

Ramadan fasting and digestive disorders: SEPAHAN systematic review No. 7

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BACKGROUND: During Ramadan, the 9th month in the Hijri lunar calendar, healthy adult Muslims are obliged to fast from sunrise to sunset. The fast of Ramadan has significant health effects and is the most commonly researched religious fasting. In this study, we will investigate available findings on the effects of Ramadan fasting on gastrointestinal (GI) signs, symptoms, and diseases. **METHODS:** We searched PubMed, Google Scholar, Iran Medex, and Scientific Information Database (SID) for related articles in English or Farsi. Editorial articles and case reports were excluded. **RESULTS:** Of 2312 articles found, 23 articles fulfilled our inclusion criteria and were included. Ramadan fasting seems to increase peptic ulcer complications (peptic ulcer perforation and bleeding) and have a deteriorating effect on patients with chronic peptic ulcer diseases on drug therapy, but not on duodenal ulcer patients under treatment. Healthy individuals might experience minor GI symptoms but no serious complications have been reported. Studies regarding the incidence of acute appendicitis and peptic ulcer diseases are not in agreement, but acute mesenteric ischemia, hyperemesis gravidarum and primary small bowel volvulus seem to be increased during Ramadan. No increase in idiopathic intussusception is observed during Ramadan and fasting does not appear to impose serious risks on patients with an inflammatory bowel. **CONCLUSIONS:** Fasting is generally safe for healthy individuals, but might be hazardous to patients with various GI diseases and may increase the risk of complications in this group.

KEYWORDS: Ramadan Fasting, Islamic Fasting, Gastrointestinal Diseases, Gastrointestinal Signs and Symptoms.

BACKGROUND

With 1.57 billion followers worldwide, Islam is the world's second largest religion.^[1] During Ramadan, which is the 9th month of the Islamic lunar calendar, all adult Muslims are obliged to fast; i.e. refrain from eating, drinking, smoking and engaging in sexual activities from sunrise to sunset.^[2]

Ramadan lasts 29 to 30 days each year. Since the Islamic calendar (the Hijri calendar) is a lunar calendar, the first day of Ramadan advances 11 to 12 days each year compared to the Gregorian calendar. Hence Ramadan occurs in different times of the seasonal year over a 33-year cycle.^[2,3]

Depending on the season Ramadan falls in, and also the latitude, the duration of the fast varies between 11 and 18 hours in the north and in tropical countries.^[4]

All adult Muslims are required to fast with the exemption of the sick, the travelers and menstruating, pregnant or lactating women; however, many of the individuals, who could be considered exempt, decide to fast.^[2,4]

During the month of Ramadan, eating patterns

change. Individuals consume two relatively large meals, one before the dawn (Sahur) and the other right after the sunset (Iftar). The food consumed during Ramadan is usually rich and high in protein and fat.^[5,6] The alteration in circadian rhythm is also of significance: the individuals become more active after sunset and in the night and they may also become sleep deprived.^[2,7]

The month of Ramadan is a religious festival and fasting is mainly a ritual for Muslims to practice self-control and self-discipline, and empathize with the impoverished. Moreover, fasting during Ramadan has significant health effects and is the most commonly researched religious fasting.^[8]

In the past two decades, studies have been conducted to evaluate the impact of fasting in Ramadan on the gastrointestinal (GI) tract. Nonetheless, the findings have been heterogeneous, and therefore, no consensus exists regarding how GI tract might be affected by the fasting in Ramadan.

In a retrospective study over a 10 year period, Bener et al. did not find an increase in the frequency of peptic ulcer disease during Ramadan.^[9] Moreover, Tavakkoli et al. found no correlation between

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Ramadan fasting and the severity of inflammatory bowel diseases (IBD) in the patients.^[10]

Other studies however suggest that peptic ulcer perforation is significantly increased during the fasting of Ramadan.^[2,11]

Furthermore, Ozkan et al. found that significantly more patients were diagnosed with acute upper GI hemorrhage during Ramadan compared with a non-Ramadan month and suggested that fasting during Ramadan “reactivates and aggravates the severity and complications of pre-existing GI diseases like peptic ulcer and gastritis”.^[12] Another study came to the conclusion that Ramadan fasting can increase acute upper GI bleeding, but fasting patients do not have a poorer prognosis than non-fasting patients.^[13]

To our knowledge, there is no review article on the impact of Ramadan on GI tract to date. The aim of this paper is to systematically review the published literature regarding the effect of Ramadan on the GI tract.

METHODS

Literature search

Data were obtained by a search of the published literature cited in PubMed, Google Scholar, Scientific Information Database (SID) and Iran Medex. Search of all databases from inception to present was performed and the last search was conducted on March 11, 2012.

A search of PubMed was carried out. PubMed query was: (((Ramadan) AND "Signs and Symptoms, Digestive"[Mesh]) OR Ramadan [Title]) OR Islamic fasting) OR Ramadhan. The term “Ramadhan” is a less frequently used variant of “Ramadan”.

Google Scholar was searched for articles with the terms “Ramadan” and “Islamic fasting” in their title. Only articles in the following subject areas were searched: medicine, pharmacology and veterinary sciences (the limitation was chosen from “articles and patents”, in advanced scholar search). Articles with equivalent Farsi terms in their titles were also searched in all subject areas.

Likewise, the databases Iran Medex (www.iran-medex.com) and SID (www.sid.ir) were searched for articles including “Ramadan” and “Islamic fasting” and their equivalent terms in Farsi, in all fields. The aim was to especially identify articles in Farsi and articles in local journals.

Reference lists from potentially relevant articles were also hand searched to identify any additional studies that may have been missed using the computer-assisted search strategy.

Study selection criteria

Two investigators reviewed the titles and abstracts of all citations identified by the literature search. Full texts of the potentially relevant studies were retrieved and the selection criteria were applied. The selection criteria were: (1) data presenting articles of studies comparing GI signs, symptoms and diseases before and/or during Ramadan with those of after Ramadan, or comparing GI signs, symptoms and diseases between fasting and non-fasting subjects; (2) published in full manuscript; and (3) in English or Farsi only. Editorial articles and case reports were excluded.

Data extraction

Eligible articles were reviewed by two reviewers, and data were extracted. From each eligible article, data were extracted on first author, year of publication, title, journal, study population, sample size, main study outcome and findings, study design and methods, and the demographic factors taken into consideration in the study. The extracted data were then entered into a table. A summary of that table is presented in this article (Table 1).

RESULTS

With the above described searches, 476 articles were found searching PubMed. Search of Google Scholar identified 1322 articles and search of Iran Medex and SID databases led to identification of 363 and 151 articles, respectively. Reviewing the titles and abstracts, followed by the review of the full manuscripts of potentially relevant articles, identified 23 articles that met our inclusion criteria (Figure 1). Characteristics and findings of the selected articles are summarized in table 1.

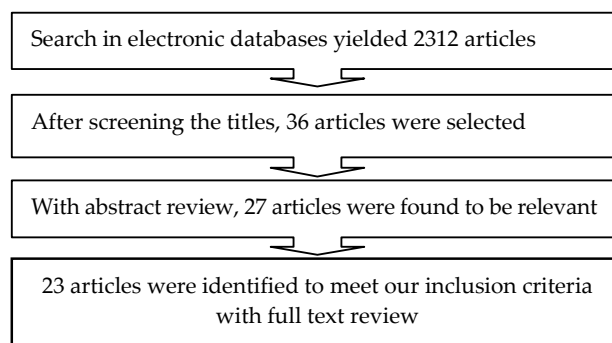


Figure 1. Diagram of the searches for the systematic review of the gastrointestinal effects of Ramadan fasting

Table 1: Relationship between Ramadan fasting and gastrointestinal disorders based on previous publications

| Row # | First author | Design (case-control, cohort, RCT,) | # of observations (participants under analysis) | Setting (population or geographic location) | Main exposure(s) or variable under study | Main outcome(s) | Magnitude of effect(s) or brief of findings | Explanations (e.g. if the study was only on women, or only on a specific age group, etc.) |
|-------|-------------------------------------|-------------------------------------|---|--|--|---|---|---|
| 1 | Al-Kaabbi S. ^[22] | Cross sectional | 516 | Patients with PUD | Ramadan | PUD | No increase was found in PUD incidence during Ramadan compared to periods before and after Ramadan. More patients had DU in Ramadan compared to the period before Ramadan (55% vs. 39.3%, $p < 0.05$). | The study period included almost 3 months, the month of Ramadan and a period of time before and after it. |
| 2 | Bener A. ^[9] | Cross sectional | 470 | Patients treated for PUD | Ramadan | PUD and PPU | Frequency of PUD and PPU was higher in the month after Ramadan compared to that of Ramadan ($p > 0.05$ and $p = 0.008$ respectively). | Patients treated in Ramadan and the month after, during a 10-year period |
| 3 | Chong VH. ^[23] | Cross sectional | 1661 | Patients referred for upper GI endoscopy to a referral centre | Ramadan | Upper GI endoscopy referrals and findings | There was less workload for the endoscopy centre during Ramadan. Number of the patients referred to the centre: BR: 603, R: 397, AR: 661 ($p < 0.05$) More patients with GI bleeding were referred during Ramadan. Percentage of patients referred with the indication of GI bleeding to the total number of patients referred: BR: 10.9%, R: 16.6%, AR: 13.5% ($p = 0.153$) There was no significant difference in endoscopic findings in the esophagus and stomach. More duodenal ulcer diseases were encountered during and after Ramadan. Percentage of patients with duodenal ulcer disease in the total number of patients referred: BR: 7.5%, R: 14.1%, AR: 12.6% ($p = 0.001$) | Patients referred a month before, during, and a month after Ramadan over a 4-year period |
| 4 | Darvish Moghadam S. ^[21] | Cohort | 125 | Healthy fasting volunteers | Fasting | GI symptoms | GI symptoms (nausea, vomiting, diarrhea, constipation, etc.) occurred in 58.4% of volunteers. However, symptoms were mild and none of the volunteers stopped fasting due to severity of GI symptoms. Women had 1.7 times more GI symptoms than men ($p < 0.02$). | All participating individuals fasted for more than 21 days. |
| 5 | Davoudabadi A. ^[14] | Cross sectional | 1256 | Patients with acute appendicitis (diagnosis confirmed by pathology report after surgical excision) | Ramadan | Acute appendicitis | Significantly less patients underwent surgery for acute appendicitis during Ramadan compared to other months ($p < 0.0001$) and most patients underwent surgery for acute appendicitis in the month after Ramadan ($p < 0.001$) | Patients aged from 15 to 70 years, admitted during 3 consecutive Hijri years |
| 6 | Davoudabadi A. ^[15] | Cross sectional | 1773 | Patients with acute appendicitis (diagnosis confirmed by pathology report after surgical excision) | Ramadan | Acute appendicitis | The incidence of acute appendicitis is significantly reduced during Ramadan, while it increases sharply in the month after Ramadan ($p < 0.001$). | Patients aged from 15 to 70 years, admitted during 3 consecutive Hijri years |
| 7 | Donderici O. ^[25] | Cross sectional | 1114 | Patient hospitalized for PUC | Ramadan | PUC | PUC increased with Ramadan fasting. Share of patients with PUC among the total number of patients hospitalized: BR: 14.3%, R: 20.5%, AR: 15.4% (difference between R and BR: $p < 0.05$) Difference between R and AR: $0.1 > p > 0.05$) Female patients tended to develop more hemorrhage and perforation during Ramadan than male patients ($0.05 > p > 0.01$). | Patients admitted one month before, during, and one month after Ramadan during a 6-year period |
| 8 | Duke JH Jr. ^[28] | Cross sectional | 26 | Patients with primary small bowel volvulus | Ramadan | Primary small bowel volvulus | There was a tenfold and ninefold increase in the incidence of primary small bowel volvulus in the two fasting months (Ramadan) during the study. 73% of cases presented during Ramadan. | Duration of the study was 13 months, the first and last month was Ramadan. |

Table 1: Relationship between Ramadan fasting and gastrointestinal disorders based on previous publications (Continue)

| Row # | First author | Design (case-control, cohort, RCT,) | # of observations (participants under analysis) | Setting (population or geographic location) | Main exposure(s) or variable under study | Main outcome(s) | Magnitude of effect(s) or brief of findings | Explanations (e.g. if the study was only on women, or only on a specific age group, etc) |
|-------|---------------------------------|-------------------------------------|---|--|--|--|---|---|
| 9 | Elnagib E. ^[24] | Cross sectional | 58 | Patient with PPU | Ramadan | PPU | The incidence of PPU increased in Ramadan, 37.9% of perforations occurred during Ramadan. | Patients admitted during a period of two and a half years. |
| 10 | Emami MH. ^[13] | Cohort | 236 | Patients admitted to a hospital with AUGIB | Fasting | AUGIB causes; Dyspeptic symptoms; prognosis of AUGIB | The fasting group had more DU (38% vs. 19.5%), but this was only significant for 20 to 60-year old patients ($p < 0.05$). The frequency of esophageal varices was higher in the non-fasting group (11.7% vs. 3.7%, $p < 0.05$), which was significant for patients more than 40 years old. In the fasting group 38% and in non-fasting group 18.9% had a history of dyspeptic symptoms ($p = 0.001$, OR = 2.62). There was no significant difference between the two groups in terms of the outcome of AUGIB and prognosis, but mortality was higher in the fasting than the non-fasting group (12.5% vs. 3.7%, $p = 0.016$). | Patients admitted from the 10th day of Ramadan until one month after during a 2-year period. Fasting group consisted of patients who were fasting at least 10days before admission. |
| 11 | Gocmen E. ^[3] | Cross sectional | 1408 | Patients admitted to surgical emergency unit | Ramadan | PPU; Acute mesenteric ischemia | PPU nearly doubled during Ramadan compared to the months before and after (BR: 7.7%; 95%CI 1.05-1.10, R: 16.0%; 95%CI 1.12-1.19, AR: 7.9%; 95%CI 1.05-1.10). There was a more than twice increased ratio of acute mesenteric ischemia during Ramadan (BR: 1.6%; 95%CI 1.00-1.02, R: 3.7%; 95%CI 1.02-1.05, AR: 1.4%; 95%CI 1.00-1.02) | Patients admitted one month before, during and one month after Ramadan during a 4-year period. |
| 12 | Hosseini-Asl K. ^[19] | Cohort | 39 | Patients with endoscopically proven DU | Fasting | Treatment of DU | Fasting did not have a deteriorating effect on healing of duodenal ulcer and patients with active duodenal ulcer could fast, receiving the treatment employed in the study. A 94.4% cure in the fasting group and a 95.5% cure in the non-fasting group was detected | All patients were receiving Omeprazole as a treatment. |
| 13 | Jastanjah S. ^[27] | Cross sectional | 27 | Patients with perforated duodenal ulcer | Ramadan | Duodenal ulcer perforation | There was no increase in the prevalence of perforation of duodenal ulcer during Ramadan. | Patients admitted during a 7-year period. |
| 14 | Kucuk HF. ^[26] | Cross sectional | 260 | Patients undergoing urgent operation for perforated duodenal ulcer | Ramadan | Duodenal ulcer perforation | The incidence of duodenal ulcer perforation was higher in Ramadan. The number of patients undergoing surgery per Ramadan was 10 while that of non-Ramadan months was 3.8 ($p < 0.018$). History of dyspepsia significantly increased the risk of perforation in fasting people in Ramadan compared to the non-Ramadan group ($p < 0.05$) | within a 5-year period |
| 15 | Kuruvilla MJ. ^[30] | Cross sectional | 114 | Patients with intestinal obstruction | Ramadan | Intestinal obstruction | There were no cases of idiopathic intussusception during or immediately following Ramadan. | Duration of the study was 30 months. |
| 16 | Malik GM. ^[18] | Cohort | 38 | Patients with endoscopically proven PUD | Fasting | Treatment of PUD | Chronic PUD was difficult to cure during Ramadan fasting and fasting might be hazardous to patients with PUD. The non-fasting group showed no change after Ramadan. All fasting patients with ADU healed. 7 of 8 patients with active CDU bled during Ramadan. 7 of 8 patients with HDU showed no change, one developed a new active ulcer. One patient had a CGU, he bled during Ramadan. | All patients were receiving an H2 blocker drug as a treatment. |

Table 1: Relationship between Ramadan fasting and gastrointestinal disorders based on previous publications (Continue)

| Row # | First author | Design (case-control, cohort, RCT,) | # of observations (participants under analysis) | Setting (population or geographic location) | Main exposure(s) or variable under study | Main outcome(s) | Magnitude of effect(s) or brief of findings | Explanations (e.g. if the study was only on women, or only on a specific age group, etc) |
|-------|--------------------------------|-------------------------------------|---|--|--|-----------------------------|---|--|
| 17 | Malk GM. ^[17] | Cohort | 80 | Patients with endoscopically proven PUD | Fasting | Treatment of PUD | Chronic PUD was difficult to cure during Ramadan fasting and fasting might be hazardous to patients with PUD. All patients with ADU (4 of 4) showed signs of healing. In the group of patients with CDU (16 patients), 62.5% (10 patients) bled during the study, while others showed no change on the repeat endoscopy. In patients with HDU (20 patients), 85% (17 patients) showed no change, but the others developed new ADU. One patient had CGU and bled during the fasting period. No changes were detected after Ramadan in non-fasting patients. | All patients were receiving Ranitidine as a treatment. |
| 18 | Mehrabian ^[20] | Cohort | 84 | Patients with DU | Fasting | Treatment of DU | DU healed in 75.5% of non-fasting and 85.7% of fasting patients (p = 0.05). | All patients were receiving Omeprazole as a treatment. |
| 19 | Ozkan S. ^[12] | Cross sectional | 71 | Patients presenting with AUGIB | Ramadan | AUGIB | The number of patients diagnosed with AUGIB during Ramadan was higher than that of the non-Ramadan month (p < 0.05). | Patients aged > 16 admitted during Ramadan and a non-Ramadan month (2 months after Ramadan) in one year. |
| 20 | Rabiner-son D. ^[29] | Cross sectional | 211 | Patients with hyperemesis gravidarum | Ramadan | Hyperemesis gravidarum | Hyperemesis gravidarum was more frequent in Ramadan. Patients admitted in Ramadan/The total number of patients admitted: 76/211 (p < 0.05) | Pregnant Muslim women during the first trimester admitted during an 11-year period. |
| 21 | Sulu B. ^[16] | Cross sectional | 992 | Patients with acute appendicitis (diagnosis confirmed by pathology report after surgical excision) | Ramadan | Acute appendicitis | Ramadan did not increase the frequency of acute appendicitis. Percentage of patients with acute appendicitis undergoing surgery: BR: 37.1%, R: 32.1, AR: 30.8% (p > 0.05) | Patients aged > 10 diagnosed during Ramadan, the month before and the month after, over a 4-year period |
| 22 | Tavakkoli H. ^[10] | Cohort | 60 | Patients with IBD in remission | Ramadan Fasting | Severity of symptoms of IBD | Ramadan did not cause aggravation in IBD patients' symptoms. Mean score of CAI in UC patients: BR: 2.97±2.33, AR: 1.88±1.67 (p = 0.005) CAI decreased in UC male patients (BR: 3.5, AR: 1.7; p = 0.008) but not in UC female patients (BR: 2.5, AR: 2; p = 0.3). In CD patients, mean score of CDAI was: BR: 102.5, AR: 92.5 (p = 0.6) There was no difference in patients' scores or changes of scores and type of disease between fasting and non-fasting patients. | 26 patients did not fast, 5 patients fasted for all 30 days and 29 patients fasted for 1-29 days |
| 23 | Torab FC. ^[11] | Cross sectional | 116 | Patients with intraoperatively confirmed PPU | Ramadan | PPU | There was a significant increase in the admission of patients with PPU during Ramadan (p < 0.004) | Patients aged > 18 diagnosed over a period of 4 years and 3 months. |

PUD: Peptic ulcer disease

DU: Duodenal ulcer PPU: Perforated peptic ulcer GI: Gastrointestinal BR: Before ramadan

R: Ramadan AR: After ramadan PUC: Peptic ulcer complications

AUGIB: Acute upper GI bleeding

ADU: Acute duodenal ulcer

CDU: Chronic duodenal ulcer

HDU: Healed duodenal ulcer

CGU: Chronic gastric ulcer

IBD: inflammatory bowel disease

CAI: Colitis activity index

UC: Ulcerative colitis

CD: Crohn's disease

CDAI: Crohn's disease activity index

Acute appendicitis

Three articles were found to have investigated the effect of Ramadan on the incidence of acute appendicitis.^[14-16] Davoudabadi et. al investigated medical records of all patients admitted to the hospital with acute appendicitis and undergoing surgery during a 3-year period.^[14] The findings showed that the incidence of acute appendicitis was significantly lower during Ramadan, compared to other months; however, it is significantly high in the month after Ramadan and also during *Muharram*, the first month of the lunar Hijri calendar. Another study with a very similar design was carried out,^[15] and the results were in accordance with those of the previous study. A more recent study on the other hand, compared the incidence of acute appendicitis during Ramadan, with that of the month before and after Ramadan.^[16] The incidence of acute appendicitis reported by this study was higher in Ramadan compared to the following Hijri month, and hence the results of this study did not confirm those of the other two. Furthermore this study reported that there was no significant difference between Ramadan and the month before and after it in terms of frequency of perforation ($p > 0.05$).

Treatment of Peptic Ulcer Diseases

Two cohort studies evaluated the effect of fasting on the treatment of peptic ulcer diseases (PUD).^[17,18] In both studies, a number of fasting and non-fasting patients received an H₂-blocker drug during Ramadan and were endoscoped before and after Ramadan. Patients in both fasting and non-fasting groups would take their drugs at Sahur and Iftar. In both studies, the condition of patients in the fasting group improved or worsened, while no change was detected in the non-fasting group on repeated endoscopy. Healing of erosive duodenitis (ED) was also evaluated in both studies. In the first study,^[17] 56.25% of fasting patients with ED showed no change, while the rest showed signs of healing. In the second study,^[18] fasting patients with ED had completely healed after Ramadan. Findings of the two studies were generally in agreement, but the name of the drug was not mentioned in the second study.

Treatment of Duodenal Ulcer

In two cohort studies, fasting and non-fasting patients with duodenal ulcer (DU) had been compared in terms of their treatment response to Omeprazole.^[19,20] Endoscopic evaluation was performed before and after Ramadan. In both studies, patients received 40mg of Omeprazole per day. Both studies suggested that patients with DU could fast while on the previously described drug regimen.

GI symptoms in healthy individuals

We found only one study regarding the effect of fasting on GI symptoms in healthy individuals.^[21] GI symptoms occurred in 58.4% of the participants. The most prevalent GI symptoms were belching, bloating and fullness sensation; the three symptoms had an overall prevalence of 19.9% (values were not reported separately); while the least prevalent GI symptom was diarrhea with a prevalence of 0.6%. Other GI symptoms and their prevalence were as follows: mouth dryness and bitter taste in the mouth (18.7%), epigastric pain and discomfort (11.7%), early starvation (10.5%), early satiety (9.9%), loss of appetite (8.8%), heartburn (5.3%), abdominal pain, flank pain and periumbilical pain (5.3%), constipation (5.3%), nausea and vomiting (4%). Fasting patients were divided into two groups with different diets: one group had a light meal like breakfast, and the other a large meal for Sahur. Respectively 55.2% and 59.4% of individuals in the first and second group experienced GI symptoms, but this finding was not statistically significant ($p > 0.4$). Moreover, most of the upper GI symptoms were found to correlate with some dietary components. Upper GI symptoms included: mouth dryness and bitter taste in the mouth, heartburn, epigastric pain and discomfort, nausea and vomiting, early starvation, early satiety and loss of appetite. GI symptoms and correlated dietary components were as follows: mouth dryness and bitter taste in the mouth with carbohydrate intake ($p < 0.04$), nausea and vomiting with fat and protein intake ($p < 0.02$), early starvation and loss of appetite with all of the mentioned dietary components. There was also a correlation between the overall upper GI symptoms and dietary components ($p < 0.05$).

Frequency and incidence of PUD

Regarding the frequency of PUD, Al-Kaabi et al. found no increase during Ramadan,^[22] and Bener et al. reported a higher frequency of PUD in the month after Ramadan, compared to that of Ramadan.^[9] Additionally, Chong et al. reported that a higher percentage of patients referred to an endoscopy center, had duodenal ulcer during Ramadan, compared to the preceding and following months ($p = 0.001$).^[23] They also observed that more patients were found to have gastric ulcers in Ramadan, but the difference was not significant ($p = 0.09$).

Frequency of Peptic Ulcer Perforation

Several studies were carried out to evaluate the frequency of peptic ulcer perforation (PUP) in Ramadan. Most of these studies showed that the frequency of PUP is increased during Ramadan,^[3,9,11,24] and only one study has reported that frequency of PUP is lower in

Ramadan, compared to the following Hijri month.^[9] Donderici reported that peptic ulcer complications are more frequent during Ramadan compared to periods before and after.^[25] Peptic ulcer perforation and duodenal ulcer perforation were significantly more frequent during Ramadan, compared to periods before and after Ramadan ($p < 0.01$).

Frequency of Duodenal Ulcer Perforation (DUP)

Of three studies, two reported an increase,^[25,26] and one reported no change^[27] in the frequency of DUP in Ramadan.

Inflammatory Bowel Diseases

Only one study was found evaluating the severity of symptoms in IBD patients before and after Ramadan, and it had suggested that Ramadan fasting does not impose serious risks on IBD patients.^[10]

Acute Upper GI Bleeding frequency, causes and prognosis

Donderici et al. reported that among patients with peptic ulcer complications, the ratio of patients with acute upper GI bleeding (AUGIB) was significantly higher during Ramadan compared with the months before Ramadan ($0.05 > p > 0.01$), but the same difference after Ramadan had no statistical significance.^[25]

Emami et al. compared the causes of AUGIB (DU, erosive gastritis, gastric ulcer, esophageal varices, Mallory-Weiss, obscure AUGIB, and other causes) in fasting and non-fasting patients, and found no correlation between fasting and different causes of AUGIB, except for DU and esophageal varices.^[13] DU was more frequent in the fasting group and the frequency of esophageal varices was significantly higher in the non-fasting group. In this study patients were also compared in terms of the outcome of AUGIB. Rebleeding in hospital, need for surgery, mean volume of infused packed cell, mean number of days in hospital, and mortality rates were compared. Both groups were similar and no statistically significant difference was detected, except for mortality: the mortality rate was higher in the non-fasting group (12.5% vs. 3.7%, $p = 0.016$).

Another study showed that a higher number of patients were diagnosed with AUGIB in Ramadan compared to a non-Ramadan month.^[12] No statistically significant difference was found between the two groups regarding the outcome of AUGIB (admission to gastroenterology, admission to CU, discharge, and admission to general surgery). In addition, this study reported a

higher frequency of DU, esophageal varices and gastric ulcers in AUGIB patients during Ramadan ($p < 0.05$).

Other findings

Studies also showed an increase in primary small bowel volvulus,^[28] hyperemesis gravidarum,^[29] and acute mesenteric ischemia,^[3] and a decrease in admission of patients with idiopathic intussusception^[30] during Ramadan.

DISCUSSION

Our systematic review demonstrated that fasting is generally safe for healthy individuals, but might be hazardous to patients with certain GI diseases and could increase the risk of complications in this group.

The findings regarding the effect of Ramadan on the incidence of acute appendicitis are inconsistent. In two of the studies only patients aged 15 to 70 years were included, since children are exempt from fasting and the elderly might be unable to fast and are therefore also exempt.^[14,15] However, this was not taken into consideration in the third study.^[16] The three studies were all retrospective studies.

Although, the findings of both cohort studies evaluating the effect of fasting on PUD patients on H₂-blocker treatment were in agreement, both studies had some limitations.^[17,18] In both studies, all of the patients in the non-fasting group took the prescribed drug regularly, while 14.03% and 21.73% of the patients in the fasting group were drug defaulters in the first and the second study, respectively. The authors of the first study also stated that the small sample size was another limitation of their study.^[17]

DU ulcer healing in patients receiving Omeprazole, a proton pump inhibitor drug, seems to not be negatively affected by fasting.^[19,20] Mehrabian et al. explain that the use of proton pump inhibitors and Helicobacter pylori eradication play an important role in the treatment of DU, and patients under treatment can fast and will not face an increased risk of complications.^[20]

It has even been claimed that long-term hunger may contribute to healing of persistent ulcers by improving the control of stomach secretion.^[31]

Healthy individuals only experience minor GI symptoms and no serious complication has been reported. Individuals having a light meal like breakfast for Sahur were not significantly different from those

having a large meal, in terms of incidence of GI symptoms. Fasting women tended to be affected by GI symptoms more than fasting men.^[21]

In the two studies evaluating the incidence of PUD, the number of patients presenting with PUD was higher in the month after Ramadan compared to that of Ramadan.^[9,22]

Experiments carried out with rats have definitely shown ulcer-forming effects of long-term hunger.^[32-34] In animal studies, the ulcer inducing effect of long-term hunger was mostly related to the weakening of the defense mechanisms, especially by reducing the volume of the mucus.^[33] The fact that drinking of water is also prohibited from dawn to sunset during fasting may cause weakening of another defense factor by leading to dehydration.^[25]

It has been reported that in humans, the 24-hour mean gastric pH decreases after the 10th day of fasting. This decrease could contribute to aggravation of PUD in patients. Moreover, the increase in gastric acidity was observed during the day (i.e. fasting hours), which suggests giving antiulcer drugs as late as possible at night during Ramadan in fasting patients.^[35]

The majority of studies show that PPU in general and DUP in particular, increase during Ramadan. All of the studies on this matter were retrospective. In one study, it was reported that in the group of patients with PPU, In one study, it was reported that in the group of patients with PPU, the average age of women was higher during Ramadan ($p < 0.01$), while the average age of men was significantly lower during Ramadan ($0.05 > p > 0.01$), both compared to the average ages in periods before and after Ramadan.^[25]

Tavakkoli et al. reported that although fasting imposes physiological stress on the body, it does not have a significant deteriorating effect on IBD patients in remission. They suggested that IBD patients who were in remission and on maintenance therapy with no comorbidities, might fast. However, the sample size of the study was small and there were limitations in data collection, as the authors stated.^[10]

AUGIB was shown to be more frequent during Ramadan but no statistically significant difference was found between fasting and non-fasting patients regarding the outcome of AUGIB. Although, one study found a lower mortality rate in the fasting group, authors explained that the difference might be due to the younger age in this group; patients in the non-fasting group

were older, since the elderly are more likely to be unable to fast.^[13]

Findings on the increase in primary small bowel volvulus,^[28] mesenteric ischemia,^[3] and hyperemesis gravidarum,^[29] and the decrease in idiopathic intussusception^[30] remain to be investigated more, before a definitive conclusion can be made.

Studies show that generally, people with various diseases are at a higher risk of complications due to Ramadan fasting. This might be in part because patients' compliance with medication therapy drastically decreases during Ramadan. This is a matter of significance especially since patients with chronic diseases often insist on fasting, even though they are not permitted to by the Islamic rules. These patients tend to change the intake time and dosing of drugs arbitrarily and without taking medical advice.^[36]

Given that a high percentage of the society struggles with GI diseases, and considering that a reported number of approximately one billion Muslims partake in the fast of Ramadan each year,^[37] the importance of conducting studies to evaluate the GI effects of Ramadan fasting is abundantly clear. To draw a definitive conclusion, further studies with larger sample size are required. Moreover, studies on some prevalent GI disorders, such as the functional GI disorders, are lacking and such studies are recommended to be conducted in the future.

In addition, this review provides background knowledge for the Ramadan track of The Study on the Epidemiology of Psychological, Alimentary Health and Nutrition (SEPAHAN).^[38] The data of this study will estimate the impact of Ramadan fasting on common GI symptoms alteration that will be published later by the same study group.

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