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Ramadan Fasting and its Health Benefits: What's New?

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Abstract

Fasting is one of the five pillars of Islam. Fasting entails more than abstaining from food and drink, fasting improves impulse control and aids in the development of good behavior. The holy month of Ramadan falls on the 9th month of the lunar calendar. Ramadan is a month-long fasting period that takes place between dawn and sunset. Some people with diabetes and those who are sick or have certain medical conditions may be exempt. The majority of people with diabetes, on the other hand, choose to fast; even against medical advice. Many studies have been conducted to determine the health benefits of fasting. Apart from the benefits to the body's organs, Ramadan fasting is also beneficial for the growth of the gut microbiota and gene expression and is believed to impact the body's autophagy process. Furthermore, Ramadan fasting has an impact on mental health; TC and LDL were lower, while HDL and TG were higher, lowers inflammation, and oxidative stress markers.

Introduction

Fasting, which entails complete abstinence from food and drink, has been practiced in various religions since antiquity, including Islam and Judaism. Every year, during the lunar month of Ramadan, Muslims around the world conduct. Islamic fasting, with an estimated 2 billion Muslims participating. Fasting during Ramadan is an Islamic rule, so Muslims fast for 29–30 days in a row every year. During Ramadan, all healthy Muslim adults (who do not have any specific health problems) must fast from dawn to dusk and refrain from eating, drinking, smoking, intercourse, and a variety of other activities. This may last for more than 18 h/day, depending on the latitude [1], [2].

Ramadan fasting is one of Islam's five pillars, commemorating the revelation of the Holy Quran to Prophet Muhammad, peace be on him. All healthy Muslims who have reached puberty must fast for a month (29–30 days), which is a time for spiritual introspection and closeness to God. Between the hours of dawn and sunset, followers must abstain from eating and drinking and utilize oral medications, sexual activity, and smoking. During Ramadan, it is thought that spiritual rewards for good deeds are multiplied, and there is a strong urge to fast, even among those who may be exempt, such as the elderly, youngsters, and the infirm, and pregnant women. Fasts that have been missed should be performed at a later date, such as after one's health has been restored or after the birth of a child. Fasting outside of Ramadan (when the rest of the community is not fasting) can be difficult, which may deter people from using the exemptions that have been allowed. Those who are chronically disabled might make up for missed fast days by giving Fidya, which is a food or money donation to the impoverished [3], [4], [5], [6].

Many Muslims believe that specific diseases or heightened dangers should be declared as Fatwas or religious edicts, depending on the school of Islam they follow. Nonetheless, these judgments must be made on an individual basis based on the physicians' recommendations. In some schools of Islam, such Fatwa is produced on a nearly annual basis prior to the start of the holy month through elaborate cooperation among high-ranking Islamic jurisprudence experts, academicians, and medical practitioners [2].

The traditional Ramadan eating habit is to eat one major meal after sundown and one smaller meal before dawn; however, some Muslims eat another meal before sleeping. During Ramadan, Muslims eat a wider variety of meals than they do the rest of the year. During Ramadan, sugary meals and beverages are also consumed more frequently. When a child reaches puberty, all healthy Muslims are obligated to fast. Fasting is not required for those who are at risk of deterioration such as sick people, traveling, pregnant, breastfeeding, menstruation, or disabled. Despite this,

many Muslims who are eligible for an exemption opt to fast are still doing Ramadan [7].

Fasting has been the subject of numerous scientific studies as a potential non-pharmacological intervention for improving health and increasing longevity. Caloric restriction (CR), alternate-day fasting (ADF), and dietary restriction (DR) are the three most widely studied fasts. The reduction of kilocalorie (kcal) intake by a certain percentage (typically 20–40%) of *ad libitum* consumption is known as calorie restriction (CR). It has been proven that CR improves health and lengthens life. ADF is divided into two 24-h periods: during the "feast period," fasters may eat as much as they want; during the "fast period," food consumption is limited or stopped entirely. DR is defined as reducing one or more dietary components (usually macronutrients) with little to no reduction in total calorie intake. According to research, neither carbohydrate nor lipid restriction extends life. While religious fasting is done largely for spiritual reasons, it can also significantly impact one's physical health. As a result, the health implications of religious fasting have recently been the topic of scientific investigation, with the majority of studies conducted in the previous two decades [7].

Ramadan fasting is similar to ADF fasting in that both include feast and fast periods. Ramadan fasting feast days and fast periods are each 12 h long on average; for both the feast and fast periods of ADF, this equates to half of 24 h. Fasting should not make healthy adult Muslims weak; rather, it should increase their health and stamina. About 50 research articles on the medical ethics of fasting were presented at the first International Congress on "Health and Ramadan," held in Casablanca in 1994. It was proposed that Ramadan fasting would be an excellent recommendation for the treatment of mild to moderate diseases such as non-insulin-dependent diabetes, essential hypertension, weight management, and for the rest of the digestive tract, which involves reducing blood sugar levels, cholesterol levels, and lipid profiles. Patients with serious illnesses, such as type 1 diabetes, coronary artery disease, kidney stones, and other conditions, should be exempted from fasting and should not be allowed to fast [7], [8].

The main goals of this month-long process are to shape the practitioners' behavior and life patterns in such a way that they become ideal human beings. To accomplish this, one must refrain from listening, speaking, hearing, or thinking negatively about others. The effects of this purification procedure are expected to persist for the next few months before the process is completed [8].

Muslim Population around the World

The number of Muslims is predicted to reach 1.9 billion in 2019, accounting for almost 24% of the global population [9]. In 2015, 1.8 billion people identified as Muslims, or roughly 24.1% of the world's population. The following are the approximate Muslim percentages of the overall population in various geographic regions: 93% in Middle East and North Africa (MENA), 83% in Central Asia, 42% in Southeast Asia, 31% in South Asia, 29–31% in Sub-Saharan Africa, 1.5% in Oceania, roughly 5% in Europe, and 1% in the Americas. The MENA region, in particular, has a large and rising Muslim population. Muslims account for about a quarter of the world's population, with nearly 1.6 billion adherents as of 2010. By 2050, the number of Muslims is expected to rise by 73%, making Islam the world's fastest-growing religion for the next four decades [10]. The majority of countries with a majority Muslim population are in less-developed portions of the world, and sickness affects less-developed countries disproportionately (Figure 1). The population patterns in developing Islamic nations are changing dramatically as a result of rapid modernization. Increases in life expectancy, urbanization, and a reduction in the burden of infectious disease will all contribute to a rise in disease prevalence in future generations [11]. Similarly, major changes in development in these areas have a negative impact on lifestyle; some of the consequences of development include increased levels of poor-quality nutrition and sedentary behavior, which enable weight gain and raise the risk of cardiovascular disease. Another issue to be concerned about is smoking, which is becoming more prevalent in low- and middle-income nations and is linked to diabetes and cardiovascular disease [12].

While the global population is forecast to rise by 32% over the next few decades, Muslims are expected to grow by 70%, from 1.8 billion in 2015 to nearly 3 billion in 2060 [9]. Muslims accounted up 24.1% of the world's population in 2015. They are predicted to account for more than three-quarters of the world's population in 45 years (31.1%).The primary drivers of Islam's expansion are simple demography. For starters, Muslims have more children than the other seven major religious groups studied in the study. Muslim women have 2.9 children on average, which is much more than the next highest group (Christians, at 2.6) and the overall non-Muslim average (2.2). Muslim fertility outnumbers non-Muslim fertility in every major region with a significant Muslim population. Muslim population growth is also aided by the fact that Muslims have the youngest median age of all major religious groups (24 in 2015), more than 7 years younger than non-Muslims [9].

Psychological Effects of Ramadan Fasting

Fasting, according to Muslims, entails more than abstaining from food and drink. Fasting also

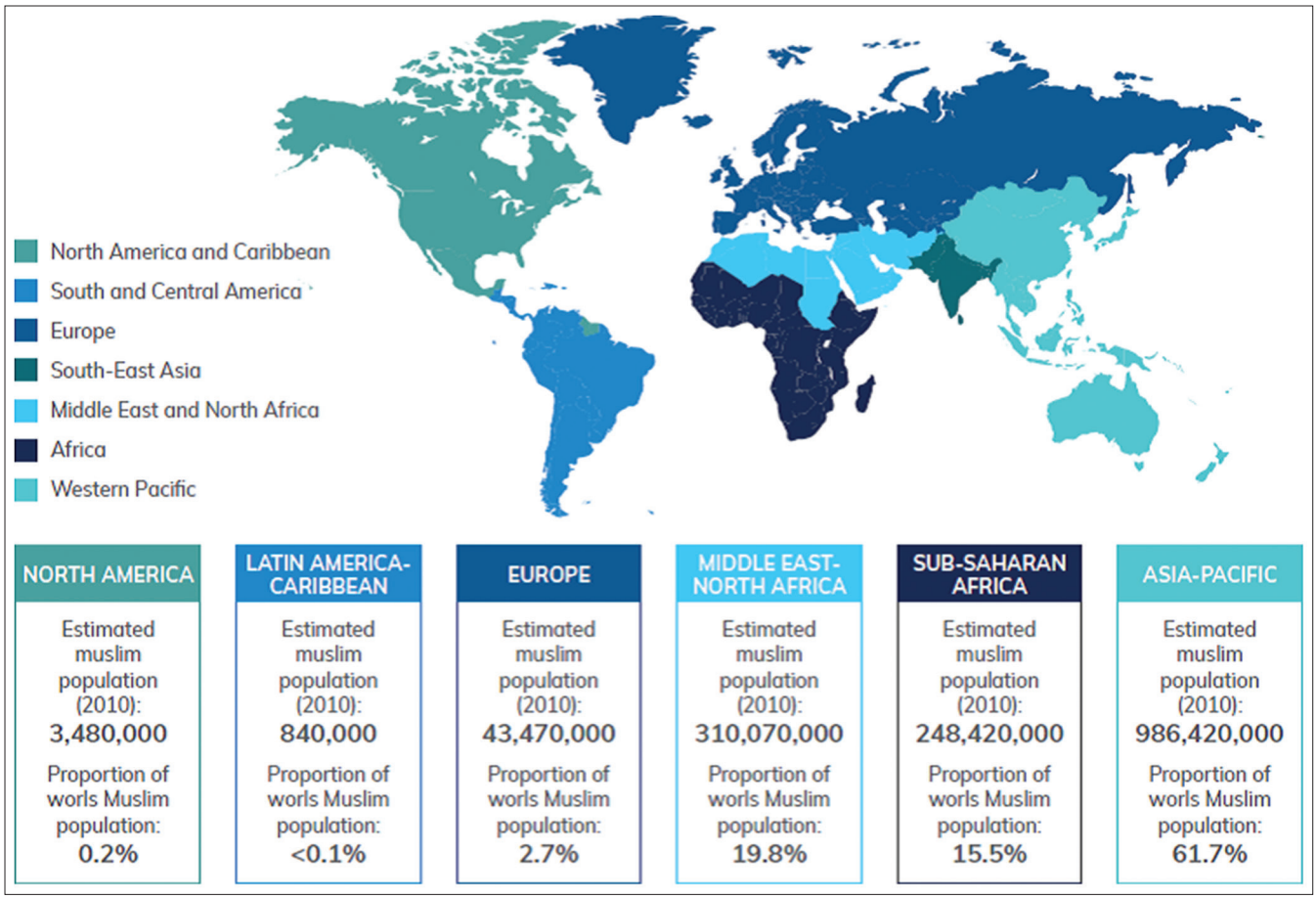

Figure 1: Estimated Muslim population in various countries in the world [3]

entails refraining from lying in words and deeds and refraining from ignorant and indecent speech, debating, fighting, and having lustful thoughts. As a result, fasting improves impulse control and aids in the development of good behavior. This purification of body and soul harmonizes an individual's inner and outer spheres. Muslims want to improve their health by eating less and living a healthier lifestyle. Food overindulgence is discouraged, and eating only enough to alleviate hunger pain is encouraged. Muslims believe that they should be active, attend to all their responsibilities, and never skip a beat [8].

Muslims consider Ramadan to be a blessed month since the Quran was revealed to Prophet Muhammad, peace be on him, during it, and it is the month of fasting when Allah's rewards for good actions are much more than at any other time. This usually results in a strong and ardent desire to do everything possible to seek God's presence and pleasure. During the month of Ramadan, Muslims practice a variety of additional types of devotion in addition to fasting. Therefore, it is not surprising that many Muslims, who fall in the exempt categories, including those with illness, are loath to take advantage of this concession. The reasons for such a strong desire to retain the fast are easy to assume or deduce. Perhaps one of the most important factors is that the sick person believes he or she would be failing to fulfill his or her responsibility as a Muslim, despite the fact that he or she is aware of the exemption offered in the event of such a condition. Many academics, however, who are aware of the potential major health risk for some people with medical illnesses, believe that those who refuse to fast against medical advice are committing a grave religious error because their health may be jeopardized. Indeed, the collaboration between medical and religious specialists is necessary to guarantee that those who do not fast due to a medical condition understand that they are rewarded in the same way as those who fast and should not feel guilty [3].

Fasting is thought to aid in the promotion of chastity and modesty, as well as the prevention of sin, the outburst of uncontrollable lusts and desires, and unrealistic expectations. During Ramadan, Muslims seek to purify their bodies and souls while also increasing their good deeds. On a cultural level, believers seek to develop and apply the most virtuous qualities to their daily lives. They strive to treat others with kindness, generosity, and mercy, as well as patience and anger control. In essence, Muslims are attempting to develop their moral character and habits, which they consider to be good [8].

Fasting during Ramadan is intended to help people develop spiritual, moral, and social qualities. It sends out a message of equality among society's

members. Charity and the genuine practice of the concept of neighborhood and hospitality are given special attention to the poor, who benefit from it. Apart from assisting in the attainment of body and soul purity through this self-purification process, addressing these socially significant issues is bound to assist people in letting go of everything that is not socially desirable. It is also critical to put the concept of neighborhood into practice. The neighborhood concept eventually spreads to the rest of the world [8].

During Ramadan, Muslims are not allowed to drink alcohol or smoke in any manner. Those who are addicted to such behaviors should now be the greatest time to break them, as they are harming their health and wasting their money. They should continue to abstain from these behaviors for the remainder of their lives, as they have done for the past month. Fasting has been made compulsory in order to achieve equality between the rich and the poor; the rich experience hunger and therefore fulfill their commitments to the poor. One of the most significant benefits of fasting throughout this month is that it instills in a person the habit of expressing the truth. Fasting during Ramadan is a form of self-discipline. For those who are heavy smokers, or frequent eating habits, or drink coffee very often, it is a good way to break the habit, hoping that the Effect will continue after the month is over [8].

Ramadan is a month of self-control, self-purification, truthfulness, and self-training, with the goal of continuing the training after Ramadan ends. Fasting has the benefit of drawing attention to the impoverished, which benefit from charity and the faithful implementation of the concept of neighborhood and hospitality [8].

Physiological Effects of Ramadan Fasting

The physiological implications of fasting during Ramadan on both homeostatic and endocrine functions are numerous. Ramadan fasting affects not only meal timings, but also sleeping habits and circadian rhythms, all of which might impair a person's metabolic status [3]. Individuals who fast during Ramadan are less likely to consult their doctors. It is hardly surprising, then, that potentially invasive research has been difficult to undertake, resulting in a scarcity of direct evidence about the Ramadan Fasting's physiological effects. Obtaining evidence for guidelines can be challenging, and asking people to volunteer for Ramadan-related projects can be even more difficult. Studies can also take longer to complete because Ramadan only happens once a year, leaving only a tiny window of opportunity to collect data. Much of the knowledge obtained thus far has come from studies with subjects who had fasted for more than 48 h. However, many additional studies of the Ramadan Fasting have lately been undertaken, with fresh and updated evidence on several aspects emerging [3], [13].

The Ramadan Fast has an effect on many aspects of human physiology, including sleeping patterns and circadian rhythmicity, fluid balance, energy balance, and glucose homeostasis, to name a few. It is a significant departure from traditional eating habits, as well as sleep and wakefulness routines. The Ramadan Fast is distinct from other types of fasting (Figure 2) [14]; since no food or drink is consumed during daylight hours, the time between meals is much longer during Ramadan than during other months of the year. This has major implications for physiology, with changes in the frequency and severity of variations in a number of homeostatic and endocrine processes as a result. The length of the fast has an effect on the physiological changes that occur; this is especially true when Ramadan falls during the longer summer days, when higher latitudes have the most daylight hours. In the summer, for example, the Ramadan fasting day in Scandinavian countries will last more than 17 h [3].

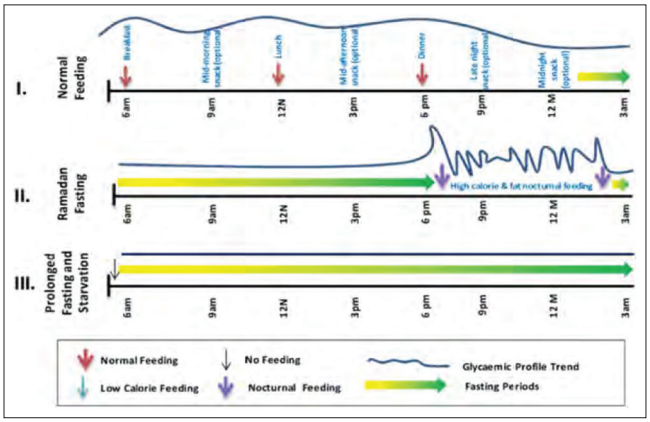

Figure 2: Changes in eating habits and energy intake were observed during different fasting times. The three feeding and fasting patterns mentioned above are regular feeding, Ramadan fasting, and extended fasting and starvation. Hourly discrepancies in eating patterns between different fasting models are depicted in the diagram: Hourly timings of fasting, feeding, and energy intake (meals) are shown every day in relation to fasting cycles (arrows) and expressed in glycemic regulation (trend) [14]

During Ramadan, sleeping habits are invariably disrupted. Sleep is usually broken before dawn to enable Muslims to feed before the fasting period starts (Suhoor). After that, most people will go back to sleep and wake up a second time to start the day. Some Muslims who are fasting can sleep in the afternoon. Many people would remain awake until midnight or later after the evening meal (Iftar). According to a recent meta-analysis, total sleep time (TST) is decreased by around 1 h during Ramadan. This resulted in a 1-point rise in the Epworth sleepiness scale, indicating increased daytime sleepiness (ESS). Another study looked at the Effect of Ramadan fasting on sleep-wake cycles in physically active people and found similar TST reductions. Sleep deprivation has been linked to a reduction in glucose tolerance, and the connection

between sleeping time and insulin resistance has resurfaced as a topic of medical interest. Short sleep time is also linked to weight gain, particularly in younger people [15], [16].

The major finding of Faris *et al*. comprehensive review and meta-analysis is that Ramadan and related activities have an impact on sleep duration and daytime sleepiness. Total sleep time was 7.2 h at the start of the study, although it reduced by 1 h throughout Ramadan. Fasting during Ramadan was observed to affect daytime sleepiness, as seen by reduced Epworth sleepiness scale scores. Fasting people's overall sleep time might be reduced due to a variety of circumstances. For starters, throughout Ramadan, people's eating habits shift. When compared to individuals who may stay awake all night, those who get up early to eat the predawn meal suhoor had fewer interruptions in early morning rapid eye movement (REM) sleep. Mealtime disruption has an impact on the circadian rhythm. Late-night-dinner eating has a deleterious impact on circadian rhythm and hormone release regardless of fasting. Sleeping on an empty stomach induces gastric reflux and lowers diet-induced thermo genesis, both of which decrease sleep quality. When sleep begins, core body temperature drops, while increases promote awake, and late-night-dinner eating may produce an increase, causing sleep latency to be prolonged. 30 min before bedtime, but not 3–3.5 h before bedtime, reduces nocturnal sleep time. Second, melatonin impacts circadian rhythm by having a smaller and later night peak, a flatter serum concentration slope, and lower nocturnal melatonin levels during Ramadan [15]. On the other hand, intermittent fasting has no effect on melatonin's circadian cycle. Total sleep time fell in adults during Ramadan, probably due to a delay in sleep due to a delay in the start of work in several Muslim nations throughout Ramadan. Despite the fact that there is a delay in rising time during Ramadan, the delay in bedtime is more pronounced, which explains the lower total sleep time [15].

Fasting has physiological effects: Lower blood sugar, lower cholesterol, and lower systolic blood pressure. Fasting during Ramadan would be an excellent treatment option for mild to moderate, stable non-insulin diabetes, obesity, and essential hypertension [16]. Fasting is a potent therapeutic technique that can aid in the recovery of persons suffering from mild to severe health problems. A recent study on inactive volunteers found that religious rituals such as fasting during the holy month of Ramadan can lower stress, anxiety, and depression in certain people [3], [17].

A meta-analysis by Cui *et al*. revealed that alternate-day fasting is a potentially preferable option to daily calorie restriction in normal-weight and overweight subjects. Body-related biomarkers, such as weight, BMI, and so on, were effectively lowered by the alternate-day fasting technique. Alternate day fasting demonstrated a lesser potential for weight management when compared to complete calorie restriction [18].

Health Benefits of Ramadan Fasting

Circadian rhythm effects

During Ramadan Fasting, sleeping patterns are invariably disrupted. Sleep is usually disrupted before dawn to allow Muslims to eat before the fasting period starts (Suhoor). After then, most people will go back to sleep and wake up a second time to start the day. Some Muslims who are fasting may nap in the afternoon. Many people will stay awake until midnight or later after the evening meal (Iftar). Reduced overall sleep time, delayed sleep, decreased sleep period time, decreased rapid eye movement (REM) sleep length, reduced proportion of REM sleep, an increased proportion of non-REM sleep, and increased sleep latency are all effects of Ramadan tolerance [3], [19], [20].

It cannot be overstated how abrupt and dramatic the change from routine and "natural" mealtimes and sleep/wakefulness habits is during Ramadan. Between sunset and sunrise, eating times shift from daytime to darker hours. This can directly affect the body's circadian rhythm, resulting in cardio metabolic shifts. Fasting during Ramadan has been shown to influence several hormone rhythms. Serum leptin, ghrelin, cortisol, and melatonin levels are among them [19].

The white adipose tissue secretes leptin, a satiety hormone. Because of its effects on the hypothalamus, it has a deleterious impact on feeding. Leptin plays a role in bone metabolism and immunity as well. Between Ramadan and non-Ramadan, there are various patterns of leptin secretion. Leptin levels grow in healthy people in response to meals. Its secretion follows a 24-h cycle, peaking between 10 p.m. and 3 a.m. Weight and body fat are both strongly correlated with leptin levels. The effects of Ramadan on serum leptin appear to be linked to the shifts in eating times. Ramadan fasting leptin levels were substantially greater in the morning than in the pre-Ramadan period, but evening levels were similar to those of pre-Ramadan [21], [22].

Ghrelin is a peptide hormone that stimulates appetite. Ghrelin levels in the blood are high before meals and diminish thereafter. As a result, ghrelin levels and fluctuations may change during RF. However, during the RF, no significant variations in ghrelin were identified in persons of a healthy weight. In a more recent study of overweight and obese people, ghrelin levels were found to be significantly lower in the last week of Ramadan [23], [24].

Cortisol is the main glucocorticoid hormone produced by the adrenal cortex and controlled by the hypothalamus and pituitary. Cortisol secretion has a diurnal rhythm, peaking in the morning and trough in the evening. It is also a source of stress, as a result of physical and psychological stress, levels rise. In the context of the RF, all of these considerations

may be relevant. Cortisol has a significant impact on blood glucose levels as a result of its effects on insulin sensitivity. A spike in blood glucose is linked to a high level of cortisol. There have been few studies on cortisol changes during Ramadan that take into account circadian rhythms. When compared to the pre-Ramadan period, researchers discovered lower morning cortisol levels and higher evening cortisol levels during Ramadan [25]. In the few research that have looked at cortisol circadian rhythmicity during Ramadan fasting, this reduction in the morning to evening cortisol ratio appears to be constant [3], [25].

Glycemic changes in healthy individuals during ramadan fasting

Fasting can be separated into three parts depending on how long it lasts: The post absorptive period, which lasts 6–24 h; the gluconeogenic phase, which lasts 1–10 days; and the protein conservation phase, which lasts more than 10 days. The RF is a post-absorptive condition with a partial overlap into the gluconeogenic phase since it is an intermittent form of fasting. The fast is broken at sunset by a feasting session. The central nervous system and many other tissues prefer to utilize glucose produced by glycogen breakdown during a fast [3].

After eating, increases in blood glucose levels induce insulin secretion, which causes the liver and muscles to store glucose as glycogen in healthy people. Circulating glucose levels drop, and insulin secretion is suppressed during fasting. Increased release of glucagon and catecholamine stimulates glycogenolysis and gluconeogenesis, raising blood glucose levels [4]. For about 12 h, liver glycogen will supply enough glucose to the brain and peripheral tissues. Fasting times are usually longer than 12 h, suggesting that they are a condition of sporadic glycogen loss and replenishment. As glycogen reserves are exhausted, and insulin levels are low, adipocytes release fatty acids, which are oxidized to produce ketones, which can be used as fuel by a variety of organs while leaving glucose for the brain and erythrocytes [26]. Several studies have looked at insulin sensitivity. Many of these studies discovered a connection between Ramadan fasting and evening hypercortisolism and insulin resistance. Ajabnoor *et al*. found that the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) before Ramadan to 4.51 in the morning during Ramadan. For pre-Ramadan and Ramadan increased from 1.98 in the morning the corresponding evening values were 4.94 and 12.01, respectively. In a series of studies by Spiegel *et al*., sleep was reported to have important modulatory effects on glucose regulation, and recurrent sleep loss was associated with marked negative alterations of parameters of glucose tolerance. As a result, Ramadan Fasting should be regarded as an insulin resistance condition [21], [27].

Fasting during Ramadan is strongly discouraged by the medical community for diabetic people. Major epidemiological research of 12,243 diabetic people who fasted throughout Ramadan in 13 Islamic countries found a significant prevalence of acute complications. However, a few short studies imply that complication rates may not be considerably higher. Hypoglycemia, one of the acute complications that can be found when fasting Ramadan, can be caused by a decrease in food consumption, which is a well-known risk factor. Fasting throughout Ramadan has not been proven to reduce the rate of hypoglycemia in diabetic patients. Lifestyle modification and adjusting the blood sugar lowering drugs during Ramadan increase the risk of hypoglycemia. Glycemic control in diabetic individuals who fasted throughout Ramadan has deteriorated, improved, or remained unchanged. Excessive medication dosage reductions to prevent hypoglycemia may have resulted in hyperglycemia. The risk of severe hyperglycemia was considerably higher in patients who reported an increase in food and/or sugar intake [4], [26].

Fasting during Ramadan presents significant obstacles for people with diabetes. Despite these obstacles, many people continue to fast. The most common side effects of fasting are hypoglycemia and hyperglycemia. Summer fasting periods can last anywhere from 15 to 18 h/day, and they're usually done in hot, humid weather, which can contribute to problems like dehydration. Diabetic patients confront significant hazards of hypoglycemia and hyperglycemia regularly. Nevertheless, studies have shown that fasting may increase these events' likelihood. The Diabetes and Ramadan-Middle East and North Africa (DARMENA) Type 1 Diabetes Mellitus (T1DM) study report was just released. According to the Diabetes and Ramadan-Middle East and North Africa (DARMENA) Type 1 Diabetes Mellitus (T1DM) study, 48.5% of participants fasted the whole Ramadan. Before Ramadan, the rate of verified and severe hypoglycemia was similar. While hypoglycemia rose significantly during Ramadan compared to before Ramadan in the DARMENA Type 2 Diabetes Mellitus (T2DM) research, 10.4–4.9%, respectively [3], [28].

Similarly, during Ramadan, more excellent rates of hyperglycemia have been documented. The EPIDIAR study found that persons with T2DM, whether they have diabetic keto acidosis (DKA) or not, have a 5-fold increased risk of hyperglycemia. Ahmedani *et al*. discovered symptomatic hyperglycemia in 33.3% of T1DM patients and 15.4% of T2DM patients. People with T1DM appear to be at an increased risk of these problems. According to a recent global survey of 1054 people with type 1 diabetes, 27% were able to fast for the entire month of Ramadan, and 39% had no incidents of hypoglycemia. In contrast, studying diabetic patients who fasted for 21 revealed that 28% of those who fasted for 21 days or less did so because of diabetes-related

conditions. In addition, 45% and 60% of respondents said they had hyperglycemia or hypoglycemia, respectively, and 7% needed hospitalization [29], [30], [31].

According to several reported data, ADF is the best diet plan for decreasing fasting insulin, glucose, and HOMA-IR. On the other hand, insulin resistance did not differ significantly between the two groups. It was hypothesized that ADF combined with exercise could lower insulin resistance, but more research is needed [32], [33].

Healthy individuals' lipid changes during Ramadan

According to a number of studies, fasting during Ramadan has been related to improved lipid profiles in healthy people. A meta-analysis published in 2014 involving 30 articles found no overall improvement in high-density lipoprotein (HDL) or triglyceride (TG) levels but major substantial decreases in low-density lipoprotein (LDL) levels. Ramadan fasting causes a significant rise in high-density lipoprotein cholesterol and a significant decrease in low-density lipoprotein cholesterol, according to other reports [8], [34].

The effects of Ramadan fasting on athletes' lipid profiles have been documented. When compared to a pre-Ramadan assessment, the results showed that TC and LDL were lower, while HDL and TG were higher during Ramadan. After Ramadan, there was a decrease in TG and very-low-density lipoprotein and an increase in HDL. TC and LDL levels returned to pre-Ramadan levels after the Ramadan fasting time [1].

The main finding of Kul *et al*. meta-analysis was that LDL and FBG levels dropped after Ramadan fasting in both sex groups and the total group as compared to levels before Ramadan. Furthermore, while the female subgroup's body weight, total cholesterol, and triglyceride levels were the same, HDL levels increased. On the other hand, fasting during Ramadan causes men to lose weight. In males, there was also a significant drop in total cholesterol and LDL levels and a minor decrease in triglyceride levels. HDL levels did not change in men as they did in women. It is clear from this evidence that Ramadan fasting can successfully modify body weight and several biochemical parameters compared to pre-Ramadan levels of participants. Fasting is thought to be a viable non-pharmacological intervention for enhancing health and lengthening life. Religious fasting is frequently a time of tremendous spiritual growth, but it can also be a period of significant physical improvement. During the holy month of Ramadan, there is a shift in eating habits, with larger meals compensating for lower food intake frequency. Previous studies demonstrated that total body weight was significantly reduced despite minor decreases in total energy intake. Weight loss may be ascribed in part to the efficient utilization of body fat during Ramadan fasting [34].

The systematic review conducted by Cui, *et al*. found significant decrease differences between the alternate-day fasting (ADF) group and the control group in the total cholesterol ($p = 0.001$), low-density lipoprotein ($p = 0.01$), and triglycerides ($p = 0.02$). The ADF group had the same effect as the control group in aspects of high-density lipoprotein ($p = 0.27$). The findings of this meta-analysis show that ADF has a positive impact on cardiovascular health. Alterations in cholesterol metabolism, as we all know, have long been known to be potent predictors of developing cardiovascular events, even in the early stages of atherosclerosis. In metabolic syndrome, obesity, and diabetes, aberrant cholesterol metabolism, such as decreased intestinal cholesterol absorption and high cholesterol production, played a key role. By lowering triacylglycerol and boosting LDL particle size and adiponectin concentration, this diet plan may have cardioprotective effects in individuals. The findings of this meta-analysis show that ADF has a positive impact on cardiovascular health. Alterations in cholesterol metabolism, as we all know, have long been known to be potent predictors of developing cardiovascular events, even in the early stages of atherosclerosis. In metabolic syndrome, obesity, and diabetes, aberrant cholesterol metabolism, such as decreased intestinal cholesterol absorption and high cholesterol production, played a key role. This diet plan may have cardio protective effects in individuals by lowering triacylglycerol and boosting LDL particle size and adiponectin concentration [32], [35], [36].

To the best of our knowledge, the Mediterranean and some low-carbohydrate diets help people maintain a healthy weight and lower their risk of heart disease. It would be interesting to see how ADF affects weight loss and cardiovascular outcomes when paired with a Mediterranean or low-carbohydrate diet in future research. Combining diet and exercise are more beneficial than either diet or exercise alone in improving cholesterol levels. This diet plan may have cardio protective effects in individuals, lowering triacyl glycerol and boosting LDL particle size and adiponectin concentration. Obesity has previously been linked to glucose and insulin levels. As a result, managing and controlling glucose levels and insulin resistance are critical. At the same time, the considerable reduction in fasting insulin could be attributable in part to the decrease in body weight and total body fat. In the ADF group, we discovered a substantial loss of lean mass. Because ADF may aggravate muscle loss in those at risk for sarcopenia, this should be taken into consideration. According to certain research, adequate/excessive protein consumption during weight loss can help to prevent lean mass loss [37], [38], [39], [40], [41], [42].

Acute coronary syndrome (ACS) is a term that refers to a group of disorders in which blood flow to the coronary arteries is restricted. Unstable angina and myocardial infarction are examples of such disorders (MI). There is no obvious link between fasting during Ramadan and an increase in acute cardiac

events, according to the evidence. During Ramadan, echocardiography and angiographic tests revealed no apparent differences between persons who were fasting and those who were not. Fasting during Ramadan was also found to have some beneficial effects in several studies. When compared to times outs, there was a considerable reduction in the number of ACS incidents during Ramadan. When compared to alternate day fasting alone, new research found that exercise plus alternate day fasting resulted in the greatest reductions in cardiometabolic risk variables and the least loss of lean mass [3], [17].

Fasting during Ramadan and intestinal microbiota

Along with a variety of other environmental and genetic factors, gut microbiota has recently emerged as an important player in the development of chronic diseases such as obesity and diabetes [3]. Recent research indicates that dietary changes, such as intermittent fasting, play a major role in altering the gut microbiota in ways that favor the immune system and body metabolism [43]. Furthermore, it has been discovered that a beneficial improvement in gut microbiota influences body fat composition through transforming white adipose tissue into more mitochondria-dense browned tissue through a mechanism known as “browning or being,” which helps to increase energy consumption and reduce the risk of obesity [3], [43].

The gut microbiota is important for energy metabolism and lipid balance, and germfree or microbiota-depleted rats are less prone to obesity and metabolic syndrome. According to the findings, every other day fasting (EODF) treatment may modify microbiota compositions and help to avoid a high-fat diet (HFD)-induced obesity and metabolic diseases. The effect of EODF on metabolic disorders in control and microbiota-depleted DIO mice was examined to further define the function of gut microbiota in mediating the therapeutic benefits of the EODF regimen. In control mice, EODF therapy reduced obesity and hepatic steatosis while also improving insulin sensitivity, but not in microbiota-depleted mice, according to the findings. In control mice, EODF treatment reduced obesity and hepatic steatosis, as well as increased insulin sensitivity, but not in microbiota-depleted mice, demonstrating that EODF’s benefits are dependent on gut microbiota [43].

Recent research suggests that dietary changes, such as intermittent fasting, significantly alter the gut microbiota in ways that benefit the immune system and body metabolism. Furthermore, it has been discovered that a positive change in gut microbiota affects body fat composition by converting white adipose tissue into more mitochondria-dense browned tissue through a process known as “browning or beiging,” which helps to increase energy expenditure and reduce the risk of obesity [3].

The impact of Ramadan fasting on the gut microbiota has not been thoroughly investigated. Microbial richness was significantly increased at the end of the Ramadan fasting season, according to a pilot study (N = 9) conducted in Turkey; however, no substantial differences in phylogenetic diversity metrics were found. The findings in humans are supported by studies in model organisms such as mice, which demonstrate the significant changes in gut microbiota that may occur when fasting is practiced. In healthy mice, intermittent fasting has recently been discovered to reshape the intestinal microbiota, with the duration of the regular fasting period being a key influencing factor [44], [45].

The human salivary microbiota has been studied as a non-invasive way to learn more about the bacteria that are shed from oral surfaces. Oral and general health may be mirrored by this form of microbiota. Recent research on salivary microbiota and 16S ribosomal deoxyribonucleic acid (rDNA) from 64 obese individuals fasting during Ramadan found a statistically significant difference in the phylum Candidatus Sacchari bacteria/TM7 at the end of Ramadan compared to pre-Ramadan. The meaning of this move is unclear at this time [3], [46].

Fasting during Ramadan and gene expression

While genes are fundamentally set and cannot be modified during a person’s life, it is well known that dietary and lifestyle choices influence human gene expression, potentially modulating the risk of chronic diseases like diabetes. This impact of dietary and lifestyle choices is manifested through epigenetic mechanisms such as histone acetylation and DNA methylation are two factors that influence gene expression levels. The epigenetic effect of Ramadan fasting has piqued people’s interest recently. Fasting during Ramadan has been shown to have an effect on CLOCK, a fundamental component of the circadian biological clock, antioxidant enzyme-controlling genes (TFAM, SOD2, and Nrf2), and metabolic and aging-controlling genes in several studies (SIRT1 and SIRT3). CLOCK gene expression was much higher in the morning than in the evening during the pre-fasting month (Sha’ban) than during the Ramadan fasting month, according to Ajabnoor *et al*., a finding that could be explained by the changes in sleep patterns experienced during Ramadan fasting days. This large change in CLOCK gene expression has a negative impact on glucose homeostasis, which could explain the documented changes in insulin secretion patterns and increased insulin resistance during Ramadan. These findings emphasize the possible negative consequences of staying up late during Ramadan, a frequently practiced habit in many Islamic communities [3].

Madkour *et al*. observed 56 overweight and obese people and discovered that, at the end of

Ramadan, relative gene expressions for antioxidant genes were significantly upregulated by varying degrees as compared to usual safe controls. Genetic research revealed clear evidence of downregulation in the metabolism-controlling gene, which coincided with a non-statistically significant decrease in gene expression at the end of Ramadan. These findings indicate that Ramadan fasting improves gene expression of anti-inflammatory and antioxidant regulatory genes, suggesting that Ramadan fasting can protect non-diabetic obese people from oxidative stress and its metabolic-related derangements [3], [47].

Elevated expression of ant oxidative stress genes (TFAM, SOD2, and Nrf2) during Ramadan month shows that RIF is associated with increased levels of ROS generation and hence may result in oxidative stress in fasting people according to one theory. In their review, "Extending life duration by increasing oxidative stress," Ristow and Schmeisser upheld this position. According to the scientists, several longevity-promoting therapies, such as calorie restriction and intermittent fasting may converge by driving mitochondrial oxygen consumption to boost ROS production. These dietary changes may act as molecular signals, causing natural defense systems to activate, resulting in enhanced stress resistance and lifespan, known as mitohormesis or mitochondrial hormesis [47].

The effect of fasting on mental wellbeing during Ramadan

Ramadan has many spiritual and mental benefits, including the opportunity to self-reflect on areas of life that require improvement as well as doing good deeds, the ability to develop spiritually through prayers, and the opportunity to spend more time with loved ones and community members. Islam teaches and empowers the person to attain inner peace and tranquility. Individuals reinforce their faith, read and listen to recitations of the Qur'an, and engage in prayers during Ramadan, all of which have been related to lower rates of depression, anxiety, and stress, as well as improved memory. Fasting during Ramadan has also been shown in studies to have mental health effects, such as reducing anxiety, depression, and stress levels in healthy people. Another study of healthy graduate students found that fasting improved self-acceptance, self-sufficiency, social ties, and personal development. Another study of Muslim graduate students found that fasting improved self-acceptance, self-sufficiency, social relations, and personal growth [3], [48].

Ramadan fasting promotes the growth of moral and social virtues like genuine compassion and empathy for the less fortunate. Furthermore, Ramadan is a holy month during which people show hospitality and perform nice activities that aid in the feeling of satisfaction. The social parts of Ramadan are as essential. People strengthen their relationships with family, friends, and community members and improve their social interactions in general. Maintaining healthy relationships can help people grow more emotionally intelligent by satisfying their desire for contact, love, and affection. Many individuals look forward to Ramadan and note it on their calendars. Ramadan is a significant social event that promotes connection while combating emotions of isolation and loneliness [3].

The effect of Ramadan fasting on inflammatory and oxidative stress markers

Fasting during Ramadan lowers inflammation and oxidative stress markers. This may have a short-term protective impact against health conditions that can be harmful in the form of systemic inflammation and elevated levels of oxidative stress, both of which are predisposing factors for a variety of chronic diseases associated with modern society [49].

The best-known evidence on the effects of Ramadan intermittent fasting on pro-inflammatory cytokines (IL-1, IL-6, and TNF-α), a general inflammatory marker (hs-CRP), and an oxidative stress marker (MDA) in healthy adults is summarized in a review by Faris *et al*. (both obese and non-obese). The research included in this review found a variety of results when comparing the effects of Ramadan intermittent fasting on key inflammatory and oxidative stress markers at the conclusion of Ramadan month to pre-fasting (baseline) levels. The I statistics was low, indicating little heterogeneity, indicating that a meta-analysis was necessary. Overall, Ramadan intermittent fasting had a minor impact on inflammatory and oxidative stress markers, implying that fasting Muslims may experience some short-term protection against low-grade systemic inflammation and oxidative stress. According to a meta-analysis of body weight changes during Ramadan intermittent fasting, this drop in inflammatory and oxidative stress markers could be ascribed to weight loss during the fasting month. IL-6, IL-1, and TNF - are among the major pro-inflammatory adipokines that predispose the metabolic derangements associated with obesity [49].

Fasting throughout Ramadan may boost ant oxidative and anti-inflammatory systems. Increased levels of pro-inflammatory cytokines have been linked to an increased risk of inflammatory disorders (such as diabetes), insulin resistance, cardiovascular disease, and atherosclerosis. On the other side, Islamic fasting has been shown to reduce pro-inflammatory cytokines such as TNF- and IL-6, resulting in an improvement in the human body's inflammatory status. Fasting throughout Ramadan may also lower levels of other inflammatory indicators including homocysteine and C-reactive protein. Evidence suggests that one month after Ramadan fasting, the level of IL-6 may remain significantly low, which is thought to be a long-term health advantage of Ramadan fasting [50].

The digestive system's effect on Ramadan fasting

At Iftar, the body's immediate need is for readily accessible energy sources in the form of glucose for all living cells, especially the brain and nervous system. A well-balanced diet lowers blood cholesterol, lowers stomach acidity, avoids constipation and other digestive issues, and promotes an active and stable lifestyle. "Fasting brings a wholesome physiological rest for the digestive tract and central nervous system, and normalizes metabolism," wrote Cott in his 1975 book "Fasting as a Way of Life." The results of Ramadan fasting among Muslims and similar reduced energy intake situations among non-Muslims indicate that a high-fat diet containing poly-unsaturated fat, which accounts for about 36% of total energy, may be beneficial in lowering blood cholesterol and uric acid levels and improving protein retention in the body [8], [51].

The digestive organs (digestive tract, enzymes, and hormones) can rest for 14 h during fasting; whereas when not fasting, the vital organs of digestion will work continuously to digest food for approximately 18 h, when fasting the organs in our bodies take a break from hard work grind food. Because the stomach is empty while fasting, food is more easily absorbed and nasty germs are unable to live, allowing us to avoid a variety of ailments. As a result, fasting can have an impact on the health of the stomach's digestive system. During fasting, changes in eating patterns produce various changes in the body, particularly in the digestive tract. Fasting allows the digestive system to relax, which can help to reduce the risk of digestive disorders or even cure them. The stomach is also not filled with food for several hours while fasting. Stomach acid production will decrease at this time to avoid acid erosion of the stomach wall. As a result, fasting may have an impact on the health of the gastric digestive system [52].

Sadeghpour *et al*. conducted a systematic review and found that fasting is typically safe for healthy people, but it may be dangerous for patients with specific GI illnesses and may increase the risk of problems in this group. The results of studies on the impact of Ramadan on the occurrence of acute appendicitis are mixed. Only patients aged 15–70 years old were included in two of the investigations, because children are excused from fasting and the elderly may be unable to fast and hence are also exempt. The third study, on the other hand, did not take this into account. All three investigations were retrospective in nature. Fasting appears to have little Effect on the healing of duodenal ulcers in people who are taking Omeprazole, a proton pump inhibitor. Proton pump inhibitors and Helicobacter pylori eradication are vital in the treatment of DU, and patients who are taking them can recover quickly and have a lower risk of problems. Long-term hunger has also been suggested as a way to aid in the healing of recurrent ulcers by increasing the control of stomach discharge. Healthy people only have minor gastrointestinal discomfort, and no significant complications have been reported. In terms of GI symptoms, individuals who ate a small meal, such as breakfast for Suhoor, were no different from those who ate a substantial meal. Fasting women were more likely than fasting men to experience GI discomfort [53], [54].

In clinical practice guidelines, it is often recommended to restrict diets and exercise if someone wants to lose weight. Traditional weight-loss approaches (e.g., daily calorie restriction) have poor control and compliance, despite the fact that the effect is positive. Intermittent fasting regimens, particularly ADF protocols, are advocated in many pieces of literature based on this foundation. The big unanswered question is whether ADF's effects can help people lose weight [33].

Nutrition Plan for Ramadan

The Ramadan Nutrition Plan (RNP) is a mobile and web-based tool that allows health-care professionals (HCPs) to tailor medical nutrition therapy (MNT) for diabetic patients during Ramadan fasting. The RNP also has a patient site that offers Ramadan education and dietary programs, which may be especially valuable for diabetics who do not have access to HCPs. MNT plays a critical function during this fasting phase, not only in maintaining optimal diabetes management but also in assisting overweight and obese type 2 diabetes (T2DM) patients in improving their lifestyle and losing weight. Ramadan, in fact, provides a great chance for patients to channel the power and discipline required to adhere to MNT, allowing them to maintain optimal glycemic control beyond Ramadan [55], [56].

When compared to normal therapy, structured MNT for Ramadan has been demonstrated to enhance fasting blood glucose levels, triglycerides, and the rate of pre-dawn and pre-bed self-monitoring blood glucose (SMBG) in persons with T2DM. Furthermore, structured MNT for Ramadan comprises pre-Ramadan education and personalized energy and macronutrient prescriptions, as well as the addition of a diabetes-specific formula of at least 1 serving per day during Suhoor or a snack (if needed) to increase nutritional intake adequacy. The RNP is built on ideal MNT principles and includes meal plans for a variety of countries and regions throughout the world. Dietary recommendations, on the other hand, should be adapted to a person's lifestyle needs, age, co morbidities, and other medical needs. Based on the basic framework described in this chapter, the RNP is still a work in progress that would benefit from additional contributions from HCPs of many nationalities. As a result, a comprehensive worldwide menu resource will be created [3], [55], [57].

Fasting Ramadan during the COVID-19 Pandemic

Despite all of the known health benefits of fasting, there is considerable question this Ramadan about whether fasting is safe during the current outbreak. COVID-19 has infected millions of individuals, causing hundreds of thousands to suffer serious sickness and tens of thousands to die. It is sometimes stated that Ramadan Fasting causes dry lips and throat, which increases the chance of catching the virus. Although prominent health and religious authorities have debunked this idea, the evidence presented in this regard is neither reliable nor indisputable [2].

In terms of immunological improvements, it has been shown that Ramadan fasting has no impact on the immune system. On the contrary, a growing body of evidence suggests that fasting during Ramadan can help the immune system fight infections. Increased serum levels of certain immunoglobulin's, such as IgA, may play a role in this immunoprotective impact. Furthermore, some complement system elements (such as C4) have been shown to increase during Ramadan Fasting, shielding individuals from a wide range of microorganisms. Scientific evidence confirms many of this immunoprotective effects. Clinical evidence supports many of these immunoprotective effects. For example, past research has shown that fasting during Ramadan can protect against tuberculosis and reduce the chance of infection in healthy persons [2], [17].

Fasting for at least 3 days causes the body to begin creating new white blood cells, allowing the immune system to be rejuvenated and better able to fight infection. Although long-term fasting has been proven to reduce the quantity of white blood cells in humans and animals, blood cells return when they are re-fed. In this approach, Ramadan fasting (intermittent fasting throughout Ramadan, time-restricted feeding, and alternate day fasting) pushes the body to consume glucose and fat stores, as well as a significant number of white blood cells. As a result, changes in the body induce stem cells in the immune system to regenerate new cells. Various studies, on the other hand, have confirmed that cytokine storms are an important mechanism of corona viruses, which produce large amounts of inflammatory cytokines such as IFN-α, IFN-γ, IL-1β, IL-6, IL-12, IL- 18, IL-33, TNF-α, G-CSF, IP-10, MCP-1, MIP-1A, TGF-β, as well as chemokine such as CXCL9 and CX Supporting immune function and improving individual resistance are proved to be critical in combating COVID19, and the most significant approaches to build and raise personal immunity are to avoid overeating calories and to engage in a proper exercise routine [17].

For Ramadan-fasted persons, exercise training can be a major difficulty, especially during COVID-19 breakouts. The inability to eat and drink for several hours before and during exercise sessions can result in low levels of endogenous fuel, as well as dehydration, which can last until the end of the activity. Furthermore, daytime sleepiness, feelings of heightened malaise, and lethargy are all characteristics that can lead to unfavorable mood changes in Muslim sportsmen. When compared to the non-Ramadan period, Ramadan fasted individuals may experience higher degrees of weariness and perceived effort in response to the same amount of labor or exercise training during the month of Ramadan [17].

Ramadan Fasting and Autophagy

Autophagy is derived from the Ancient Greek words auto, which means "self," and phagin, which means "to feed," so autophagy literally means "self-feeding." Autophagy is the cell's normal, regulated, and destructive mechanism for degrading and recycling unwanted or dysfunctional components. When the body's energy supply (starvation) is inadequate to sustain it, autophagy is the body's mechanism for eliminating all the broken down, old cellular components such as organelles, proteins, and cell membranes. After conducting experiments in yeast cells in his own laboratory, Ohsumi suggested and verified the mechanism of autophagy. In his work, Oshumi cultivated mutant yeast that lacked vacuolar degradation enzymes while also starving the cells to trigger autophagy. The findings revealed that the vacuoles were packed with small vesicles that had not decomposed within hours, and these vesicles were dubbed autophagosomes. Oshumi's research concluded that autophagy existed in yeast cells, and he was awarded the Nobel Prize in Physiology or Medicine in 2016 for his discoveries [58], [59].

Autophagy is a catabolic mechanism found in all eukaryotic species. Autophagy research has exploded in popularity in the past decade, due to its ability to describe the fundamentals of cellular and organismal metabolism. Autophagy has been the central regulating point in controlling the human body's homeostasis, regulating everything from basic metabolic functions within cells to diseases such as aging, cancer, neurodegenerative disorders, and lysosomal disorders [60].

As previously mentioned, Ramadan Fasting is a state of starvation or null energy induced by the complete cessation of food and water intake during fast periods; thus, Ramadan Fasting can be classified as an inducer of autophagy. Goal of rapamycin (TOR) complex 1 (TORC-1) is inactivated in mammalian cells when they are starved, causing TORC-1 to dissociate from ULK (the mammalian homolog of yeast Atg1), preventing TORC1 from phosphorylating Atg13 and ULK1 (or ULK2) and inducing autophagy. After autophagy has been triggered, it will go through a

sequence of steps that include membrane nucleation, elongation, maturation, fusion, and degradation. Following autophagy activation, cytoplasmic materials (protein aggregates and organelles) are sequestered by a phagophore, a pre-autophagosomal single membrane structure (nucleation). The phagophore membrane then extends and enwraps its cargo, forming the autophagosome, a double-membrane vesicle (elongation). The autophagosome unites with a lysosome to produce an autolysosome (maturation), where acid hydrolases destroy the enwrapped cargo (degradation). After being carried back into the cytosol by membrane permeases, the disintegrating macromolecules can either be utilized to create proteins or oxidized by the mitochondria to generate ATP for cell survival [61] (Figure 3).

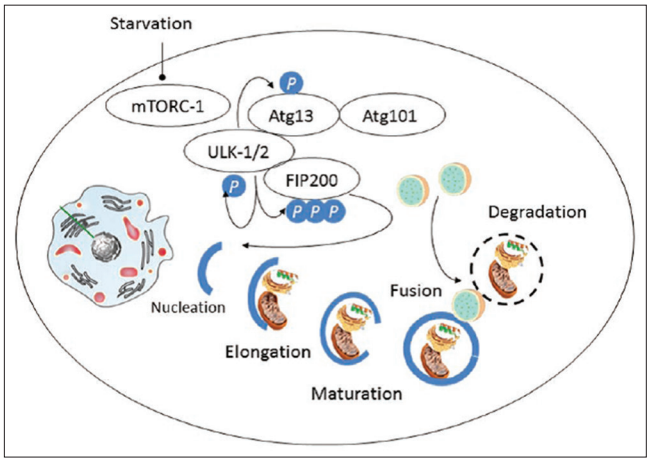

Figure 3: A state of hunger triggers the activation of autophagy [61]

In summary, malnutrition occurs during Ramadan fasting, and autophagy is triggered to eliminate protein aggregate and other cellular debris for recycling, resulting in a health gain. Autophagy is triggered during RF by glycogen depletion and a metabolic shift through ketosis, which may occur between days 3 and 5 of fasting. Fasting improves GH secretion at the same time, so a synergistic action of autophagy and growth hormone may be able to replace old and weakened cells with new ones, preventing the pathological phase [58].

Conclusion

Ramadan fasting, which is an obligation for every Muslim, who is able to carry it out, turns out to have a lot of health benefits on the condition that we maintain a diet during breaking and dawn. Autophagy, which has good health benefits, can be triggered through Ramadan fasting. Further studies are needed to see the relationship between autophagy and fasting in the month of Ramadan.

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