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Impact of fasting on human health during Ramadan

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ABSTRACT

Ramadan fasting is a religious practice observed by millions of Muslims worldwide. Firstly, the experimental studies were searched on different websites like PubMed, Science direct, and google scholar to find out the latest research regarding Ramadan fasting. Studies have shown that Ramadan fasting influences body weight, blood glucose, insulin, lipid levels, and blood pressure. However, the effects of fasting on mental health and specific health conditions such as cardiovascular diseases, cancer or metabolic disorders vary depending on individual factors. Because, fasting duration, the presence of chronic diseases, and obesity are all factors that can alter the outcomes. Until now, Multiple studies on Ramadan fasting's impact on health have been conducted but certain limitations make the results inconclusive. We hope to gain a better understanding of the potential benefits and risks associated with this religious practice. Ultimately, this knowledge can be used to inform healthcare professionals and individuals who are participating in Ramadan fasting. Further research is necessary to explore underlying mechanisms and optimize fasting protocols for chronic disease patients. Overall, this review emphasizes the need for further research on the effects of Ramadan fasting on human health and its potential as a tool for improving health outcomes in diverse populations.

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1. INTRODUCTION

Ramadan is a month of fasting observed by approximately 1.8 billion Muslims worldwide. It is considered one of the five pillars of Islam, alongside the testimony of faith, charity, pilgrimage, and daily prayer. Fasting is characterized as refraining from consumption for varying periods of time, and is associated with positive impacts on the human body, including increased longevity. Religious fasting involves a fasting regimen undertaken for spiritual or religious purposes, and can be defined as a nutritional model characterized by various degrees of caloric control and abstinence from foods. Hence, fasting is becoming increasingly popular around the world [1]–[3]. Currently, Ramadan fasting is a topic of active research and ongoing debate. While several studies have been conducted to investigate the potential health benefits and risks associated with Ramadan fasting, although the results have been coflicting and the evidence is still ambiguous. Furthermore, a study was conducted on healthy Muslims to determine the impacts of fasting on blood parameters and body composition, revealed that fasting during Ramadan has a positive impact on certain biochemical factors, specifically high-density lipoprotein (HDL) levels and liver function test (LFT), in 216 cirrhotic individuals before and during the period of Ramadan, increase in the serum level was

observed after one month of Ramadan [4]. Subsequently, the slight improvement in LFT might be associated with the change in cytokines and sleeping patterns. Therefore, a fasting routine similar to Ramadan, coupled with nutritional education before commencing the fast, could be more advantageous and efficient for spiritual and overall wellness [5]. In addition, It is worth noting that previous studies have reported considerable differences in lipid profiles during Ramadan fasting, which may be influenced by factors such as ethnicity, geographical location, and dietary habits. Some studies have suggested that diurnal fasting during Ramadan leads to small reductions in inflammatory markers such as IL-1 (Interleukin-1), CRP/hs-CRP (High sensitivity-C-Reactive Protein), TNF-α (Tumor Necrosis Factor-alpha), and IL-6 (Interleukin-6). IL-1, IL-6, and TNF-α are important proinflammatory cytokines that are widely investigated in clinical settings and have important roles in the immune response. They are also linked to persistent low-grade systemic inflammation, which may lead to cardio-metabolic disorders, particularly in obese people [6]. While CRP/high-sensitivity directly contributes to cardiovascular disease, hence lowering them may reduce acute inflammation and increase atheroprotection [7]. On the other hand, the oxidative stress marker malondialdehyde (MDA) is a molecule that has been investigated extensively in relation to oxidative stress and lipid peroxidation. It is a reactive aldehyde compound formed as a consequence of the peroxidation of polyunsaturated fatty acids (PUFAs) in cell membranes. This process takes place when PUFAs in cell membranes are exposed to oxidative stress, such as reactive oxygen species (ROS), which can be generated by a variety of physiological and pathological processes [8]. Therefore, this type of fasting may have the potential to protect against elevated inflammatory and oxidative stress markers, and consequently reduce the risk of adverse health effects in healthy people [9].

Moreover, the comprehensive analysis of the two-research conducted separately on animal and human evaluated the impacts of Ramadan and non-Ramadan intermittent fasting (IF) on gut flora. Most animal and human studies found that fasting has favourable effects on the makeup and structure of the gut microbiome, including increased expression of beneficial bacteria such i) muciniphila, ii) fragilis, Bacteroides, and butyric acid-producing Lachnospiraceae. However, fasting diet duration, the presence of chronic diseases, and obesity are all factors that can alter the outcomes. Future research, especially clinical studies, should assess the effects of fasting regimens, particularly Ramadan, on the prevention and treatment of illnesses via altering the composition of the gut microbiome [10].

Recently, andras and his co-workers revealed in research on hypertensive metabolic syndrome patients that fasting and refeeding can reduce cardiometabolic risk. At three months post-intervention, a 5-day fast followed by a modified Dietary Approach to Stop Hypertension diet reduced systolic blood pressure, as well as reduced antihypertensive medication use, and body-mass index more than the diet alone. Whats more, Fasting affected the gut microbiota and short-chain fatty acid-producing bacterial taxa and gene modules. Fasting may lower blood pressure by affecting particular immune cells and microbiome bacteria, according to the research. Fasting may treat metabolic syndrome patients' high blood pressure non-pharmacologically [11]. In addition, it is investigated that Patients with type 2 diabetes may safely fast throughout Ramadan provided they monitor their blood sugar levels and modify their medications accordingly. Better results may be seen when medicine is combined with modifications in food and lifestyle. If you follow your doctor's orders and watch what you eat, you can avoid both hypoglycemia and hyperglycemia [12].

On the other hand, unfavorable effects of fasting have been recorded on noncommunicable illnesses, These include dehydration, hypoglycemia, and weight loss, changes in sleep patterns, cognitive performance and fluctuations in mood, weight, and a variety of other alterations [13]–[16]. Since fasting is a condition of negative energy balance, many fasting regimens have been utilized to promote weight reduction as well as other health advantages. Until now, there have been several studies examining the effects of fasting during Ramadan on various aspects of health but due to certain limitations that make the study inconclusive. i) Controlled studies: Future studies should employ well-controlled research designs that involve appropriate control groups to compare the effects of fasting on healthy individual to non-fasting healthy individual. ii) Multidisciplinary approach: To gain a comprehensive understanding of the impact of Ramadan fasting on human health, studies should involve a multidisciplinary team of experts, including nutritionists, physicians, and researchers in various fields. iii) Confounding factors: Ramadan occurs at different times of the year, and other factors such as weather, physical activity, and sleep patterns can affect the outcomes of studies. iv) Sample size: Many studies have small sample sizes, making it difficult to draw definitive conclusions about the impact of Ramadan fasting on human health. A larger sample size is needed to increase the statistical power of the study. v) Difficulty in measuring dietary intake: Measuring dietary intake during Ramadan can be challenging as fasting individuals may consume irregular and variable amounts of food at different times of the day. This can make it difficult to accurately assess the impact of fasting on nutrient intake. vi) Differences in populations: Ramadan fasting practices differ across different countries, cultures, and ethnicities, making it challenging to generalize findings to other populations.

To address these limitations, more rigorous and comprehensive studies are needed that include diverse populations with a range of health conditions, and that examine the potential benefits and risks of fasting in more detail. It is also important to provide appropriate education and guidance to individuals who are fasting during Ramadan, to ensure that they are following safe and healthy practices that can minimize any negative impacts on their health.

The aim of this review article is to provide a comprehensive overview of the latest research on the impact of Ramadan fasting on human health. We hope to gain a better understanding of the potential benefits and risks associated with this religious practice. Ultimately, this knowledge can be used to inform healthcare professionals and individuals who are considering participating in Ramadan fasting.

Fasting is regarded as a fundamental practice by many faiths across the globe due to the favorable impact it has on the human body, both spiritually and physically [8]. The health impacts of religious fasting have been investigated for decades, particularly in the past 30 years. Few transdisciplinary scholars have looked beyond the individual level for these repercussions. Fasting has an impact on individual, communal, environmental, and planetary well-being, "a balanced mind and a healthy body" [17], [18]. The time and duration of fasting in Ramadan, Christianity, Buddhism, Judaism, and the Daniel Fast has been discussed in Figure 1. The main difference between Ramadan fasting and other fasting is the time schedule and complete restriction from consumption of any food or fluids even medication is not permitted.

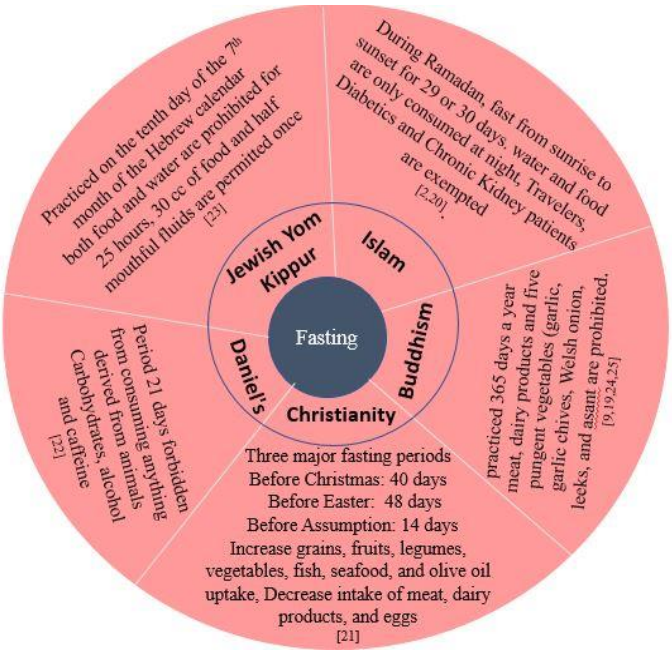

Figure 1. Duration of fasting in different religions along with abstinence from food and water, [2], [9], [19]–[25]

2. RESEARCH METHOD

We conducted a search on different websites, PubMed, science direct, and google scholar using the keyword “Ramadan, Human health, positive and negative effects of ramadan. The resulting articles were classified as either original or review articles. To identify the most recent review articles, we sorted the included papers by year of publication. We then reviewed the original articles that were published after the most recent review article. This approach allowed us to select the latest studies and articles on topics such as weight, energy balance, diabetes, cardiovascular risk, autophagy and cancer, gut microbiome and kidney function.

3. RESULTS AND DISCUSSION

3.1. Energy balance

Inadequate consumption of carbohydrates, proteins, and fluids during fasting periods may affect one's health and ability to exercise. Given that there is less glycogen stored in the liver and muscles, there is less energy available to support muscle activity and maintain blood glucose levels [26]. On the other hand,

there is mounting evidence that various calorie-restricted diet plans have positive effects on reducing inflammation, burning fat, boosting the immune system, and, most importantly, increasing healthy life spans in both animal models and people [22], [27].

During the Holy month of Ramadan, while fasting for 12 to 24 hours, the frequency of meals is decreased from 3-5 to only 2 meal daily [28]. Thus, the management of a healthy, balanced diet is essential for maintaining both healthy weight and person's general nutritional health, therefore, the amount of energy used is crucial [26]. Nevertheless, it can be challenging to maintain a healthy, balanced diet over the long term due to a variety of factors influencing energy intake, such as cultural and lifestyle differences. According to recent data, the energy intkae in daily routine for adults during non-fasting periods is, 2250 kcal/day (female 2,010 and male 2,600 kcal/day) in the United Kingdom while, 2300 kcal/day (female 2,010 and male 2,600 kcal/day) were oberved in the United States of America, followed by 2255 kcal/day (female 2,010 and male 2,600 kcal/day) in Australia. According to the statistics, an average adult eats around 2268 kcal per day (females consume 2,003 kcal per day, and men take 2,533 kcal per day), along with that some environmental factors like habits of more eating and daily activities (exercise, labour) could influence the amount of calories intake. Though there is no agreement as to the anthropometric quantities or as to energy or kilocalories intake against balanced energy being required for the human body [29].

Energy intake and body mass have been reported to be increased in Saudi Muslims and on the other hand reduced in people from many several countries like India, Sudan, and Malaysia [30]. However, one study documented neither of these parameters to be affected. Ramadan fasting in people from Tunisia and the United Arab Emirates [31]. The difference in the energy balance is attributed to the different food choices and habits, as well as the diverse socioeconomic status cultures, and customs of Muslim countries around the world. The alteration in body mass is mostly comparatively minor. Also, in the first two weeks of fasting, the weight of the body seems to be greater [32]. Many factors have been suggested to describe Ramadan fasting encouraged body mass loss. Few of the studies revealed i) low energy diet: 16 young adult male fasting subjects reduced two meals a day, which was associated with reduced energy balance and weight loss. While fasting subjects were permitted to eat as they wanted at each meal, ii) a slight - moderate dehydration secondary to decreased salt intake was observed [33], [34].

Ramadan meal planning becomes an important component for effective Ramadan fasting due to unavoidable changes in eating habits and related physiological adjustments in hormone levels and circadian rhythms. This is especially important for individuals with chronic conditions such as diabetes. To ensure a healthy Ramadan, it is recommended to have a balanced "Ramadan Plate" containing carbohydrates (40-50% of total daily calorie intake) from low-glycemic index and high-fiber foods, protein (20-30% of total daily calorie intake) from non-red meat sources and legumes, and reduced fat intake (35% of total daily calorie intake) from mostly mono- and poly-unsaturated fatty acids. Suhoor, the pre-dawn meal, should provide 30-40% of the day's energy intake, iftar 40-50%, and snacks 10-20% as needed [29].

3.2. Energy gastrointestinal (gut) microbiota

The gut microbiome of human, consists of millions of species of bacteria, viruses, fungi, and parasites (e.g., bacteria, viruses, fungi, parasites), may be affected by a variety of environmental variables (e.g., nutrition and diet) [35]. On the other hand, a number of studies have shown that unfavourable alterations in the gut microbiome may be connected to the onset of a number of chronic illnesses, metabolic diseases, liver conditions, neurodegenerative disorders, including cancer, and others [34], [36]–[39]. Some research has shown that fasting diets can also alter the microbiota. According to a recent comprehensive analysis by Mousavi *et al*. the effects of Ramadan fasting on some types of bacteria, including *Akkermansia muciniphila* and Bacteroides, are beneficial to overall health [10].

A bacterium is a well-studied group among this consisting of gram-negative Bacteroidetes and gram-positive Firmicutes [39]. They are partially determined and most beneficial to the host, and some species are neither harmful nor beneficial. These species are known as “Normal flora” or “Microbiota.” It has been predicted that 500-1,000 various species of bacteria populate the human body [40]. The critical role of these microbes includes the maintenance of homeostasis, metabolism of dietary fiber into short-chain fatty acids, providing the vital nutrients, and ensuring healthy immune system development. However, disruption of the gut microbiota's stability can result in immunologic dysregulation, and the development of many diseases including, inflammatory bowel disease, C*lostridium difficile* infection, irritable bowel syndrome, obesity, asthma, and neurodevelopmental disorders such as autism [41], [42].

The gastrointestinal tract maintains several functions of sleep-wake or robust circadian, rhythms. For example, during the daytime, gastric evacuation and blood flow are higher than the night and in the evening time, and the metabolic response to a glucose load is slower than in the morning [43]. Therefore, it is plausible that frequently disrupted circadian profiles can negatively impact the function of the gastrointestinal tract, metabolism, and health [44]. Diet modulates the diversity of the gut microbiome, which has a robust

circadian rhythm that is influenced by food signals [45], [46]. Studies on animals (rodents) have shown that the gastrointestinal microbiome is highly dynamic, with daily cyclical fluctuations in compositional diversity. Fasting may have direct effects on the gut microbiota, which is a diverse, complex, and extensive community of microorganisms that inhabit the intestinal tract. Variations in the metabolic function and composition of gut microbiota in obese individuals may allow an obese microbiota to extract more energy from food than a lean microbiota, thereby influencing net energy absorption, storage, and expenditure [47], [48].

Obesity caused by a poor diet destroys cyclical microbiota fluctuations. In one study, feeding rodents was restricted, but the availability of food during the active night period partially compensated for cyclical fluctuations [49]. Therefore, the periodic variations of intestinal microorganisms induced by day and night feeding and fasting rhythms contribute to the diversity of the intestine. The microbiota is also a mechanism through which the intestinal microbiome influences the host's metabolism. A prolonged fasting period (i.e., gastrointestinal rest) may also result in decreased intestinal permeability, thereby reducing postprandial endotoxemia and systemic inflammation, both of which typically increase with obesity. The brain-intestinal pathway is activated in the brain during fasting to promote energy balance by enhancing intestinal epithelial integrity, according to recent biological research presented by Salk Institute researchers. Eventually, jet-lag-induced dysbiosis in both humans and mice promotes adiposity and glucose intolerance, which can be transferred to a sterile mouse via faecal transplantation [50]–[54].

Recently it has been observed, in two different cohorts and found the significant effect of Ramadan fasting on the gut microbiome by demonstrating that human physiologic surrogate markers like blood glucose and BMI or body mass index are improved by intermittent fasting, which is particularly linked to an upregulation of butyric acid-producing Lachnospiraceae, thus Intermittent fasting.positively regulate the gene expression of Lachnospiraceae, but still there are some limitation to conclude the results accurately due to lack of nonfasting control group for young adults [38]. In conclusion, A fasting schedule seems to have positive impacts on the intestinal microbiota. Further well controlled study, in term of sex, age and sample size may significantly advance this field by examining how fasting positivley affect the human gut microbiome.

3.3. Metabolic variations during ramadan

Metabolic health encompasses cellular, cardiovascular, and cardiorespiratory health and well-being. Clinically, body adiposity, anthropometrics, blood pressure, and blood-based indicators including serum lipids and blood glucose may assess metabolic health [55]. How the body reacts to fasting is conditional on how long the fast lasts. And it takes in various nutrients from the meal as digestion progresses [56]. In order to function, a fasting person must draw upon its reserves of nutrients. Having a steady supply of glucose prompts the body to adjust its hormones in order to access the nutrients it has stored. Hormones like insulin, for instance, instruct cells to absorb and use glucose from the blood. Fasting during Ramadan led to a decrease in insulin production and an increase in anti-insulin hormones like glucagon and epinephrine, which allow the body to access glycogen and fat stores in the event that external sources of energy are unavailable. After about 24 hours, a healthy adult will have used all of their glycogen stores and will be preparing fresh glucose by metabolising stored proteins, including muscle tissue [57]. Furthermore, to study the metabolic variations during Ramadan, Kul and his colleagues performed a meta-analysis of pre- and post-Ramadan BMI, triglyceride, and fasting blood glucose levels across sexes, to assess how Ramadan fasting affects people's metabolic health [58].

The key conclusion of this meta-analysis was that after Ramadan fasting, both sexes and the overall group had lower levels of low-density lipoprotein and fasting blood glucose compared to levels before Ramadan. It is worth noting that, in the female subgroup, HDL levels were increased while BMI was unchanged, and total cholesterol and triglyceride levels were unchanged. In addition, men had significant decreases in their total cholesterol, low-density lipoprotein or LDL, and triglyceride levels, while triglyceride levels were only slightly reduced. Finally, this evidence shows that fasting throughout Ramadan may significantly alter weight [58].

In the support of the previous study, Mirmiran *et al*. revised the earlier systematic review and meta-analysis, while concluding that in people who appear to be in good health, fasting during Ramadan has no appreciable impact on blood LDL cholesterol, triglycerides and total cholesterol. In contrast, fasting during Ramadan raises LDL cholesterol levels while lowering HDL and very low-density lipoprotein cholesterol (VLDL-C) levels. In addition, fasting during Ramadan was further studied by Hassan *et al*. in healthy, non-athletic adults to determine its influence on glucometabolic indicators (insulin, leptin, fasting glucose, adiponectin) [59], [60].

According to the authors, fasting during Ramadan considerably reduces fasting glucose while not affecting insulin, insulin resistance, leptin, or adiponectin. Therefore, concluding that fasting during Ramadan does not have any negative effects on metabolism and may even enhance glucometabolic markers, particularly fasting glucose levels in healthy individuals. To determine the impact of fasting during Ramadan

on MetS components among healthy Muslims, Jahrami *et al*. performed a meta-analysis. Fasting during Ramadan has been shown to improve health in several ways, including lowering risk factors like waist circumference, blood sugar, and triglycerides while raising good cholesterol levels like HDL-cholesterol [61]. Auspiciously, fasting from before sunset to the onset of sunset in Ramadan allows for a mild and healthy change for utilizing fats and glycogen for energy without the protein metabolism related to longer fats.

3.4. Changes observed in the diet and weight during the Ramadan fast

Observing the wide range of cultural and geographic diversity among the cohorts during Ramadan and the resulting variations in fasting durations and eating patterns, make it difficult to get the accurate results about changes in body weight and diet [12]. The main nutritional alteration during Ramadan is a reduction in the number of meals. However, several studies have shown that people do not reduce their daily calorie consumption while fasting. Despite this, persons who fast often decrease their weight and body fat [62], [63]. According to research conducted on young women in Jordan, fasting during Ramadan had no impact on their calorie intake, intake of macronutrients, or level of overall physical activity. These women continue to lose weight, as well as their BMI is falling, and their percentages of body fat and water are also falling [64]. Similarly, it was shown that Malaysian people consumed more protein and fat after 21 days of fasting, but their total calorie intake remained unchanged. However, their waist to hip circumference ratio reduced. Moreover, Gaeini *et al*. have conducted a detailed investigation and meta-analysis to ascertain how fasting during Ramadan affects levels of leptin and adiponectin, two of the primary hormones involved in regulating hunger and fullness [35].

Leptin levels were found to be significantly lower in those who had fasted during Ramadan. The levels of adiponectin were not significantly altered by fasting throughout Ramadan. In the sub-group investigation, normal-weight persons had a greater leptin reduction than overweight/obese adults. The authors suggest that Ramadan fasting may reduce leptin levels, especially in persons of normal weight. Interestingly, it works best in men of average weight [56]. Fasting resulted in a considerable weight reduction of an average of 3 pounds in men and women, according to recent study studies from Asia, Africa, North America, and Europe [65]. East Asians lost the greatest weight, with the majority of it recovering after a few weeks of Ramadan. During Ramadan, West and East Asian groups reduced their daily calorie consumption, but African communities increased their daily calorie intake. Both increased and decreased calorie intake are due to changes in carbohydrate intake and were related to a different culture and traditional foods eaten during this period, making the study more complicated and ambiguous to achieve accurate results, so specific control studies related to the same age, gender, culture, and food intake must be considered before studying the positive or negative impact of ramadan fasting on human health [12].

Another study designed by Zouhal *et al.* [66] found that Ramadan intermittent fasting improves body composition and inflammatory biomarkers in obese middle-aged men without impairing their hepatic or renal function. The improvements in body composition (weight, body mass index, body fat percentage, and waist-hip ratio) occurred later in Ramadan (30 days) but not in the middle of Ramadan, and they persisted for 21 days after RIF. In addition, declines in IL-6 and TNF- began towards the middle of Ramadan and persisted until the conclusion of Ramadan and 21 days afterward [66]. To summarize, the results of the previous studies indicate that Ramadan fasting results in significant weight loss, reduction in fat-free mass and fat mass. The greater the initial BMI, the greater the amount of weight loss. Additionally, those who are overweight or obese lose a significant amount of fat mass (as a percentage of weight), and those who are normal weight do not experience this Ramadan fasting effect [57]. Since these benefits were achieved without any exercise or dietary intervention, encouraging individuals to exercise and providing dietary guidance and support during and after Ramadan fasting could enhance the positive effects and prevent a return to pre-fasting weight and body composition. Thus, Ramadan fasting may be a suitable starting point for addressing obesity, but it is important to develop strategies to maintain its beneficial effects beyond the fasting period.

3.5. Ramadan fast and cardiovascular disease

There are some evidences that cardiovascular factors may enhance the lipid panel during Ramadan. According to one research, LDL levels declined while high-density lipoprotein (HDL) levels rose during Ramadan's fast [67], [68]. Males who fasted during Ramadan had lower total triglycerides and cholesterol, whereas women had greater HDL levels, according to various recent research. Both men and women had lower LDL cholesterol levels. Such lipid profile changes are associated with a reduction in cardiovascular risk. Over the course of 10 years, the individual at risk for cardiovascular disease exhibited a significant increase in coronary heart disease risk after fasting for at least ten days [26]. In most cases, the lipid profiles of fasting people returned to normal several weeks after Ramadan.

A meta-analysis was carried out by Jahrami *et al*. [69] in order to determine the influence that fasting throughout the month of Ramadan has on cardiometabolic risk factors in healthy persons. In the study's authors showed that while Ramadan fasting raised HDL cholesterol, but it also lowered total cholesterol, LDL cholesterol, very low-density lipoprotein cholesterol, triglycerides, and diastolic blood pressure [69]. When comparing heart rates before and after Ramadan,they found no difference in resting heart rate, Authors suggest that healthy people may have temporary protection from cardiovascular disease due to Ramadan fasting's favorable effects on cardiometabolic risk variables [69]. Al-Jafar *et al.* meta-analysis's first suggested that fasting during Ramadan could have a positive impact on both systolic and diastolic blood pressure [70].

Additionally, several studies have investigated and found no link between Ramadan fasting and cardiac mortality or morbidity, according to Khafaji *et al.* observational study of patients with the chronic coronary syndrome (CCS), as defined by the European Society of Cardiology (ESC) [71]. Furthermore, 29% of patients reported improved cardiac symptoms. In individuals with CCS and normal left ventricular function, Mousavi *et al.* observed similar results. Over six years, Temizhan *et al.* [69] evaluated the incidence of ACS in 1,655 patients at a single center before, during, and after Ramadan, using the ESC's definition of ACS. They found no statistically significant increases or decreases in the occurrence of ACS during Ramadan compared to the previous or subsequent month. Within three months of undergoing percutaneous coronary intervention, patients who fasted during Ramadan had a greater risk of major cardiac events than those who did not fast during Ramadan [72], [73].

Fasting during Ramadan appeared to significantly reduce systolic and diastolic blood pressures in people using diuretics, and this was well tolerated without complication in a prospective observational study evaluating the safety of diuretic therapy in patients with hypertension. Fasting during Ramadan has been linked to improved blood pressure control and arterial compliance in patients with hypertension, regardless of renal function [74], [75].

3.6. Diabetes

Diabetes patients are more susceptible to both hyperglycemia and hypoglycemia while they are fasting [26]. In order to effectively monitor and modify insulin administration, it is advised against fasting or to fast only while under the supervision of a doctor. Diabetes must be controlled using insulin. Based on modifications made in real-time throughout Ramadan, insulin administration should be postponed. Utilising an insulin pump is advised [64]. Before fasting, diabetic people who do not use insulin and manage their blood sugar with food or oral drugs should also consult a doctor before fasting. According to studies, people with type 2 diabetes had lower fasting and postprandial blood sugar levels throughout Ramadan. Overall, Ramadan seems to help with blood sugar control [12].

In addition to improving glycemic control, progresses in lipid profile and inflammatory markers were also noted. A few weeks after the end of fasting, fasting blood glucose and blood lipids returned to fasting levels, and inflammatory markers decreased for a more extended period [76], [77]. Diabetic patients must be recommended to take a moderate intake of carbohydrates and fat during dinner and add complex carbohydrates to the pre-dawn diet, diabetic patients during Ramadan receive medical care before fasting, and nutrition and physical exercise counseling are essential. Furthermore, patients with diabetes should be aware that if they have severe hypoglycemia after fasting, they should eat breakfast to restore normal blood sugar levels. Additionally, Aydin *et al*. have demonstrated that fasting throughout Ramadan improved glycemic indices in patients with type 2 diabetes. Fasting during Ramadan significantly reduces fasting plasma glucose, according to a comprehensive review and meta-analysis. Fasting blood sugar levels decreased in all three treatment groups (monotherapy, oral combination therapy, and many therapies (such as dietary changes or oral antidiabetics combined with insulin), as shown by subgroup analysis. The levels of postprandial plasma glucose, glycated hemoglobin, and fructose amine did not alter during Ramadan compared to pre-Ramadan levels. Oral combo therapy led to a considerable reduction in BMI on its own. The authors find that postprandial plasma glucose and fructose amine levels are unaffected by Ramadan fasting. Interestingly, fasting throughout Ramadan had a beneficial effect on both body mass index and fasting plasma glucose [78], [79].

In conclusion, both healthy people and those with diabetes type 2 can benefit from fasting throughout Ramadan. According to epidemiological studies conducted in 13 Muslim-majority nations in Asia, the Middle East, Northern Africa, hypoglycemic episodes increased among diabetes patients (types 1 and 2) during Ramadan [80]. During Ramadan, diabetes patients had low incidence of hypoglycemia who fasted and no reports of fatal hypoglycemic events [81]. This is supported by the findings of Almulhem *et al*. results, which revealed conflicting evidence relating fasting in Ramadan to either an increased or reduced risk of cardiovascular events in diabetes [64], When Ramadan falls during the summer (when there are more daylight hours), it can be difficult to observe the fast. Therefore, diabetic patients who plan to fast during Ramadan should adhere to the most recent advice [82]. This may be accomplished if medical professionals

become aware of the advantages and disadvantages of Ramadan fasting for those with type 2 diabetes. The positive impacts of fasting and potential negative consequences on human health that have been uncovered in various research are included in Table 1.

Table1. Effect of fasting on human health during ramadan

Outcome	Health Benefits	References
Activation of the brain-intestinal pathway	Brain while fasting improves gut epithelial integrity to regulate energy balance.	[53]
↓Insulin; ↑Glucagon	During fasting, the body modifies hormones to access stored glucose, maintaining a stable glucose level in the body.	[83]
Weight ↑or weight↓	In Asian, African, North American, and European average of 3 pounds weight reduction were observed in men and women, except Saudi Muslims experience a weight increase.	[84]
Total Triglycerides	Fasting reduces the level of total triglycerides in both men and women. Alterations in lipid profiles indicate a reduction in cardiovascular risk.	[58]
Postprandial blood glucose	Patients with type 2 diabetes had lower blood glucose levels after a meal while fasting.	[85]
Blood sugar control	Fasting during Ramadan improves glucose management.	[85]
Inflammatory markers	Inflammatory markers decreased for a more extended period after Ramadan fasting.	[76], [77]
Dietary Restriction	Restricting one's diet has been demonstrated to help prevent age-related illnesses including cancer, diabetes, neurological diseases, and cardiovascular conditions.	[85], [86]
Starvation of Nutrients	As a stress response, most cultured cells and organs including livers and muscles undergo autophagy when starved of nutrition	[87]
Dietary intervention	Food intervention may reduce the incidence of tumors and enhance the efficacy of radiotherapy and chemotherapy.	[88]
Dietary regimens	Fasting and calorie restriction are being studied for their potential effects on cancer.	[89]
Intermittent fasting	In a model of colon cancer, breast cancer, pancreatic cancer, lung cancer, and hepatocellular cancer, intermittent fasting improved the chemotherapeutic response to anticancer drugs and tyrosine kinase inhibitors.	[35]
Inflammatory bowel disease	Interrupting gut microbiota stability may induce immunologic dysregulation and various illnesses, including inflammatory bowel disease.	[42]
Diabetes	During periods of fasting, people with diabetes are more likely to experience hyperglycemia and hypoglycemia.	[80]
Dehydration	Dehydration may cause fatigue, muscular cramps, dizziness, confusion, and fainting during Ramadan.	[90], [91]
Chronic kidney disease	Fasting may damage renal tubular cells in chronic kidney disease patients.	[92]
Kidney stone disease	People with kidney stone disease can also be affected by fluid restrictions, but the evidence is not clear.	[93]
Chronic kidney disease	Fasting may exceed the risk of chronic renal disease for those with high blood pressure, body weight, lipids, and glomerular filtration rate.	[94]

3.7. Renal or kidney function

Dehydration is a problem, During Ramadan, when eating and drinking are forbidden between dawn and dusk. Previous research has shown that people drink less water overall throughout the month of Ramadan. The body responds by producing less urine and but urine is more concentrated, which may lead to diminished renal function [95]. The worst of the fluid deficit occurs in the third week of Ramadan, although the situation normally improves by the end of the month. In cold and humid areas, this may not be a problem at all [42].

Dehydration can be a life-threatening complication if proper precautions are not taken to ensure rehydration during non-fasting periods [23]. As a result, total body water may be used to assess hydration status in addition to other measures including urine osmolality, urine specific gravity, and blood parameters like plasma and serum osmolality. Ibrahim *et al*. [20] showed that eighteen healthy boys (mean age=22.02.4 yrs.) experienced substantial increases in urine-specific gravity measurements, with mean values above 1.020, indicating hypohydration during Ramadan. However, serum osmolality reduced dramatically during Ramadan but remained within normal norms. Homeostatic processes kept serum osmolality normal [20].

In contrast, another study revealed fasting during Ramadan has no impact on serum osmolality in the Emergency Department. When the other biochemical values were correlated with fasting days, glucose exhibited a negative association while sodium and potassium had a positive correlation [96], in addition, the study suggested about patients with a history of diabetes or past electrolyte abnormalities who are also fasting during Ramadan should be closely monitored in the emergency department (ED) and made aware of these biochemical consequences [96]. More study seems to be needed to examine the impact of fasting during Ramadan on serum osmolality. If severe signs of dehydration present themselves, such as lethargy, muscular cramps, dizziness, disorientation, or imminent fainting, necessary actions should be followed to treat the condition of dehydration. In healthy persons, renal function and the production of urine are not altered

throughout the month of Ramadan, even though the body has a greater need to concentrate urine at this time. The reduction of fluid intake, on the other hand, raises worries about the effects it will have on those who have chronic renal illness. However, there are concerns about the effects of fluid restriction on individuals with chronic kidney disease. Although there is no conclusion, some evidence suggests that people with chronic kidney disease during fasting may cause damage to renal tubular cells [91], [92].

Furthermore, a number of publications have been published to help researchers fully grasp how Ramadan fasting affects Chronic Kidney Disease (CKD) patients, who has kidney failure or on dialysis. Therefore, Sixty Chronic Kidney Disease patients who have fasted for whole month during Ramadan were investigated by Mbarki and his colleagues to determine their renal function. The researchers found that acute renal failure (ARF) may have started in 11.7% of CKD patients, who experienced a decrease in GFR of 25% and a rise in serum creatinine that was 442.1 mol/L higher than the original serum creatinine level [97]. Nasrallah *et al*. [98] observed that after one week of fasting during Ramadan, serum creatinine rose by 60.4% compared to non-fasting CKD patients who served as the control group, with substantial unfavourable effects in fasted CKD patients (eGFR =27.7 mL/min/1.73 m2). Furthermore, three months after the conclusion of Ramadan, 23% of fasting CKD patients still had increased plasma creatinine levels, with no discernible difference from the control group of CKD patients who did not fast [98]. The researchers came to the conclusion that CKD progression rather than fasting was more likely to blame for the increase in creatinine levels. In a prospective study of 65 CKD (stage 3) patients, a 26.5 mol/L increase in blood creatinine was seen in 33% of participants. Chowdhury *et al*. analysed the risk of proteinuria and ARF in 68 CKD stage 3 diabetic individuals who fasted for 19 hours and compared them to 61 participants in the same group who did not fast [99]–[101].

Nonetheless, the benefits of fasting on lipids, glomerular filtration rate, blood pressure, and body weight may exceed the danger for those who have advanced stages of chronic renal disease. If they want to fast, those with chronic renal illness need to be monitored by a doctor. Although the research is conflicting, people with kidney stone disease may also have fluid restrictions. However, other research indicated a link between renal stone development and Ramadan fasting and an increase in renal stone formation during the first week of Ramadan [64].

Many other studies have revealed that there is no correlation between the two [102]. People with a history of renal stones who want to fast during the Holy month of Ramadan should pay proper consideration to their fluid intake and drink enough amount of water from dusk to dawn to achieve the recommended 24 hours urine output. In those with increasing levels of renal impairment Fasting in Ramadan is associated with an increased risk of injury; however, this is not always the case in the aforementioned articles. Fasting may be safe for some patients with stable CKD up to Stage 3 who are not on dialysis, but those on hemodialysis or peritoneal dialysis are at very high risk unless they are well monitored [103].

In conclusion, healthy people don't seem to have any decline in renal function throughout the month of Ramadan. In CKD patients, however, results are inconsistent, and the reasons for this variation across the trials that have been conducted are not always clear. Possible explanations for the conflicting results include individual variations in the study populations' CKD severity, non-fasting hydration levels, fasting days, fasting length, and lifestyle factors including physical activity level may explain the inconsistent findings.

3.8. Autophagy and cancer

The term "autophagy" originates from Ancient Greek, where the word "auto" means "self" and "phagin" means "to eat." Therefore, "autophagy" can be translated literally as "self-eating" or "self-devouring." According to Klionsky [104], autophagy is the natural, controlled, and destructive mechanism of the cell that eliminates components that are either superfluous or malfunctioning so that they can be recycled. When there is not enough of an energy supply (also known as hunger), autophagy kicks into gear to remove all of the broken down and old cellular components such as organelles, proteins, and cell membranes from the body [104]. Yoshinori Ohsumi was awarded the Nobel Prize in physiology and medicine in 2016 for his elucidation of the morphological and molecular mechanisms of autophagy in the 1990s [105], [106].

Autophagy is a conserved lysosomal catabolic mechanism by which cells destroyed and recycle the exogenous and endogenous components to maintain the homeostasis of the cell [107], [108]. The function of autophagy in cancer is complex, and its role may vary depending on numerous biological factors, such as tumour type, progression phase, genetic landscape, activation of oncogenes, and inactivation of tumour suppressor genes [109], [110]. Therefore, autophagy can be associated with either preventing the development of cancer or allowing cancer cell proliferation, adaptation, survival, and metastasis [111], [112]. In preclinical studies, dietary restriction has been shown to increase lifespan and diminish age-related diseases such as cancer, diabetes, neurodegenerative diseases, and cardiovascular diseases [88]. Dietary restriction induces metabolic and cellular changes in prokaryotic to animal organisms that permit adaptation to periods of limited nutrient availability [16]. The central variation includes a decrease in blood glucose

levels and growth factor signalling, as well as the initiation of stress resistance pathways that influence cell growth, glucose metabolism, protection against oxidative stress, inflammation, and cell death [86].

As an adaptive response to an adverse environment, nutrient deprivation induces autophagy in the majority of cultured cells and organs, such as the liver and muscles [87]. According to studies, dietary intervention can reduce tumour incidence and enhance the efficacy of radiotherapy and chemotherapy in a variety of tumour models, spotlighting dietary manipulation as a possible adjunct to standard cancer treatments [88]. Among several dietary regimens that were evaluated, fasting and caloric restriction is the method under investigation in oncology [89]. The in-vitro and in-vivo studies have explored that intermittent fasting enhanced the chemotherapeutic response to doxorubicin, cisplatin, cyclophosphamide, sorafenib, oxaliplatin, mitoxantrone, etoposide, gemcitabine, temozolomide, and tyrosine kinase inhibitors in a model of neuroblastoma, melanoma, glioma, fibrosarcoma, and colon cancer, breast cancer, pancreatic cancer, lung cancer, and hepatocellular cancer. The earlier studies required a better understanding of the molecular mechanisms induced by fasting in order to identify the circumstances in which fasting may be beneficial as an adjunct to cancer therapy [113].

In conclusion, during Ramadan fasting (RF), malnutrition occurs, and autophagy is activated to clear protein aggregates and other cellular garbage for recycling, resulting in a health benefit. During RF, glycogen depletion and a metabolic change into ketosis, which may occur between days 3 and 5 of fasting, activate autophagy. Because fasting enhances growth hormones (GH) secretion, a synergistic action of autophagy and growth hormone may be able to replace old and weakened cells with new ones, to halt the pathogenic process [114]. In addition, it is necessary to keep in mind that autophagy can be inactivated by increasing calorie intake, as reported previously that most Muslims increase their uptake of calories during Ramadan fasting [115]. In order to determine the consequences that fasting during Ramadan (RF) has on human health, further study is required. This is of utmost significance since, according to the findings of a research conducted by El Ati *et al.* in 1995, the amount of calories consumed during Ramadan fasting seems to rise in some Muslim communities. It is important to keep in mind that the amount of calories consumed might have an effect on autophagy, which is a process that occurs in cells. Because of this, depending exclusively on alternate-day fasting (ADF) or Ramadan fasting may not be adequate to get the maximum health advantages of either method, particularly in those individual who gorge themselves during feast periods [115]. It is suggested to combine calorie restriction (CR) with alternate day fasting (ADF) or Ramadan fasting (RF) in order to elicit the best health-related biomarker and longevity. However, there are some limitations to keep in mind the health status of the individual having diabetes, chronic kindney problems while exploring the relationship between autophagy and fasting. Therefore, for future research on cancer or tumorigesis it is highly recommended to use animal model study.

4. CONCLUSION

The metabolic effects of fasting during Ramadan are complicated, vary from person to person, this month has the potential to be used as a weight loss paradigm if fasting is performed consciously, it can reduce obesity that's help in the control of cardiovascular diseases, while fasting has been observed effective in the cancer pateints. Nontheless, certain studies found adverse effect of fasting on diabetic and chronic kidney disease patients, however they need specialized counsel if Ramadan fasting is judged appropriate in the first place. Futher research need to explore the posive impacts of the alternate day fasting, Ramadan fasting, and calorie restrictions on cancer and tumorigenesis. In conclusion, fasting has the potential to provide significant health benefits, but the effects may vary depending on the individual and the specific circumstances. Careful consideration and guidance are necessary to ensure that fasting is a safe and effective practice for each individual.

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