the 29th day of Ramadan and four months after Ramadan. They investigated Plasma Granulysin, triglyceride (TG), Cholesterol (Chol), low-density lipoprotein (LDL), and High-density lipoprotein (HDL), FBS, Uric acid, and CRP. They found that the mean concentrations of CRP serum on the 29th day of Ramadan were significantly lower than after Ramadan, which shows Fasting caused modulation in the CRP level but did not affect the immune system. A study by Bahijri et al., 2015²⁵ investigated the effect of Ramadan fasting on secretory patterns of PTH, markers of bone metabolism, and serum immunoglobulins for healthy young volunteers before (Shaban) and 2 weeks into Ramadan. Calcium, phosphorus, magnesium, albumin, alkaline phosphatase, 25-OH vitamin D, intact PTH (iPTH), and immunoglobulin (Ig) A, M, and G were measured, the levels of immunoglobulin M remained stable, with no significant increase or decrease. and Ramadan fasting was not shown to result in drastic disturbances.

Mohammadzade et al., 2017²⁷ performed a study on the effect of fasting during Ramadan on biochemical parameters and inflammatory markers. The studies were done on 30 healthy fasting men, blood samples were taken one week before Ramadan, during the last week of Ramadan, and four weeks after Ramadan. Serum interleukin-6, high sensitivity C-reactive protein, fasting blood sugar (FBS), insulin, total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein levels were measured. No significant change was observed in the results and the showed that the inflammatory factors do not change significantly during and after fasting.

Orucunun et al., 2019³⁴ conducted a study on 30 fasted female subjects during Ramadan month. They investigated the red blood cells (RBC) and total White blood cells (WBC) before the 3rd and 28th day of the Ramadan month using a fully automatic hematological

analyzer. The results of Lymphocytes percent and Neutrophils percent were significantly increased during the Ramadan fasting period as compared to the pre-Ramadan fasting period. WBC count decreased significantly at the end of the Ramadan month as compared with pre-Ramadan fasting.

In addition, A cross-sectional study for Mushtaq et al., 2019²² at Federal Urdu University of Arts, Science & Technology investigated the effect of Ramadan fasting on plasma adiponectin and TNF- α levels for 55 females and 55 males, age 20 and 40 years fasting in Ramadan, the Plasma adiponectin and TNF-alpha levels were assayed with ELISA kits. Fasting in Ramadan significantly decreased TNF- α (pg/mL) levels of post-obese males and females than Pre-Ramadan-groups. fasting showed a beneficial effect on health. A cohort study was done by Alam et al., 2019²⁹ on 78 adult men who were fasted for 29 consecutive days from sunrise to sunset in Pakistan, aged 20 to 85 years, All CRP level <2 mg/l during the fasting period and a similar trend were observed for TNF α . Most SASP molecules were decreased after the fasting period, heightened levels of IL-8 and IL-6 suggest that some inflammatory markers may be elevated by recurrent circadian fasting. The results highlighted that circadian fasting is beneficial at the cardiometabolic and inflammatory levels. According to the review results of Massoud et al., 2020²³. Ramadan fasting has a positive influence on the body weight, lipid and glucose levels, while exerting antioxidative effects, increasing longevity, and improving the renal and immune function.

In an additional study of Mindikoglu et al., 2020²⁸ An untargeted serum proteomic profiling was performed using ultra-high-performance liquid chromatography/tandem mass spectrometry for 14 healthy fasted people from dawn to sunset for over 14 h daily for 30 consecutive days. Samples of Serum were collected before 30-day of fasting, at the end of 30-day of Ramadan, and one week after 30-day intermittent fasting. the results highlighted that 30-day fasting can be a preventive and adjunct therapy in cancer, DNA repair, cytoskeleton remodeling, immune system, and cognitive function.

The impact of Ramadan fasting on Respiratory structure and function in healthy people

Siddiqui et al., 2005³⁷ studied the impact of

Ramadan fasting on pulmonary function values in Healthy people. They found no significant change in the pulmonary function parameters during fasting in Ramadan compared to before the Ramadan period. However, FVC was decreased significantly after the Ramadan period compared to Ramadan. Relative Topre-Ramadan Baseline Values, there was no change in spirometric variables during Ramadan fasting.

In addition, Subhan et al.,2006³⁸ determined the effect of Ramadan fasting on the expiratory flow rates in healthy subjects. There was a significant reduction in body mass in Ramadan compared to pre- and post-Ramadan. They found no significant changes in expiratory flows during Ramadan as compared to the pre-Ramadan period. forced expiratory flow rates at 75%-85% of the vital capacity showed a significant increase in the post-Ramadan period compared to Ramadan. Their results show that Ramadan fasting did not affect expiratory flow rates in healthy subjects.

Moosavi et al.,2007³⁹ assessed changes in lung volume during and after Ramadan fasting. They found that the mean of FEV1% increased both during fasting and after Ramadan. Moreover, the mean vital capacity and peak expiratory flow rate were significantly increased during Ramadan. Although the mean maximum mid-expiratory flow decreased at the beginning of Ramadan, however, it was subsequently increased significantly. The researchers concluded that fasting increased lung volume and improved lung function. Moosavi et al.,2007⁴⁴ designed a cohort study that included 117 healthy male subjects' professors and student volunteers, to evaluate the changes in pulmonary volume during and after Ramadan fasting. All participants underwent spirometry 10 days prior to Ramadan, two times during Ramadan, and one time 10 days post-Ramadan. Although the mean maximum mid-expiratory flow decreased at the beginning of Ramadan and significantly increased subsequently, MEF50%, and MEF 75% increase at the beginning of Ramadan and decreased subsequently the result clarifies that fasting increases lung volumes and might improve pulmonary function.

The study of Askari et al.,2015⁴⁷ evaluated the total and differential white blood cells, inflammatory biomarkers, and respiratory symptoms in fifteen

asthmatic patients compared with a matched control group of fourteen healthy volunteers before and after the one-month fasting. There was no negative impact found on the pulmonary function, total white blood cells, and inflammatory biomarkers on healthy nor on asthma subjects.

In a study by Soori et al., 2016³⁶, the effects of Ramadan fasting on respiratory muscle strength were investigated in a group of 35 fasting healthy males, maximal inspiratory muscle pressure (MIP) and peak inspiratory flow (PIF) were measured in the last week of Ramadan month in summer, after 3 months of Ramadan the measurements were repeated in 12 individuals. the results showed Ramadan fasting may cause reduction of respiratory muscle strength through reduction of body weight but no other effects.

Latiri et al., 2015⁴⁵ Evaluated the effect of Ramadan Fasting on Spirometric values in 29 non-smoking healthy males (mean age of 27±6 yrs) fasting during Ramadan for at least the 5 past years for three periods, before-Ramadan, mid-Ramadan and, after – Ramadan, the results showed Ramadan fasting did not have any significant changes in the spirometric only affected FEV1 and FVC of healthy male adults.

Askari et al., 2016⁴² investigated the pulmonary function tests (PFT) and respiratory symptoms, in 15 asthmatic patients compared with 14 healthy volunteers who had no history of respiratory complaints. They measured PFT before and after the one-month fasting duration. The results showed that the values of MCH, MCHC in both groups, and monocyte counts in asthmatic patients. Respiratory symptoms in asthmatic patients were non-significantly increased and wheezes were significantly reduced following Ramadan fasting in the asthmatic group of patients.

Latiri et al., 2017⁴⁰ conducted a study of whether Ramadan Fasting affects Spirometric values in Twenty-nine nonsmoking healthy males during fasting month for three periods before-Ramadan, mid-Ramadan, and after-Ramadan, to conclude, RF did not have any significant changes in the spirometric values of nonsmoking healthy adult males.

The study of Roy A. & Bandyopadhyay A. 2018⁴¹ aimed to investigate the effects of Ramadan fasting

on lungs function tests (PFTs) in Fifty sedentary nonsmoking healthy young Muslim male individuals aged 20 to 25 years without any history of pulmonary or other diseases were recruited by simple random sampling from Kolkata, India. Participants completed the American Thoracic Society questionnaire for their personal demographic data, health status, PFTs were within the normal range and did not show any significant variation during the RIF and RIF did not affect the normal range of PFTs in young Muslim males.

The Study was done by Sayeed et al., 2018⁴³ to determine the effect of Ramadan fasting on spirometric parameters for 50 apparently healthy young adults aged between 17-27 years. It was done at three different time points: First: 5–10 days before the start of Ramadan (pre-Ramadan); second: Within 10 days of the beginning of RF (Ramadan); third: Within 7 days of the end of Ramadan (post-Ramadan). There were no statistically significant differences between the three phases, RF does not have any significant effect on PFTs as assessed by spirometry. Hence, the diagnosis and prognosis of a respiratory disorder made on spirometry findings are reliable and need no error correction with an individual is fasting.

In another study of Dodderi & Philip, 2018⁴⁸ aimed to measure the pulmonary function of thirty-seven healthy adults between 18-23 years volunteers, Twenty non-fasting and seventeen fasting healthy adults, Individuals under fasting performed spirometry tracings across the 1st week of fasting, last week of fasting and one week after breaking of fasting, the results showed reduced pulmonary function in fasting volunteers during 1st week and last week of fasting, with the increase in pulmonary function 1st-week post breaking of fasting and the study concludes that fasting in Ramadan improves the pulmonary function. Fraj et al., 2019⁴⁶ Evaluated the weather of Ramadan Fasting affects Spirometric values in a group of 36 healthy males adolescents aged 12 to 15 years for three periods Before-Ramadan, Mid-Ramadan and Post-Ramadan, to conclude, Ramadan Fasting did not have interaction effect in the spirometric values of healthy male adolescents.

Conclusion

In Ramadan, as the COVID-19 continues to spread

globally, and people go on to self-isolate in their homes and most of them afraid of getting sick, moreover, they work to strengthen their immunity. healthy people wanted to consider the religious license to break their fast in consultation because fasting during Ramadan may have a negative effect on the immune system, pulmonary function, and increase the risk of infection. however, guidelines statements that help to guide healthy people in addressing these issues are not clear, moreover, There has been no research on the impact of fasting on an increased risk of COVID-19 disease, for this purpose, we performed this review, in this review, our aimed to collect the current evidence regarding the effect of Ramadan fasting on the immune system and respiratory structure and function in healthy subjects. We can conclude that:

1. Ramadan fasting has been shown no negative impact on the immune system in healthy people.
2. Fasting in Ramadan may improve the immune system function.
3. Ramadan fasting has been shown no negative impact on the respiratory system in healthy individuals.
4. fasting in Ramadan may improve pulmonary function.
5. Ramadan fasting doesn't increase the chances of getting sick with the COVID-19.
6. Studies of healthy people have shown that Ramadan fasting is safe

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Author's contributions

BQ, participated in the design of the study, data collection, and drafted the manuscript. BQ, KSF and AOA contributed to the e writing of the manuscript. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

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