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Brief Report

Efficacy of Levofloxacin and Metronidazole-Based Triple Therapy in Eradicating *Helicobacter pylori* in Patients with Chronic Recurrent Epigastric Pain: A Prospective Study in Zakho, Iraq

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Abstract

Background: Antibiotic resistance and adverse effects pose significant challenges to the effectiveness of *Helicobacter pylori* eradication therapies, such as clarithromycin-based triple therapy. Alternative treatments, including bismuth quadruple therapy, are effective in cases of clarithromycin resistance. Levofloxacin and metronidazole-based triple therapy have demonstrated high success rates with fewer side effects, making it a preferred option following clarithromycin treatment failure.

Objectives: This study aimed to evaluate the effectiveness of levofloxacin and metronidazole in eradicating *H. pylori* among patients with chronic epigastric pain in Zakho, Iraq. It also assessed the accuracy of diagnostic tests, patient history, and post-treatment confirmation of eradication.

Methods: A prospective study was conducted involving 100 patients with chronic epigastric pain at Zakho General Teaching Hospital. Diagnosis was performed using the fecal antigen test, urea breath test (UBT), and endoscopy with biopsy. Patients were treated with a 14-day regimen comprising levofloxacin, metronidazole, and either esomeprazole or pantoprazole.

Results: Of the 100 participants, 66% were female, with a mean age of 37.85 years. The fecal antigen test, performed on 60 patients, showed a positivity rate of 96.5%, while the UBT, conducted on 40 patients, revealed a positivity rate of 97.5%. The highest infection rate was observed in the 51 - 60 age group. The 14-day levofloxacin and metronidazole regimen achieved a 99% eradication rate with minimal side effects.

Conclusions: This study underscores the high efficacy of levofloxacin and metronidazole-based therapy for *H. pylori* eradication. It highlights the importance of non-invasive diagnostic methods, enhanced patient follow-up, and international collaboration to achieve optimal treatment outcomes.

Keywords: *Helicobacter Pylori*, Levofloxacin and Metronidazole, 14C-Urea Breath Test, Gastritis, Stool Antigen Test (SAT)

1. Background

Eradicating *Helicobacter pylori* often alleviates symptoms, underscoring the importance of early diagnosis and treatment. Diagnostic methods include the urea breath test (UBT), fecal antigen tests for detecting active infections, histology for examining biopsy samples, stool PCR tests for assessing antibiotic resistance, and serological tests to detect anti-*H. pylori* antibodies (1-3).

Helicobacter pylori eradication therapies, such as clarithromycin-based triple therapy, face challenges due to antibiotic resistance and side effects, which can impact patient adherence (4). Alternative treatments include bismuth quadruple therapy, which is particularly beneficial in cases of clarithromycin resistance (5). Levofloxacin- and metronidazole-based triple therapy, which combines levofloxacin, metronidazole, and proton pump inhibitors (PPIs), has shown high success rates with fewer severe side effects, making it a preferred option following clarithromycin-

based treatment failure (6). However, increasing antibiotic resistance to drugs like metronidazole and clarithromycin remains a significant challenge, driven by factors such as over-prescription and patient noncompliance. This emphasizes the need for judicious antibiotic use and consistent monitoring (7).

2. Objectives

This study aims to assess the efficacy of levofloxacin-metronidazole therapy in *H. pylori* eradication in Zakho, Iraq. It also seeks to evaluate diagnostic tools such as the fecal antigen test, UBT, and endoscopy for *H. pylori* detection, document patient histories of *H. pylori* tests and treatments, and confirm post-treatment eradication while identifying any correlations with patient histories or characteristics.

3. Methods

3.1. Study Design

This prospective study, conducted from July 2022 to October 2023 in Zakho, Iraq, enrolled 100 patients with chronic, recurrent epigastric pain.

3.2. Inclusion and Exclusion Criteria

Eligible patients had chronic epigastric pain, a positive *H. pylori* test (via fecal antigen test, UBT, or biopsy), and a history of incomplete *H. pylori* eradication. Exclusions included individuals under 18 years old, those resistant to levofloxacin/metronidazole therapy, or those who had previously received bismuth quadruple therapy. The study adhered to the STROBE checklist (8).

3.3. Patient Assessment

Patients' *H. pylori* test history, prior treatments, confirmatory tests, and PPI usage were reviewed. Diagnostic methods were determined based on recent PPI use: Fecal antigen testing for recent PPI users and UBT for those who had been off PPIs for two weeks. Endoscopy was used for patients with negative fecal antigen test results.

3.4. Sample Size and Data Collection

Data were collected using the census method and gathered through structured questionnaires, which were recorded electronically to cover medical history, demographics, and clinical outcomes, ensuring a comprehensive analysis.

3.5. Sample Collection

Endoscopic tissue samples were stored at 2 - 8°C, while stool samples were either preserved or frozen at -20°C to maintain sample integrity.

3.6. Diagnostic and Assessment Tools

The UBT (14C- UBT) required fasting for six hours, discontinuation of antibiotics for four weeks, and PPI discontinuation for two weeks, with elevated labeled carbon indicating *H. pylori*. The fecal antigen test detected *H. pylori* antigens using the EpiTuub® lateral flow immunoassay. Histological examination involved formalin-fixed, paraffin-embedded biopsy specimens.

3.7. Treatment Regimens

Patients received a triple therapy regimen comprising esomeprazole or pantoprazole (40 mg/day), levofloxacin (750 mg/day), and metronidazole (500 mg three times daily) for 10 - 14 days, followed by 2 - 4 weeks of PPI monotherapy.

3.8. Statistical Analysis

Descriptive statistics provided an overview of the data. Inferential methods, including chi-square and Kruskal-Wallis H tests, were used for in-depth analysis. Multivariate techniques such as logistic regression and multivariate analysis of variance (MANOVA) were employed to control for potential confounders and explore relationships between variables. Hypothesis testing was performed at a significance level of $P < 0.05$. Data processing was conducted using statistical package for the social sciences (SPSS) version 27.0.

3.9. Potential Confounders

Confounders, including prior medication use, dietary habits, and demographic factors, were adjusted for using multivariate regression analyses to ensure accurate outcomes.

4. Results

This study, conducted in Zakho, Iraq, from July 2022 to October 2023, evaluated the efficacy of levofloxacin- and metronidazole-based triple therapy for *H. pylori* eradication in patients with chronic epigastric pain.

4.1. Demographic Characteristics of Study Patients

Of the participants, 66% were female and 34% were male, with an average age of 37.85 years (SD = 1.18). In the 15 - 25 age group, females comprised 72.73%, and the largest age group was 31 - 40 years (44%). The 26 - 30 age range showed the highest gender disparity, with females constituting 90%. A chi-squared test revealed a significant gender disparity ($P < 0.001$) and a significant deviation in age distribution ($P < 0.001$), as shown in Table 1.

Table 1. Distribution of Study Participants by Age Group and Gender [a]

Age Group	Female	Male	Total
15 - 25	8 (72.73)	3 (27.27)	11
26 - 30	9 (90.00)	1 (10.00)	10
31 - 40	29 (65.91)	15 (34.09)	44
41 - 50	11 (55.00)	9 (45.00)	20
51 - 60	5 (62.50)	3 (37.50)	8
> 60	4 (57.14)	3 (42.86)	7
Total	66	34	100

[a] Values are expressed as No. (%).

4.2. Laboratory Results for Helicobacter pylori Tests

Among the 60 patients tested using the fecal *H. pylori* antigen test, 96.5% showed positive results. For the 40 patients tested with the UBT, the positive rate was 97.5%. Negative results were minimal: 2.5% for the UBT and 3.5% for the fecal antigen test, as shown in Table 2.

Table 2. Frequency and Percentage of Lab Results for *Helicobacter pylori* Tests

Test	Frequency Positive	Positive Rate (%)	Frequency Negative	Negative Rate (%)
Fecal *Helicobacter pylori* Ag	58/60	96.5	2	3.5
Urea breath test	39/40	97.5	1	2.5
EGD and biopsy for *Helicobacter pylori*	3/3	100	-	-

Abbreviation: EGD, esophagogastroduodenoscopy.

4.3. Distribution of Test Results by Gender

The positive rates were 37.88% for females and 41.18% for males, with males exhibiting a slightly higher *H. pylori* prevalence based on both diagnostic tests. The Kruskal-Wallis H test found no significant gender differences in detection rates ($P = 0.3679$).

4.4. Treatment Regimens

Patients received levofloxacin, metronidazole, and either esomeprazole or pantoprazole for 10 or 14 days, with 71% on the 14-day regimen. Side effects were minimal, with 93% of patients reporting none. Post-treatment, *H. pylori* was eradicated in 99% of cases, demonstrating high efficacy and tolerability (Figure 1).

5. Discussion

Globally, *H. pylori* infection rates average 50.8% in developing nations, compared to 34.7% in developed regions (9). This study reported a 33.33% prevalence in Zakho, with higher rates among males. Similar studies by Pshtewan and Khoshnaw (10, 11) showed prevalence rates of 53.3% in Erbil, 51.2% in Sulaymaniyah, and 28% in Dohuk, emphasizing the need for localized research to understand regional variations.

Only 3% of patients in this study were diagnosed using esophagogastroduodenoscopy (EGD) and biopsy, reflecting the invasive nature of this method. The study prioritized non-invasive diagnostics, aligning with global trends favoring patient-friendly approaches (12).

The fecal antigen test demonstrated 96.5% accuracy, proving its reliability as a non-invasive, quick diagnostic option (13). With accuracy exceeding 90%, stool antigen testing (SAT) is both cost-effective and convenient for detecting *H. pylori*, as noted by Cardos et al. (14) and Elbehiry et al. (15). Its utility extends to post-treatment assessments, making it invaluable across patient demographics.

The UBT yielded a 97.5% positivity rate, with minimal false negatives, supporting its reliability in diagnosing *H. pylori*. These findings align with Gomollon et al. (16), who confirmed UBT's high sensitivity and specificity.

Using the Kruskal-Wallis H test, no significant age-based differences in *H. pylori* detection were found ($P \approx 0.4159$). However, the 51 - 60 age group exhibited a

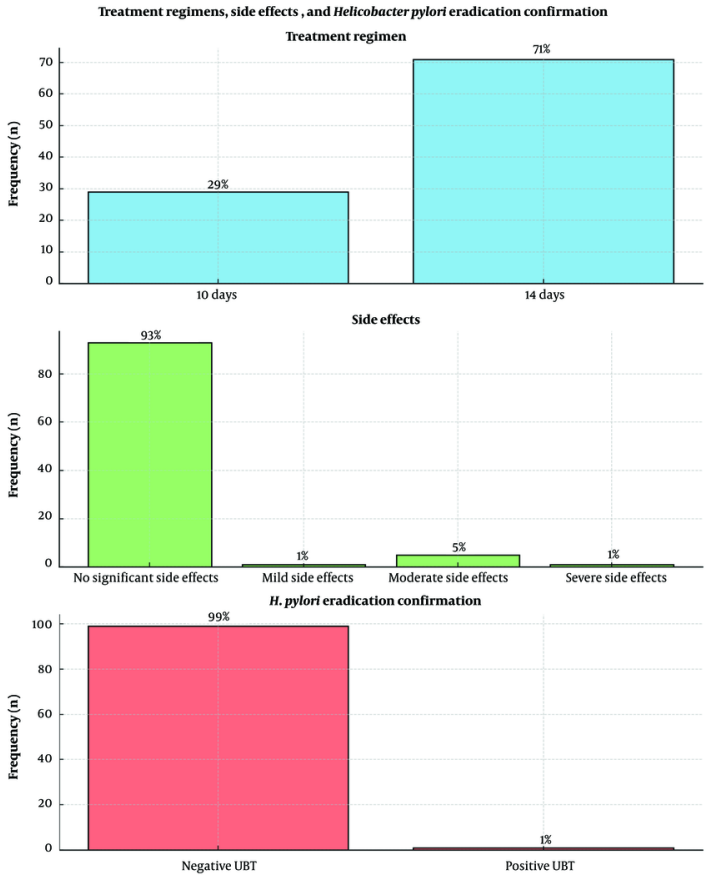

Figure 1. Treatment regimens, side effects, and *Helicobacter pylori* eradication confirmation in studied patients

higher susceptibility, potentially due to prolonged exposure or delayed diagnoses. This highlights the need for targeted interventions for older demographics to mitigate *H. pylori*-associated risks (17).

The study evaluated one of the primary *H. pylori* treatment regimens using levofloxacin and metronidazole combined with either esomeprazole or pantoprazole. Treatment duration (10 or 14 days) was based on infection severity, with 71% of patients receiving the 14-day regimen for enhanced efficacy.

Levofloxacin's superior efficacy over clarithromycin, especially in resistant regions, was evident, corroborated by Keikha et al. (6). Studies from northeastern Poland also demonstrated levofloxacin-based triple therapy (L-TT) as a potent treatment option (18).

Using UBT to assess treatment outcomes, this study achieved a 99% *H. pylori* eradication rate. The high success rate, combined with minimal adverse effects, underscores the effectiveness and safety of the modified regimen.

5.1. Practical Significance and Implications

This study highlights age-related variations in *H. pylori* prevalence, advocates for non-invasive diagnostic methods, and demonstrates the efficacy of levofloxacin-metronidazole therapy. It provides valuable insights for improving patient outcomes and contributes to clinical practice and policy-making.

5.2. Study Limitations

Despite the significant sample size, selection and recall biases may affect the generalizability of the findings. Unvalidated instruments and uncontrolled confounders present potential measurement errors and causality issues in this cross-sectional study, highlighting the need for further research.

5.3. Conclusions

This study offers valuable insights into *H. pylori* prevalence, diagnostic methods, and treatment efficacy. It underscores age and gender patterns, advocates for non-invasive diagnostics, and highlights the superior efficacy of levofloxacin-metronidazole therapy. Policymakers should allocate resources to support these findings to optimize *H. pylori* management.

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Footnotes

Authors' Contribution: All stages of this study, including its concept and design, data acquisition, analysis and interpretation, drafting, critical revision, statistical analysis, administrative support, and supervision, were conducted by M.A.

Conflict of Interests Statement: The author declares no conflicts of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after its publication.

Ethical Approval: This Study approved by the Scientific and Ethics Committee, University of Zakho, Kurdistan, Iraq, under reference number OCT2022/E06 on 01/10/2022.

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