

# Ramadan Fasting and Patients with Cancer: state of the art and future prospects

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## 1. Abstract

Ramadan fasting represents one of the five pillars of the Islam creed. Even though some subjects (among which patients) are exempted from observing this religious duty, they may be eager to share this particular moment of the year with their family and peers. However, there are no guidelines or standardized protocols that can help physicians to properly address the issue of patients with cancer fasting in Ramadan and correctly advising them. Moreover, in a more interconnected and globalized society, in which more and more Muslim patients live in the Western countries, this topic is of high interest also for the general practitioner. For this purpose, we carried out a systematic review on the subject. Our main findings are that: 1) very few studies have been carried out, addressing this issue; 2) evidence concerning quality of life and compliance to treatment is contrasting and scarce; 3) generally speaking, few patients ask their physicians whether they can safely fast or not. For these reasons, further research could be performed, given the relevance and importance of this topic.

**2. Keywords:** cancer; drug compliance and adherence; quality of life; Ramadan fasting; stomia

## 3. Introduction

The Arabic word *Islam* means peace, purity and total submission to the will of Allah (the Lord of the worlds, *Rabb al-'alameen*) by conforming inwardly and outwardly to His law. The religion of Islam is based on five pillars (*arkan al-Islam*). Ramadan fasting (*as-sawm*) is considered one of the five pillars of the creed, together with the faith declaration (*as-shahada*), the ritual prayers (*as-salah*), the pilgrimage to Mecca at least once in lifetime for those who are financially and physically able (*al-hajj*), and charity or almsgiving (*zakat*).

The Holy month of Ramadan, the ninth month of the Muslim lunar calendar (*Hijra*), is of great value and significance among Muslims, representing the month of the descent of the *Qu'ran*.

Ramadan is not only abstinence from food and drinking, but also from smoking, medication and sexual intercourses (*Surat 2 "Al-Baqarah", ayyat 183*).

Ramadan fasting is not, however, a prolonged or continuous fasting, but consists of alternate fasting and feasting (re-feeding) periods [1]. Pre-dawn meal is termed as *suhoor*, whilst after-sunset meal is called *iftar*. Ramadan duration is variable, since the Islamic calendar is a lunar one and therefore the Islamic year contains 354 days (instead of 365, as in the Gregorian or solar calendar). For this reason, the Ramadan month occurs 11 days earlier every year, and may fall in any period of the year. Therefore, mean fasting duration is usually 12-14 hours, but depending on the place and the year it can last also up to 18 hours [1,2] or even 22 hours, in the extreme latitudes [1].

Pre-puberal and puberal children, menstruating, pregnant and breast-feeding women, sick people, debilitated older subjects; travelers are exempted from this religious duty (*Surat 2 "Al-Baqarah", ayyat 185-186*). However, they could be willing to fast and share the spirituality of this month with their family and peers [3].

It is a common saying that religion promotes healthy lifestyles. However, the relationship between a religion and cancer has been often overlooked or poorly addressed from a scientific, rigorous point of view [4], especially in terms of physiology [5]. Among the few studies available in the literature, Mills and collaborators investigated Seventh-Day Adventists. This religious group does not consume tobacco, alcohol or pork and is characterized by lower cancer-related morbidity rates than the general population, even though the risk for prostate and endometrial cancer was higher [6]. Fraser noticed that non-vegetarian Seventh-Day Adventists were significantly more affected by colorectal and prostate cancer than vegetarian Seven-Day Adventists [7, 8]. Seventh-Day Adventists present also a particular relationship between cancer risk and allergy [11]. Ogata and coworkers found a lower mortality from respiratory cancers among Zen Buddhists with respect to the general population [8]. Sriplung and collaborators found that a lower incidence of cervical and breast cancers in Muslim than in Buddhist females. Further, they noticed a lower incidence of prostate cancer in Muslim males. Independent of sex and year of diagnosis, the incidence of lung, liver, non-Hodgkin lymphoma (NHL), and colorectal cancers was lower in Muslims [9]. Islamic beliefs can have an impact on access to breast or cervical cancer screening programs and therefore should be carefully taken into account by health workers in the field of Public Health [1].

The effects of Ramadan fasting on patients suffering from cancer is not a mere academic topic or of limit interest for only the Arabic countries. In a globalized society, the physicians have to face with issues like the management of cancer in Muslim patients that to want to fast during Ramadan, since more Muslims live in the Western societies [4]. However, information is sparse and no guidelines or standardized protocols exist [3].

In principle, clinical investigations carried out among patients suffering from cancer fasting during Ramadan could have broad, translational implications. The effects of fasting on cancer have been extensively studied: starvation-induced changes in genome organization, chromatin remodeling and in metabolic pathways, modulating, for example, glucose, insulin-growth factor (IGF) and other related enzymes and proteins may increase the effectiveness of chemotherapy [5,6,7]. Fasting could have a positive impact on drug pharmacokinetics, and could contribute to reducing its side-effects, improving the chemotherapeutic index and overcoming at least partially the issue of drug-resistance [5,6,7]. Furthermore, fasting has a beneficial impact on the renewal of stem-cells and on the immune system, in particular on natural killer cells, as well as on the oxidant system, thus enabling cancer growth control [8,9,10,11]. To this respect, different kinds of cancer have been investigated, such as pancreatic [12], breast [13,14,15], lung [16], colorectal [17] and prostate [18] cancer, and even glioma [19]. The impact of fasting has been assessed on different drugs [20,21], like irinotecan [22,23], doxorubicin [24], as well as on new recent anti-blastics, including erlotinib [16], tyrosine kinase inhibitors [25], and sirtuin [26], among others.

Effects of fasting on tumor have been assessed both on neo-adjuvant and adjuvant therapy [15]. Further, fasting seems to sensitize tumor cells and increase the outcome of radiation therapy [19].

Warburg. However, despite that this topic has attracted an impressive body of research [27,28], little is known

both in terms of molecular mechanisms and clinical outcomes about the difference among the various existing kinds of fasting, such as periodic diet [29], calories restriction [30], dietary restriction [31] or dietary manipulation [28], intermittent [13,18] or short-term fasting [24], and prolonged fasting [8,10,14], among others. Lv and collaborators in a recently published systematic review and meta-analysis concluded that while the roles of ketogenic diet and of caloric restriction in controlling cancer are quite established, evidence of the effectiveness of intermittent fasting is still insufficient [32]. Furthermore, most of these studies have been conducted in animal models: therefore, there is an urgent need for more investigations in human [33].

Ramadan represents a unique laboratory for studying the effect of fasting in cancer patients, using a multidisciplinary approach. Aspects such as diabetic patients [] or with renal [], infectious or cardiovascular diseases [] have been already reviewed.

For this purpose, we have carried out a systematic review that could be helpful for general practitioners. We have mined different databases: namely, ISI/Web of Science (WoS), MEDLINE/PubMed, Scopus, Scirus, Directory of Open Access Journals (DOAJ), and Google Scholar.

#### **4. Ramadan and Cancer: quality of life and adherence to religious worship**

Kuzu and collaborators [4] investigated quality of life and compliance to religious duties (such as praying and fasting) in 178 patients living with a permanent colostomy. 75 underwent abdominoperineal resection (APR, or Miles' operation), 51 sphincter-saving resection, and 52 anterior resection including sigmoid colectomy. Quality of life was measured with the Medical Outcomes Study Short Form 36 Health Survey (SF-36) and a questionnaire with items about work, sexual life, and compliance to religious worship. They found that a significantly number of patients in the APR ~~abdominoperineal resection~~ group stopped praying daily (either alone or in a mosque) and fasting during Ramadan. They concluded that colorectal cancer, besides affecting quality of life, has a profound impact on religious worship. They authors recommended a preoperative counseling, involving local religious authorities.

Celasin and coworkers [5] carried out a prospective study recruiting 93 Muslim patients after surgery for colorectal carcinoma: 50 underwent APR, 22 sphincter-saving resection and 1 anterior resection including sigmoid colectomy. Quality of life was assessed pre- and postoperatively at 15-18 months with the SF-36 questionnaire and a modified version of the American Society of Colorectal Surgeons (ASCRS) Fecal Incontinence questionnaire. Life standards, including religious practice, were measured using the Ankara University Life Standard Questionnaire (AULSQ). Authors found that religious worship (praying alone, praying in mosques, fasting during Ramadan and purifying alms) was not significantly different among the groups. Probably this was the effect of a proper religious counseling and its importance, advocated by Kuzu and collaborators in the previous article [4], is here confirmed.

Zeeneldin and co-authors [6] conducted a cross-sectional study during Ramadan, August-September 2009, investigating 102 patients suffering from breast cancer (31%), acute leukemia (24%), colorectal cancer (7%), non-Hodgkin lymphoma (5%), bladder cancer (4%), lung cancer (4%), and laryngeal cancer (4%). Treatments included chemotherapy, radiotherapy, hormonal therapy, and nonspecific therapy in 42%, 31%, 10%, and 17%, respectively. Co-morbidities were present in 22% of the patients. Authors found that 40% of patients did not fast during Ramadan, 36% and 24% were partial and complete fasters. Being female patients, having a good and stable performance status, suffering from a non-metastatic solid tumor, and receiving non-intravenous chemotherapy as outpatients were found to be predictor of compliance to fasting. However, only 46% of patients sought the treating oncologist advice on whether they could fast.

Altuntas and coworkers [7] carried out a prospective study investigating 56 patients with a cancer-related fecal stoma over two periods of Ramadan to analyze the effect of fasting on nutritional and metabolic status and quality of life. 14 patients were fasting. They had their stoma for a longer period of time than patients in the non fasting group, and the proportion of patients with a permanent stoma was higher in the fasting group than in the non fasting group. Ramadan fasting had almost no influence on quality of life.

Tas and collaborators [8] performed a survey of 701 adult Turkish Muslim cancer patients during the month of Ramadan in 2012. Before diagnosis of cancer, 93.1% of the patients used to fast completely or partially. After

diagnosis of cancer, this rate fell down to 15%: 83.9% of patients who fasted before diagnosis, gave up observing the religious duty. Patients who decided to go on fasting after the diagnosis of cancer thought that observing Ramadan would have led to Patients who were females, those with good performance status, those without any comorbid disease (in particular, diabetes mellitus), who had non-metastatic disease, those with history of surgery, young, those treated with radiotherapy and those being treated with single agents, oral chemotherapeutic agents or not receiving drugs being in the follow-up period were more likely to be fasting than others. The fasting ones suffered from lymphoma, urogenital cancer (in particular, testicular tumor) and breast cancer; conversely, the rate of fasting status among patients with lung and gastrointestinal cancer was quite low. Gynecologic, head and neck, sarcoma, and skin cancers did not correlate with fasting status. Only 20.8% of all patients asked their physician whether it was alright for them to fast and physicians generally had a negative attitude towards fasting (83.2%). 13.3% of physicians allowed patients to choose whether to fast or not. Physicians were concerned about the possibility of fasting in patients at risk of tumor lysis syndrome, taking nephrotoxic drugs or other drugs that could lead to vomiting, diarrhea or renal failure. The authors concluded that majority of cancer patients are not fasting during the month of Ramadan, and a small part of patients consult this situation to their physician.

## **5. Ramadan and Cancer: adherence to drug treatment**

Drug compliance during Ramadan generally tends to fall, as noticed by some scholars [9-11]. Other authors, such as Zeeneldin and coauthors [12], however, have found that Ramadan fasting does not impair patient's adherence to treatment. During Ramadan 2010, 139 patients suffering from breast cancer were asked about compliance to fasting and religious duties as well as to treatment with oral hormonal therapy (OHT) in Ramadan and in the preceding month. Tamoxifen and aromatase inhibitors were used in 64% and 36%, respectively. Adherence rates to OHT during Ramadan and before were 94.2% and 95.7%, respectively (not statistically significant). Non-adherence prior to Ramadan and shorter duration of OHT were predictors of non-adherence during Ramadan, whilst fasting status, age, performance status, presence of metastases and type of OHT were not good predictors of adherence.

## **6. Results and Discussion**

Despite our extensive search, we managed to find only 6 studies addressing the issue of patients suffering from cancer fasting during Ramadan: in particular, 5 focusing on the impact of fasting on quality of life and compliance to worship, and 1 focusing on adherence to drug treatment. Despite the importance and relevance of this topic and given the burden imposed by the cancer, very few scholars have investigated the impact of Ramadan fasting on the health of patients with tumor.

The effect of Ramadan on quality of life appears to be controversial: whilst three studies confirm this relationship, two other researches fail to find any impact. Also the effect of fasting on compliance to worship seems to be quite contrasting.

As far as the compliance to drug treatment is concerned, there is only 1 study available and therefore it is not possible to collect any evidence.

## **7. Conclusions**

There is a strong need for evidence-based suggestions and guidelines [3]. Very few studies are available, with contrasting findings.

This could be done within a multidisciplinary team, made up of an oncologist, a nutritionist, a psychiatrist or a psychologist. Patients should be carefully checked and assessed, considering both the clinical symptoms and the laboratory exams. Also psychological aspects, such as motivation, and patient preferences and adherence/compliance to treatment should be investigated and taken into account.

A diagnosis of cancer is always difficult to cope with and in Muslim subjects can have a varying impact,

depending also on the degree of religiosity of the subjects itself. Errihani and colleagues found that in practicing Muslims cancer is seen as a divine test and as such accepted, whilst non practicing Muslims feel guilty and begin to practice []. Therefore, the level of spirituality/religiosity plays a major role in supporting the patient during the health-care process and can influence the clinical outcome. However, as found by the study of Tas and collaborators [], the communication between the patient and the physician is not always characterized by an open disclosure and a frank dialogue. This is further complicated by the fact that the situation is rather delicate and the doctor, if not culturally competent or sensitive, could be left with dilemmas because of the cultural/religious beliefs and attitudes of the patient [].

Patients suffering from metastatic, disseminated, aggressive tumor, lysis syndrome, taking nephrotoxic drugs which could cause diarrhea, vomiting or renal failure, or with a history of non-compliance with therapy and dietary modifications should not fast during the month of Ramadan.

In conclusion, if stable, patient's eagerness to fast should be taken into account and even encouraged, since spirituality plays a key role in cancer. The patient feels indeed himself/herself more active being involved in the religious activities, and less depressed and isolated [3].

A particular aspect that should be addressed is the management of terminal patients during Ramadan. From the literature, it is known that some Muslim patients with terminal illnesses may express a strong spiritual and religious wish [13,14]. This calls for cooperation between the family and the interdisciplinary palliative care team. On the contrary, some scholars, like Tas and collaborators [8] have shown that there is poor cooperation between physician and patient. Facing patients' needs is likely to have a great positive impact on the patient's sense of wellbeing.

However, once again, also this topic has been poorly explored. Further research in the field is needed.

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