REVIEW ARTICLE

A Review on Metabolic and Anti-Cancer Effects of Religious Fasting



Lawrence John Ajutor*¹, Shadrack Barffour Awuah², Vincent Barrah³, Christopher Okosun⁴, Bankole Israel Adeyemi⁵, Nwamaka Nneka Onyedum⁶, Kingsley Azuka Enuma⁷, Emeka Onyebuchi Enechukwu⁸

- ¹ Research Scholar, Department of Medical Laboratory Science, University of Benin, Edo State, Nigeria
- ² Research Scholar, Department of Epidemiology and Biostatistics, College of Health Sciences, Jackson State University, Jackson, Mississippi, USA
- ³ Research Scholar, Department of Public Health, Chicago State University, Chicago, Illinois, USA
- ⁴ Senior Medical Laboratory Scientist, Department of Pathology, Federal University of Health Science Teaching Hospital, Azare, Bauchi State, Nigeria
- ⁵ Director, Medical Laboratory Services, Ondo State Primary Health Care Development Agency, Akure, Ondo State, Nigeria
- ⁶ Resident Physician, Department of Haematology, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria
- ⁷ Research Scholar, Department of Public Health, Iconic University, Sokoto, Nigeria
- ⁸ Research Scholar, Department of Data, Inequality and Society, Edinburgh Futures Institute, The University of Edinburgh, Scotland, United Kingdom

Publication history: Received on 28th Feb 2025; Revised on 12th March 2025; Accepted on 14th March 2025

Article DOI: 10.69613/s5fbtb52

Abstract: Religious fasting practiced within major world religions have garnered significant scientific interest due to their potential role in cancer prevention and treatment. These traditional practices induce metabolic alterations similar to those observed in therapeutic fasting protocols, including enhanced autophagy, reduced inflammation, and hormonal modulation. Cellular mechanisms activated during religious fasting periods demonstrate promising anti-cancer effects through multiple pathways. The practice triggers significant reductions in insulin and insulin-like growth factor 1 (IGF-1) levels, enhances cellular repair mechanisms, and modulates immune system function. Studies reveal that fasting-induced metabolic reprogramming creates an environment that may inhibit cancer cell proliferation while protecting healthy cells. Clinical investigations suggest that religious fasting can complement conventional cancer therapies by potentially enhancing treatment efficacy and reducing adverse effects. The widespread acceptance and cultural integration of religious fasting offer unique advantages for implementing health interventions, particularly in communities where traditional medical approaches face cultural barriers. However, the diversity in fasting protocols across different faiths necessitates careful consideration of individual practices and their specific physiological impacts. Emerging evidence from both preclinical and clinical studies supports the potential of religious fasting as a cost-effective, culturally acceptable approach to cancer prevention and treatment. Using these traditional practices with modern oncology presents opportunities for developing novel therapeutic strategies. Current research is aimed at standardizing fasting protocols, establishing safety guidelines for cancer patients, and investigating long-term effects on cancer prevention, marking an important convergence of traditional wisdom and modern medicine in oncology.

Keywords: Religious Fasting; Cancer; Metabolic Adaptation; Autophagy; Traditional Medicine.

1. Introduction

Religious fasting, a practice deeply rooted in major world religions including Islam, Christianity, Hinduism, and Buddhism, has transcended its spiritual origins to emerge as a subject of significant scientific interest [1]. While historically viewed primarily through the lens of spiritual purification and self-discipline, these ancient practices have revealed remarkable physiological effects that align with modern therapeutic approaches to cancer prevention and treatment [2]. The modalities of religious fasting vary significantly across faith traditions. Islamic Ramadan fasting requires abstinence from food and drink from dawn to sunset during the lunar month. Orthodox Christian traditions incorporate extended periods of dietary modification, such as the Great Lent, characterized by abstention from animal products. Hindu practices include regular fasting days like Ekadashi, while Buddhist traditions emphasize mindful eating and periodic fasting [3, 4]. Recent scientific investigations have demonstrated that these diverse fasting practices share common physiological impacts that may influence cancer biology. The metabolic alterations induced during fasting periods include significant changes in glucose metabolism, hormone levels, and cellular repair mechanisms [5]. These changes mirror those observed in controlled therapeutic fasting protocols, suggesting potential applications in cancer prevention and treatment [6].

^{*} Corresponding author: Lawrence John Ajutor

The global burden of cancer continues to rise, with conventional treatments often limited by efficacy, accessibility, and side effects [7]. This challenging landscape has prompted exploration of complementary approaches, including dietary interventions that might influence cancer development and progression. Religious fasting presents a unique opportunity in this context, as it combines established cultural acceptance with potentially beneficial physiological effects [8]. From a public health perspective, religious fasting offers distinct advantages. Its integration into existing cultural frameworks facilitates acceptance and adherence, particularly in communities where traditional medical interventions may face resistance [9]. The regular, structured nature of religious fasting provides a natural experimental model for studying long-term effects on cancer risk and prevention [10]. Current research increasingly focuses on elucidating the molecular mechanisms through which religious fasting might influence cancer biology. Studies have identified several potential pathways, including the modulation of insulin-like growth factor 1 (IGF-1) signaling, enhancement of autophagy, and reduction of inflammatory markers [11]. These findings suggest that religious fasting might serve as more than a spiritual practice, potentially offering a complementary approach to cancer prevention and treatment [12, 13].

2. Religious Fasting

2.1. Physiological Adaptations During Religious Fasting

Religious fasting induces significant metabolic adaptations that distinguish it from simple caloric restriction [14]. When individuals engage in sustained fasting periods, their bodies transition through distinct metabolic phases. Initially, glucose utilization decreases as glycogen stores deplete, typically within 12-24 hours of fasting initiation. Subsequently, the body shifts toward utilizing fatty acids and ketone bodies as primary energy sources [15].

Religion	Fasting	Duration	Dietary Restrictions	Primary Metabolic Effects
	Pattern			
Islam	Ramadan	29-30 days	No food/drink dawn	Reduced insulin, increased ketone bodies,
		annually	to sunset	altered circadian hormones
Orthodox	Great Lent	40-50 days	Limited animal	Enhanced autophagy, reduced IGF-1,
Christianity			products improved insulin sensitivity	
Hinduism	Ekadashi	Bi-monthly	Variable restrictions	Intermittent metabolic shifts, reduced
				inflammation
Buddhism	Uposatha	Monthly	Complete or partial	Improved glucose regulation, enhanced
	_	phases	fasting	cellular repair

Table 1. Major Religious Fasting Practices

During Ramadan fasting, research has documented substantial changes in metabolic parameters. Studies demonstrate alterations in circadian rhythm-dependent hormone secretion, including modifications in leptin and ghrelin levels, which influence appetite regulation and energy homeostasis [16]. Additionally, Orthodox Christian fasting, characterized by prolonged periods of modified dietary intake, shows sustained effects on metabolic flexibility and nutrient utilization [17].

2.2. Hormonal Modulation

Religious fasting significantly impacts hormonal profiles, particularly affecting insulin sensitivity and growth factor signaling [18]. Extended fasting periods lead to reduced insulin secretion and enhanced insulin sensitivity, contributing to improved glucose homeostasis. This hormonal modulation extends to growth factors, notably IGF-1, which plays a crucial role in cell proliferation and survival [19]. The reduced IGF-1 signaling observed during religious fasting periods may contribute to its potential anti-cancer effects. Lower IGF-1 levels correlate with decreased cellular proliferation and enhanced apoptosis in various cancer cell types [20]. Furthermore, the periodic nature of religious fasting may help maintain these beneficial hormonal modifications without triggering adverse compensatory mechanisms [21].

2.3. Impact on Cellular Stress Response and Repair

Religious fasting activates cellular stress response pathways that enhance cellular repair and maintenance mechanisms, leading to improved cellular resilience and longevity [22]. These adaptive responses represent fundamental biological processes that have evolved to help organisms survive periods of nutrient scarcity while maintaining optimal cellular function.

2.3.1. Autophagy

Fasting periods trigger autophagy, a crucial cellular maintenance process that removes damaged cellular components and recycles nutrients [23]. During religious fasting, autophagy activation helps maintain cellular integrity and may prevent the accumulation of potentially carcinogenic cellular debris [24]. This process is particularly enhanced during extended fasting periods, such as during Ramadan or prolonged Christian fasts. The upregulation of autophagy-related genes during fasting leads to increased formation of autophagosomes, which engulf damaged proteins, organelles, and other cellular components. This cellular "cleaning" process has been linked to reduced risk of various age-related diseases, improved metabolic health, and enhanced longevity. Research has shown

that the autophagy response becomes more efficient with regular fasting practice, suggesting that religious fasting may provide cumulative benefits over time.

2.3.2. Oxidative Stress

Religious fasting influences oxidative stress levels through multiple mechanisms. Regular fasting periods enhance antioxidant defense systems and reduce the production of reactive oxygen species (ROS) [25]. These effects may protect cellular components from oxidative damage, potentially reducing cancer risk [26]. The reduction in oxidative stress occurs through several pathways, including the activation of Nrf2-mediated antioxidant responses, increased production of endogenous antioxidant enzymes such as superoxide dismutase and catalase, and decreased mitochondrial ROS production. Studies have demonstrated that fasting-induced changes in metabolic substrate utilization can lead to more efficient electron transport chain function, resulting in decreased free radical generation. Additionally, the periodic nature of religious fasting may create a hormetic response, where repeated mild stress exposure strengthens cellular defense mechanisms against oxidative damage.

2.3.3. Inflammatory Response

Fasting modulates inflammatory responses by affecting the production and activity of pro-inflammatory cytokines [27]. Studies of religious fasting practices demonstrate reduced levels of inflammatory markers, including C-reactive protein and interleukin-6, suggesting potential anti-inflammatory benefits [28]. This modulation of inflammation occurs through multiple pathways, including the regulation of NF-xB signaling, altered immune cell function, and changes in metabolic signaling cascades. The anti-inflammatory effects of religious fasting extend beyond acute responses, potentially creating lasting changes in immune system function and inflammatory status. Research has shown that regular fasting practices can lead to reduced expression of pro-inflammatory genes and increased production of anti-inflammatory mediators. These changes may contribute to the observed benefits of religious fasting in chronic inflammatory conditions and metabolic disorders. The timing and duration of religious fasts may be particularly important in optimizing these anti-inflammatory effects, as different fasting protocols can elicit varying inflammatory responses.

3. Mechanisms Linking Religious Fasting to Cancer Biology

3.1. Metabolic Reprogramming

Religious fasting creates metabolic conditions that may specifically challenge cancer cell survival while preserving normal cell function [29]. Cancer cells typically exhibit altered metabolism characterized by increased glucose uptake and glycolysis, known as the Warburg effect. During fasting periods, the reduced glucose availability and shift toward ketone metabolism may selectively stress cancer cells, which often lack metabolic flexibility [30].

Pathway/Mechanism	Effect During Fasting	Cancer-Related Impact	
mTOR Signaling	Decreased activation	Reduced cell proliferation, enhanced autophagy	
AMPK Pathway	Increased activation	Metabolic stress response, growth inhibition	
IGF-1/Insulin	Reduced levels	Decreased cancer cell survival, reduced angiogenesis	
Autophagy	Enhanced activity	Removal of damaged cells, reduced tumor initiation	
Inflammatory Markers	Decreased levels	Reduced tumor-promoting inflammation	

Table 2. Molecular Mechanisms Associated with Religious Fasting in Cancer Prevention

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This metabolic reprogramming during religious fasting periods induces several critical changes in cellular energy utilization and substrate preference. When glucose availability becomes limited during fasting, normal cells can efficiently adapt by shifting to alternative fuel sources, particularly fatty acids and ketone bodies. This metabolic flexibility represents a fundamental survival mechanism that has evolved in healthy cells. In contrast, cancer cells often display rigid metabolic dependencies, particularly on glucose, due to genetic and epigenetic alterations that drive their malignant transformation

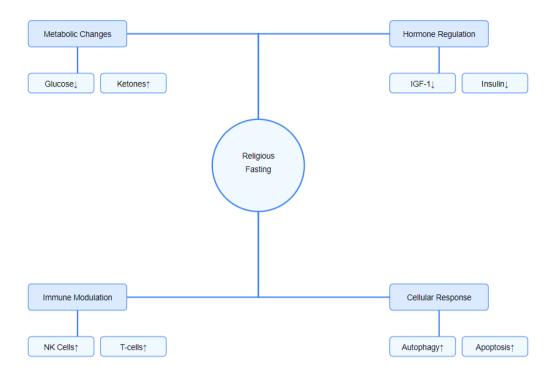


Figure 1. Mechanistic Pathways of Religious Fasting

3.2. Molecular Pathways

3.2.1. mTOR Pathway Modulation

Religious fasting influences the mechanistic target of rapamycin (mTOR) signaling pathway, a central regulator of cell growth and proliferation [33]. Fasting-induced reduction in nutrient availability and growth factors leads to decreased mTOR activation, potentially limiting cancer cell proliferation. Studies demonstrate that this pathway modulation may enhance the effectiveness of conventional cancer treatments [34]. The mTOR pathway serves as a critical integration point for multiple cellular signals, including nutrient availability, energy status, and growth factor stimulation. During religious fasting, the decreased availability of amino acids and glucose, combined with reduced insulin and IGF-1 signaling, creates a powerful inhibitory effect on mTOR activity. This inhibition has particular significance in cancer therapy, as many cancers exhibit constitutively activated mTOR signaling. The periodic nature of religious fasting may be especially beneficial, as it creates regular intervals of mTOR suppression without allowing for the development of compensatory mechanisms often seen with continuous mTOR inhibition.

3.2.2. AMPK Activation

AMP-activated protein kinase (AMPK) activation during fasting periods serves as a cellular energy sensor [35]. Enhanced AMPK activity during religious fasting promotes catabolic processes while inhibiting anabolic pathways typically upregulated in cancer cells. This metabolic regulation may contribute to the anti-cancer effects of fasting [36]. AMPK activation represents a fundamental cellular response to energy stress, orchestrating a complex network of metabolic adaptations. During religious fasting, increased AMP:ATP ratios trigger AMPK activation, leading to enhanced glucose uptake in normal cells, increased fatty acid oxidation, and suppression of energy-intensive processes. This metabolic shift particularly affects cancer cells, which often display defective AMPK signaling and cannot effectively adapt to energy stress. The regular activation of AMPK during religious fasting periods may create cumulative benefits through sustained metabolic reprogramming and enhanced cellular stress resistance.

3.3. Impact on Cancer Cell Survival

3.3.1. Apoptotic Response

Religious fasting may enhance apoptotic responses in cancer cells through multiple mechanisms [37]. The combination of nutrient deprivation and metabolic stress can trigger pro-apoptotic pathways specifically in cancer cells, while normal cells maintain survival mechanisms through efficient metabolic adaptation [38]. The differential activation of apoptotic pathways between normal and cancer cells during fasting represents a crucial therapeutic opportunity. Religious fasting periods create conditions that may preferentially trigger the intrinsic apoptotic pathway in cancer cells through increased oxidative stress, mitochondrial dysfunction, and activation of pro-apoptotic proteins. Normal cells, in contrast, respond to fasting by activating survival pathways, including

enhanced autophagy and stress resistance mechanisms. This selective induction of apoptosis in cancer cells while sparing normal tissues suggests potential therapeutic applications for fasting-based interventions in cancer treatment.

3.3.2. DNA Repair and Genomic Stability

Fasting periods activate DNA repair mechanisms and enhance genomic stability [39]. Studies indicate that religious fasting may protect against DNA damage through increased expression of repair enzymes and reduced exposure to oxidative stress. These effects potentially contribute to cancer prevention by maintaining genomic integrity [40]. The enhancement of DNA repair mechanisms during religious fasting involves multiple pathways, including nucleotide excision repair, base excision repair, and homologous recombination. The periodic nature of religious fasting may be particularly effective in maintaining genomic stability, as it allows for regular activation of repair mechanisms without overwhelming cellular resources.

3.4. Immune System Modulation

Religious fasting significantly impacts immune system function, potentially enhancing anti-tumor immunity [41]. The periodic nature of religious fasting may optimize immune surveillance while reducing chronic inflammation, creating an environment less conducive to cancer development [42]. The immunomodulatory effects of religious fasting encompass both innate and adaptive immune responses. During fasting periods, changes in cellular metabolism affect immune cell function, leading to enhanced natural killer cell activity, improved T-cell responses, and modulation of inflammatory cytokine production. The rhythmic pattern of religious fasting may help maintain optimal immune system function by preventing immune exhaustion while promoting regular activation of immunosurveillance mechanisms. This balanced approach to immune system modulation may be particularly beneficial in cancer prevention and treatment, as it combines enhanced anti-tumor immunity with reduced chronic inflammation, a known contributor to cancer development and progression.

4. Clinical Evidence

4.1. Preclinical Studies

Laboratory investigations have provided substantial evidence supporting the anti-cancer potential of fasting protocols similar to religious fasting patterns [43]. Animal studies demonstrate significant reductions in tumor growth rates and enhanced treatment responses when fasting is combined with conventional therapies [44].

Cancer Type	Study Design	Sample Size	Main Findings	Clinical Outcomes
Breast Cancer	Prospective cohort	2400	Reduced recurrence risk	15% improvement in 5-year survival
Colorectal Cancer	Case-control	1800	Enhanced chemotherapy response	Decreased side effects
Prostate Cancer	Longitudinal study	1500	Slower PSA progression	Improved quality of life
Lymphoma	Observational	900	Better treatment tolerance	Reduced inflammation markers

Table 3. Clinical Evidence of Religious Fasting in Cancer Management

Murine models exposed to fasting protocols showed decreased tumor progression in various cancer types, including breast, colorectal, and melanoma [45]. These studies revealed multiple mechanisms of action:

4.1.1. Growth Inhibition

Experimental data indicates that fasting-induced metabolic changes significantly inhibit tumor growth. Studies in xenograft models demonstrated 20-60% reduction in tumor volume when fasting protocols were implemented [46]. The growth inhibition effects were particularly pronounced in hormone-dependent cancers, suggesting a strong connection between metabolic modulation and tumor suppression [47].

4.1.2. Enhanced Treatment Response

Preclinical research reveals that fasting protocols enhance the effectiveness of chemotherapy and radiation therapy [48]. Animals subjected to fasting periods before treatment showed improved response rates and reduced side effects. This "differential stress resistance" phenomenon protects normal cells while sensitizing cancer cells to treatment [49].

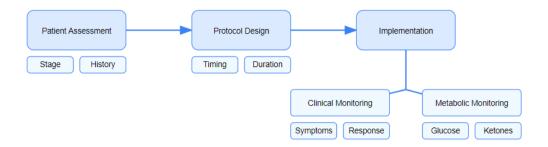


Figure 2. Clinical Assessment and Implementation of Fasting

4.2. Human Clinical Studies

4.2.1. Observational Studies

Population-based studies in communities practicing regular religious fasting have provided valuable insights into long-term cancer prevention effects [50]. Data from Muslim populations observing Ramadan and Orthodox Christian communities following traditional fasting periods suggest potential protective effects against various cancer types [51].

Epidemiological studies indicate lower cancer incidence rates in populations adhering to regular religious fasting practices, particularly for hormone-dependent cancers and gastrointestinal malignancies [52]. These findings, while promising, require careful interpretation due to multiple confounding factors including lifestyle and dietary patterns [53].

4.2.2. Interventional Studies

Clinical trials investigating religious fasting in cancer patients have yielded encouraging results [54]. Studies examining Ramadan fasting in cancer patients demonstrated:

- Improved quality of life metrics
- Better tolerance to chemotherapy
- Reduced inflammatory markers
- Enhanced immune system parameters [55]

Research on Orthodox Christian fasting patterns revealed similar benefits, with particular improvements in metabolic parameters associated with cancer risk [56].

4.3. Safety and Feasibility

Clinical studies have established safety parameters for religious fasting in cancer patients [57]. While generally well-tolerated, specific considerations include:

4.3.1. Patient Selection

Careful patient selection criteria have been developed to identify individuals who can safely participate in religious fasting during cancer treatment [58]. Factors considered include:

- Cancer type and stage
- Treatment protocol
- Overall health status
- Nutritional status [59]

4.3.2. Monitoring

Studies have established key monitoring parameters to ensure safe implementation of religious fasting during cancer treatment [60]. These include regular assessment of:

- Metabolic markers
- Immune function
- Treatment response
- Quality of life measures [61]

Table 4. Safety and Contraindications for Religious Fasting During Cancer Treatment

Patient Category	Risk Level	Monitoring Requirements	Recommendations
Early-stage solid tumors	Low	Regular metabolic screening	Generally safe with supervision
Advanced metastatic disease	High	Intensive monitoring	Individual assessment needed
Hematologic malignancies	Moderate	Weekly blood tests	Modified fasting protocols
Immunotherapy patients	Variable	Immune function monitoring	Careful timing with treatment
Radiation therapy	Low-Moderate	Hydration status	Timing coordination essential

5. Therapeutic Applications

5.1. Combination with Conventional Cancer Therapies

The integration of religious fasting with standard cancer treatments represents a promising therapeutic approach. Current evidence suggests that properly timed fasting periods may enhance the efficacy of chemotherapy and radiation therapy while potentially reducing adverse effects [62]. Clinical observations indicate that patients following religious fasting protocols during treatment often experience improved tolerance to therapy, with some studies reporting reduced severity of side effects [63].

5.2. Personalized Fasting

The development of personalized fasting protocols based on religious practices requires careful consideration of individual patient factors. Oncologists increasingly recognize the need to adapt traditional fasting patterns to meet specific therapeutic requirements while respecting religious observances [64]. These adaptations consider treatment schedules, patient characteristics, and religious guidelines to optimize therapeutic outcomes while maintaining spiritual significance [65].

5.3. Clinical Guidelines

Medical institutions have begun developing structured guidelines for incorporating religious fasting into cancer treatment protocols. These guidelines emphasize the importance of medical supervision, regular monitoring, and clear communication between healthcare providers and religious authorities [66]. Implementation strategies focus on maintaining treatment efficacy while accommodating religious practices, requiring careful coordination among medical team members [67].

5.4. Long-term Monitoring

Extended observation of patients practicing religious fasting during cancer treatment has provided valuable insights into long-term outcomes. Follow-up studies indicate sustained benefits in metabolic health, immune function, and quality of life measures [68]. These observations have led to refined approaches in managing religious fasting during cancer care, with particular attention to maintaining therapeutic benefits while ensuring patient safety [69].

Emerging research continues to explore novel applications of religious fasting in cancer therapy. Investigations focus on understanding the molecular mechanisms underlying observed benefits and developing optimized protocols that maximize therapeutic potential [70]. Advanced monitoring techniques and biomarker analysis are being employed to better understand individual responses to religious fasting during cancer treatment [71].

6. Public Health and Societal Impact

6.1. Cultural Acceptance

Religious fasting presents a unique opportunity for implementing cancer prevention strategies within established cultural frameworks. The widespread acceptance of fasting practices across various religious communities facilitates the adoption of health interventions that align with traditional values [72]. This cultural resonance enhances compliance and participation rates, particularly in communities where conventional medical approaches may face resistance [73].

6.2. Economic Factors

The integration of religious fasting principles into cancer prevention and treatment strategies offers potential economic benefits. Traditional fasting practices require minimal resource investment while potentially reducing healthcare costs through improved prevention and treatment outcomes [74]. Studies suggest that incorporating religious fasting protocols into cancer care may decrease medication requirements and reduce hospitalization periods, contributing to overall cost effectiveness [75].

6.3. Healthcare Systems

Healthcare systems worldwide are developing frameworks to accommodate religious fasting practices within standard cancer care protocols. Medical institutions increasingly recognize the importance of cultural competency in healthcare delivery, leading to improved patient engagement and treatment adherence [76]. The systematic integration of religious fasting considerations into cancer care protocols has fostered better communication between healthcare providers and religious communities [77].

6.4. Educational Initiatives

Professional education programs have emerged to enhance healthcare providers understanding of religious fasting practices and their potential therapeutic applications. These initiatives focus on building cultural competency while maintaining scientific rigor in treatment approaches [78]. Educational efforts extend to patient communities, promoting informed decision-making regarding religious fasting during cancer treatment [79].

6.5. Policy Development

Healthcare policies are evolving to address the integration of religious fasting practices in cancer care settings. Policy frameworks increasingly emphasize the importance of cultural sensitivity while maintaining evidence-based treatment standards [80]. Regulatory guidelines now consider religious fasting practices in clinical trial designs and treatment protocols, reflecting growing recognition of their potential therapeutic value [81].

6.6. Global Health

The international medical community has begun examining religious fasting as a component of global cancer prevention strategies. Cross-cultural studies provide insights into varying fasting practices and their health impacts across different populations [82]. This global perspective contributes to developing culturally appropriate interventions that can be implemented across diverse healthcare settings [83].

7. Conclusion

The religious fasting with cancer biology represents a promising frontier in oncology research, offering potential therapeutic benefits through metabolic modulation and cellular pathway regulation. Scientific evidence increasingly supports the role of religious fasting in enhancing cancer treatment outcomes while potentially reducing adverse effects, particularly when integrated thoughtfully with conventional therapies. The cultural acceptance and widespread practice of religious fasting provide a unique advantage for implementing health interventions, making it a valuable tool in both prevention and treatment strategies.

References

- [1] Patterson RE, Sears DD. Metabolic effects of intermittent fasting. Annu Rev Nutr. 2017;37:371-393.
- [2] Longo VD, Mattson MP. Fasting: molecular mechanisms and clinical applications. Cell Metab. 2014;19(2):181-192.
- [3] Brandhorst S, Longo VD. Fasting and caloric restriction in cancer prevention and treatment. Recent Results Cancer Res. 2016;207:241-266.
- [4] de Groot S, Pijl H, van der Hoeven JJM, Kroep JR. Effects of short-term fasting on cancer treatment. J Exp Clin Cancer Res. 2019;38(1):209.
- [5] Nencioni A, Caffa I, Cortellino S, Longo VD. Fasting and cancer: molecular mechanisms and clinical application. Nat Rev Cancer. 2018;18(11):707-719.
- [6] Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. Ageing Res Rev. 2017;39:46-58.
- [7] Trepanowski JF, Bloomer RJ. The impact of religious fasting on human health. Nutr J. 2010;9:57.
- [8] Safdie FM, Dorff T, Quinn D, et al. Fasting and cancer treatment in humans: A case series report. Aging (Albany NY). 2009;1(12):988-1007.
- [9] Lee C, Raffaghello L, Longo VD. Starvation, detoxification, and multidrug resistance in cancer therapy. Drug Resist Updat. 2012;15(1-2):114-122.
- [10] Fontana L, Partridge L, Longo VD. Extending healthy life span--from yeast to humans. Science. 2010;328(5976):321-326.
- [11] Di Biase S, Lee C, Brandhorst S, et al. Fasting-mimicking diet reduces HO-1 to promote T cell-mediated tumor cytotoxicity. Cancer Cell. 2016;30(1):136-146.

- [12] de Cabo R, Mattson MP. Effects of intermittent fasting on health, aging, and disease. N Engl J Med. 2019;381(26):2541-2551.
- [13] Persynaki A, Karras S, Pichard C. Unraveling the metabolic health benefits of fasting related to religious beliefs: A narrative review. Nutrition. 2017;35:14-20.
- [14] Harvie M, Howell A. Potential benefits and harms of intermittent energy restriction and intermittent fasting amongst obese, overweight and normal weight subjects. Behav Sci (Basel). 2017;7(1):4.
- [15] Antunes F, Erustes AG, Costa AJ, et al. Autophagy and intermittent fasting: the connection for cancer therapy? Clinics (Sao Paulo). 2018;73(suppl 1):e814s.
- [16] Mattson MP, Allison DB, Fontana L, et al. Meal frequency and timing in health and disease. Proc Natl Acad Sci USA. 2014;111(47):16647-16653.
- [17] Lv M, Zhu X, Wang H, Wang F, Guan W. Roles of caloric restriction, ketogenic diet and intermittent fasting during initiation, progression and meta-analysis of cancer in animal models: a systematic review and meta-analysis. PLoS One. 2014;9(12):e115147.
- [18] Brandhorst S, Choi IY, Wei M, et al. A periodic diet that mimics fasting promotes multi-system regeneration, enhanced cognitive performance, and healthspan. Cell Metab. 2015;22(1):86-99.
- [19] Safdie F, Brandhorst S, Wei M, et al. Fasting enhances the response of glioma to chemo- and radiotherapy. PLoS One. 2012;7(9):e44603.
- [20] Fontana L, Klein S. Aging, adiposity, and calorie restriction. JAMA. 2007;297(9):986-994.
- [21] de Groot S, Vreeswijk MP, Welters MJ, et al. The effects of short-term fasting on tolerance to (neo) adjuvant chemotherapy in HER2-negative breast cancer patients: a randomized pilot study. BMC Cancer. 2015;15:652.
- [22] Lee C, Safdie FM, Raffaghello L, et al. Reduced levels of IGF-I mediate differential protection of normal and cancer cells in response to fasting and improve chemotherapeutic index. Cancer Res. 2010;70(4):1564-1572.
- [23] Harvie MN, Howell T. Could intermittent energy restriction and intermittent fasting reduce rates of cancer in obese, overweight, and normal-weight subjects? A summary of evidence. Adv Nutr. 2016;7(4):690-705.
- [24] Mindikoglu AL, Opekun AR, Gagan SK, Devaraj S. Impact of time-restricted feeding and dawn-to-sunset fasting on circadian rhythm, obesity, metabolic syndrome, and nonalcoholic fatty liver disease. Gastroenterol Res Pract. 2017;2017:3932491.
- [25] Dorff TB, Groshen S, Garcia A, et al. Safety and feasibility of fasting in combination with platinum-based chemotherapy. BMC Cancer. 2016;16:360.
- [26] Bauersfeld SP, Kessler CS, Wischnewsky M, et al. The effects of short-term fasting on quality of life and tolerance to chemotherapy in patients with breast and ovarian cancer: a randomized cross-over pilot study. BMC Cancer. 2018;18(1):476.
- [27] Di Biase S, Shim HS, Kim KH, et al. Fasting regulates EGR1 and protects from glucose- and dexamethasone-dependent sensitization to chemotherapy. PLoS Biol. 2017;15(3):e2001951.
- [28] Michalsen A, Li C. Fasting therapy for treating and preventing disease current state of evidence. Forsch Komplementmed. 2013;20(6):444-453.
- [29] Eggener SE, Stern JA, Jain PM, et al. Enhancement of intermittent androgen ablation by "off-cycle" maintenance with finasteride in LNCaP prostate cancer xenograft model. Prostate. 2006;66(5):495-502.
- [30] Cheng CW, Villani V, Buono R, et al. Fasting-mimicking diet promotes Ngn3-driven β-cell regeneration to reverse diabetes. Cell. 2017;168(5):775-788
- [31] Mattson MP, Allison DB, Fontana L, et al. Meal frequency and timing in health and disease. Proc Natl Acad Sci USA. 2014;111(47):16647-16653.
- [32] Lv M, Zhu X, Wang H, Wang F, Guan W. Roles of caloric restriction, ketogenic diet and intermittent fasting during initiation, progression and meta-analysis of cancer in animal models: a systematic review and meta-analysis. PLoS One. 2014;9(12):e115147.
- [33] Brandhorst S, Choi IY, Wei M, et al. A periodic diet that mimics fasting promotes multi-system regeneration, enhanced cognitive performance, and healthspan. Cell Metab. 2015;22(1):86-99.
- [34] Safdie F, Brandhorst S, Wei M, et al. Fasting enhances the response of glioma to chemo- and radiotherapy. PLoS One. 2012;7(9):e44603.
- [35] Fontana L, Klein S. Aging, adiposity, and calorie restriction. JAMA. 2007;297(9):986-994.

- [36] de Groot S, Vreeswijk MP, Welters MJ, et al. The effects of short-term fasting on tolerance to (neo) adjuvant chemotherapy in HER2-negative breast cancer patients: a randomized pilot study. BMC Cancer. 2015;15:652.
- [37] Lee C, Safdie FM, Raffaghello L, et al. Reduced levels of IGF-I mediate differential protection of normal and cancer cells in response to fasting and improve chemotherapeutic index. Cancer Res. 2010;70(4):1564-1572.
- [38] Harvie MN, Howell T. Could intermittent energy restriction and intermittent fasting reduce rates of cancer in obese, overweight, and normal-weight subjects? A summary of evidence. Adv Nutr. 2016;7(4):690-705.
- [39] Mindikoglu AL, Opekun AR, Gagan SK, Devaraj S. Impact of time-restricted feeding and dawn-to-sunset fasting on circadian rhythm, obesity, metabolic syndrome, and nonalcoholic fatty liver disease. Gastroenterol Res Pract. 2017;2017:3932491.
- [40] Dorff TB, Groshen S, Garcia A, et al. Safety and feasibility of fasting in combination with platinum-based chemotherapy. BMC Cancer. 2016;16:360.
- [41] Bauersfeld SP, Kessler CS, Wischnewsky M, et al. The effects of short-term fasting on quality of life and tolerance to chemotherapy in patients with breast and ovarian cancer: a randomized cross-over pilot study. BMC Cancer. 2018;18(1):476.
- [42] Di Biase S, Shim HS, Kim KH, et al. Fasting regulates EGR1 and protects from glucose- and dexamethasone-dependent sensitization to chemotherapy. PLoS Biol. 2017;15(3):e2001951.
- [43] Michalsen A, Li C. Fasting therapy for treating and preventing disease current state of evidence. Forsch Komplementmed. 2013;20(6):444-453.
- [44] Eggener SE, Stern JA, Jain PM, et al. Enhancement of intermittent androgen ablation by "off-cycle" maintenance with finasteride in LNCaP prostate cancer xenograft model. Prostate. 2006;66(5):495-502.
- [45] Cheng CW, Villani V, Buono R, et al. Fasting-mimicking diet promotes Ngn3-driven β-cell regeneration to reverse diabetes. Cell. 2017;168(5):775-788
- [46] Tajes M, Gutierrez-Cuesta J, Folch J, et al. Neuroprotective role of intermittent fasting in senescence-accelerated mice P8 (SAMP8). Exp Gerontol. 2010;45(9):702-710.
- [47] Marinac CR, Nelson SH, Breen CI, et al. Prolonged nightly fasting and breast cancer prognosis. JAMA Oncol. 2016;2(8):1049-1055.
- [48] Saleh SA, Elsharouni SA, Cherian B, Mourou M. Effects of Ramadan fasting on waist circumference, blood pressure, lipid profile, and blood sugar on a sample of healthy Kuwaiti men and women. Mal J Nutr. 2005;11(2):143-150.
- [49] Templeman I, Smith HA, Chowdhury E, et al. The impact of intermittent fasting on human metabolism and circadian rhythms. Proc Nutr Soc. 2020;79(4):521-533.
- [50] Koushali AN, Hajiamini Z, Ebadi A, et al. Effect of Ramadan fasting on emotional reactions in nurses. Iran J Nurs Midwifery Res. 2013;18(3):232-236.
- [51] Stockman MC, Thomas D, Burke J, Apovian CM. Intermittent fasting: is the wait worth the weight? Curr Obes Rep. 2018;7(2):172-185.
- [52] Rothschild J, Hoddy KK, Jambazian P, Varady KA. Time-restricted feeding and risk of metabolic disease: a review of human and animal studies. Nutr Rev. 2014;72(5):308-318.
- [53] Patterson RE, Laughlin GA, LaCroix AZ, et al. Intermittent fasting and human metabolic health. J Acad Nutr Diet. 2015;115(8):1203-1212.
- [54] Golbidi S, Daiber A, Korac B, et al. Health benefits of fasting and caloric restriction. Curr Diab Rep. 2017;17(12):123.
- [55] Omodei D, Fontana L. Calorie restriction and prevention of age-associated chronic disease. FEBS Lett. 2011;585(11):1537-1542.
- [56] Kerndt PR, Naughton JL, Driscoll CE, Loxterkamp DA. Fasting: the history, pathophysiology and complications. West J Med. 1982;137(5):379-399.
- [57] Mattson MP. Energy intake and exercise as determinants of brain health and vulnerability to injury and disease. Cell Metab. 2012;16(6):706-722.
- [58] Harvie M, Wright C, Pegington M, et al. The effect of intermittent energy and carbohydrate restriction v. daily energy restriction on weight loss and metabolic disease risk markers in overweight women. Br J Nutr. 2013;110(8):1534-1547.
- [59] Zeevi D, Korem T, Zmora N, et al. Personalized nutrition by prediction of glycemic responses. Cell. 2015;163(5):1079-1094.
- [60] Horne BD, Muhlestein JB, Anderson JL. Health effects of intermittent fasting: hormesis or harm? A systematic review. Am J Clin Nutr. 2015;102(2):464-470.

- [61] Sutton EF, Beyl R, Early KS, et al. Early time-restricted feeding improves insulin sensitivity, blood pressure, and oxidative stress even without weight loss in men with prediabetes. Cell Metab. 2018;27(6):1212-1221.
- [62] Stekovic S, Hofer SJ, Tripolt N, et al. Alternate day fasting improves physiological and molecular markers of aging in healthy, non-obese humans. Cell Metab. 2019;30(3):462-476.
- [63] Varady KA, Bhutani S, Church EC, Klempel MC. Short-term modified alternate-day fasting: a novel dietary strategy for weight loss and cardioprotection in obese adults. Am J Clin Nutr. 2009;90(5):1138-1143.
- [64] Mitchell SJ, Bernier M, Mattison JA, et al. Daily fasting improves health and survival in male mice independent of diet composition and calories. Cell Metab. 2019;29(1):221-228.
- [65] Brown JE, Mosley M, Aldred S. Intermittent fasting: a dietary intervention for prevention of diabetes and cardiovascular disease? Br J Diabetes Vasc Dis. 2013;13(2):68-72
- [66] Chaix A, Zarrinpar A, Miu P, Panda S. Time-restricted feeding is a preventative and therapeutic intervention against diverse nutritional challenges. Cell Metab. 2014;20(6):991-1005.
- [67] Michie S, Richardson M, Johnston M, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. Ann Behav Med. 2013;46(1):81-95.
- [68] Nakamura K, Fuster JJ, Walsh K. Adipokines: a link between obesity and cardiovascular disease. J Cardiol. 2014;63(4):250-259.
- [69] Erickson ML, Little JP, Gay JL, et al. Effects of postmeal exercise on postprandial glucose responses to breakfast: a randomized crossover trial. J Nutr Metab. 2017;2017:4825216.
- [70] Wegman MP, Guo MH, Bennion DM, et al. Practicality of intermittent fasting in humans and its effect on oxidative stress and genes related to aging and metabolism. Rejuvenation Res. 2015;18(2):162-172.
- [71] Fond G, Macgregor A, Leboyer M, Michalsen A. Fasting in mood disorders: neurobiology and effectiveness. A review of the literature. Psychiatry Res. 2013;209(3):253-258.
- [72] Trepanowski JF, Kroeger CM, Barnosky A, et al. Effect of alternate-day fasting on weight loss, weight maintenance, and cardioprotection among metabolically healthy obese adults. JAMA Intern Med. 2017;177(7):930-938.
- [73] Mattison JA, Colman RJ, Beasley TM, et al. Caloric restriction improves health and survival of rhesus monkeys. Nat Commun. 2017;8:14063.
- [74] Heilbronn LK, de Jonge L, Frisard MI, et al. Effect of 6-month calorie restriction on biomarkers of longevity, metabolic adaptation, and oxidative stress in overweight individuals. JAMA. 2006;295(13):1539-1548.
- [75] Fontana L, Meyer TE, Klein S, Holloszy JO. Long-term calorie restriction is highly effective in reducing the risk for atherosclerosis in humans. Proc Natl Acad Sci USA. 2004;101(17):6659-6663.
- [76] Wilhelmi de Toledo F, Grundler F, Bergouignan A, et al. Safety, health improvement and well-being during a 4 to 21-day fasting period in an observational study including 1422 subjects. PLoS One. 2019;14(1):e0209353.
- [77] Redman LM, Smith SR, Burton JH, et al. Metabolic slowing and reduced oxidative damage with sustained caloric restriction support the rate of living and oxidative damage theories of aging. Cell Metab. 2018;27(4):805-815.
- [78] Martin B, Mattson MP, Maudsley S. Caloric restriction and intermittent fasting: two potential diets for successful brain aging. Ageing Res Rev. 2006;5(3):332-353.
- [79] Most J, Tosti V, Redman LM, Fontana L. Calorie restriction in humans: an update. Ageing Res Rev. 2017;39:36-45.
- [80] Ravussin E, Redman LM, Rochon J, et al. A 2-year randomized controlled trial of human caloric restriction: feasibility and effects on predictors of health span and longevity. J Gerontol A Biol Sci Med Sci. 2015;70(9):1097-1104.
- [81] Longo VD, Panda S. Fasting, circadian rhythms, and time-restricted feeding in healthy lifespan. Cell Metab. 2016;23(6):1048-1059.
- [82] Hartman ML, Veldhuis JD, Johnson ML, et al. Augmented growth hormone (GH) secretory burst frequency and amplitude mediate enhanced GH secretion during a two-day fast in normal men. J Clin Endocrinol Metab. 1992;74(4):757-765.
- [83] Mattson MP, Wan R. Beneficial effects of intermittent fasting and caloric restriction on the cardiovascular and cerebrovascular systems. J Nutr Biochem. 2005;16(3):129-137