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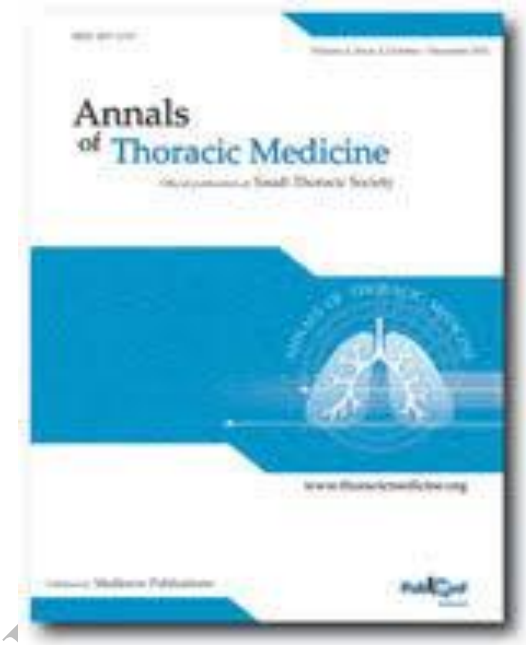

Ramadan intermittent fasting and immunity: An important topic in the era of COVID-19

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Abstract

With the growing pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome (SARS)-related coronavirus (SARS-CoV-2) infection, a parallel growing interest arose concerning the preventive therapies, dietary behaviors, and remedies that may boost the immunity of against SARS-CoV-2 infection. Further, as Ramadan intermittent religious fasting that is practiced by about one and a half billion people throughout the globe is coincide this year with COVID-19 pandemic, a growing debate rose concerning the expected impact of fasting during Ramadan month and the associated dietary and lifestyle behaviors on the body's immunity against the pandemic infection. Published literature was searched to find out how intermittent fasting and its model of Ramadan affect the various aspects related to the body's immunity against microbial infections. Intermittent fasting was found to impact immunity by changing different related elements, including oxidative stress and inflammation, metabolism, body weight, and body composition. Dietary and lifestyle modifications during Ramadan month and their impact on immunity, such as water intake and hydration status, sleep duration and timing, caloric intake and mealtime, and social and religious activities, were addressed. Further research is warranted to figure out how intermittent fasting during Ramadan affects immunity against SARS-CoV-2 infection.

***Keywords*:** COVID-19, Corona virus, Infection, Inflammation, Diurnal fasting

1. Introduction

In December 2019, the new severe acute respiratory syndrome (SARS)-related coronavirus (SARS-CoV-2) firstly emerged in Wuhan, China. It then spread rapidly worldwide to be declared as a pandemic by the World Health Organization (WHO) in March 2020. The disease caused by the new SARS-CoV-2, known as coronavirus disease 2019 (COVID-19), is associated with increased morbidity and mortality, representing substantial global public health concerns [1]. It is not an exaggeration to say that what the world is going through at present represents a pivotal historical moment and a position in the contemporary history of humankind that is similar to the historical viral and bacterial pandemics in the last century.

According to the recent WHO report [2], respiratory infections can be transmitted through droplets in different ways according to the different droplet sizes. Recent evidence showed that the COVID-19 coronavirus is primarily transmitted through contact routes and respiratory droplets. This droplet transmission occurs when a person is in close contact with another one who is carrying the virus. Therefore, the normal person is at risk of having her/his mouth and nose mucosae or ophthalmic tissue (eye conjunctiva) exposed to potentially infective respiratory droplets. Also, the transmission may occur through fomites in the immediate environment around the infected person [3]. Therefore, the transfer of the COVID-19 coronavirus can occur either by indirect contact with surfaces in the immediate environment or with objects used on the infected person or by direct contact with infected people [2].

Fasting during the Muslims' holy month of Ramadan represents one of the five pillars of Islam. Ramadan month is the ninth month in the lunar calendar, during which around one and half billion Muslim population abstains from food, drink, and smoking from dawn to sunset for a period ranging from 12 to 20 hours based on the season and geographical location [4].

Further, religious gatherings (such as group prays in the Mosques) and social parties (such as family and friend invitations for *Iftar*, the breakfast meal at sunset) especially for the extended family members, which characterize many Arab and Muslim communities; all are

among the most distinguishing community behaviors characterize the holy month of Ramadan [5].

With the current health burden of COVD-2019 and the precaution raised by the WHO, especially the necessity of keeping throat wet, there is an ongoing debate by the scientific and puplic communities (by some) around whether or not adult Muslims should fast Ramadan month, which is expected to start on April 24, 2020. As such, it is not clear whether fasting Ramadan negatively impacts the body's immunity, and hence causing expansion of the COVID-19 outbreak among the Muslim communities.

Therefore, we intended in this review to revise the available literature pertaining to the impact of intermittent fasting (IF) regimens, and particularly diurnal Ramadan intermittent fasting (RIF), on the immune response against microbial infections, with particular attention toward viral infections and coronavirus, when available.

2. Material and Methods

Google Scholar, ScienceDirect, PubMed/MEDLINE, CINAHL, EBSCOhost, Cochrane EMBASE, ProQuest Medical, Web of Science, and Scopus databases were searched**.** Keywords used in searching literature included “Ramadan”, “intermittent fasting”, “fasting regimen”, “immune response”, “immunity”, “infection”, “viruses”, “Corona virus”, and “COVID-19”. Original research, systematic reviews, and meta-analyses, along with narrative review articles were collected and reviewed for their significant findings on the impact of fasting regimens and RIF on immunity and immune response against microbial infections. Other related aspects that affect immunity, such as oxidative stress (OS) and inflammation, were collected as well. Both human and *in vivo* animal studies mimicking RIF and other fasting regimes were reviewed as well. Studies conducted on both healthy and disease patients were considered to highlight the impact of IF and RIF on different sectors of people in any population group.

3. Results

3.1 . Intermittent fasting, inflammation, and immunity

Recent reports indicated that severe COVID-19 patients might exhibit features of systemic hyper-inflammation designated as cytokine storm [6]. This inflammatory storm is characterized by a sharp burst in the inflammatory cytokines interleukin [IL]-6, IL-1β, and tumor necrosis factor (TNF)-α) and interferon (IFN)-γ [6, 7]. It is well reported that the imbalance in the production of proinflammatory cytokines like IL-6, TNF-*α*, IL-1, IFNs type I and II, IL-10 contributes to immune dysfunction and mediates inflammation of the tissues [8]. Further, insulin-like growth factor-1 (IGF-1) has been implicated in the etiopathogenesis of the neuroinflammation and associated with age-related neurodegenerative diseases [9]. Several studies have been conducted on the immunomodulatory and proinflammatory effects of RIF on healthy adults. In this regard, our team performed relevant research that started in 2009 and published in 2012 [10]. In that study, 50 (29 women and 21 men) healthy volunteers were recruited. Circulating proinflammatory cytokines IL-6, IL-1β, and TNF)-α, immune cells (lymphocytes, total leukocytes count, granulocytes and monocytes) were tested before and at the end of RIF month (after 28 days of daily fasting for about 15 hours) and again one month after the end of Ramadan month. The serum levels of the proinflammatory cytokines IL-6, IL-1β, TNF-α, were significantly lower (P<0.05) during Ramadan as compared to their levels before Ramadan or after the cessation of RIF. Moreover, the numbers of immune cells significantly reduced during Ramadan, but remained within the normal reference ranges.

We further confirmed these significant reductions in the proinflammatory cytokines in our recent study on the impact of RIF on visceral adiposity and serum adipokines in overweight and obese individuals [4]. In this study, which involved 61 (38 women and 23 men) overweight and obese subjects, we found significant decreases in the serum levels of cytokines IL-6 and TNF-α, as well as the level of IGF-1, coinciding with a significant increase in the anti-inflammatory cytokines IL-10 and IL-10/IL-6 ratio [9]. These findings imply that RIF attenuates the inflammatory status of the body by decreasing the levels of proinflammatory cytokine expression and decreasing circulating levels of leukocytes without adversely impacting the immune response. Another recent study assessed the pure effect of RIF on proinflammatory cytokines while controlling for lifestyle changes that may affect systemic inflammation, such as sleep duration and timing, meal composition and

caloric intake, and energy expenditure, and multiple sample were collected around the clock to account for circadian changes in the cytokines levels.[11] The study reported RIF led to significantly decreased plasma levels of cytokines (IL-1β, IL-6, and IL-8), particularly IL-1β and IL-6 across 24 h.[11]. In line with our studies, others also highlighted the positive impact of IF on ameliorating the IGF-1 levels [12]. IGF-1 has been shown to augment proinflammatory cytokine levels.[13]

Another study assessed the effect of RIF on circulating levels of immune complex (CIC) and immune indices before and after Ramadan in blood samples of 120 healthy volunteers [14]. The results revealed no significant differences in the CIC level at the end of RIF in comparison with the pre-fasting level, implying that RIF does not harm the immune status of healthy people. The same group found no adverse effect of RIF on the respiratory bursts of neutrophils [15] at the end of RIF month in comparison with the pre-fasting levels. Based on their studies, the investigators speculated that innate immunity response for intracellular infection factors during RIF was not decreased; in fact, it increased, indicating the beneficial effect of fasting to protect against bacterial infection. This speculation was supported by research on an experimental animal model using middle-aged BALB/c mice, which demonstrated the ability of IF to increase the efficiency of the immune system in resisting the pathogenic bacteria *Salmonella typhimurium* that causes the famous typhoid fever [16].

This anti-inflammatory and neuroprotective effect of IF against bacterial infection was also shown in another animal model. In one study, rats were subjected to IF (alternate-day fasting diet) for thirty consecutive days after being injected with toxic inflammatory lipopolysaccharides compounds. [17] The study showed that IF induces adaptive responses in the brain and periphery that can suppress inflammation and preserve cognitive function in the animal model of systemic bacterial infection [17]. Further evidence on the neuroprotective and anti-inflammatory effect of IF (alternate day fasting) was shown on Sprague-Dawley rats exposed to IF for three months.[18] IF stimulates IFN-γ mediated neuroprotective signaling in the hippocampus, suggesting a role for this cytokine to protect neurons in animal models against neurodegenerative disorder, severe epileptic seizures, stroke [18]. IFN-γ is known to be an extremely multipurpose cytokine that can carry out countless biological activities that are essential to other interferons. Failure in the IFNγ-IFN-γR system severely hampers host immune responses. IFN-γ has been shown to activate

macrophages and improve their ability to mount an effective immune response through enhancing antigen processing and presentation, and activating natural killer (NK) cells.[19] The protective effects of IFN-γ can be seen in the pathogens, including viral infections, as enhanced survival of neurons infected with Varicella-zoster virus is observed post-IFN-γ treatment.[20] Additionally, IFN-γ have been shown to be effective blocking Ebola virus infectivity.[21] The anti-viral effects of IFN-γ work through the stimulation of RNA-activated protein kinase R and adenosine deaminase RNA specific-1, where the anti-viral actions involve either viral multiplication or genomic stability.[19] However, the effect of IFN-γ on SARS-CoV-2 needs further.

Adawi et al., [22] systematically reviewed 45 studies that assessed the effect of fasting during the month of Ramadan on immunity. By examining the collected articles, they conclude that fasting during Ramadan was associated with mild transient changes in the immune system, which return to the basal pre-Ramadan status shortly afterward. They also reported, in cardiac patients, that fasting during Ramadan entailed beneficial effects in the alleviation of oxidative stress.

In addition to the studies dedicated to the investigation of RIF on human health and immunity, other studies have been conducted on the impact of different forms of fasting, including IF, time-restricted feeding (TRF), alternate-day fasting, and the simulated diet of fasting-mimicking. One study investigated the effect of TRF (a pattern similar to fasting Ramadan) on 40 adult and young adult volunteers.[23] It demonstrated a reduction in the numbers of NK cluster of differentiation (CD) 56+ and CD15+.[23] These data support the ability of TRF to prevent the age-associated perturbations that contribute to immunosenescence [23].

Apart from the direct effect of RIF on inflammatory and immunomodulatory factors that mediate the immune function, other physiological impacts such as changes in body weight and composition during Ramadan may have an indirect effect on the body's immunity and ability to fight pathogenic infections. Recent findings highlighted the significant impact that obesity and metabolic syndrome impose on pathogen defense and immunity function. These include the alterations in leukocyte development, phenotypes, and activity; disruption of lymphoid tissue integrity; and the coordination of adaptive and innate immune responses.

These changes are associated with an overall adverse effect on immunity from infection [24]. Excessive adipose tissue has been reported to be implicated in the impaired immunity that obese people suffer from. It has been reported that T-cells infiltrating the adipose tissue display activation markers, and regulatory T-cell populations increase within adipose tissue [25]. Beside, adipocytes do not only work as a storage site for lipids but also they secrete a variety of adipocytokines such as adiponectin and leptin [26]. These two hormones, in addition to their vital role in body weight regulation, play a significant role in inflammation and immune function [26, 27]. It is believed that cells of the innate immune system mediate physiological changes present in obesity. Cells from the adaptive immune system play roles in both lean and obese conditions. Researchers believe that obesity has numerous synergistic interactions with viral infections. Bacterial infections in the setting of obesity also alter in comparison with healthy weight [28].

RIF has been shown to reduce weight. Several meta-analyses have documents weight reduction during Ramadan fasting despite being conducted in a free-living unconstrained environment and not giving the participant any advice on lifestyle or dietary modifications.[29-31]. A recent systematic review and meta-analysis on RIF and body weight (on 4176 participants from 85 studies conducted in 25 countries) [32] and metabolic syndrome components (on 4326 participants from 85 studies conducted in 23 countries) [32] showed that RIF was associated with a significant reduction in the body weight (about 1 kg), with substantial decreases in the metabolic syndrome components, namely fasting glucose, systolic blood pressure serum triglycerides, and waist circumference, concomitant with a significant increase in the HDL-cholesterol. Further, other systematic review showed a significant reduction in body fat mass and fat percent at the end of the fasting month of Ramadan [29].

3.2.Intermittent fasting and infection

A study tested the effect of fasting in Ramadan on the body's ability to fight the pathogenic bacterial infection by *Mycobacterium tuberculosis*, which causes tuberculosis, of thirty fasting volunteers. [33] It demonstrated that fasting during Ramadan was associated with a reduction in the disease with this pathogen by increasing the numbers of macrophages. The study also showed the ability of fasting to increase the secretion of INF-γ, which is known to stimulate the anti-microbial immune mechanisms against infections with bacteria or viruses, as discussed above.[33]

Most interestingly, studies of fasting and immunity were not limited to healthy people. A study that was conducted on Muslim patients infected with the Human Immunodeficiency Virus (HIV) showed the absence of any negative impact of RIF on modifying the frequency of antiretroviral therapy. [34]. In this study, fasting HIV patients on antiretroviral therapy were shifted from twice-daily dosed to once-daily dosed without significant changes in cluster differentiation CD4 cell counts, viral load, or hematocrit levels in comparison with the twice-daily dose therapy non-fasting patients.

In another scientific review on the IF and other forms of dietary restrictions, it appeared that such dietary modifications could promote anti-inflammatory effects and to decrease the biological rate of aging. Such changes may alleviate and possibly reverse a variety of autoimmune disorders as well as immunosenescence by killing damaged and old cells and replacing them with functional young ones [35]. This protective effect of IF against the autoimmune disease was evident in the animal model of experimental autoimmune encephalomyelitis (EAE). Using female mice (C57BL/6) injected with myelin oligodendrocyte glycoprotein antigen to induce EAE, IF for 35 days after immunization resulted in a significant reduction in the incidence and induction of EAE, and significantly reduced the severity of disease [36]. The authors concluded that IF might play a possible role in the treatment of multiple sclerosis patients. This finding was further supported by Cignarella and colleagues [37] who found that IF ameliorates the clinical course and pathology of the multiple sclerosis mouse model (EAE) induced in animals. This was manifested in the ability of IF to increased gut bacteria richness, enrichment of the Bacteroidaceae, Lactobacillaceae, and Prevotellaceae families and enhanced antioxidative

microbial metabolic pathways. Further, they reported that IF altered T cells in the gut with a reduction of IL-17 producing T cells and an increase in regulatory T cells.

3.3. Inyermittent fasting and oxidative stress

It has been established that an increase in pro-inflammatory and oxidative stress factors participate in weakening the immunity and increases the risk of infection. Oxidative stress (OS) and inflammation are strictly related pathophysiological processes, one of which can be easily induced by another. Thus, both processes are simultaneously found in many pathological conditions [38], and involved in the etiopathogenesis of many acute, chronic [39-41] and infectious [42-44] diseases [45]. Several mechanisms have been proposed to explain the distinct relationship between oxidative stress, inflammation, and infection. One of these mechanisms is that OS plays a pivotal dual role in infections.

Free radicals protect against the invading pathogens, which in turn can cause tissue damage during the resulting inflammation. In the process of infection, there is a generation of reactive species by several enzymes, such as nitric oxide synthase, myeloperoxidase, and nicotinamide adenine dinucleotide phosphate (NADPH) oxidase. On the other hand, reactive oxygen species can be generated, by cytochrome P450, xanthine oxidase, and some metals. Some pathological changes arising during infection can be attributed to OS, and the generation of reactive species in infection can even have fatal consequences [44]. Further, the two related processes, inflammation, and oxidation could be the link between anxiety, aging immunosenescence [46].

In a recent systematic review and meta-analysis study on the impact of RIF on inflammatory and oxidative stress markers in healthy subjects, Faris et al. reviewed the inflammatory markers IL-1, IL-6, TNF-α, and C-reactive protein (CRP), as well as the oxidative stress marker malondialdehyde (MDA). Based on explicit inclusion and exclusion criteria, 12 studies involving 311 participants distributed, over eight countries were solicited. Studies were distributed as follows: 3 studies from Iran, two from Turkey, two from Saudi Arabia, one from Jordan, one from the United Arab Emirates, one from Denmark, one from the Netherlands, and one from Indonesia. The results revealed that RIF was associated with a small to medium reductions in TNF-α (expressed in terms of the effect size measure of Hedge's g value = -0.371) and IL-6 (Hedge's g = -0.407) and minimal reductions in MDA (Hedge's g = -0.219), IL-1 (Hedge's g value = -0.016), and CRP (Hedge's g = -0.119) [47].

A recent examined the effect of RIF on the genetic expression of three genes that augment the processes of preventing oxidation and inflammation in nearly 60 healthy adults.[48] Results of the study showed that RIF was associated with significantly increased expression of these genes, namely Mitochondrial transcription factor A (*TFAM*) superoxide dismutase 2 (*SOD2*), and nuclear factor erythroid 2 related factor 2 (*Nrf2*) genes at high levels of 90.5 %, 54.1% 411.5%, respectively, as compared to their levels before Ramadan. These results suggest the ability of RIF to protect against oxidative stress and inflammation responsible for weakening the immune system and reducing its defense against infection [48]. This antioxidative stress effect of RIF was further supported by an animal model that mimics the 12hour/day, 30-day of RIF model. Forty male carbon tetrachloride-intoxicated Wistar rats were exposed to RIF mimicking model, and the results showed significant reductions in CRP and MDA parameters for oxidative stress [49]. In a similar RIF mimicking model, Shawky et al. showed that IF caused a considerable increase in neutrophil phagocytic activity, phagocytic index, and brain neurotransmitters (norepinephrine and serotonin) [50].

3.4.Water intake, dehydration, and immunity against infection

It is well established that immunopathology of airway surface liquid is adversely affected by dehydration disease, and that any defects in the functioning of the mucociliary escalator compromise the mucociliary clearance of inhaled pathogens may favor microbial lung infection [51]. Indeed, RIF 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 RIF versus Nineveh fasting regimens (refrainment from food and drink from morning till sunset for three consecutive days) during the three consecutive days as well as the difference between the fasting period and four weeks following the fasting period in both groups.[52] In this study, RIF (for an average of 15 h for 29 consecutive days, n = 40) and Nineveh fasting (60 h of nonstop fasting, n = 26) were compared. No significant difference was found in the mucociliary clearance time between the RIF and control (4 weeks after the fasting period).[52].

Insuffieinct water intake is one of the most compelling and challenging claims that were raised about the possibility that RIF may induce susceptibility to COVID-19 infection. Although RIF dictates refrain from food and fluid, even water, intake, no available evidence

supports that RIF is associated with dehydration, and no detrimental effects on health have been directly attributed to negative water balance during Ramadan month in healthy subjects [53]. Changes in functional water volume may be more important clinically than gross differences in total body water [54]. In one study, gross total body water statistically decreased [55], and it was non-significant in another study [48]. However, in both studies, gross total body water remained within the normal range of 30-46 kg [56]. Further, total water and fluid intake showed a significant increase during the night hours of Ramadan month in comparison to the pre-fasting intakes (1131±967 ml/day before vs. 1691±796 ml/day at the end of Ramadan)[55].

Water deprivation is functionally characterized by maximum urine concentration. In 20 Malaysian Muslims, urine was collected before, during, and after RIF each in the morning, afternoon, and overnight [57]. The authors found that RIF did not affect the overnight urine volume or osmolality, indicating that the fasting subjects were probably not subjected to severe water deprivation. During Ramadan, the osmolality of the urine samples collected in the afternoon was very high, indicating effective water conservation and a decreased obligatory urine output and maximum urinary concentration.[58]

Among the clinical consequences of dehydration is that dehydration and low fluid intake are associated with increased risk of developing renal calculi [59]. Evidence supporting the lack of adverse effects of RIF on the body's hydration status comes from a study that was conducted to compare the prevalence of renal colic (RC) in Ramadan with other months of the lunar year. Records of 574 subjects (398 males and 176 females) who were admitted to the two medical centers of a city in a hot region of Iran were reviewed.. Twenty-seven males (63%) and 16 females (37%) were admitted in Ramadan, and 37 males (70%), and 160 females (30%) in other months ($p<0.4$) of the year.[60] There was also no significant difference between the frequency of admissions in Ramadan and mean admission during the other months of the year [60].

In a more recent prospective observational study that was conducted to evaluate the effects of RIF on the number of RC visits and laboratory results of patients with RC. Results from 176 patients (89 before Ramadan and 87 in Ramadan) with RC revealed that RIF did not

change the number of RC hospital visits. Moreover, although fasting causes some changes in urinary metabolites, there was no enough evidence that these changes increased urinary calculus formation [61].

3.5.Impacts of ritual and social behaviors during Ramadan month

At the sunset breakfast meal (*Iftar*), social gatherings, many times in buffet style, are frequent in many communities. It is worth noting that talking about fasting the month of Ramadan does not stop with the social and nutritional habits and behaviors that accompany it. This virtuous month of Ramadan is not only a month of fasting, but also a social, devotional month in every sense of the word, and what people gather in prayers and worship and on iftar tables is far from our minds. Perhaps this is one of the biggest challenges facing Muslim societies during Ramadan. The adverse effect of RIF on the immune system that has been refuted is not a challenge. Still, the real problem is those societal behaviors that may be a source of renewed infection in light of talking about the recurrence of the virus outbreaks in the coming seasons. Also, the nature of the food prevailing in the month of Ramadan, which is predominantly sugar and fat, weakens immunity and reduces the efficiency of this device in defending and curbing the virus. It is well established that the typical diet rich with refined sugars, salt, and saturated fat is associated with an increased risk of infection [62].

Several mechanisms have been proposed for the adverse effect of an unhealthy diet on immune function. More attention has been given to the dietary impact on the gut microbiota and the mechanisms by which unhealthy food choices and dietary patterns are encoded into our genes and our gut. It has been reported that the overabundance of macronutrients and calories that compose the modern diet may all lead to reduced control of infection, increased inflammation, and increased risk for allergic and auto-inflammatory disease [62, 63].

Therefore, fasting performers have to eat balanced food rich in vegetables, fruits, legumes, and nuts rich in micro-nutrients (vitamins and minerals) and polyphenols that boost the immune system and may help in combating COVID-19 coronavirus infection [64, 65]. A mounting body of evidence indicates that the ingestion of fruits high in polyphenols, carbohydrates, and metabolites effectively supports human body performance, with added

benefits including enhancement of anti-viral and oxidative capacity through fruit metabolites, and increased plasma levels of gut-derived polyphenols [40, 66].

Further, multivariate logistic regression analysis for data of seventy-eight patients with COVID-19 from China indicated that a history of smoking was a risk factor of disease progression [67], and smoking has been reported to be the most likely factor associated with the negative progression and adverse outcomes of COVID-19 [68]. This may lead to speculation that RIF may favor a protective environment against SARS-CoV-2 infection and reduce the burden of COVID-19 during Ramadan month, providing that deliberately smoking is one of the things that invalidate the fast during Ramadan [69]. Also, the spiritual conditions characterizing the month of Ramadan may trigger many smokers to quit smoking, which is looked at as a useful faith-based smoking cessation intervention [70] providing that numerous religious scholars and institutions in North African and Middle Eastern countries have declared smoking to be *haram* (prohibited) [71, 72].

It should also be noted that fasting and the accompanying drought in the throat constitute a risk factor for infection, which compels the fasting persons to stay away and guard against infection points and commitment to social distancing to ward off danger from the other side. Here, a distinction is made between the effect of individual fasting on the one hand, and the social customs and behavior associated with the blessed month of Ramadan on the other.

Another behavioral risk factor for reduced immunity that may accompany the fasting month is the significant reductions in sleep duration and the disturbances in sleep pattern, as revealed by a recent meta-analysis on RIF and sleep [73]. This work showed that total sleep time significantly decreased by about one hour (from 7.2 hours per night before Ramadan to 6.4 hours during Ramadan), while the daytime sleepiness measure using the Epworth sleepiness scale score increased slightly from 6.1 before Ramadan to 7.0 during Ramadan. These changes in sleep quantity and quality are ascribed to the religious and social activities practiced during the night hours of Ramadan [73, 74]. It well established that insufficient sleep can increase organism susceptibility to infection through weakening immunity and that sleep deprivation is associated with increased susceptibility to viral infections [75, 76]. This relationship is explained by the fact that partial sleep deprivation is associated with transiently impaired mitogen proliferation, the decreased human leukocyte antigen-

DR isotype, the upregulated CD14, and the variations in CD4 and CD8 that we observed in temporal relationship with [77].

4.Conclusion

In conclusion, this is a summary of the most prominent scientific studies published on the impact of the practice of fasting in all its forms, including fasting the month of Ramadan, on the immune response and the health and efficiency of the immune system. These studies were conducted in humans and animals, and their results showed a combination of the ability to fast to improve the body's resistance to bacterial infections. At its minimum levels, these studies did not show any adverse effect of fasting on the immune system, which refutes the claimed adverse impact of RIF on immunity. The false claim that there is a possible adverse effect of fasting on increasing the severity of the impact of the COVID-19 on the immune system is nullified. However, it should be noted from the scientific point of view that none of these scientific studies did test the effect of fasting in the month of Ramadan on the COVID-19 coronavirus infection.

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Abbreviations:

CD: Cluster of differentiation
CIC: Circulating levels of immune complex
COVID-19: Coronavirus disease 2019
CRP: C-reactive protein
EAE: Experimental autoimmune encephalomyelitis
HDL-cholesterol: High-density lipoprotein-cholesterol
HIV: Human Immunodeficiency Virus
IF: Intermittent fasting
IFN: Interferon
IGF-1: Insulin-like growth factor-1
IL: Interleukin
MDA: Malondialdehyde
NADPH: Nicotinamide adenine dinucleotide phosphate
NK: Natural killer
Nrf2: Nuclear factor erythroid 2 related factor 2
OS: Oxidative stress
RC: Renal colic
RIF: Ramadan intermittent fasting
SARS: Severe acute respiratory syndrome
SARS-CoV-2: Severe acute respiratory syndrome-related coronavirus
SOD: Superoxide dismutase
TFAM: Mitochondrial transcription factor A
TNF: Tumor necrosis factor
WHO: World Health Organization

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