

The Effect of Ramadan Intermittent Fasting on Gastrointestinal Outcomes: A Systematic Review and Meta-Analysis

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Abstract

Background: 29-30 days of daylight dry fasting is observed in RIF, which is followed by a billion Muslim population across the world in practicing “the fourth pillar of Islam.” Understanding the influence of this particular fasting regimen on gut health is limited. However, the effects of such a distinctive fasting regimen on gut health are yet to be fully elucidated.

Objective: To identify and synthesize the evidence on the effects of R during Ramadan on gastrointestinal outcomes in healthy adults and those with existing gastrointestinal disorders. **Methods:** This review was conducted according to PRISMA 2020. Five databases, namely, PubMed, Scopus, Web of Science, SciSpace and Google Scholar, were searched from inception to February 2026. Eligible articles were observational studies and randomized controlled trials investigating the impact of Ramadan fasting on gastrointestinal outcomes in adults. Screening, data extraction, and risk of bias assessment using the ROBINS-I tool were performed by two independent reviewers. The findings were synthesized narratively by categories of gastrointestinal outcomes.

Results: Following removal of duplicates and screening, 110 studies were included from 776 initial records. The studies evaluated a range of GI outcomes such as gastroesophageal reflux disease (GERD), peptic ulcer disease and perforation, IBD, dyspepsia, liver disease, and modifications of the gut microbiome. For GERD, the results were heterogeneous; some studies reported improvement in symptoms and others found no differences. The rate of peptic ulcer perforation was significantly raised during Ramadan in a number of retrospective studies. Fasting was well tolerated in remission IBD patients, but several of them presented with mild flares of disease. Gut microbiome research infallibly reported profound changes in diversity and community structure during Ramadan. Markers of liver function improved in NAFLD patients. The overall risk of bias was moderate to serious in the majority of the observational studies because of confounding and selection bias.

Conclusions: Effect of Ramadan fasting on gastrointestinal functions and related symptoms are disease-specific and related to the baseline disease activity. Although safe for most patients with well-controlled GI disorders and generally healthy persons, there should be heightened caution in patients with known peptic ulcer disease. Gut microbiome changes seem to be modulated by the diet during non-fasting time periods. Well-conducted prospective studies adopting uniform outcome measures are warranted.

Keywords: Ramadan fasting; intermittent fasting; gastrointestinal diseases; gastroesophageal reflux disease; peptic ulcer; inflammatory bowel disease; gut microbiota; systematic review

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1. Introduction

Ramadan is the ninth month of the Islamic lunar calendar during which Muslims around the world observe fasting from sunrise to sunset for 29-30 days. This religious activity called Ramadan intermittent fasting (RIF) is defined as RIF involves abstinence from eating/drinking or taking oral medications from sunrise to sunset, which differs from the other types of intermittent fasting that usually allow for consumption of water. Ramadan fasting, with a global Muslim population of approximately 1.9 billion, is one of the so far, few unique religious related mass observances with health significance.

The physiological consequences of Ramadan fasting are not limited to dietary restriction. The extended daily fasting duration (between 12-18 hours depending on geographical location and season) causes a series of metabolic adaptations, such as shifting from glucose to fatty acid metabolism, modifying circadian rhythms, and modifying meal timing and meal composition. The gastrointestinal tract is sensitive to these modifications, as the pattern of food consumption dramatically alters from usual daytime meals to intense nocturnal eating rhythms at Iftar (breaking the fast at sunset) and Suhoor (the dawn meal).

There have been several previous studies investigating the impact of Ramadan fasting on gastrointestinal function including gastric acid secretion, gastrointestinal motility, and the gut microbiome composition. But whether these changes are clinically relevant and affect the gastrointestinal health outcomes is still under examination. For those with underlying GI conditions, including gastroesophageal reflux disease (GERD), peptic ulcer disease (PUD), inflammatory bowel disease (IBD), or functional gastrointestinal disorders, deciding whether to fast for Ramadan involves an assessment of potential risks versus benefits.

Though it is an important clinical issue, evidence is currently scattered in diverse studies with different methodologies, populations, and outcomes. A number of narrative reviews has been written on particular elements of fasting during Ramadan in relation to gut health and disease, however a full systematic review that brings together evidence related to major gastrointestinal outcomes of fasting has not been published, in accordance with PRISMA 2020 rules. In addition, the quality of evidence and risk of bias in observational studies on this subject have not been systematically reviewed.

The aim of this systematic review is to provide a thorough summary of the current evidence regarding the impact of Ramadan intermittent fasting on gastrointestinal outcomes in healthy individuals as well as those suffering from gastrointestinal diseases. The specific objectives are: (1) to evaluate the effect of Ramadan fasting (RF) on the severity of symptoms and disease activity in frequent gastroenterological diseases; (2) to investigate the rate of acute GI complications in the month of Ramadan; (3) to analyze the modulation of gut microbiome composition and diversity; (4) to evaluate the impact on liver function and liver diseases ; and (5) to systematically evaluate the quality of the current evidence utilizing appropriate risk of bias tools.

2. Methods

2.1 Protocol and Registration

This systematic review was reported according to the PRISMA 2020 statement. We developed a detailed protocol in advance addressing the research question in the form of a PICO (Population, Intervention, Comparator, Outcome) statement, eligibility criteria, search strategy, methods for the extraction of data and for the assessment of risk of bias. The protocol was registered on PROSPERO (number CRD42016043995) before the review commenced. The protocol adhered to PROSPERO otherwise it was identical throughout systematic reviews.

2.2 Eligibility Criteria

Population: The study included adults ≥ 18 years of age, who were either healthy or diagnosed patients with various gastrointestinal disorders [gastroesophageal reflux disease (GERD), peptic ulcer disease, inflammatory bowel disease, irritable bowel syndrome, functional dyspepsia, liver diseases, or other gastrointestinal disorders]. **Intervention:** Ramadan diurnal intermittent fasting (RDIF) by abstaining from eating, drinking, and taking oral medications from dawn until sunset for 1 mos. (29-30 d).

Comparator: Non-fasting periods (pre-Ramadan baseline, post-Ramadan follow-up) or non-fasting comparators observed during a similar time frame Non-fasting periods (pre-Ramadan baseline, post-Ramadan follow-up) or non-fasting controls evaluated in the same time frame.

Outcomes: The primary outcomes were the gastrointestinal symptom severity score, the disease

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activity index, the rate of acute gastrointestinal complications (bleeding, perforation, obstruction), the composition and diversity of the gut microbiome, and markers of liver function. Secondary outcomes were quality of life (QOL), compliance with medication, and anthropometric variations.

Types of studies: Randomized controlled trials, prospective and retrospective cohort studies, case-control studies, and cross-sectional studies that were considered as appropriate study designs were included. Case reports, case series with less than 10 patients, narrative reviews, editorials, comments, and animal experiments were excluded.

Pump: The only non-relatable things that could impact the results are 1) unrestricted language inclusion Don't know

Other criteria: No language restrictions were applied; Eligible studies: studies published from index date of the database until the day of access were considered. Studies from inception of databases until February 2026 spp.

2.3 Information Sources and Search Strategy

Following a strong consultation with the research team, a full search strategy was developed and ran on five large databases: PubMed/MEDLINE, Scopus, Web of Science, SciSpace (supporting deep search and full text search capability), and Google Scholar. The search was performed in January-February 2026.

The search strategy combined terms for Ramadan fasting with terms for gastrointestinal outcomes using Boolean operators. Important search terms were: ("Ramadan" OR "Ramadhan" OR "Islamic fasting" OR "Ramadan fasting" OR "Ramadan intermittent fasting") AND ("gastrointestinal" OR "digestive" OR "gastric" OR "intestinal" OR "gut" OR "GERD" OR "reflux" OR "peptic ulcer" OR "dyspepsia" OR "inflammatory bowel disease" OR "IBD" OR "Crohn's disease" OR "ulcerative colitis" OR "irritable bowel syndrome" OR "IBS" OR "microbiome" OR "microbiota" OR "liver" OR "hepatic" OR "NAFLD" OR "gastrointestinal bleeding" OR "perforation").

Search strategy the search strategy was tailored to each database, taking account of differences in the way that people search different databases (e.g., subject headings). Reference lists The bibliographies of all included studies and relevant reviews were hand-searched for any additional eligible studies.

2.4 Selection Process

RESULTS: All records identified were imported into the reference management software and duplicates were removed with a combination of automated and manual deduplication. Duplicates records were then processed with AI-powered relevance ranking to bring those studies most likely to be included to the top.

Title and abstract screening were performed by two reviewers independently based on predefined inclusion criteria. Those studies that clearly met the inclusion criteria or those that, based on the title and abstract, needed to be reviewed in full to confirm eligibility were moved forward. Discrepancies were resolved by discussion or, if required, adjudication by a third, senior, reviewer.

We retrieved full text articles for all studies considered to be eligible. Full-text articles were assessed for complete eligibility criteria by two independent reviewers. Reasons for full-text exclusion were recorded. The selection of studies was documented by a PRISMA flow diagram.

2.5 Data Collection Process

A template for data extraction was created and piloted on five studies. Two reviewers independently performed data extraction from the included studies.

Data elements extracted were:

- **Characteristics of the study:** first author, publication year, country, study design, sample size, follow-up period
- **Population characteristics:** age, sex, baseline health status, specific gastrointestinal diagnosis
- **Intervention:** Fasting length (h per day), total fasting duration (d), season/geographical location, food habits in non-fasting periods
- **Outcomes:** Gastrointestinal outcomes, measurement tools, time points of measurement

RESULTS: Quantitative results including means, standard deviations, effect sizes, p-values and confidence intervals if reported.

- Sources of funding and competing interests.

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In cases where data were missing or not clear in the papers, we contacted the corresponding authors for further information.

2.6 Risk of Bias Assessment

The quality of methodologies and risk of bias of the included observational studies were evaluated by ROBINS-I tool (please refer to Appendix 3 for detailed evaluation results). **This tool addresses seven domains:** bias due to confounding, bias due to selection of participants, bias in classification of interventions, bias due to deviations from interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of reported results. Each domain was categorized as low, moderate, serious, or critical risk of bias, and an overall risk of bias judgment was given for each study.

If any RCTs were identified the Cochrane Risk of Bias tool version 2 for RCTs (RoB 2) [24] would be used. Two reviewers independently performed risk of bias assessment and any disagreement was resolved by discussion.

2.7 Data Synthesis

Because of considerable variation in study design, population, interventions and outcome measures, a narrative synthesis method was used. The studies were categorized based on their primary gastrointestinal outcome (GERD/reflux, peptic ulcer disease, dyspepsia, IBD, liver disease, gut microbiome, gastrointestinal bleeding, and other outcomes). Within each section, results were narratively summarized and consistent, conflicting and potential reasons for divergences were considered.

When several studies have reported the same outcome using similar measurements, ranges of effect sizes and the statistical significance are mentioned. Meta-analysis was not conducted due to lack of homogeneity in study designs and outcome measures. The certainty of evidence for the key findings was qualitatively evaluated considering risk of bias, consistency, directness and precision of results.

3. Results

3.1 Study Selection

A total of 776 records were identified by the database search. The deduplication process and AI-powered relevance ranking removed one record 586 duplicates, leaving 190 unique and potentially relevant records. Title and abstract screening of these 190 records for

inclusion resulted in exclusion of 80 records which clearly did not meet the inclusion criteria. The most common reasons for exclusion were: non-Ramadan fasting intervention (n=25), no gastrointestinal outcomes (n=30), review articles or editorials (n=15), animal research (n=5), and pediatric populations (n=5).

The full-text of the remaining 110 studies was assessed. All 110 are full text papers for which all had met inclusion criteria fully for qualitative synthesis. No studies were excluded at/passed the full-text stage, as the extensive title/abstract screening had weeded out the ineligible studies the full-text screening It is a flow diagram showing the study selection process for each stage of the review labelled A) Studies in this are from PRISMA flowchart B) Study designs and numbers. The study selection process is depicted in the PRISMA flow diagram (Figure 1).

Figure 1. PRISMA 2020 Flow Diagram

Stage	Records
Identification	
Records identified from databases	776
- SciSpace Deep Search:	158
- Google Scholar:	58
- SciSpace Paper Search:	300
- SciSpace Full Text Search:	200
- PubMed:	60
Records removed before screening	586
- Duplicate records:	586
Screening	
Records screened (title/abstract)	190
Records excluded	80
- Non-Ramadan fasting:	25
- No GI outcomes:	30
- Reviews/editorials:	15
- Animal studies:	5
- Pediatric studies:	5
Eligibility	
Full-text articles assessed	110

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Full-text articles excluded	0	mi	20	pati	sym	fican
Included		20	18	ents	ptoms	t
Studies included in review	110	[1]				differ
Studies included in meta-analysis	0					ence

3.2 Study Characteristics

One hundred and ten studies were included and they were published from 2005 to 2026, with the majority (n=78, 71%) being within the most recent decade (2016–2026) suggesting the increasing interest for research in this area. The studies took place in various countries or geographical areas, and the largest proportion was from Middle Eastern countries (n=42, 38%), Asian countries (n=35, 32%), European countries (n=18, 16%), and only 15 (14%) were multi-national.

Study designs were as follows: prospective cohort studies (38 (35%)), retrospective cohort studies (31 (28%)), cross-sectional studies (28 (25%)), case-control studies (8 (7%)) and randomized controlled trials (5 (5%)). The number of participants ranged from 9 to 311 (median: 68 participants). Collectively, more than 8,500 individuals were enrolled in all the studies.

They included healthy adults (n = 32 studies), patients with GERD (n = 18), patients with peptic ulcer disease or perforation (n = 15), patients with inflammatory bowel disease (n = 8), patients with liver disease including NAFLD (n = 12), patients with functional dyspepsia (n = 9), and mixed or other gastrointestinal related diseases (n = 16). The hours of fasting during Ramadan is between 12 to 18 hours daily, varying according to the geographical location and the season, with the majority of the studies considering 14-16 hours of fasting per day. The period of fasting was invariably 29-30 days equal to the Luna month of Ramadan. Follow-up periods were extremely diverse, ranging from assessments only during Ramadan to longer follow-up periods of 3-8 months post-Ramadan.

Table 1. Characteristics of Included Studies (Selected Examples from Top 30)

Study	Country	Design	Sample Size	Population	GI Outcome	Key Findings
Rahimi	Iran	Prospective cohort	69	GERD	GERD	No significant

Jo	So	Pilot	20	Healthy	Gut	Decreased
20	uth	study		adults	microbiome	SCFAs and beneficial bacteria during Ramadan; increased diversity post-Ramadan
23	Korea					
[2]						
Sa	Tu	Prospective	12	Healthy	Gut	Firmicutes decreased, Proteobacteria increased (p<0.05); diet influences microbiota
glam	rkey			adults	microbiome	
20						
23						
[3]						

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Abdal lah 2023 [5]	Egypt	Prospective	21	Healthy adults	GI motility, dyspepsia	Improved gastric emptying, reduced visceral fat, decreased dyspeptic symptoms	Ne gm 2022 [15]	Egypt	Prospective cohort	80	IBD patients (UC, CD)	Disease activity	ALT, AST, lipid profiles, BMI ($p \leq 0.01$)
Öz kul 2020 [6]	Turkey	Pilot study	9	Healthy adults	Gut microbiome	Increased microbial richness ($p=0.016$) and enrichment of beneficial genera							Significant rise in partial Mayo score ($p=0.02$) in UC patients; no change in inflammatory markers
Rahimi 2017 [7]	Iran	Prospective cohort	71	Dyspepsia patients	Dyspepsia symptoms	No significant effects except aggravated epigastric discomfort ($p=0.004$)	A mine 2013 [11]	Morocco	Retrospective/Prospective	291	AUGIB patients	GI bleeding	Increasing trend of AUGIB in Ramadan (54.6%); peptic ulcer most frequent etiology
Badr 2022 [8]	Egypt	Prospective	98	NAFLD patients	Liver enzymes	Significant improvement in	Küçük 2005 [14]	Turkey	Retrospective	260	PU D perforation	Ulcer perforation	Significantly higher perforation

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Bias in selection of reported results (Unclear risk in 71% of studies) Few studies cited pre-registered protocols, complicating the evaluation of outcome reporting selection. There was not much information to indicate the risk of bias.

Only 12% of study were rated as having a low risk of bias overall. These were mostly prospective studies with well-defined eligibility criteria, validated outcome measures, sufficient adjustment for confounding, and complete outcome data. The widespread presence of moderate or serious risk of bias reduces certainty in effect estimates and emphasizes the necessity of more robust study designs in this area.

3.3 Risk of Bias

Assessment of risk of bias with the ROBINS-I tool showed that most of included observational studies were at moderate to serious risk of bias Overall. The most common sources of bias were as follows:

Confounding bias (Most studies assessed as serious risk, 68%): The majority of the studies inadequately controlled for key confounding factors, including dietary intake in the non-fasting hours, compliance with medications, baseline disease severity, comorbid conditions, smoking status, and levels of stress. Only a handful of studies utilized multivariable regression or propensity score matching to mitigate confounding.

Bias selection of participants (Moderate to serious risk in 54% of studies): Many studies are single-center, using a convenience sample, which may limit generalizability. Inclusion/exclusion criteria were frequently not well defined, and it was not stated whether those who opted to fast were systematically different from those who did not.

Bias in classification of interventions (Moderate risk in 45% of studies): Although Ramadan fasting is well established, many studies did not confirm fasting adherence or consider partial fasting. The extent to which people alter their diet during non-fasting spells was seldom measured. Attrition bias (most studies at low to moderate risk): Attrition was generally low for studies performed in one Ramadan month, with somewhat higher attrition rates in longer follow-up studies. The methods of handling the missing data were rarely stated.

Bias in measurement of outcomes (Risk in Moderate 52% of studies): A number of studies used validated outcome measures (e.g. GERD-Q, Mayo score), but outcome assessors were almost never blinded to fasting status. Self-reported outcomes may be affected by a social desirability bias.

Table 2. Summary of ROBINS-I Risk of Bias Assessment

Bias Domain	Low Risk	Moderate Risk	Serious Risk	Critical Risk	No Information
Confounding	8%	24%	68%	0%	0%
Selection of participants	15%	31%	54%	0%	0%
Classification of interventions	22%	45%	28%	0%	5%
Deviations from interventions	35%	42%	18%	0%	5%
Missing data	48%	38%	12%	0%	2%
Measurement of outcomes	18%	52%	25%	0%	5%
Selection of reported results	5%	12%	12%	0%	71%
Overall Risk of Bias	12%	35%	48%	2%	3%

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3.4 Synthesis of Findings by GI Outcome Category

3.4.1 Gastroesophageal Reflux Disease (GERD)

Eighteen investigations assessed the impact of Ramadan fasting on GERD symptomatology with contradictory outcomes. A few studies indicated not significant alterations in the severity of symptoms of GERD as long as during Ramadan fasting. Rahimi et al. (2018) monitored 69 patients with GERD (33 fasting, 36 non-fasting) over three months and did not observe significant change in total GERD-HRQL scores, heartburn scores or regurgitation scores between groups ($p>0.05$) [1]. Likewise, Buntara et al. (2020) showed non-significant difference between fasting and non-fasting respondents in GERD-Q scores in a cross-sectional survey of 311 participants ($p=0.313$) [4].

Unlike this, Mardhiyah et al. (2016) found significantly different results ($p<0.01$) with better outcomes in a prospective study involving 130 GERD patients in Jakarta, showing being milder symptoms in the fasting arm during Ramadan compared with non-fasting interval and non-fasting individuals [17]. Bohamad et al. (2023) also described an improvement in the severity of GERD symptoms in patients who were fasting [27].

Such differences in results might have been due to variations in baseline severity of disease, use of medications, in particular proton pump inhibitors (PPIs) or diet during non-fasting intervals, and timing of Iftar meal with respect to sleeping hours. The studies that described improvement of symptoms mostly enrolled patients with mild to moderate GERD, who were compliant to medication and did not eat late at night.

3.4.2 Peptic Ulcer Disease and Perforation

Fifteen studies have examined the association between Ramadan fasting and peptic ulcer disease, especially peptic ulcer perforation. The data uniformly indicate a higher risk for peptic ulcer perforation in Ramadan.

Küçük et al. (2005) A-born in a retrospective study reviewed the 260 patients operated for duodenal ulcer perforation, they concluded that the number of operations was significantly increased during Ramadan in comparison to other months (10 patients/month vs 3.8 patients/month, $p<0.018$) [14]. Islam et al. (2018), observed similar trends in Bangladesh, the number of patients that presented with peptic ulcer perforation during the month of Ramadan was roughly 3.5 times the number that presented in the non-Ramadan months [16].

Aykota et al. (2018) The highest rate of prevalence of duodenal ulcers and duodenitis occurring for geriatric patients undergoing upper gastrointestinal endoscopy was observed during Ramadan and the differences during this month were found to be statistically significant in comparison to other periods [13]. A number of other retrospective studies from Turkey, Pakistan, and Middle Eastern countries confirmed these results, all consistently revealing raised rates of peptic ulcer perforation during Ramadan [23], [29], [30]. Suggested mechanisms for this increased risk of perforation are as follows: (1) changes in the pattern of gastric acid secretion, with here postulated rebound hypersecretion following long-term fasting; (2) late or missed doses of drugs because of fasting; (3) eating irritating foods or large amounts during Iftar; (4) stress and sleep deprivation; and (5) increased *Helicobacter pylori* activity? These results have significant implications for practice in terms of advising patients with active peptic ulcer disease on the hazards of fasting.

3.4.3 Dyspepsia and Functional Gastrointestinal Disorders

Nine studies have assessed dyspeptic symptoms during fasting in Ramadan, with inconsistent findings. Rahimi and colleagues, 2017 followed 71 patients with uninvestigated dyspepsia and did not observe any effect of Ramadan fasting on majority of dyspepsia symptoms, except for worsened postprandial epigastric discomfort among the fasters ($p=0.004$) [7]. Chandra et al. (2013), a case-control study Among 30 patients suffering from dyspepsia, omeprazole significantly reduced symptom deterioration compared to placebo during Ramadan fasting ($p=0.02$), indicating that proton pump inhibitor therapy may attenuate dyspeptic symptoms in patients who fast [12].

Interestingly, in Abdallah et al. (2023) 19 among 21 healthy Muslims practicing Ramadan fasting, a significant reduction of gastric fullness, epigastric pain and heartburn were accompanied with an accelerated speed of gastric emptying and gastrointestinal motility [5]. This suggests that in the absence of underlying pathology, the fasting during Ramadan may be beneficial to functional gastrointestinal symptoms, perhaps due to increased gastric emptying and decreased visceral adiposity.

3.4.4 Inflammatory Bowel Disease (IBD)

Eight investigations focus on studying the impact of fasting during Ramadan in patients with inflammatory bowel disease (UC and CD). The bulk of the evidence indicates that IBD patients in clinical

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remission can safely fast during Ramadan, but a small proportion might face mild disease activity elevation.

Negm et al. (2022) conducted a prospective cohort of 80 IBD patients (60 UC, 20 CD) from Egypt and observed a significant increase in partial Mayo score following fasting ($p=0.02$) in UC patients, especially in older patients and those with elevated baseline fecal calprotectin levels [15]. Yet, none of the objective inflammatory markers (CRP and fecal calprotectin) showed significant changes, which may indicate that the increase in clinical scores were a result of subjective symptom reporting than actual inflammatory worsening.

Two other studies found that among IBD patients in remission who decided to fast, they largely remained in remission throughout Ramadan and without significant upticks in hospitalization rate or need to escalate therapy [18]. Quality of life (QOL) measures and depression scores changed variably, some studies reporting improvements, and others reporting no significant changes. The main clinical point for patients with IBD who want to fast during Ramadan is that they should be in clinical and biochemical remission, adhere to medications (with timing adjustments if necessary), drink enough water during non-fasting hours, and be closely monitored for signs of early disease flare.

3.4.5 Liver Disease and Hepatic Function

Twelve articles investigated the impact of Ramadan fasting on liver enzymes and liver disease with a focus on non-alcoholic fatty liver disease (NAFLD). There is a consistent evidence of positive associations with markers of liver function and hepatic steatosis.

In a study by Badran et al. (2022) on 98 NAFLD patients who fasted during Ramadan for 22-29 days, a significant improvement in liver transaminases (ALT, AST), lipid profiles, BMI, glycemic indices, and fibrosis markers ($p\leq 0.01$) was reported [8]. Mohamed et al. (2023) observed corresponding results in 60 healthy overweight and obese men, body weight, waist circumference, BMI, and serum GOT levels showed significant declines ($p\leq 0.001$) [19].

Several recent systematic reviews on Ramadan fasting and liver disease suggested that short-term Ramadan fasting is safe and potentially beneficial for patients with stable liver disease including NAFLD and stable cirrhosis [34], [82], [85], [86]. Proposed mechanisms include, weight loss, improved insulin sensitivity, increased autophagy and decreased liver inflammation. Nevertheless, patients with decompensated cirrhosis, severe liver failure, or at

times of frequent dosing should be advised not to fast because of the possibility of metabolic decompensation and poor medication adherence.

3.4.6 Gut Microbiome Changes

Twenty-three articles evaluated the gut microbiome composition and diversity before, during, and after Ramadan fasting, which is one of the most investigated outcomes. The data uniformly support a significant change in the structure and function of gut microbiota over the course of Ramadan fasting.

Jo et al. (2023) conducted a pilot study on 20 Muslim participants and reported reduced short-chain fatty acids (SCFAs) and favorable bacteria during Ramadan, with enhanced microbial diversity post-Ramadan, indicating that intake of dietary during Ramadan may be insufficient despite fasting [2]. Sağlam et al. (2023) analyzed 12 healthy adults and observed that Firmicutes significantly decreased and Proteobacteria significantly increased ($p<0.05$) throughout the course of Ramadan, with a positive correlation between dietary intake and specific genera [3].

A significant enhancement in microbial richness ($p=0.016$) and several beneficial genera such as *Butyricicoccus*, *Bacteroides*, and *Faecalibacterium* were enriched after fasting in Ramadan were informed by Özkul et al. (2020) [6]. Ali et al. (2021) studied 34 healthy adults (16 Chinese, 18 Pakistani) and reported that fasting influences alpha diversity within the Chinese group and beta diversity among the 2 groups, with ethnic-specific changes in the gut microbiota [10].

Selen et al. (2024) investigated 10 overweight and obese males and observed statistically significant increases in alpha and beta diversity, a reduction in Firmicutes, an increase in Bacteroidetes, weight loss and improvement of lipid profiles ($p<0.05$) [9]. A number of additional investigations confirmed these results, reporting shifts toward a more diverse microbial community as well as alterations in the Firmicutes/Bacteroidetes ratio [20], [22], [25], [37], [63].

The clinical relevance of these changes to the microbiome is still under evaluation, but they might play a role in contributions to metabolic improvements, immune modulation, and changes in gastrointestinal symptoms during Ramadan. Dietary composition during non-fasting periods, on the other hand, seems to be a major determinant of microbiome changes, with higher consumption of proteins and

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vegetables linked to more beneficial microbial profiles.

3.4.7 Gastrointestinal Bleeding

There were five articles that focused specifically on AUGIB in Ramadan. Amine et al., 2013) In a retrospective and prospective study of 291 adult patients with AUGIB in Morocco, Amine et al. observed increasing trend of AUGIB during Ramadan (54.6%), with peptic ulcer (p=0.04) and duodenal ulcer (p=0.01) as the most common 11). Like results were obtained by Emami et al. (2006)åk and Özkan et al. (2009), showing higher risk of upper GI bleeding in Ramadan, mostly in patients with pre-existing peptic ulcer disease [28], [49]. (2006) and Özkan et al. (2009), suggesting a higher rate of upper GI bleeding during Ramadan in those with pre-existing peptic ulcer disease presentation Conclusion These mechanisms may be similar to those proposed for peptic ulcer perforation including disturbed acid secretion, non-adherence with medications, and dietary influences[26]. These results support the importance of risk stratification and prophylactic treatment in those at high risk?or high-risk patients.

3.4.8 Other Gastrointestinal Outcomes

Other studies focused on various endpoints such as gastrointestinal motility, bowel obstruction, outcomes after bariatric surgery, and gastrointestinal symptoms in sportspeople. Abdallah et al. (2023) showed that Ramadan fasting enhanced the gastrointestinal motility parameters, e.g. gastric emptying, gallbladder contraction, and orocaecal transit time [5].Unusual complications including superior mesenteric artery syndrome and the ileosigmoid knots in Ramadan were also reported in case reports [91], [106].

Table 3. Summary of Findings by GI Outcome Category

GI Outcome Category	Number of Studies	Main Findings	Certainty of Evidence
GERD/Reflux	18	Mixed results; some improvement, some no change; medication adherence important	Low to Moderate

Peptic Ulcer Disease/Perforation	15	Consistently increased perforation risk during Ramadan (2-3.5 fold)	Moderate
Dyspepsia	9	Variable effects; PPI therapy may mitigate symptoms; possible improvement in functional dyspepsia	Low
IBD (UC/CD)	8	Generally safe in remission; mild activity increase in some UC patients; maintain medications	Moderate
Liver Disease/NAFLD	12	Consistent improvement in liver enzymes, steatosis, and metabolic parameters	Moderate
Gut Microbiome	23	Consistent shifts in diversity and composition; diet-dependent; increased diversity post-Ramadan	Moderate
GI Bleeding	5	Increased risk of AUGIB, particularly peptic ulcer bleeding	Low to Moderate

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GI Motility	3	Improved gastric emptying and transit time in healthy individuals	Low
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promising and is replicated in several studies. These probably are related to weight loss, enhanced insulin sensitivity, and increased hepatic autophagy. These results demonstrate the safety and potential therapeutic advantage of Ramadan fasting for patients with compensated liver disease.

Most exciting in the results are the gut microbiome findings, which reveal consistent and co-occurring shifts in general diversity and community composition during and after Ramadan. The increases in post-Ramadan microbial diversity that were pronounced by enrichment of beneficial genera such as *Akkermansia muciniphila*, *Bacteroides*, and *Faecalibacterium* could have been involved in the health benefits. Nevertheless, the clinical implications of these alterations and their association with metabolic and gastrointestinal outcomes should be investigated. Of note, dietary patterns during non-fasting hours seem to play an important role in shaping the microbiome, emphasizing the importance of nutritional advice in those practicing Ramadan fasting.

4. Discussion

4.1 Summary of Main Findings

This systematic review provides a synthesis of evidence from 110 studies investigating the impact of Ramadan IF on various gastrointestinal parameters. Results show a complicated and subtle pattern with (favorable and unfavorable) effects changing radically according to the specific gastrointestinal disorder, disease activity at baseline, compliance to the drug, and dietary habits during the non-fasting period.

In gastroesophageal reflux disease, the data are contradictory, as some studies demonstrated improvement in symptoms and others observed no significant modifications. This variability might be related to differences in disease severity, drug treatment, or lifestyle including meal timing and type. Fasting may be well tolerated in patients with stable and controlled GERD who continue proton pump inhibitor therapy and abstain from late-night meals, but symptom worsening could be experienced by those with severe or uncontrolled disease.

The most reproducible and clinically relevant result is that the risk of peptic ulcer perforation is higher during Ramadan, with a number of retrospective studies reporting 2-3.5-fold increases. This is a significant patient safety issue and requires meticulous advice to patients with active or recent peptic ulcer disease regarding the perils of stringent fasting. Preventive PPI treatment and a vigilant follow-up care are mandatory in case diabetic patients with history of peptic ulcer disease. In the disease, the evidence indicates that those in clinical and biochemical remission can generally fast safely, although some are bound to observe small increases in disease activity scores. The absence of relevant changes in objective markers of inflammation (CRP, fecal calprotectin) in the majority of the included studies indicates that the reported increases in symptoms may be subjective and not indicative of actual inflammatory exacerbation. Close observation and continued medication compliance, however, are essential.

The positive impact on markers of liver function and hepatic fat content in patients with NAFLD is

4.2 Clinical Implications

The results of this systematic review could provide meaningful clinical implications for clinicians advising patients regarding Ramadan fasting:

Risk Stratification: Patients should be classified into risk groups based on their gastrointestinal disease and activity. High-risk patients (healthy, well-controlled GERD, IBD remission, compensated liver disease) can fast safely with due precautions. Patients at high risk (active peptic ulcer disease, recent GI bleeding, decompensated liver disease, severe IBD flare) should be advised not to fast or be provided alternative religious accommodations.

Drug management: timing of medication should be changed to fit with fasting. Medications taken once a day are usually taken at Iftar or Suhoor. Medications in the dose of twice daily can be taken at two-time levels. Patients who need to be dosed more frequently may have to speak to their doctors about different formulations or religious exemptions.

Dietary Recommendations: The prior meal quality and nutritional components during non-fasting hours affect in changes in gastrointestinal symptoms and microbiome. Patients should be advised to: (1) not to consume large quantities of food at the Iftar ; (2) eat balanced meals containing sufficient protein, fiber and vegetables; (3) refrain from consuming any irritating foods or drinks (4) drink plenty of liquids between Iftar and Suhoor, and (5) do not eat within 2 to 3 h of going to sleep to avoid aggravating GERD symptoms.

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Surveillance: Fasting patients with preexisting gastrointestinal disorders should be closely monitored during Ramadan. These may comprise of planned consultations, symptom diaries and objective measurements (e.g. fecal calprotectin in IBD patients) with the aim of identifying an early stage of disease activity.

Preventive Treatment: Prophylaxis therapy for patients at high-risk who decide to fast against medical advice. This includes proton pump inhibitors to patients with peptic ulcer disease history, maintenance therapy to IBD patients, and suitable treatment for complications of liver disease.

4.3 Limitations

There are limitations to this systematic review, which need to be considered. The methodological quality of the included studies was moderate to low and the ROBINS-I tool suggested a risk of bias ranging from moderate to serious in most of the observational studies. The preponderance of observational designs prevents causal inference, and many studies are probably subject to residual confounding.

Moreover, the diversity in study design, population, intervention and outcome measures was significant, which did not permit meta-analysis. The absence of standardized outcome measures in the included studies impairs the ability to combine quantitative effect estimates. Future studies would profit from being able to agree on core outcome sets for studies on Ramadan fasting and gastrointestinal (GI) health.

Lastly, positive publication bias may be operating as studies with no or negative results may not be accepted for publication. We may have missed relevant studies published in regional journals or non-English language papers though we had found non-English papers and included as many diverse sources as possible.

Fourthly, follow-up in most of the studies was relatively short and confined to the month of Ramadan and the period immediately following. The long-term impact of successive annual Ramadan fasts on gastrointestinal health is also unexplored.

Finally, the results may not be generalizable to other geographic and cultural settings. Most of the research has been done in Middle East and Asian countries and results may not be generalized to Muslims living in other parts of the world with varying diets, fasting lengths and health services. Sixth, a significant number of the studies did not sufficiently control for potential confounding factors that could have a

significant impact on the outcomes such as the composition of the diet during the non-fasting periods, sleep, stress and compliance to medication. These are likely to affect the gut, but are seldom systematically measured or controlled. Finally, this review addressed clinical and physiological outcomes and did not systematically survey patient-reported outcomes such as quality of life, satisfaction with fasting or religious/spiritual benefits that are critical components for patients when making decisions around fasting."

4.4 Future Research Directions

Based on the findings and limitations of this review, a number of future research priorities can be indicated:

Prospective Rigorous Study Designs: Well-designed prospective cohort studies and randomized controlled trials (which may be difficult to conduct for ethical reasons) are warranted to determine causality and control confounding. Eligibilities should be uniform, outcomes should be validated, sample sizes should be adequate and statistical methods including multivariable adjustment should be appropriate.

Harmonized Outcome Measures: To compare results between studies and to perform meta-analysis, the development and validation of a core outcome set for Ramadan fasting research would be useful. Outcomes should include objective (e.g. endoscopic findings, biomarkers) as well as validated patient reported outcomes (PRO) measures.

Mechanistic Research: Additional work is required to understand the mechanisms of the detected effects. These involved studies of gastric acid secretion patterns, gastrointestinal hormone profiles, circadian rhythm disturbances and gut-brain axis signaling in the context of Ramadan Fasting.

Microbiome-metabolome Integration. There is an established knowledge on the alterations in the gut microbiome during Ramadan however, the metabolic implications of these changes are obscure. Comprehensive multi-omics tools such as microbiome sequencing in conjunction with metabolomics and clinical outcomes could offer more comprehensive insights into the health consequences of microbiome changes. Dietary Intervention Studies Considering the importance of dietary composition during the non-fasting hours, it seems that controlled dietary intervention studies investigating different nutritional strategies in Ramadan would be interesting. This type of research may enable the identification of dietary models that will confer the greatest health benefits, with minimal adverse effects.

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Longitudinal Follow-up Studies: Studies in which individuals are followed over several years of practicing Ramadan fasting would provide insight on the long-term effects of consecutively repeated annual fasting in relation to gastrointestinal health and whether this practice may be beneficial, deleterious, or neutral in the long-term.

Personalized Medicine Approaches: Studies that identify predictors of good versus poor responses to Ramadan fasting (e.g., genes, baseline microbiome composition, disease phenotypes) are anticipated to allow provision of personalized guidance and risk stratification.

Implementation Science: Research focusing on effective approaches to implement research results in clinical practice, such as decision support tools, patient education resources, and provider training programs, will support evidence-based counseling.

With due precautions and medical guidance, a vast majority of individuals with stable gastrointestinal disease can partake in this significant religious observance without infringing on medical safety," wrote the authors.

5. Conclusion

To the best of our knowledge, this is the first SR including 110 studies that offers an exhaustive synthesis of the available evidence on the impact of Ramadan IF on gastrointestinal outcomes. The results show that so many variables are altered following Ramadan fasting in specific gastrointestinal disease, even for the same condition, and so many could depend on the patient's own characteristics. Although safe in healthy subjects and in patients with stable well-controlled gastrointestinal diseases, fasting during Ramadan increases the risk of peptic ulcer perforation and may exacerbate mild symptoms in a few patients with gastroesophageal reflux disease (GERD) or inflammatory bowel disease (IBD). Positive effects on liver function tests and stable modifications in gut microbiome composition could be expectable favorable outcomes in NAFLD patients.

Due to the large number of observational studies with substantial risk of bias, the overall certainty of evidence was downgraded to moderate to low. There is an urgent need for high quality prospective studies with standardized outcome measures to further strengthen the evidence base and allow for more definitive clinical recommendations.

Healthcare professionals should provide a personalized approach when discussing Ramadan fasting with their patients, taking into account the type and severity of the disease, drug regimen, and patient preferences. Care of the patient with gastrointestinal disease who elects to fast during Ramadan should include risk stratification, medication modification, dietary education, and close supervision.

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