





# Fasting Challenges among Patients with Cancer; Focus on Ramadan Fasting: A Systematic Review

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(Received 18 Feb 2025; accepted 19 May 2025)

#### **Abstract**

**Background:** We evaluated the effects of fasting on cancer treatment outcomes, gathering evidence separately from human clinical trials and in vitro (animal) studies.

**Methods:** A comprehensive search was conducted using the PubMed, Scopus, and Web of Science databases. Studies were included if they examined the effects of fasting on cancer treatment outcomes in vitro or in human subjects, regardless of study design, sample size, or country of origin.

Results: A total of 16 studies were included, consisting of 6 in vitro and animal studies and 10 human clinical trials. In vitro and animal studies consistently showed that fasting enhances the efficacy of chemotherapy and reduces its toxic side effects. Human clinical trials indicated that short-term fasting could decrease chemotherapy-induced side effects such as nausea, fatigue, and immunosuppression while improving overall response rates. However, the number of clinical trials is limited, and there is significant variability in study designs, fasting protocols, and endpoints.

Conclusion: Fasting may serve as a beneficial adjunct to cancer therapy, particularly in mitigating chemotherapy-induced side effects and enhancing treatment efficacy. Despite these promising results, further large-scale, well-designed clinical trials are necessary to confirm these findings and establish standardized fasting protocols. Future research should also investigate the long-term effects of fasting and its impact on different cancer types and treatment modalities. While some patients may fast without significant adverse effects, the primary concern should always be their safety and well-being.

Keywords: Fasting; Cancer therapy; Chemotherapy; Hormonal therapy

#### Introduction

Fasting, particularly intermittent and prolonged fasting, has gained considerable attention in recent years for its potential health benefits, especially concerning cancer treatment (1). Fasting

involves voluntarily abstaining from food and, in some cases, beverages for a specific period. This practice has deep roots in various religious, cultural, and health traditions (2).

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With Muslims making up over 20% of the world's population (3), fasting is a significant aspect of the Islamic holy month of Ramadan. During this month, adult Muslims are expected to fast from sunrise to sunset, unless they are ill or traveling (1, 4). Consequently, Muslim patients often ask their doctors about the safety and impact of fasting on their health (5).

By 2030, approximately 26 million new cancer cases and 17 million cancer deaths are projected each year (6). Chemotherapy is a cornerstone of cancer treatment but can lead to several debilitating side effects, including immunosuppression, fatigue, nausea, and organ toxicity. These side effects can severely affect patients' quality of life and limit the dosage and frequency of chemotherapy administered (7). Emerging evidence suggests that fasting may protect normal cells from the toxic effects of chemotherapy while making cancer cells more susceptible to treatment. This phenomenon, known as differential stress resistance, is believed to be mediated by various molecular and cellular mechanisms, including reduced signaling of insulin-like growth factor 1 (IGF-1), enhanced autophagy, and altered metabolic pathways (8).

In the context of cancer therapy, fasting is hypothesized to enhance the efficacy of treatments such as chemotherapy and radiation therapy while minimizing their adverse effects. However, there is no established protocol for selecting patients who can safely tolerate fasting (9-11). This creates a dilemma for Muslim cancer patients (12). The issue remains controversial among oncologists, influenced by their personal experiences, judgments, and the specific conditions of the patients.

This literature review aimed to systematically evaluate the effects of fasting on chemotherapy and other cancer treatments, drawing on evidence from both in vitro studies and human clinical trials. By synthesizing the available data, this review seeks to provide a comprehensive understanding of the potential role of fasting in cancer therapy and identify areas for future research.

#### **Methods**

#### Eligibility Criteria

This systematic review included studies that investigated the effects of fasting on cancer patients. Both in vitro and human studies were considered, regardless of study design, sample size, or country of origin. Eligible studies included those that examined the impact of fasting on chemotherapy, hormonal therapy, or radiation therapy (EBRT).

#### **Information Sources**

The following databases were searched for relevant studies: PubMed, Scopus, and Web of Science until October 2024.

# Search Strategy

The search strategy utilized a set of Medical Subject Headings (MeSH) terms, including fasting, Ramadan fasting, cancer therapy, chemotherapy, hormonal therapy, and treatment outcomes. Boolean operators were employed to refine the results across the following databases: PubMed, Scopus, and Web of Science. The full syntax for PubMed was: ("Fasting" OR "Ramadan fasting") AND ("Cancer" OR "Chemotherapy" OR "Hormonal therapy"). This provided clarity on how the study was conducted.

#### Study Selection

The study selection process involved several steps:

- 1. Initial Screening: Titles and abstracts of all identified studies were screened for relevance.
- 2. Full-Text Review: Full texts of potentially relevant studies were retrieved and assessed for eligibility based on the inclusion criteria.
- 3. Data Extraction: Data were extracted from the included studies using a standardized form. Extracted data included study design, sample size, type of fasting, cancer type, treatment modality, and key outcomes.

## Risk of Bias Assessment

The risk of bias in the included studies was assessed using appropriate tools based on study

design. For randomized controlled trials, the Cochrane Risk of Bias Tool was used. For observational studies, the Newcastle-Ottawa Scale was applied. In assessing the risk of bias for in vitro studies, the following criteria were considered: reproducibility of experimental procedures, clarity and relevance of documented outcomes, and measures to minimize observer bias, such as blinded assessments or standardized data collection protocols.

#### Results

The initial search of the database included Pub-Med, Scopus, and web of science, yielded a total of 2,462 papers. After the initial screening of titles and abstracts, 381 papers were selected for further review. Following a more detailed screening process, which included full-text assessment, 16 studies met the inclusion criteria and were included in the final analysis. The selection process is illustrated in the PRISMA flow diagram (Fig. 1).

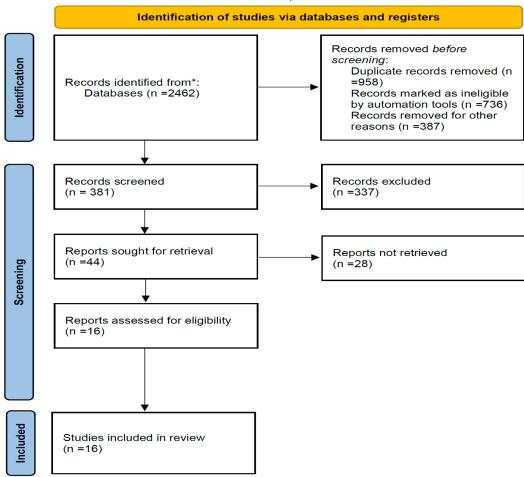


Fig. 1: PRISMA diagram of study

#### Risk of Bias Assessment Results

The risk of bias in included studies was evaluated using standardized tools tailored to each study design. For randomized controlled trials, the Cochrane Risk of Bias Tool identified low to moderate risk across domains, such as sequence generation and blinding. Observational studies were assessed using the Newcastle-Ottawa Scale, revealing moderate risk related to participant selection. In vitro (animal) studies presented challenges in standardization, with methodological reproducibility identified as a key factor influencing risk assessment. These findings highlight the importance of interpreting results within the context of inherent variability across study types.

In the present review, effects of fasting on cancer cells in animal studies, and then human studies were reported. In human review studies, different cancers were evaluated separately, and finally, studies related to fasting in Ramadan were reported.

# Effects of fasting on cancer cells (animal studies)

Recent studies have explored the impact of fasting on cancer treatment, particularly in animal models. These studies suggest that fasting can significantly influence the effectiveness of cancer therapies and the body's immune response to tumors (13-18).

Fasting has been shown to reprogram the metabolism of natural killer (NK) cells, a type of white blood cell that targets cancer cells. This reprogramming helps NK cells survive in the nutrient-deprived environment around tumors and enhances their cancer-fighting abilities (14).

In mice, periods of fasting led to a drop in glucose levels and an increase in free fatty acids, which NK cells used as an alternative energy source. This metabolic shift improved the NK cells' ability to attack cancer cells (14).

Table 1 summarized key findings from various animal studies, focusing on different types of cancers and fasting durations.

# Effects of fasting on cancer patients (human studies)

Some human studies have been conducted on cancer and fasting, and they have mostly been descriptive. In some cancers there have been more studies, likely due to higher prevalence and better patients' performance, which will be discussed in details. Tiwari et al in a narrative review study reported, cancer patients who fast prior and following chemotherapy had less gastro intestinal side effects such as nausea, vomiting, mucositis and abdominal pain (19).

European Society for Clinical Nutrition and Metabolism recommended regular nutrient intake for cancer patients during chemotherapy, to avoid weight loss and impairing immune system (20); but this approach can be outdate because patients with early stage cancers have good performance status with low risk of cachexia and malnutrition and may have weight gain during treatment; another point is DSR in fasting cancer cells that can result in tumor cells death in preclinical models (21).

A recent studies revealed that intermittent fasting (about 18 hours) during adjuvant chemotherapy in patients with breast cancer was well tolerated as well as reduced chemotherapy side effects (22) (4, 9, 23-25).

We have summarized below key findings from various human studies, focusing on different types of cancers and fasting durations.

#### Breast and colorectal Cancer

In a number of studies, fasting has been associated with increased quality of life in breast cancer patients (26-28). Many patients who have had breast cancer need to use long term oral hormonal therapies to reduce cancer recurrence and increase survival. Most of patients who use oral hormonal therapies like tamoxifen have good drug compliance during Ramadan fasting (1, 29-31).

In a study that was performed among patients with a history of hormone positive breast cancer, most of them (94%), who had received hormonal therapy- including tamoxifen or aromatase inhibitors- before Ramadan, could continue drugs during the holy month. Patients often changed the eating time of drugs from daytime to nighttime. Fasting did not impact negatively on their drug compliance with treatment (29).

Factors that are related to drug non-adherence during Ramadan include history of non-adherence and short duration of hormone therapy (30). In a study which was conducted in Marco, 209 patients who received EBRT during Ramadan month were evaluated; about 39.2% of the patients were fasting during treatment in

Ramadan month; and they tolerate it well without significant complications (32).

### Chronic myeloid leukemia (CML)

Tyrosine kinase inhibitor (TKI) is the cornerstone treatment of patients with CML; but using TKIs during Ramadan fasting is not studied widely; in a retrospective study that was conducted in Qatar, 49 patients' laboratory data who need using TKI during Ramadan fasting were evaluated and concluded that using TKIs during fasting did not significantly change complete blood count parameters and BCR-ABL levels (33-35).

There was a case report about a 49 year old woman with CML who took nilotinib once instead of twice per day during fasting in Ramadan month and remained in major molecular response (36).

# Chronic lymphocytic leukemia (CLL)

Novel agents, such as Venetoclax and Bruton tyrosine kinase inhibitors (BTKIs), are frequently

used in chronic lymphocytic leukemia (CLL) patients who need treatment. Fasting during using these agents are challenging due to concerns for possible changes in their efficacy and side effects. A Pharmacology-Based Review declares that dehydration during fasting may rise the risk of tumor lysis syndrome (TLS); another concern is increasing the risk of gastro-intestinal bleeding in patients receiving BTKIs (37). Raucci et al (49), and Trojani et al (28) reported, fasting help to Delay of CLL progression, improve improved outcomes, and reduce of chemotherapy toxicity.

### Multiple myeloma (MM)

Obesity is a modifiable risk factor for MM (37) and may increase the risk of progression of asymptomatic myeloma (monoclonal gammopathy of undetermined significance and smoldering MM) to MM (38-40). Prolonged nightly fasting is an effective strategy for weight loss and cancer prevention (41, 42); and can modify the risk of MM progression (13).

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Authors	Year	Country	Exper- imental Subject	Type of cancer	Fasting type and du- ration	Type of Treat- ment	Effect of Fasting on Treatment
Lee et al.(13)	2012	USA	Mice	Breast cancer	48 hours	Doxo- rubicin	Enhanced efficacy of chemotherapy, reduced side effects, and increased survival rates.
Delconte et al.(14)	2024	USA	Mice	cancers	24 hours twice a week	None (Dietary Inter- vention)	Improved survival of natural killer cells, enhanced cancerfighting ability.
Lv et al.(15)	2014	China	Mice	Any can- cers	Various duration	Various chemo- therapies	Caloric restriction and keto- genic diet showed anti-cancer effects; intermittent fasting effects were less clear
Di Biase et al(18).	2016	USA	Mice	Any can- cer	24-48 hours	Cyclo- phos- phamide	Increased cancer cell death, reduced tumor growth.
Simone et al.(16)	2018	USA	Mice	Breast cancer	24-48 hours	Various chemo-therapies	Enhanced therapeutic effects, reduced adverse effects.
Vernieri et	2022	Italy	Mice	Any can-	5-day	Standard	Reduced blood glucose and

Table 1: Continued...

These studies suggest that fasting or fasting-mimicking diets can enhance the efficacy of cancer treatments and reduce side effects in human subjects with various types of cancer, including MM, CML, and CLL.

Effect of Ramadan fasting on cancer patients

Ramadan fasting is a religious obligation for healthy Muslims after they reach puberty. However, individuals with acute or chronic medical conditions may be exempt from this obligation based on their health status. Despite our exten-

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sive search, we were only able to find six studies that address the issue of cancer patients fasting during Ramadan. Specifically, five of these studies focus on the impact of fasting on quality of life and compliance with religious practices.

In reviewing the literature on the topics of fasting during Ramadan and cancer, only one study evaluated the effect of fasting on treatment.

In A cross-sectional study that investigated the effects of Ramadan Intermittent Fasting (RIF) on inflammatory cytokines and immune biomarkers in healthy individuals, the results showed that immune cell counts decreased during Ramadan but stayed within normal ranges. This indicates that RIF reduces inflammatory status by lowering pro-inflammatory cytokine expression, body fat, and circulating leukocyte levels (45).

A cross-sectional study at the National Cancer Institute (NCI) in Egypt during Ramadan 1430 (August-September 2009) found that 40% of Muslim cancer patients did not fast. Of the remaining patients, 36% partially fasted (fasting 0% to 99% of the day), and 24% fasted completely. Only 45% consulted their oncologist about fasting (3).

A cross-sectional survey was conducted during Ramadan (July-August) in 2013, involving 620 cancer patients and 187 healthcare professionals from various clinics across Iran. Only 76 (13%) fasted for at least one day, with 41 (7%) fasting the entire month for religious reasons. The main reasons for refraining from fasting included lack of physical strength (403 patients, 65%) and excessive thirst (141 patients, 23%). Additionally, 275 (44%) consulted their physician about fasting, and over 50% of physicians advised against it for those recently hospitalized, undergoing chemotherapy, or post-surgery. Most healthcare professionals (68%) believed that cancer survivors should not fast, even if symptom-free (1).

Tas and collaborators conducted a 2012 survey of 701 adult Turkish Muslim cancer patients during Ramadan. They found that fasting patients primarily had lymphoma, urogenital cancers (especially testicular tumors), and breast cancer, while those with lung and gastrointestinal cancers fasted less frequently. Most patients asked their phy-

sicians if fasting was permissible, but 83.2% of physicians were against it, with only 13.3% allowing patients to make their own choice. Concerns included risks for those susceptible to tumor lysis syndrome or taking nephrotoxic medications and treatments that could cause vomiting, diarrhea, or renal failure (46).

In 49 patients participated in the study. Imatinib was the most commonly used tyrosine kinase inhibitor (TKI), prescribed to 25 patients (51%), followed by nilotinib in 15 patients (30.6%), dasatinib in 8 patients (16.3%), and ponatinib in only 1 patient. Repeated measures ANOVA showed a decrease in mean white blood cell count, neutrophils, and BCR-ABL levels after Ramadan compared to before and during the period, though these changes were statistically insignificant (33).

A prospective study was conducted to assess the impact of fasting for 15 to 16 hours on the nutritional status and quality of life of 56 patients with cancer-related fecal stomas over two Ramadan periods. The fasting participants showed significantly higher albumin levels and pre-albumin levels, along with better global health scores. Additionally, those who fasted had a longer duration of stoma use, averaging 9 months compared to 4.5 months in the non-fasting group. A majority of fasting participants (92.9%) expressed that they would feel sad if they were unable to fast (47).

Patients with colorectal cancer who received intravenous chemotherapy were evaluated during Ramadan month. The study was conducted in Riyadh, Saudi Arabia and the impact of fasting on tolerability of chemotherapy side effects and tumor markers level was investigated. This study confirms that fasting was well tolerated among most of (73%) these patients. The level of CEA and LDH did not change significantly (24).

#### **Discussion**

This systematic review aimed to evaluate the effects of fasting on chemotherapy and other cancer treatments. It included a thorough analysis of

both in vitro and human studies sourced from databases such as PubMed, Scopus, Web of Science, and SID.

The findings from in vitro and animal studies consistently showed that fasting can enhance the effectiveness of chemotherapy while reducing its toxic side effects. These studies highlighted mechanisms like differential stress resistance, where fasting protects normal cells and makes cancer cells more vulnerable to treatment.

Although there are fewer human clinical trials, they provided promising evidence that short-term fasting can alleviate chemotherapy-induced side effects such as nausea, fatigue, and immunosuppression. Additionally, fasting seems to improve the overall response to chemotherapy in patients with various types of cancer, including breast cancer, CML, CLL, and MM.

Ramadan fasting is significant for Muslims, but its effects on cancer patients are not well studied. Research shows that many cancer patients choose not to fast due to their physical limitations and medical advice, those who do often consult their healthcare providers encounter with varying opinions among physicians. Some studies indicate fasting may not significantly affect certain health aspects, but others warn of potential risks, especially for patients undergoing intensive treatments. (3, 24, 29, 45-47).

Therefore, fasting decisions should be personalized, considering the patient's health status, type of cancer, and treatment regimen. Discussing intentions with healthcare providers is crucial for ensuring safety.

Despite these encouraging results, the review identified several limitations. The number of clinical trials remains limited, and there is considerable variability in study designs, fasting protocols, and outcome measures. Moreover, the long-term effects of fasting on cancer treatment outcomes are still unclear.

#### Heterogeneity and Data Synthesis

In this systematic review, heterogeneity was inherently high due to the inclusion of studies with diverse designs, endpoints, and biological systems, including human clinical trials and in vitro

(animal) studies. To manage this heterogeneity, data synthesis was performed separately for each category. Findings from in vitro studies were presented independently from those derived from human studies, reflecting the different study designs and their unique contexts. This approach adheres to the principles of narrative synthesis, ensuring that meaningful comparisons and conclusions could be drawn within each category.

# Clinical Relevance of Preclinical Findings

In vitro and animal studies provide crucial insights into the underlying mechanisms by which fasting might enhance cancer therapy, such as differential stress resistance, autophagy induction, and metabolic reprogramming of cancer cells. While these findings are foundational, their direct applicability to clinical settings is limited due to differences in study conditions, biological systems, and endpoints.

To bridge this gap, human studies remain the cornerstone for assessing clinical effectiveness. These studies, albeit fewer in number, demonstrate the potential of fasting to mitigate chemotherapy-induced side effects and improve treatment outcomes. Our synthesis of preclinical and clinical data aims to present a comprehensive understanding of fasting's role in cancer therapy while acknowledging the limitations of translating preclinical findings to clinical practice. Future research should continue to focus on well-designed human trials to confirm these insights and establish standardized guidelines for fasting interventions in cancer therapy.

#### Conclusion

The results from both animal and human studies suggest that fasting can enhance the efficacy of chemotherapy and reduce its side effects across various types of cancer. However, while preclinical studies provide robust evidence, clinical trials are still limited and further research is needed to establish standardized fasting protocols and confirm these findings in larger patient populations. However, further large-scale, well-designed clini-

cal trials are needed to confirm these findings and establish standardized fasting protocols. Future research should also explore the long-term effects of fasting and its impact on different cancer types and treatment modalities. While some cancer patients may fast (Ramadan) without serious issues, the decision should be individualized, as fasting can impact health parameters. The guidance of healthcare professionals is essential for making informed choices.

# Journalism Ethical considerations

Ethical issues (Including plagiarism, informed consent misconduct, data fabrication and/or falsification, double publication and/or submission redundancy, etc) have been completely observed by the authors.

# Acknowledgements

No external funding or institutional support was received for this study. All contributors are listed as co-authors.

#### **Conflict of Interest**

The authors declare that there is no conflict of interests.

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