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The Protective Effects of Ramadan Fasting against Cancer: Exploring Metabolic, Cellular, and Epigenetic Mechanisms

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ABSTRACT

Fasting, particularly the fasting during Ramadan, is becoming very common due to the potential health benefits of which it is inclusive of its anti-cancer properties as well as therapy. It is mentioned in a recent study that intermittent fasting, as during Ramadan, induces some alterations in the metabolism, physiology, and epigenetics, which could suppress cancer growth. The problem that this study seeks to address is the deficiency of scientific honesty and transparency in explaining the mechanisms by which Ramadan fasting affects cancer development and treatment response. The research seeks to systematically update the literature to evaluate the protective mechanisms of Ramadan fasting against cancer progression based on scientific transparency. The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines for executing sound and transparent reporting. The key findings are that fasting controls metabolism towards increased production of ketone bodies, reduced availability of glucose, and reduced levels of insulin and insulin-like growth factor-1 (IGF-1)—vital modulators of cancer cell growth. Also, fasting increases the DNA damage response (DDR), stimulates cellular homeostasis through autophagy, and decreases oxidative stress, thereby inhibiting malignant transformation. Epigenetically, fasting regulates non-coding RNAs, DNA methylation, and histone modification, which act to activate tumor suppressor genes and silence oncogenes. The most significant finding is that Ramadan fasting is of immense potential as an adjuvant intervention in cancer therapy. These findings have crucial implications for integrative oncology practice, dietary intervention, and public health policy in the integrative oncology setting.

1. Introduction

Fasting has been associated with spiritual cleansing and personal discipline in many religions and cultures. Muslim communities worldwide fast throughout Ramadan. The scientific community is studying the health benefits of this 29- or 30-day religious fasting that prohibits food and drink from dawn to sunset [1]. Ramadan fasting is a controlled intermittent fasting approach that may help prevent and treat cancer. Fasting is shown to activate autophagy, regulate IGF-1, decrease reactive oxygen species, and change gene expression patterns to stop cancer development [2]

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Traditional Islamic beliefs use biological processes to prove fasting's health benefits. Verse 2:184 of the Quran states, “And fasting is better for you if you only knew,” implying that fasting improves spiritual health and overall well-being. Ash-Shu'ara 26:80 "And when I am ill, it is He who cures me." (This passage may relate to fasting's restorative effects, including cancer prevention and metabolic health. According to Prophet Muhammad (peace be upon him), one can find health through fasting when he said, "Fast, and you shall be healthy" (Sunan Ibn Majah, Hadith 3448). Current scientific investigations demonstrate that fasting produces important modifications to cellular homeostasis while affecting cancer cell survival, together with cell proliferation processes and resistance capabilities [3]. Autophagy stands as a key cellular detoxification process of fasting, which removes damaged cells while minimizing cancer development potential [4]. This study investigates the metabolic, molecular, and epigenetic factors behind Ramadan fasting's cancer-protective effects. The study functions as a bridge linking traditional Islamic practices with contemporary scientific achievements within public health, together with biomedical sciences domains. The extensive biological effects of fasting studied in this work strengthen ongoing scientific proof, which suggests that fasting works as a non-medication intervention to prevent cancer and support health benefits.

Cancer remains a leading cause of disease and deaths around the world, based on projections that indicate 10 million fatalities will occur in 2020 [5]. Treatment through chemotherapy as well as radiation therapy often results in severe side effects and high charges, combined with unsatisfactory long-term treatment success. Increasing demand now exists for different and supplementary methods to combat and prevent cancer. The intensity of focus on fasting during Ramadan has increased because researchers believe that it might protect against cancer, along with controlling metabolic processes and activating autophagy, and causing epigenetic changes [3]. The current scientific understanding does not fully reveal the operative mechanisms through which fasting could defend against cancer development. The research analyzes metabolic pathways together with cellular mechanisms and epigenetic processes that Ramadan fasting may use to prevent cancer.

The best possible cancer prevention methods should be readily accessible at cost-effective prices with minimal invasiveness to stop cancer development and growth. [6] report that cancer occurrences persist to rise, but numerous prevention strategies depend on drug-based solutions which prove inaccessible to certain populations, particularly those in low- and middle-income settings. Current cancer research stands almost completely devoid of studies involving fasting prevention, even though major research effort traditionally focuses on pharmaceutical therapies and lifestyle changes. Current scientific literature does not adequately explore how religious fasting affects cancer prevention across metabolic pathways and cell function while modifying epigenetic processes, even though intermittent fasting proves beneficial to cells and reduces cancer risks [7]. The lack of studies focused on cheap cancer prevention methods could produce rising cancer incidence rates and extensive healthcare costs throughout poor nations. The discovery of cancer-preventive effects from Ramadan fasting could introduce a religiously acceptable intervention method that traditional societies would adopt. The dismissal of this prospective relationship might lead to lost opportunities to enhance both public health results and respect religious practices.

Studies about fasting concentrate on examining its health advantages for both metabolic health and lifespan extension. Studies by [3] proved that periodic fasting enhances autophagy, which serves as a vital process to fight cancer. [7] determined that fasting enhances metabolic flexibility while lowering oxidative stress, which is known to reduce cancer risks. The investigation of Ramadan fasting with its unique fasting-feeding pattern for inhibiting cancer risks remains poorly studied in research. The analysis conducted by [1] revealed that Ramadan fasting reduces oxidative stress markers and inflammation, yet the study remained unclear about its effects on cancer development pathways. Current cancer research primarily examines temporary metabolic changes instead of sustained evaluations of cancer reduction practices. Research gaps demonstrate why scientists must conduct a complete investigation about how Ramadan fasting affects cancer prevention through metabolic systems, cellular changes, and epigenetic procedures.

This scientific work examines how Ramadan fasting acts as a cancer prevention method through the evaluation of biological pathways starting from metabolic processes to molecular mechanisms and ending at epigenetic changes. Researchers position this investigation as part of public health and biomedical science to contribute evidence about using fasting as a medicine-free approach against cancer development and overall health improvement. Knowledge about the molecular aspects of Ramadan fasting, together with its effects on cancer programs, would benefit healthcare providers, researchers, and politicians. The research findings bring vital public health consequences for Muslim-majority regions since Ramadan fasting takes place regularly in these communities. Healthcare expenditures could decrease through effective cancer prevention strategies based on fasting practices once the effectiveness has been validated by researchers. The evaluation between religious practice and medical science enables this initiative to establish evidence-based suggestions that aid integrative medicine and nutritional approaches while developing preventive care strategies that support holistic healthcare and disease prevention objectives. Research conducted through this project examines cancer prevention from a culturally suitable perspective while filling present knowledge gaps to establish innovative health interventions that are both affordable and accessible.

2. Theoretical and Empirical Literature Review

Fasting, examined from diverse theoretical perspectives, uncovers complex systems that aid in cancer prevention and therapeutic improvement. Metabolic and cellular theories highlight how fasting induces a metabolic shift that starves cancer cells of their preferred energy sources while protecting healthy cells. The Metabolic Switch Theory elucidates how ketosis inhibits glucose-dependent cancer cell proliferation by diminishing insulin and glucose levels, thereby facilitating the use of ketone bodies as an alternative energy source [3], [8], [9]. The Insulin Growth Factor-1 (IGF-1) Reduction Theory posits that diminished IGF-1 levels during fasting suppress the PI3K-AKT-mTOR pathway, hence decreasing cell proliferation and promoting death in cancer cells [10]. Cellular theories like Autophagy elucidate how fasting-induced self-cleansing eradicates damaged organelles and pre-cancerous cells, hence diminishing inflammation [11], [12]. The Differential Stress Resistance (DSR) Theory asserts that normal cells adopt a protective state during fasting, whereas cancer cells remain susceptible to therapeutic interventions [13].

Moreover, the Oxidative Stress Modulation Theory highlights fasting's function in reducing reactive oxygen species (ROS) and safeguarding cellular DNA from oxidative harm [3].

From an epigenetic and holistic health standpoint, fasting is recognized not merely as a metabolic intervention but as a multifaceted method that affects gene expression, cellular activity, and spiritual wellness. The DNA Methylation and Gene Expression Theory elucidates how fasting modifies methylation patterns, potentially inhibiting oncogenes and activating tumor suppressors [14], [15]. Ketone bodies generated during fasting suppress histone deacetylases (HDACs), hence impeding cancer cell growth and augmenting the efficacy of chemotherapy, as elucidated in the Histone Modification and Epigenetic Reprogramming Theory [16], [17]. The Non-Coding RNA Regulation Theory posits that fasting modifies miRNAs and lncRNAs, hence affecting tumor proliferation and immune response [18], [19]. Islamic and holistic health theories incorporate a spiritual aspect: the Taqwa and Spiritual Detox Theory highlights the Qur'anic perspective on fasting as a means to attain God-consciousness, mitigating stress-induced inflammation and improving immune surveillance (Koenig, 2012; Qur'an 2:183). The Circadian Rhythm and Chronobiology Theory advocates for aligning fasting with biological cycles to enhance hormonal equilibrium and immunological functionality [20], [21]. Finally, the Moderation and Prevention Theory, based on the Hadith, advocates for caloric moderation, correlating prophetic counsel with contemporary understanding of the impact of overeating on cancer progression [3]; Sunan Ibn Majah 3349).

The London Ramadan Study (LORANS) observed the effect of Ramadan fasting on metabolic profiles and chronic disease risks according to [22]. Expert researchers obtained two blood samples from 72 participants before and after the end of Ramadan. Nuclear magnetic resonance spectroscopy enabled metabolomic profiling, which analyzed the modifications of particular metabolites throughout and before the Ramadan period. Research conducted metabolic scoring (rated 0 to 100) for seven UK Biobank-associated chronic diseases to assess Ramadan fasting effects on LORANS participants. A total of 35 out of 72 participants identified as male, which represented 48.6%, while their average age came to 45.7 (±16) years. The fasting practice of Ramadan produced metabolic changes in 14 substances, including one inflammatory indicator and one amino acid, together with two glycolysis metabolites, two ketone bodies, two triglycerides, and six lipoprotein subclasses in participants independent of their body composition. Our analysis used 117.981 UK Biobank participants to develop metabolic scores for diabetes, hypertension, coronary artery disease, renal failure, colorectal cancer, breast cancer, and lung cancer. Within the sample group of LORANS post-Ramadan researchers observed decreased metabolic scores related to lung cancer by -4.74 with an effect size of 9.6% (-6.56 to -2.91 $P < 0.001$) as well as colorectal cancer scores reduced by -1.09 (-1.69 to -0.50 $P < 0.001$) and breast cancer scores decreased by -0.48 (-0.81 to -0.15 $P = 0.006$). Researchers found that the dietary restrictions of Ramadan produce temporary beneficial effects that lower the risk factors for certain chronic illnesses.

The study by [23], focused on how Ramadan intermittent fasting (RIF) affects cellular metabolism through SIRT1 and SIRT3 and antioxidant gene functions of TFAM, SOD2, and Nrf2. The study included fifty-six subjects (22 women and 34 men who were overweight or obese, together with six healthy-weight individuals) as participants. The research confirmed that obese participants exhibited higher antioxidant gene expression (TFAM, SOD2, and Nrf2) levels than controls during the final stage of Ramadan, with percentage increases reaching 90.5%, 54.1%,

and 411.5%, respectively. SIRT3 gene expression showed a large ($P < 0.001$) reduction level together with declining SIRT1 gene expression at the end of Ramadan, resulting in 61.8% and 10.4% relative magnitude changes. Results from a binary regression test confirmed a significant positive link ($P < 0.05$) between excessive caloric consumption exceeding 2000 Kcal/day as compared to <2000 Kcal/day with SOD2 and TFAM gene expression levels ($r = 0.84$ and $r = 0.9$). Genetic expression of antioxidant and anti-inflammatory, together with metabolic-regulating genes, improves due to RIF. The results indicate RIF protects people with non-diabetes and obesity from oxidative stress and metabolic disturbances in their bodies.

Scanning certain metabolites linked to cancer development revealed that cancer cells have weak resistance against nutritional starvation, according to [22], Widespread changes in growth factors and metabolite levels occur during fasting or FMDs that hinder cancer cellular adaptation and survival while improving the effectiveness of cancer therapy. Studies show that fasting and FMDs enhance the resistance of normal cells to chemotherapy while leaving cancer cells unaffected, together with their ability to regenerate normal tissue at an accelerated speed to reduce harmful treatment complications. Although most patients find fasting intolerable, medical research demonstrates that patients can safely undertake limited cycles of low-calorie FMDs. Several active clinical studies aim to determine the effects of fasting and FMDs on both adverse events triggered by treatment and treatment success measurements. According to our proposal, the fusion of FMDs with chemotherapy and immunotherapy treatments and additional therapeutic techniques has the fundamental potential to enhance clinical results and stop treatment resistance formation, and lessen negative side effects.

Another study was conducted by [20], Ramadan fasting affects autophagy pathways inside the body, together with metabolic health results among fasting healthy adults. The controlled subject study involved 50 adult participants aged 20 to 78, where 24 people fasted while 26 others did not participate in fasting activities. The researchers collected blood samples after Ramadan to measure biochemical indicators along with hematological and inflammatory markers. The investigation monitored the levels of IL-6 and hs-CRP found in fasting subjects' blood samples. The method used serum analysis through ELISA and mRNA gene expression testing with real-time PCR to evaluate autophagy marker levels of Beclin-1 and LC3β proteins and mRNA expression for Beclin-1, p62, and LC3β. The biochemical markers showed no substantial variations (except for BUN level), and inflammatory indicators (IL-6 and hs-CRP) and hematological indicators remained stable during Ramadan. The dramatic increase of Beclin-1 gene expression during fasting manifested the start of autophagy processes. The quantity of LC3β and p62 proteins decreased in peripheral blood mononuclear cells. The serum Beclin-1 levels exhibited substantial increases in fasting women who did not participate in fasting with nondiabetic controls in fasting. Biochemical as well as hematological, and inflammatory parameters do not show negative changes during Ramadan fasting. Observing Ramadan enables individuals to use autophagy as a protective mechanism when energy and vital metabolic substances decrease because of dietary restrictions.

Furthermore, [19], conducted a prospective cohort study at the oncology outpatient clinics of KAMC and KASCH, which examined CRC patients under pre- and post-fasting conditions. Researchers investigated how fasting during Ramadan impacted the tolerance of chemotherapy's adverse effects, in addition to monitoring changes in carcinoembryonic antigen (CEA) and lactate dehydrogenase (LDH) biomarker levels, which indicate certain carcinomas such as CRC. The

investigation revealed that 33 patients (89.2%) engaged in fasting activities throughout at least some of the month of Ramadan. The study showed that twenty-seven patients (73%) achieved a state of serenity through Ramadan fasting that improved their tolerance to chemotherapy adverse effects. The laboratory measurements remained unchanged when researchers evaluated results between pre-fasting examinations and 30-day Ramadan fasting. Evidence points to lower CEA and LDH levels in 46.9% and 55.6% of participants, although the difference between these groups was not statistically significant. A fasting intervention resulted in a 41% decrease of CEA levels in the studied group through statistically significant reductions in CEA values in three participants ($p=0.0283$). Data showed that fasting did not impact renal functions because both creatinine blood levels and estimated glomerular filtration rates remained identical before and after Ramadan. The research presents evidence that intermittent fasting effectively preserves safety and tolerability among CRC patients receiving chemotherapy in many current reports.

A literature review regarding Islamic fasting benefits was presented by [22]. Their search included databases Medline, PubMed, PMC, Google Scholar, ScienceDirect, and reference lists of relevant articles that used the search terms health benefits, Islamic fasting, intermittent fasting, alternate-day fasting, and time-restricted feeding, and Ramadan intermittent fasting. Research results indicated that Islamic fasting should fit into the intermittent fasting category because its pattern resembles both alternate-day fasting and time-restricted feeding protocols. Multiple research studies support the connections between intermittent fasting and a wide array of health advantages that deliver weight reduction alongside metabolic indicator improvements including insulin response control, blood pressure regulation, and enhanced lipid profile and disease prevention (diabetes, obesity, heart disease, cancer) together with protecting against brain deterioration and decreased inflammatory responses.

A study by [22] showed that a proper diet combined with movement and no alcohol or smoking, and weight management can prevent 30 to 50 percent of all possible tumors. Multiple worldwide associations have established cancer prevention guidelines based on the recommendation to eat plant-based diets, together with restricted intake of red/processed meat and sweets and processed foods, and alcohol. The potential benefits of these methods for health improvement involve their direct and indirect influence on signaling pathways that trigger cancer. [20] performed research to explain more clearly the relationships between fasting and health for the future. The study employed a literature review where recent ten-year publications qualified as inclusion, but older unimportant articles functioned as exclusion criteria. The outcomes indicate that the body conducts autophagy while fasting. The human body removes useless proteins as well as organelles and cell membranes through its natural process of autophagy. Frequent intermittent fasts cause natural body cleansing that builds cancer resistance in people. Intermittent fasting enhances overall health performance through two different mechanisms: it strengthens the immune system and helps manage diseases. During intermittent fasting, people should practice healthy lifestyle choices.

Despite accumulating evidence regarding the health benefits of Ramadan fasting, such as metabolic enhancements, modulation of gene expression, activation of autophagy, and improved chemotherapy tolerance, there exists a substantial research gap in comprehending the epigenetic mechanisms that contribute to cancer protection during Ramadan fasting. Although existing research has investigated metabolic and cellular responses, it has not thoroughly

analyzed how Ramadan fasting distinctly alters epigenetic markers (e.g., DNA methylation, histone modification, microRNA expression) that could affect oncogene suppression or the activation of tumor suppressor genes. This uncharted epigenetic aspect presents a new research opportunity to elucidate the long-term cancer-preventive effects of Ramadan fasting and differentiate it from other intermittent fasting paradigms.

3. Methodology

This study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a transparent and reproducible review process.

3.1 Eligibility Criteria (Inclusion & Exclusion)

Table 3.1: Eligibility Criteria

Criteria	**Inclusion**	**Exclusion**
Population	Human or animal studies on fasting and cancer	Studies on other types of fasting (e.g., ketogenic diet, prolonged water fasting) without mentioning Ramadan fasting
Intervention	Studies on Ramadan fasting and its biological impact	Studies on non-Ramadan fasting without comparison
Outcomes	Metabolic, cellular, and epigenetic effects of fasting related to cancer	Studies without biological mechanisms (e.g., sociological effects of fasting)
Study Type	Peer-reviewed clinical trials, experimental studies, systematic reviews, and meta-analyses	Non-peer-reviewed articles, commentaries, and opinion papers
Publication Year	Studies published in the last 10–15 years	Older studies, unless highly relevant

Source: compiled by authors

3.2 Data Sources and Search Strategy

Table 3. 2: Data source and search strategy

Databases:	PubMed, Scopus, Web of Science, Google Scholar, and ScienceDirect
Search Terms:	(“Ramadan fasting” OR “Islamic fasting”) AND (“cancer” OR “tumor” OR “oncology”) AND (“metabolism” OR “glucose metabolism” OR “insulin resistance” OR “ketogenesis”) AND (“cellular mechanisms” OR “apoptosis” OR “autophagy” OR “oxidative stress”) AND (“epigenetics” OR “DNA methylation” OR “miRNA” OR “histone modification”)
Search Filters Applied	Peer-reviewed articles, published between 2010–2025, and Human & animal studies

Source: compiled by authors

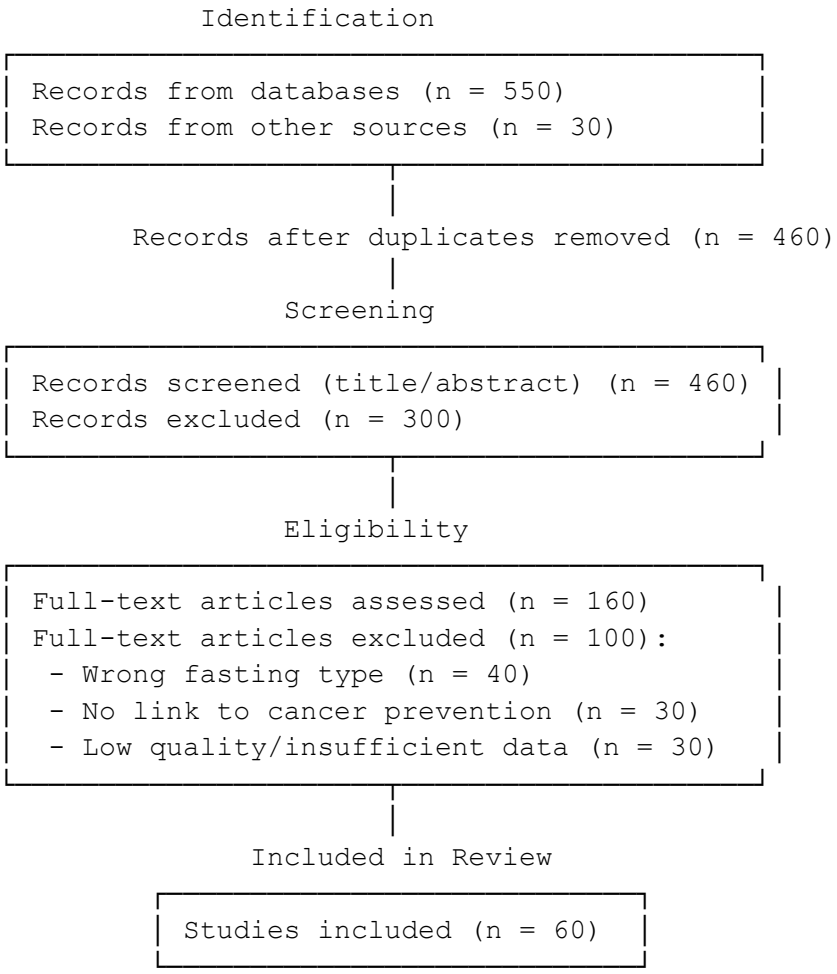
3.3 Study Selection Process (PRISMA Flowchart)

Table 3.3: Prisma Flowchart

Identification	Records identified from databases (PubMed, Scopus, Web of Science, Google Scholar, ScienceDirect): (n = 550)
	Records identified from other sources **(**manual search, citations, reports): (n = 30)
	Total records retrieved: (n = 580)
	Duplicate records removed: (n = 120)
Screening	Records screened (title and abstract level): (n = 460)
	Records excluded (irrelevant, not related to Ramadan fasting or cancer, review articles, etc.): (n = 300)
Eligibility	Full-text articles assessed for eligibility: (n = 160)
	Full-text articles excluded with reasons: (n = 100) ❖ Wrong fasting type (e.g., intermittent fasting but not Ramadan fasting) (n = 40) ❖ No direct link to cancer prevention (n = 30) ❖ Low methodological quality or insufficient data (n = 30)

Source: compiled by authors

Flowchart: Adopted Research Model (Based on PRISMA)



4. Results and Discussion

4.1 Systemic and cellular fasting response

Metabolic pathway activities shift through fasting to establish a cellular state that produces energy by using mainly adipose tissue carbon sources and, secondarily, muscle-derived carbon sources. The normal cells experience lower metabolic activity combined with reduced growth because circulating hormones and metabolites create this defense mechanism against chemotherapeutic damage. During starvation, cancer cells develop unique responses to restrictive signals in a manner that enhances their reaction to chemotherapy, along with other cancer treatments [3].

4.2 Systemic response to fasting.

The metabolic system experiences multiple changes when fasting leads to modifications in glucose, insulin, and glucagon levels as well as GH, IGF1, glucocorticoids, and adrenaline. The insulin levels fall as glucagon levels rise during the early post-absorptive period (6-24 hours), which leads to glycogen depletion in the liver and the release of glucose as the power source. Most tissue cells receive energy from free fatty acids and glycerol that arise from triglyceride degradation beyond 24 hours. Nevertheless, the brain requires both glucose and ketone bodies for operation. The brain receives sufficient power from ketone bodies during this period, but gluconeogenesis actively maintains blood glucose levels at 4 mM. The body regulates blood sugar through the actions of glucocorticoids and adrenaline, while these hormones also enhance lipolysis. GH helps gluconeogenesis briefly until it decreases IGF1 activity. The rise in IGFBP1 reduces IGF1 activity, yet the decline in leptin levels during fasting leads to increased effects of adiponectin which promotes fat breakdown. Fasting produces an environment with low glucose levels along with decreased insulin, IGF1, and leptin, but elevated glucagon, together with ketone bodies and adiponectin [5].

4.3 Cellular response to fasting.

Cells of good health activate an ancient defensive mechanism that fasting creates to extend both lifespan and health span duration. The importance of IGF1 signaling lies in its activation of AKT and mTOR through increased IGF1 levels produced by diet availability, especially when proteins are consumed. Fasting results in decreased IGF1 levels that activate FOXO transcription factors which enhance production of HO1 along with SOD and catalase enzymes thus strengthening cell protection. During fasting events, glucose levels decrease, which shuts down PKA signaling yet activates both AMPK activity and the important stress tolerance factor EGR1. The protection system provides beneficial effects on the heart as well as the entire cell resistance [10].

4.4 Dietary approaches to cancer

Cancer fasting includes two main interventions: water fasting and fasting-mimicking diets (FMDs). The prevention of DNA damage caused by chemotherapy in healthy tissues requires at least 48 hours of fasting, according to clinical research findings. This approach improves patient quality of life. Water fasting proves challenging for patients because they face difficulties and worry about their nutritional needs. FMDs provide similar fasting advantages to patients through their low-calorie, low-carb, and low-protein dietary approach, which boosts compliance rates alongside risk reduction. Primary research studies demonstrate that FMDs have low toxicity levels while simultaneously decreasing body fat, blood pressure, and blood IGF1 concentration. Research shows that combination chemotherapy with cancer fasting and FMDs administered over 3 to 4 weeks for 1 to 5 days results in no major adverse effects [12].

4.5 Ketogenic diets.

High-fat, low-carbohydrate ketogenic diets promote ketone synthesis to decrease IGF1 and insulin levels, while their influence depends on their macronutrient compositions. People use KDs for epilepsy treatment, while these diets help control blood sugar levels, although they show low anticancer properties. The murine data demonstrate positive results against glioblastoma, yet human trials require KDs together with chemotherapy treatments, radiation treatment, and PI3K inhibition. Research does not show how well KDs protect the nervous system or how diets affect chemotherapy-related tissue damage or neurocellular repair. The initiation of the refeeding phase for coordinated tissue regeneration appears only in fasting-mimicking diets and not in ketogenic diets [12].

4.6 Calorie restriction

The restriction of constant calories, together with limited specific nutrients, provides anticancer effects like periodic fasting while employing opposite mechanisms. The intake of energy content typically lowers by 20-30% under CR conditions, which leads to decreased cardiovascular risks and cancer occurrences in animal study populations that include primates. CR generates various side effects, which include cold sensitivity, muscle loss, infertility, and both osteoporosis and mood changes, resulting in heightened concerns about malnutrition for cancer patients. The combination of CR with protein restriction controls IGF1 levels in addition to minimizing fasting glucose, but singular CR administration does not affect IGF1. Medical research demonstrates that CR helps intestinal stem cells perform better through mTORC1 signaling blockage, though no scientific data exists about CR's restorative benefits on other body organs. The metabolic and protective response during fasting, together with FMDs, appears to produce advantages beyond what KD or CR can achieve [15].

4.7 Fasting and FMDs in therapy

Fasting causes chemical changes in metabolic substances and hormones, which reduce glucose and IGF1, and insulin while increasing the levels of leptin and adiponectin, leading to anticancer effects. Deleterious effects on healthy tissue receives protection from these changes mainly due to reduced levels of IGF1 and glucose. The ketone bodies produced during fasting inhibit histone deacetylases (HDACs), so tumors grow more slowly and the cells differentiate through epigenetic mechanisms122. Tests demonstrate that acetoacetate supports growth in particular cancers, including BRAF-mutated melanomas, whereas it does not stop them from progressing. Research shows that the reduction of IGF1 and glucose levels stands as the strongest proof supporting fasting and FMD's beneficial effects on cancer. The practice of fasting together with FMD diets interrupts intracellular signaling routes, including IGF1R–AKT–mTOR–S6K and cAMP PKA signaling, while simultaneously stimulating autophagy and protecting normal cells during stress situations, along with promoting anticancer immunity [10].

4.8 Differential stress resistance: increasing chemotherapy tolerability.

Through the differential stress resistance (DSR) framework, fasting enables regular cellular protection and enhances the susceptibility of cancer cells to medical

interventions. The expression of genetic factors that influence proliferation decreases during fasting, which triggers normal cells to enter a self-preservation mode that enhances their resistance to oxidative damage and chemotherapy impacts. The stress response mechanisms get disrupted by oncogenic transformations in cancer cells, so the cells become more prone to damage. The IGF1 signaling pathway becomes lowered following fasting, according to studies of yeast and mammalian biological systems, thus protecting both glial cells and neurons in addition to normal cells, but not infected cells like gliomas and neuroblastomas. Lab mice show better chemotherapeutic responses after fasting or having their IGF1 signaling pathway modified through genetic modifications, since it enhances treatment tolerance alongside minimizing cardiotoxic and immunological harm and lengthening survival time. Doxorubicin-induced cardiac damage receives protection through fasting mechanisms that reduce ROS production by autophagy and strengthen protective peptides through the cAMP-PKA-EGR1 pathway. The research supports fasting and FMDs as potential supportive cancer treatments that both improve chemotherapy outcomes and decrease side effects [20].

4.9 Differential stress sensitization: increasing the death of cancer cells.

Cancer growth shows no reaction to fasting or FMDs, yet these nutritional approaches remarkably enhance the effectiveness of chemotherapy alongside radiation and TKIs through DSS. The nutritional deficiency created through fasting works to enhance both oxidative stresses along reactive oxygen species production as well as sensitization of cancer cells to DNA-damaging therapy. Fasting modifies cancer metabolism toward oxidative phosphorylation in addition to increasing chemotherapeutic transporters, activating pro-apoptotic genes, and suppressing MAPK signaling. Cancer cells belonging to the B and T cell ALL groups and possessing glucose dependence tend to benefit the most from these advantages. Animal model research shows that when patients use fasting with standard therapies, tumor cells rarely become resistant to treatment [18].

4.10 Antitumor immunity enhancement by fasting or FMDs.

Scientific evidence demonstrates that both fasting and FMDs as individual treatments or combined with chemotherapy, help raise lymphoid progenitors to strengthen cancer immune assault. The fasted state in living subjects reduced HO1 activity in cancer cells, yet elevated its activity in intact normal cells. The decline of HO1 activity in cancer cells makes tumor-infiltrating lymphocytes attack tumors through their CD8+ cells while also potentially benefiting from regulatory T cell inhibition (Postow et al, 2015). Research conducted by investigators demonstrated that fasting together with FMDs and CR mimetics solutions enhanced anticancer immune surveillance, thus indirectly suggesting they could operate against autophagy-competent tumors but would be ineffective on autophagy-deficient ones. The practice of fasting cancer cells for two weeks in mouse colonic tumors created autophagy while decreasing CD73 enzyme activity and reducing cancer cell adenosine synthesis. The fasting process decreased macrophage CD73 expression to stop these cells from converting into M2 immunosuppressive type cells. Single studies indicate FMDs can serve as an alternative to immune checkpoint inhibitors or act alongside cancer vaccines, as well as other antitumor drugs that encompass conventional chemotherapeutic agents [19].

4.11 Anticancer diets in mouse models

Research conducted with cancer models involving animals demonstrates that both fasting procedures alongside FMDs exhibit comprehensive anticancer properties as well as potential treatment outcomes while producing organ self-healing effects. Fasting alongside FMDs provides benefits compared to costly drugs, which tend to cause harm because they achieve tumor remission as well as long-term survival of patients. Research indicates that ketogenic diets (KDs) demonstrate potent anticancer effects that control immunological activities and improve treatment results primarily for gliomas and other malignant tumors. While models show that both chronic calorie restriction (CR) and ketogenic diets possess advantageous effects over fasting, the combination with anticancer therapy presents weaker results than fasting and comes with concerns such as lean body mass loss along with patient adherence challenges. The desperate changes that short-term fasting creates in metabolic pathways make it more powerful against cancer than refeeding regenerates and heals the body. The potential therapeutic benefits, along with reduced inconvenience, of periodic FMDs or short fasting cycles make them attractive options to enhance cancer therapy results by reducing treatment side effects, mainly in aggressive cancers such as glioblastoma [16].

4.12 Fasting and FMDs in cancer prevention

Multiple studies based on both animal experiments and human population statistics show that patterned dietary approaches, including chronic calorie restriction and intermittent fasting, and fasting-mimicking diets, help prevent cancer development. The practice of CR remains difficult because people struggle to follow it and suffer negative effects. Current research focuses on finding regular eating patterns that have minimal side effects for clinical evaluation. When FMD regimens activate, they lower IGF1 and glucose while elevating IGFBP1 and ketone body production, thus creating the same indicators as fasting. When C57Bl/6 mice received two monthly FMD administrations over four days, the tumor incidence decreased to 40% compared to 70%, while mortality was extended and tumor aggressiveness reduced. The alternative day fasting protocol applied to middle-aged mice brought lymphoma occurrence down from 33% to 0% before the researchers could determine extended impacts. FMD provides a more convenient fasting plan than alternate-day fasting because it requires fewer fasting occasions each month [12].

4.13 Clinical applicability in oncology

Recent feasibility research confirms that fasting together with fasting-mimicking diets (FMDs) helps chemotherapy patients minimize their adverse effects. The voluntary fasting conducted by ten cancer patients led to no major adverse outcomes but resulted in feelings of lightheadedness, together with increased hunger. The patients also experienced alleviated fatigue and stomach issues. The protocol of short-term fasting decreased DNA breaks and blood cell number reductions that typically follow chemotherapy, according to experimental research findings. A minimum 48-hour fasting period decreased DNA damage while simultaneously tending to produce lower neutropenic conditions in patients undergoing platinum-based chemotherapy treatments. A randomized clinical study with patients who had breast or ovarian cancer proved that Fasting-Mimicking Diets defended against the fatigue effects and deterioration in quality of life from chemotherapy treatments. Research teams consisting of more than 300 participants monitor FMD's impact on chemotherapy toxicity through continuous clinical trials throughout the United States and Europe [19].

5. Conclusion

The practice of fasting triggers multiple metabolic effects along with various physiological and epigenetic effects that protect against cancer development while offering better therapeutic results. Metabolic changes from fasting lead to ketone production while reducing both cancer cell access to glucose and insulin and IGF-1 levels that manage signal proliferation through their decrease and enhance insulin-related chemical sensitivity. Autophagy develops during fasting to maintain cellular balance while eliminating defective substances that present cancer-related hazards. The treatment of cancer cells becomes more effective due to fasting-induced DSR. The lowering of oxidative stress through fasting cuts down DNA damage and malignant transformation. The practice of fasting causes significant epigenetic modifications to DNA methylation patterns and histone restructuring, together with non-coding RNA regulatory changes, which ultimately lead to tumor-suppressor activation and oncogene silencing. Different studies show how fasting can function as a supplementary method for cancer prevention and treatment, thus requiring additional clinical evaluation.

6. Future Studies and Integration of Machine Learning Approaches

While this study has explored the metabolic, cellular, and epigenetic mechanisms of Ramadan fasting and cancer prevention, it is recommended that future studies incorporate predictive modeling methods to measure complex biological interactions. Machine learning (ML) can do so. For instance, [23] demonstrated how ML models can predict stress in biological systems with predictive results beyond traditional statistical methods. The use of ML in biomedical fasting studies can improve the prediction of cancer risk, responsiveness to fasting interventions, and individualized treatment regimens. To that effect, future research must examine supervised learning models for forecasting gene expression changes induced by fasting and their association with biomarkers of cancer. Secondly, Multi-Criteria Decision-Making (MCDM) methods, like the MARCOS model and Grey PSI method, as demonstrated by [24], can be valuable tools to examine and rank fasting protocols based on multiple performance criteria such as metabolic effects, compliance of patients,

and safety. Similarly, [25] demonstrates that cutting-edge decision tools like the Z-number Parsimonious Best Worst Method (PBWM) are capable of measuring human health preferences in a sophisticated manner, which is crucial when it comes to the design of patient-specific fasting-based treatments. The combination of ML and MCDM methods will not only strengthen subsequent cancer prevention research but also bridge clinical, computational, and cultural dimensions of integrative medicine.

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