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Effect of Khat Chewing on *Helicobacter pylori* Infection Treatment Outcome Following Standard Triple Therapy: A Single-Center Study in Sana'a City, Yemen

Hind F. A. Al-Sanabani[1,*], Butheina A. A. Al-Amrani[2]

[1] Department of Pharmacology, Faculty of Pharmacy, University of Science & Technology (USTY), Sana'a, Yemen

[2] Department of Pharmacology, Faculty of Medicine and Health Sciences, University of Science & Technology (USTY), Sana'a, Yemen

* Corresponding author: Email: hendalsanabani17@gmail.com

ABSTRACT

Background: *Helicobacter pylori* infection is a well-established risk factor for gastrointestinal diseases, affecting approximately half of the global population, with higher prevalence rates in developing countries. Chewing khat is a widespread habit in Yemen and has been suggested to affect the outcome of standard triple therapy (STT) for *H. pylori* infection. Therefore, this study aimed to assess the effect of khat chewing on *H. pylori* infection treatment outcome after STT at a single center in Sana'a city, Yemen.

Methods: A single-arm longitudinal study was conducted among 123 *H. pylori*-infected patients at the internal medicine outpatient clinics of the Modern European Hospital in Sana'a, Yemen, from March to September 2024. Infection was confirmed using stool antigen testing, and all participants received STT twice daily for 14 days. Stool samples were collected at baseline and four weeks after completing STT to assess the cure rate of *H. pylori* infection. Additionally, the association between khat chewing and the outcome of STT for eradicating *H. pylori* infection was analyzed using the chi-square test, with a significance level set at $P < 0.05$.

Results: Four weeks after completing STT, the overall cure rate was 65.9% (81/123). The cure rates of *H. pylori* infection with STT were 63.5% (40/63) among khat chewers and 68.3% (41/60) among khat non-chewers. However, no statistically significant association was found between khat chewing and the outcome of STT for *H. pylori* infection (P = 0.571).

Conclusion: Approximately two-thirds of *H. pylori* infections among Yemeni patients can be successfully eradicated using STT. However, its effectiveness needs to be evaluated across different regions of Yemen. Furthermore, khat chewing appears to have no impact on the outcome of STT, highlighting the need for further studies to explore other factors that may influence the success of STT in treating *H. pylori* infection.

Keywords: *Helicobacter pylori* ▪Khat chewing ▪ Standard triple therapy ▪ Yemen

1. Introduction

Helicobacter pylori is a major cause of gastritis, peptic ulcers, gastric adenocarcinoma, and primary gastric lymphoma in industrialized and developing nations.[1]

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It is estimated to infect at least 50% of the global population, but its burden is highest in economically disadvantaged nations.[1] *H. pylori* primarily colonizes the lower part of the human stomach mucosa.[2] *H. pylori* produces urease that lowers stomach acidity and makes the stomach a more favorable habitat for *H. pylori* by converting urea into ammonia.[3] While infection rates differ across countries, poor nations have greater infection rates than developed nations. However, up to 85% of individuals infected with *H. pylori* do not exhibit any symptoms or consequences.[4]

The diagnosis of *H. pylori* infection relies on a variety of invasive endoscopy-based and non-invasive methods such as serological testing, stool examination, and breath analysis. Their use depends on local availability and patient history.[5] The most commonly used non-invasive techniques are stool antigen detection and urea breath tests. A positive stool antigen test for *H. pylori* indicates an active infection and suggests a persistent infection because of the quick antigen clearance following effective therapy.

Early detection and treatment of *H. pylori* infection are essential to prevent complications.[6] Strong acid suppressants are used in a variety of combinations with antibiotics and/or bismuth subsalicylate to treat *H. pylori*.[5] Since the bactericidal activity of antibiotics depends on antisecretory medicines raising the pH of the stomach, treatment of *H. pylori* infection is based on a combination of antimicrobial and antisecretory medications. Several antimicrobial agents, such as levofloxacin, bismuth subsalicylate, clarithromycin, metronidazole, amoxicillin, tetracycline, and rifabutin, are being used to treat *H. pylori* infections. Proton pump inhibitors (PPIs) are currently the only antisecretory agents in use. Although there are various treatment standards, triple therapy with amoxicillin, clarithromycin, and PPI for 7 to 14 days is frequently used as a first-line treatment, particularly in regions where clarithromycin resistance is low.[7] The success rates of *H. pylori* infection treatment protocols vary primarily due to drug resistance and non-compliance. Furthermore, it is believed that several variables, including age, medication sensitivity, nutrition, alcohol use, smoking habits, and gene polymorphisms, contribute to *H. pylori* eradication rates.[8]

The evergreen shrub *Catha edulis*, a member of the Celastraceae family, is generally referred to as khat. Its leaves have an astringent, somewhat sweet flavor and a strong, fragrant scent.[9] In the Arabian Peninsula and the Horn of Africa, chewing khat has been a custom for centuries. Chemicals structurally linked to amphetamines are released when khat leaves are chewed.[10] Due to its stimulant effects on the central nervous system (CNS), chewing khat is still common.[9] Furthermore, chewing fresh leaves of *C. edulis* is still a common practice with a long history in Yemeni society. Khat is chewed to relieve weariness and for its central stimulating properties.[11] Climate and environmental factors affect the chemical profile of khat leaves. Khat contains a variety of substances, including alkaloids, terpenoids, flavonoids, sterols, glycosides, tannins, amino acids, vitamins, and minerals. Cathinone, the pharmacologically active component of khat, functions similarly to amphetamine in the CNS.[9]

Chewing khat can have numerous adverse effects, including hepatotoxicity, vasoconstriction of the coronary vasculature, increased carotid intima-media thickness, cerebral stroke, and psychoneurological problems.[12] Other consequences include impaired intestinal absorption, delayed stomach emptying, a higher incidence of duodenal ulcers, and increased risk of *H. pylori* infection. Khat has been demonstrated to lower human body weight, decrease appetite, raise leptin levels, and lower blood iron, ferritin, and vitamin levels.[12]

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There is limited published data on the prevalence of *H. pylori* infection among patients with gastritis across various regions of Yemen, as well as on the evaluation of the risk factors associated with the infection.[2, 4, 6, 12, 13] Several studies have revealed a significant association between *H. pylori* infection and khat chewing.[6, 12–14] However, no published studies have assessed the effect of khat chewing on *H. pylori* eradication rates after treatment. Therefore, there is a need to conduct a study to assess the effect of khat on and the eradication rate of *H. pylori*, given the increasing rates of failure to eradicate *H. pylori* infection using the STT. Studies have shown significant reductions in *H. pylori* eradication rates with PPI-based triple therapy, with success rates of 50–70%.[15] This decrease underscores the need to study the factors influencing treatment outcomes to improve the effectiveness of treatment strategies. Therefore, this study aimed to assess the effect of khat chewing on *H. pylori* infection treatment outcome after STT at a single center in Sana'a city, Yemen.

2. Methods

2.1. Study design, population and setting

A single-arm longitudinal study was conducted among *H. pylori*-infected individuals in the internal medicine outpatient clinics at the Modern European Hospital, Sana'a, Yemen from March to September 2024.

This study enrolled patients aged 18 to 65 years who exhibited acute dyspeptic symptoms, such as epigastric pain, heartburn, abdominal pain, bloating, nausea, and/or vomiting, for at least one month and were confirmed for the first time to be infected with *H. pylori* using stool antigen tests.[17, 18] Excluded patients included those who had received PPIs, antibiotics, or H2 blockers in the two months prior to the study, as well as those with hypersensitivity to PPIs or antibiotics, pregnant and breastfeeding women, and patients with a history of malignancies, previous gastrointestinal surgery, or gastrectomy, cardiovascular diseases, diabetes, liver disease, or kidney failure.

2.2. Sample size

A minimum sample size of 139 individuals was estimated using OpenEpi, v3.01 (www.openepi.com) at a confidence level of 95%, a precision of 5%, and an expected STT failure rate of 10%. However, 146 patients with confirmed *H. pylori* infection were recruited for the study.

2.3. Data collection and laboratory investigations

Data about sociodemographic and clinical characteristics, as well as patient adherence to STT, were collected using a questionnaire administered through direct interviews with patients.

Stool samples were collected for *H. pylori* antigen testing at baseline and four weeks after completion of STT. The *H. Pylori* Antigen Rapid Test Cassette (ACON Laboratories, San Diego, USA) was used to detect *H. pylori* antigen in stool specimens, according to the manufacturer's instructions.

2.4. Treatment with STT and confirmation of cure

All patients were administered STT twice daily for 14 days.[18] The STT consisted of film-coated clarithromycin tablets (500 mg) *plus* amoxicillin tablets (1000 mg) in addition to esomeprazole tablets (20 mg).[17, 19, 20] Four weeks following the completion of treatment, stool antigen testing was used to confirm that *H. pylori* had been eradicated.[17, 18]

2.5. Data analysis

Data were analyzed using IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA). Quantitative data were presented as mean and standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. The chi-

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square test was used to test the association between khat chewing and the treatment outcome of STT, with a *P*-value of less than 0.05 considered statistically significant.

3. Results

3.1. Patients enrolled in this study

Out of 146 patients who met the inclusion criteria and received STT, 123 patients completed the study, while 23 dropped out due to loss of follow-up or low adherence (Figure 1).

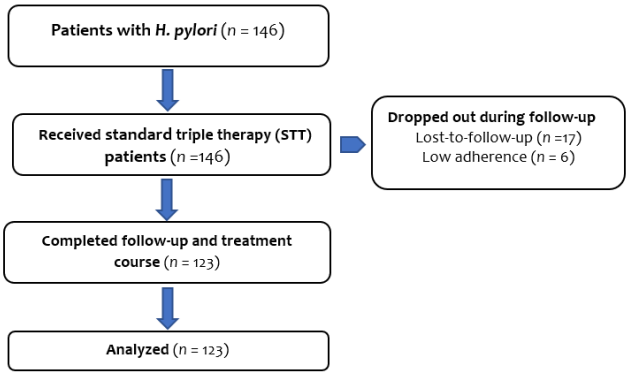

Figure 1: Flowchart of patients enrolled in this study

3.2. Characteristics of patients

The mean age of patients was 35.6±12.6 years, with females comprising the majority (61%), and over half of the participants reported chewing khat (Table 1).

Table 1: Characteristics of patients enrolled in the study*

Variable	*n* (%)
Gender	
Male	48(**39.0**)
Female	75(**61.0**)
Khat chewing	
Yes	63(**51.2**)
No	60(**48.8**)

The total number of participants in the study was 123.

3.3. Treatment outcome of *H. pylori* infection

Four weeks after completing STT, the overall cure rate was 65.9% (81/123).

3.4. Association between khat chewing and STT outcome

Table 2 shows that the cure rates of *H. pylori* infection with STT were 63.5% (40/63) among khat chewers and 68.3% (41/60) among khat non-chewers. However, no statistically significant association was found between khat chewing and the outcome of STT for *H. pylori* infection (*P* = 0.571).

Table 2: Association between khat chewing and outcome of STT for *H. pylori* infection among Yemeni patients

Khat chewing	*N*	*H. pylori* cure		P-value
		Yes *n* (%)	No *n* (%)	
Yes	63	40 (63.5)	23 (36.5)	0.571
No	60	41 (68.3)	19 (31.7)	
Total	123	81 (65.9)	42 (34.1)	

STT, standard triple therapy.

4. Discussion

H. pylori infection is a well-known risk factor for gastrointestinal illnesses. Eradication of *H. pylori* can reduce symptoms in most patients with dyspepsia and lower the risk of significant consequences, such as the development of gastric cancer.[16] Infection can be influenced by many other factors like the immune status and lifestyle choices like smoking, chewing khat, and drinking alcohol.[1]

H. pylori is widespread in Yemen, with prevalence rates ranging from 75% to 82.2%. These high rates are attributed to factors such as malnutrition, poor health practices, khat chewing, consumption of inadequately washed vegetables or those exposed to sewage contamination, and insufficient sanitation facilities.[20] The high prevalence of *H. pylori* infection in Yemen poses a significant burden on the healthcare system with low success rates of standard treatment, underscoring the need for research into factors influencing treatment outcomes to improve clinical success. The possible effect of khat chewing on the success or failure of *H. pylori* treatment remains unclear. Therefore, this study aimed to address this gap by investigating the effect of khat

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chewing on the outcome of STT among Yemeni patients.

In the present study, the eradication rate of *H. pylori* with STT (approximately 66%) was higher than in previous studies conducted in Yemen, though it still reflects a relatively low sensitivity for this first-line treatment. This finding aligns with numerous earlier studies where eradication rates were below 80%. For instance, eradication rates in Saudi Arabia, Lebanon, Iran, and Kuwait were 77.4%, 63.5%, 60.0%, and 68.6%, respectively.[23] The success rate of STT was 74.1% (43/58) in China and 74.5% in India.[24, 25] However, our result contrasts with a study in Ethiopia, where the eradication rate using STT was 83.8% (244/291).[16] Variations in eradication rates across regions can be attributed to differences in *H. pylori* strains, antimicrobial susceptibility patterns, treatment regimens, and drug metabolism. While the relationship between *H. pylori* infection and certain lifestyle factors has been explored, the impact of khat chewing on eradication rates remains unclear.

Eradication of *H. pylori* is crucial, but the best therapeutic strategy has not yet been established. The STT is the most frequently used regimen for treating *H. pylori* infection.[23] In Yemen, studies on eradication rates are limited, and no published research has examined the influence of associated risk factors, such as khat chewing, on *H. pylori* eradication outcomes. For example, a study by Gunaid et al.[26] in Yemen reported an overall eradication rate of 60% by per-protocol analysis and 49.1% by intention-to-treat analysis after six weeks of treatment. Another study by Al-Sayani and Al-Omrani[27] among Yemeni patients with liver cirrhosis found an eradication rate of 53.6% (42/79) among 79 treated patients. These findings highlight the need for further research to better understand the factors influencing *H. pylori* eradication in Yemen.

The present study found no association between Khat chewing and the rate of eradication of *H. pylori* infection. While some studies in Yemen have indicated a significant association between *H. pylori* infection and khat chewing,[6, 12] others did not.[14, 20, 28, 29] These inconsistencies may be attributed to socioeconomic factors like the lack of awareness of the methods of transmission of *H. pylori* infection. Furthermore, the Yemeni population lives under challenging war conditions that adversely affect health, income, and safety.

This study provides valuable insights into the effectiveness of standard triple therapy for eradicating *H. pylori* and the influence of khat chewing on eradication rates in Sana'a. However, the study has limitations, including a relatively small sample size, which may restrict the generalizability of the findings to the broader population. Additionally, since the research was conducted at a single center, its results and conclusions, while contributing a new perspective to the existing literature, should be interpreted with caution. Nonetheless, this study lays the groundwork for future research on this topic.

5. Conclusion

Approximately two-thirds of *H. pylori* infections among Yemeni patients can be successfully eradicated using STT. However, its effectiveness needs to be evaluated across different regions of Yemen. Furthermore, khat chewing appears to have no impact on the outcome of STT, highlighting the need for further studies to explore other factors that may influence the success of STT in treating *H. pylori* infection.

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Ethical approval and consent

The study was approved by the Research Ethics Committee of the Faculty of Medicine and Health Sciences at the University of Science and Technology (USTY) in Sana'a, Yemen (Ethical Clearance No.: 1445/001/UREC/UST). Informed consent was also obtained from all patients before their enrollment in the study.

Conflict of Interest

The authors declare no conflict of interest associated with this article.

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