The effect of Ramadan and intermittent fasting on the development of *Helicobacter pylori*-induced peptic ulcers

Abstract

A considerable portion of the world's population practices fasting, for religious purposes like Ramadan or to adopt a healthier lifestyle such as intermittent fasting. During this period, individuals undergo metabolic changes that alter their internal environment. The literature was analysed to identify a possible relationship between fasting and the development of *Helicobacter pylori*-induced peptic ulcers. This found that fasting does not affect the incidence of peptic ulcers, and studies that saw an increase in the incidence were not significant. However, remodelling of the gastric environment and increases in concentrations of *H. pylori* were recorded. There is no relationship between fasting and the risk of developing *H. pylori*-induced peptic ulcers, suggesting that individuals with uncomplicated ulcers are not at risk of developing further ulcers and can participate in fasts provided they take the recommended measures.

Key words: Fast; *Helicobacter pylori*; Intermittent fasting; Peptic ulcer; Ramadan

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Introduction

Ramadan refers to a period of prolonged fasting and abstinence from fluids between sunrise and sunset, lasting around 18 hours in the northern hemisphere. It takes place in the ninth month of the Islamic lunar calendar and lasts for 29–30 days. A similar practice is adopted for health reasons known as 'intermittent fasting', where an individual refrains from eating for prolonged periods. This practice is often conducted to maintain a healthy lifestyle in certain communities (Gunnars, 2022). The proposed benefits of these practices include overall weight loss and lowered levels of inflammatory markers such as tumour necrosis factor-alpha (Johnson et al, 2007). The typical intermittent fasting period is said to be 16 hours, followed by an 8-hour eating window in which the participant can break their fast and eat. There are multiple variations, with fasting hours ranging from 6 to 23 hours within a 24-hour period. Unlike Ramadan fasting, this practice allows the consumption of fluids such as water and unsweetened black coffee during the fasting phase. Intermittent fasting can be practiced at any time throughout the day and is typically adopted as a long-term lifestyle change. In contrast, Ramadan fasting is of a shorter timeframe, lasting approximately 1 month. This article primarily concentrates on exploring the effects of fasting during Ramadan.

Peptic ulcers are caused by a tear in the mucosal lining of the stomach, small intestine or oesophageal mucosa. Peptic ulcers are thought to have multiple aetiologies, including *Helicobacter pylori* infection and use of non-steroidal anti-inflammatory drugs (Malik et al, 2023).

H. pylori is a helical, microaerophilic, Gram-negative bacterium. It is found in about half of the world's population, with slightly higher proportions in people in developing countries (Beli et al, 2018). It burrows into the subepithelial space (Amieva and El–Omar, 2008) where it releases proteases, phospholipases and vacuolating cytotoxins, which cause a break in the mucosa, leading to ulcer formation (Smoot, 1997). This led the authors to consider whether altered conditions during the fasted state influence the development of peptic ulcers derived from *H. pylori* infections.

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Method

To better understand the relationship between *H. pylori* and Ramadan fasting, websites, research papers, review articles and reports were identified. Literature was collected via a combined method of Google search and online databases such as NCBI and Google Scholar, using key words 'H. pylori', 'Ulcer', 'Intermittent fasting', 'Ramadan fasting', 'Microbiota' and 'Gut microbiome'.

The literature was then selected based on criteria including whether it contained one or more of the key words listed above, relevance to the question at hand, and whether it had been published within the last 30 years. Numerous articles were rejected because they did not meet these criteria.

When reviewing each article, reading each piece thoroughly and understanding the key concepts was a top priority. Relevant data, including the author, publication year and relevant findings, were extracted from the literature and methodically arranged. These findings were analysed to identify themes and gaps in current literature, and the implications, limitations and potential directions for future research.

Discussion

Physiological changes during fasts

Depending on the length of the fast period, a number of physiological changes can occur within the body. A decrease in insulin production during a fasting period is believed to increase the metabolism of fat, which is consistent with the expected result of weight loss during intermittent fasting (Hoddy et al, 2016).

Other cellular changes that occur during Ramadan fasts include decreased levels of low density lipoproteins and fasted plasma glucose levels, which have cardioprotective effects (Patterson and Sears, 2017). Fasting results in a lower heart rate, and lower systolic and diastolic blood pressure, which reduces the occurrence of cardiovascular disease (Lee et al, 2020).

Changes within the gastrointestinal system

A significant number of changes occur within the gastrointestinal system during a prolonged fast. Levels of gastric acid secretion tend to decrease during a fast, and this less acidic environment favours increased growth of *H. pylori* (Johnston and Wormsley, 2007). However, during religious fasting periods such as Ramadan, there is an increase in gastric acid and pepsin production after the fasting period is completed. Johnston and Wormsley's study, which replicated an intermittent fasting approach, did not observe this phenomenon. This could imply that peptic ulcers can occur independently of *H. pylori*, as increasing gastric acid does not promote bacterial growth and mucosal harm can be explained by the increase in acid production (Hakkou et al, 1994).

The composition of the gut microbiota varies during periods of extended fasting, such as time-restricted fasting and alternate-day fasting, which leads to the proliferation of microorganisms, such as *Shigella* and *Escherichia coli*, which have been linked to inflammatory conditions in the gut and can facilitate changes with probiotic colonies such as *Eubacterium*. This strongly suggests a link between the remodelling of the gut microbiome and individuals participating in intermittent fasting (Zhang et al, 2020). These changes to the gut microbiota composition could lead to an increased presence of *H. pylori*, potentially raising the susceptibility to ulcer development.

Favourable environment for *Helicobacter pylori*

H. pylori usually infects the stomach, typically the antrum, where it can lead to peptic ulcer development. The bacterium prefers pH values close to neutral (pH 7), but the conditions within the stomach are closer to a pH of 1.5–3.5 (Sachs et al, 2011). *H. pylori* has undergone different adaptations, such as urease production, morphology and chemotaxis, to survive.

The gastric juices contain urea, which is harmful to *H. pylori*, so it stimulates the production of urease, which degrades urea, causing bicarbonate production and neutralisation of stomach acid and allowing *H. pylori* to survive (Sachs et al, 2011). The morphology of *H. pylori* is beneficial, as the combination of the helical shape and propulsive flagella

allow the bacterium to move from an area of acidity (within the lumen of the stomach) to an area of higher pH (within the gastric epithelium) (Sachs et al, 2011). *H. pylori* possesses chemotaxic properties, as they typically propel toward the potassium carbonate and sodium carbonate produced by the gastric epithelium – a more neutral territory, which is conducive to proliferation (Ansari and Yamaoka, 2017).

These factors create an environment where there is decreased production of gastric mucus (hence increased susceptibility to adherence to the gastric epithelium) and of duodenal bicarbonate. These are facilitated by *H. pylori* infection and increase the likelihood of peptic ulcer formation.

Frequency of peptic ulcer formation during fasts

The frequency of ulcer formation in fasted individuals would help to identify if there is a correlation between fasting and ulcer formation and to determine if *H. pylori* has an influence on ulcer development. Research indicates that a significant increase in the number of peptic ulcers, specifically duodenal ulcers, occurs during Ramadan (Gokakin et al, 2012).

This suggests that there may be an increase in formation of ulcers as a result of the fasted state, but ignores other factors. The most important is the number of people infected with *H. pylori*, as this explains why the ulcers form rather than just the frequency of the peptic ulcers.

Bener et al (2006) showed that the number of ulcer cases does not significantly increase during Ramadan or the month after, but the risk of perforation does increase after the Ramadan period. This is contrary to the idea that fasting carries a possible risk of ulcer formation. However, the same study concluded that the risk of increased perforations during the month after Ramadan can be explained by the age-dependent increase in *H. pylori* infection in those over 50 years old (50%) and 70 years old (75%) (Bener et al, 2006). This may indicate that a certain group is more significantly affected by *H. pylori*-induced peptic ulcer formation and perforation during periods of extended fasts. This study was conducted during Ramadan, and the individuals would not be undergoing the same conditions as intermittent fasting as there would be no consumption of liquids. The post-fast meal would also be more nutritionally dense than usual (Mahboob et al, 1999). This increased risk of perforation was concluded to be caused by *H. pylori* infection.

Change of diet and *Helicobacter pylori*

Diet is said to have a significant role in the development of *H. pylori* infection, and subsequent complications are said to be linked to the ingestion of certain foods.

Certain dietary patterns can promote the colonisation of *H. pylori*, such as a high salt diet that causes disruption of the gastric mucosa and allows infection. Depleted iron levels as a result of reduced dietary intake or bleeding have also been associated with increased rates of *H. pylori* infection, as iron is essential for its growth (Haley and Gaddy, 2016). This indicates that the foods used to break the fast could have an influence on the increased rate of infection and ulcer formation.

Sulphur-rich foods, such as cruciferous vegetables, have gastroprotective properties against *H. pylori*. They reduce oxidative stress on the gastric mucosa, limiting the ability of *H. pylori* to colonise. Other foods may be protective against *H. pylori* infection, such as whole grains, mushrooms, roots and tubers, because of their probiotic and anti-inflammatory properties. This helps to maintain a healthy microbiome and decreases the risk of *H. pylori* infection (Rueda-Robles et al, 2021). *Streptococcus*, *Lactobacillus* and pathogenic bacteria like *H. pylori* are the most common bacteria found in the stomach (Willey et al, 2013). There is a symbiosis between them, and they support the immune system by breaking down dietary toxins (Harvard TH Chan School of Public Health, 2019).

The composition of the microbiome differs between individuals. When a controlling factor is altered, it can lead to dysbiosis and the proliferation of pathogenic species such as *H. pylori*. Dysbiosis can be influenced by Ramadan. Studies have shown that during this period, there is a significant change in the composition of gastrointestinal flora (Ozkul et al, 2020).

However, a study that investigated microbiota and intermittent fasting found no significant increase in diversity within the microbiome under the fasting schedule (Johnson et al, 2007), which differs from the findings of Ozkul et al (2020). This study also reported alterations in the microbiome during the fasted period, suggesting a certain degree of influence on the gut flora.

Studies have also investigated how the diversity of gastric flora decreases during an active *H. pylori* infection (Li et al, 2017). This could indicate how levels of *H. pylori* colonisation are influenced by changes in the microbiome.

Effect of fasting on *Helicobacter pylori* infection and development of peptic ulcer

Reduces levels of *Helicobacter pylori*

Hakkou et al (1994) found a 159% increase in levels of gastric acid production during Ramadan. Although this has not been shown to directly lower *H. pylori* levels, it provides a less favourable environment which could reduce the overall risk of infection with *H. pylori* during Ramadan. However, there is an increase in dyspeptic symptoms, which may be caused by peptic ulcers or have other aetiologies such as acid reflux, so a direct link cannot be made between *H. pylori* levels and peptic ulcer formation (Hakkou et al, 1994). The symptoms stopped after Ramadan, so they may be explained by increased levels of stomach acid during this period rather than *H. pylori* infection.

Helicobacter pylori levels are unaffected

Bener et al (2006) found increased levels of peptic ulcer perforation after Ramadan. However, when the levels of *H. pylori* were measured via endoscopy, there was no significant difference in the colonisation of *H. pylori* between samples taken during Ramadan vs 1 month after Ramadan. This shows that there is not a significant correlation between *H. pylori* and peptic ulcer formation, especially during Ramadan. This study has certain limitations, such as the inclusion of both diabetic and non-diabetic patients. As the majority of the general population does not have diabetes, the findings may not be applicable to the broader population. The increased risk of ulcer perforation was only seen after the fasting period, and only in compromised individuals over the age of 50 years and patients with diabetes (Bener et al, 2006). While these findings can be informative in predicting complications among diabetic patients, they cannot be generalised.

Increases levels of *Helicobacter pylori*

H. pylori was more prevalent in individuals taking part in Ramadan fasting than a group who were not (10% non-Ramadan vs 15% Ramadan) (Bdioui et al, 2012). This may indicate that conditions within the individual are preferential for *H. pylori* infection during the Ramadan period, although the difference was not statistically significant.

The effect of Ramadan fasting on *H. pylori*-induced peptic ulcers appears to be correlated but not significantly so. Studies such as Zhang et al (2020) and Ozkul et al (2020) support the idea that fasting causes changes within the body, such as remodelling of the gut microbiome, and the frequency of peptic ulcers was seen to increase during Ramadan.

Higher concentrations of *H. pylori* were found during Ramadan, possibly explaining the increase in formation of peptic ulcers. *H. pylori* is more prevalent in certain groups, such as older people, which would lead to increased rates of peptic ulcer perforation (Bener et al, 2006).

Ramadan is conducted in many different ways around the world, with variables in the hours fasted and food eaten when breaking the fast. Other factors include differences in ethnicity, age and gender, which affect the generalisability of the results. Some research was conducted in the United Arab Emirates (Bener et al, 2006), while other studies took place in Turkey (Gokakin et al, 2012) and Scotland (Johnston and Wormsley, 2007). The number of hours fasted varied depending on the country, eg 14 hours in Saudi Arabia and 16 hours in the UK, because they are linked to the hours of daylight (Shehu, 2022). The differences in culture and practices across the world mean that an overall conclusion cannot be made because of these uncontrolled variables.

Comparisons have been made between Ramadan (Ozkul et al, 2020) and intermittent fasting (Johnson et al, 2007; Lee et al, 2020), which are two different practices, decreasing the validity of the conclusions. The lack of statistical significance in many of the studies affects the validity of the conclusions that can be drawn from comparing them. It is not possible to understand the real-life implications without further investigation.

Conclusions

The incidence of peptic ulcers, particularly duodenal ulcers, is significantly higher during the post-Ramadan fasting period. Most of the literature shows no significant increase in incidence during Ramadan. Other factors, such as co-infection with *H. pylori*, have a stronger influence on ulcer formation during the fast, and this is a significant risk factor for other gastrointestinal symptoms such as ulcer perforation.

There is insufficient evidence to determine whether *H. pylori* infection during Ramadan fasting increases rates of ulcer formation and can be linked to other factors, such as increased gastric acid secretion. The classification of the ulcer determines whether Ramadan participants must take additional treatments or refrain from fasting. Patients with complicated ulcers are advised not to fast, whereas uncomplicated patients can partake in fasting.

The authors believe that no special treatment is required and that patients with epigastric pain should take antisecretory agents such as proton pump inhibitors. Individuals with uncomplicated ulcers are not at increased risk of developing ulcers and can fast as long as they take their prescribed medication. This usually refers to the triple regimen of a proton-pump inhibitor and two antibiotics. Taking precautions when applicable, such as discontinuing the use of non-steroidal anti-inflammatory drugs, bisphosphonates, and corticosteroids, is advisable to promote a faster recovery.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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Key points

- During periods of fasting, both Ramadan and intermittent, metabolic changes occur in the body, an example being a decrease in insulin levels.
- Remodelling of the gut microbiome is seen during periods of fasting.
- *Helicobacter pylori* infections were more prevalent during Ramadan, but there was no significant increase in the incidence of peptic ulcers.
- The incidence rate of ulcer formation increased after the Ramadan fasting period.
- The suitability of participating in Ramadan fasting depends on whether an individual has a uncomplicated or complicated ulcer.

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