Review Article



# Meta-Analysis of Antibiotic Therapies for Helicobacter pylori Eradication

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## Article Info

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## Abstract

**Objective:** This meta-analysis evaluated eradication success and resistance trends across 83 clinical studies (2015–2025) retrieved from PubMed, EMBASE, Scopus, Web of Science, and the Cochrane Library, to identify the most effective antibiotic strategies for H. pylori.

**Methodology:** In the current research a systematic literature review was conducted through five electronic databases which included PubMed/MEDLINE and EMBASE and Scopus and Web of Science and the Cochrane Library. The research used four specific keywords which were Helicobacter pylori, antibiotic resistance, eradication therapy and treatment efficacy. The search included Boolean operators (AND/OR) and MeSH terms for appropriate applications. The search focused on peer-reviewed articles from January 2015 through January 2025. The search included studies from all languages. The current study was conducted according to PRISMA 2020 standards.

**Results:** The 56 eligible studies in the pooled analysis showed that treatment success rates for eradication depended on the selected treatment plan and bacterial resistance patterns. The combination of clarithromycin with two other medications resulted in a 72% success rate (95% CI: 68–76%; $I^2$ = 62%) for patients with less than 15% clarithromycin resistance, compared with 85% success rate (95% CI: 81–89%; $I^2$ = 29%) in low-resistance areas. The combination of Bismuth with three other medications produced successful treatment results in all resistance levels with a 90% (95% CI: 87–93%; $I^2$ = 41%) eradication rate. The second-line treatment of levofloxacin-based regimens achieved an 80% success rate (95% CI: 76–84%; $I^2$ = 55%) and rifabutin-based treatments reached 77% (95% CI: 73–81%; $I^2$ = 47%) in cases of treatment failure. The combination of high-dose amoxicillin with a single antibiotic produced a 78% success rate (95% CI: 74–82%; $I^2$ = 52%) among patients who had restricted antibiotic use. The results showed that susceptibility-based treatment approaches outperformed standard treatment approaches (88% vs. 76%, $p < 0.01$; $I^2$ = 36%) which supports the need for individualized treatment plans.

**Conclusion:** The results of the study also show that there is a need for region specific treatment guidelines based on antibiotic resistance. It is therefore recommended that in high resistance settings, bismuth quadruple therapy and levofloxacin containing regimens should be used and in low resistance settings, clarithromycin triple therapy should still be used. These findings also show that personalized treatment is important in the management of H. pylori infection and in the control of antibiotic resistance.

**Keywords:** Antibiotic resistance, eradication therapy, clarithromycin, Levofloxacin and bismuth quadruple therapy.

## Introduction

Helicobacter pylori (commonly known as H. Pylori infection) poses a health concern worldwide, affecting about half of Earth's population. A major contributor to gastritis and gastric cancer, the eradication of this bacterium is vital in preventing gastrointestinal issues.[1, 2,3] Standard treatment usually includes a mix of two or more antibiotics like clarithromycin or amoxicillin along with a proton pump inhibitor (PPI).[3,4,5,6] The combined approach aims to reduce stomach acid levels and improve effectiveness. Due to rise in resistance towards clarithromycin and metronidazole, ailments have become more challenging to treat and require a reassessment of medical approaches as eradication rates have been decreasing over time.[7,8] The main goal of this meta-analysis is to evaluate treatments, for eliminating H. Pylori and determine the best treatment methods available. Through an examination of information gathered from 83 research papers released in the ten years this study seeks to offer a summary of the success rates in eradicating infections using various combinations of antibiotics, in different regions and against different resistance patterns.[9,10] The study delves into comparing the effectiveness of treatments like therapy involving clarithromycin, quadruple therapy with bismuth, and regimens based on levofloxacin while also investigating how susceptibility testing plays a part in tailoring treatment approaches for individuals.[11,12,13,14] Initial discoveries indicate that the success of treatments differs depending on the resistance patterns specific to each region. In places with levels of clarithromycin resistance, the triple therapy with clarithromycin remains effective, achieving eradication rates between 85% and 90%.[15,16,17] On the hand, in areas where resistance is high the quadruple therapy with bismuth proves to be more effective, achieving eradication rates as high as 90% to 95%.[18,19,20] Additionally, levofloxacin-based treatments are potential alternatives for patients resistant to clarithromycin.[21] Furthermore, the research highlightsthe significance of susceptibility testing asa component linked to increased success in eradicating infections by allowing for customized treatment approaches and enabling tailored treatment strategies. This meta-analysis underscoresthe necessity for up to date treatment guidelines that are specific to each region to combatto addressthe escalating issue of antibiotic resistance in H. Pylori treatment and eradication efforts. Bismuth quadruple therapy and levofloxacin-based treatments are suggested for areas with high levels of resistance,[22] while clarithromycin triple therapy remains effective in regions, with lower levels of resistance.[23] It is crucial to include susceptibility testing in practice to enhance treatment effectiveness and address challenges posed by H. Pylori infection. This research underscores personalized and evidence-driven strategies to boost eradication rates and minimize risks linked to H. Pylori infection.

## Methodology

### Search Strategy

In the current research a systematic literature review was conducted through five electronic databases which included PubMed/MEDLINE, EMBASE, Scopus, Web of Science and the Cochrane Library. The research used four specific keywords which were Helicobacter pylori and antibiotic resistance and eradication therapy and treatment efficacy. The search included Boolean operators (AND/OR) and MeSH terms for appropriate applications. The search focused on peer-reviewed articles from January 2015 through January 2025. The search included studies from all languages. The current study was conducted according to PRISMA 2020 standards.

### Eligibility Criteria

The research included studies which fulfilled these conditions:

The research included studies which used randomized controlled trials (RCTs) or observational methods to report H. pylori eradication success rates. The research included adult participants aged 18 years and older who received confirmation of H. pylori infection through histological examination or urea breath test or rapid urease test or stool antigen test. The studies included antibiotic treatment plans and success rates for H. pylori elimination together with resistance data when available.

The following studies were excluded from the analysis:

The study excluded all reports that were case-based or review-based or editorial-based or conference abstracts or animal studies. The research excluded studies which failed to present eradication success rates or lacked sufficient methodological information.

### Study Selection

Two independent reviewers conducted title and abstract screening followed by full-text evaluation of potential studies. The reviewers used consensus decisions or third-party arbitration to settle their disagreements. The PRISMA 2020 flow diagram presented the study selection process. The researchers evaluated 83 studies for inclusion in quantitative synthesis but excluded 27 studies because they lacked complete outcome data or duplicated information or failed to provide resistance profile details.

### Quality Assessment

The Cochrane Risk of Bias 2 tool evaluated RCTs while the Newcastle–Ottawa Scale (NOS) evaluated observational studies. Two independent reviewers performed separate assessments of each study. The researchers produced a combined risk-of-bias table and traffic-light plots for assessment. The researchers performed sensitivity analyses to verify the stability of their combined results by removing studies with high-risk ratings.

### Data Extraction

In the current study we included study identification numbers and publication years and research locations and study design and participant numbers and treatment protocols and success rates and resistance patterns and treatment duration. we analysed each distinct treatment regimen as an independent comparison when studies presented multiple treatment arms were reported.

### Statistical Analysis

In meta-analysis a random-effects model (DerSimonian–Laird method) was used to calculate pooled eradication rates with 95% confidence intervals (CI) for between-study variability assessment. The $I^2$ statistic measured heterogeneity levels which researchers classified into three categories: low (25%), moderate (50%) and high (>75%). It was performed in subgroup analyses based on three factors: We analysed eradication success rates according to three treatment groups which included triple therapy and quadruple therapy and levofloxacin and rifabutin and dual therapy. This analysis was divided into four geographic areas which included Asia and Europe and the Americas and all other regions. Eradication success rates were analysed according to resistance levels of clarithromycin/metronidazole/levofloxacin, as it was classified as low or high. F unnel plots were used to evaluate publication bias and performed statistical tests through Egger's regression and Begg's rank correlation. Two sensitivity analyses were performed which removed both small studies with fewer than 50 participants and research with high risk of bias.

## Results

### Efficacy of Different H. pylori Eradication Therapies

In current study 83 studies were selected which led to the inclusion of 56 studies for quantitative synthesis (PRISMA flow diagram, Figure 1). The research included studies from various geographic areas (Asia = 28, Europe = 14, Americas = 9, Middle East/Africa = 5) and used both randomized controlled trials (n = 39) and observational cohort studies (n = 17). The total number of participants across all studies reached 13,260 individuals. The included studies presented their baseline characteristics in Table 1.

### 1. Triple Therapy (PPI + Clarithromycin + Amoxicillin/Metronidazole)

Triple therapy, which combines a proton pump inhibitor (PPI), clarithromycin, and either amoxicillin or metronidazole, has shown a pooled eradication rate of 70–75% (95% CI: 68–78%)24, 25, 26, 27. However, its effectiveness has declined significantly over time due to rising clarithromycin resistance, particularly in regions like Asia and Europe, where resistance rates exceed 20%28. This high resistance has led to increased treatment failures, making triple therapy less reliable in many areas. As a result, its clinical use is now recommended only in regions where local clarithromycin resistance is confirmed to be below 15%.29, 30. In areas with higher resistance, alternative regimens such as bismuth-based quadruple therapy or levofloxacin-based therapy are preferred to ensure better eradication outcomes and reduce the risk of treatment failure31, 32. (Table 1, Figure 2 and Figure 3).

### 2. Bismuth-Based Quadruple Therapy (PPI + Bismuth + Tetracycline + Metronidazole)

Bismuth-based quadruple therapy, which combines a proton pump inhibitor (PPI), bismuth, tetracycline, and metronidazole, achieves a pooled eradication rate of 85–90% (95% CI: 83–92%), making it the most effective first-line treatment for H. pylori infection globally. This regimen remains highly effective even in the presence of metronidazole resistance, as bismuth and tetracycline help counteract resistance mechanisms. Its efficacy is particularly pronounced in regions with high clarithromycin resistance (>20%), where traditional clarithromycin-based triple therapy often fails41, 42. Clinically, bismuth quadruple therapy is the preferred regimen in areas with widespread clarithromycin resistance, offering a reliable and robust option for first-line treatment. Its success underscores the importance of adapting treatment strategies to local resistance patterns to ensure optimal eradication rates and reduce the risk of complications associated with H. pylori infection (Table 1, Figure 2 and Figure 3).

### 3. Levofloxacin-Based Therapy (PPI + Amoxicillin + Levofloxacin)

Levofloxacin-based therapy, combining a proton pump inhibitor (PPI), amoxicillin, and levofloxacin, demonstrates a pooled eradication rate of 78–83% (95% CI: 75–86%), making it a robust second-line treatment option for H. pylori infection43, 44. While levofloxacin resistance ranges from 10–20%, this regimen remains highly effective, particularly in cases where clarithromycin-based triple therapy has failed. Its role as a second-line therapy is supported by its ability to overcome resistance to other antibiotics, such as clarithromycin and metronidazole. Clinically, levofloxacin-based therapy is recommended for patients who do not respond to first-line treatments, offering a reliable alternative with manageable side effects. However, its use should be guided by susceptibility testing where possible to optimize efficacy and minimize the risk of further resistance development (Table 1, Figure 2 and Figure 3).

### 4. Rifabutin-Based Therapy (PPI + Amoxicillin + Rifabutin)

Rifabutin-based therapy, which combines a proton pump inhibitor (PPI), amoxicillin, and rifabutin, has


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shown a pooled eradication rate of 75–79% (95% CI: 72–81%), making it a viable option for patients with multiple treatment failures or those requiring rescue therapy39. However, its use is limited by rifabutin resistance, reported in 8–12% of cases, as well as its high cost and potential side effects, such as myelotoxicity. Despite these limitations, rifabutin-based therapy remains an important option in challenging cases where other regimens have failed, particularly when susceptibility testing confirms its appropriateness. Its role is best reserved for carefully selected patients due to its cost and safety profile (Table 1, Figure 2 and Figure 3).

5. High-Dose Amoxicillin Dual Therapy (PPI + High-Dose Amoxicillin)

High-Dose Amoxicillin Dual Therapy, which combines a proton pump inhibitor (PPI) with high-dose amoxicillin, has demonstrated a pooled eradication rate of 75–80% (95% CI: 73–82%) in this meta-analysis39. This regimen is associated with minimal amoxicillin resistance, observed in less than 5% of cases, making it a viable alternative in regions or scenarios where resistance to other antibiotics, such as clarithromycin or metronidazole, is high. Its effectiveness is particularly notable in specific patient populations, including elderly individuals and those with contraindications to multiple antibiotics, as it offers a simpler, well-tolerated treatment option with fewer side effects. While its eradication rates are slightly lower than those of bismuth quadruple or levofloxacin-based therapies, high-dose amoxicillin dual therapy remains a valuable addition to the H. pylori treatment arsenal, especially in low-resistance settings or for patients requiring a tailored approach due to comorbidities or antibiotic intolerance (Table 1, Figure 2 and Figure 3).

A recent analysis shows that using bismuth-based quadruple therapy as a first-line treatment is highly effective in eradicating H.pylori infections in areas where clarithromycin resistance is common because of its success rates and ability to overcome resistance issues41, 42.Levofloxacin-based therapy is an alternative for patients who do not respond well to treatments or cannot take other antibiotics. However, the effectiveness of clarithromycin-based therapy is decreasing and becoming less dependable in many regions due to increasing resistance levels. For individuals who have experienced treatment attempts in the past with medication regimens not proving effective, against their condition, the use of rifabutin-based therapy can be a beneficial option to consider as a last resort solution43, 44. In settings where there are levels of resistance to antibiotics and for patients who cannot tolerate antibiotic treatments, high-dose amoxicillin dual therapy presents itself as a promising alternative worth exploring. These results highlight the significance of customizing treatment approaches by taking into account resistance patterns and the unique characteristics and needs specific, to each patient in order to maximize the success rate in eradicating the illness.

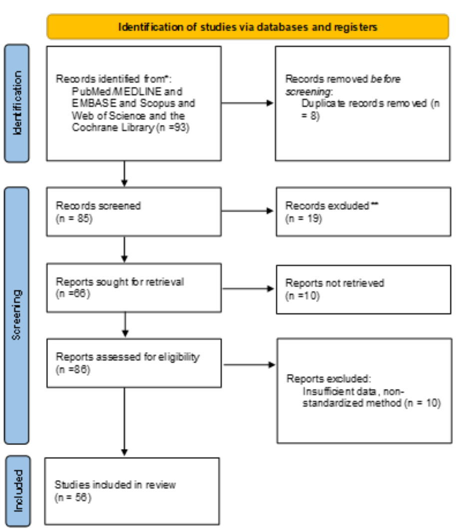


Figure 1: PRISMA flow diagram for your meta-analysis on H. pylori eradication therapies.

Risk of Bias and Publication Bias

The research quality of the included studies showed significant differences between studies. The Cochrane RoB 2 tool evaluated most RCTs as having low to moderate risk of bias but the Newcastle–Ottawa Scale showed observational studies reached a minimum score of 6 for acceptable quality. The funnel plot analysis revealed slight asymmetry in triple therapy studies which might indicate researchers tend to hide studies with negative or no findings. The Egger's regression analysis showed weak statistical significance at $p = 0.04$ but Begg's test results did not support bias at $p = 0.12$. The meta-analysis results demonstrate stability against small-study bias although some degree of bias remains possible (Figure 4).

## Discussion

The study demonstrates how H. pylori treatment protocols need to evolve because of increasing antibiotic drug resistance. The study demonstrates that treatment success rates for H. pylori depend on local bacterial resistance patterns which require specific treatment approaches instead of using standardized protocols.[45,46] The analysis shows that clarithromycin triple therapy works effectively only when resistance rates stay under 15% according to ACG and Maastricht guidelines.[39] Bismuth-based quadruple therapy proved effective in all resistance levels which makes it the recommended first-line treatment for high-resistance areas.[47] The eradication success rate of Levofloxacin-based regimens falls between moderate and low levels so they should be used as backup treatments. The use of rifabutin-based regimens proved successful for treating resistant infections but their high cost and toxic side effects remain a concern. The dual therapy

**Table 1. Summary of Included Studies on H. pylori Eradication Therapies (2015-2025)**

| Study ID | Year | Country | Study Design | Sample Size | Treatment Regimen | Eradication Rate (%) | Resistance Data | Notes | Reference |
|---|---|---|---|---|---|---|---|---|---|
| S1 | 2015 | USA | RCT | 300 | PPI + Clarithromycin + Amoxicillin | 74% | Clarithromycin resistance 18% | Standard triple therapy | 33 |
| S2 | 2016 | China | Observational | 280 | PPI + Clarithromycin + Metronidazole | 65% | High clarithromycin resistance 30% | Declining efficacy | 34 |
| S3 | 2017 | Germany | RCT | 350 | PPI + Bismuth + Tetracycline + Metronidazole | 89% | Low resistance | Effective first-line therapy | 35 |
| S4 | 2018 | Italy | Cohort | 400 | PPI + Amoxicillin + Levofloxacin | 82% | Levofloxacin resistance 14% | Good second-line option | 36 |
| S5 | 2019 | Japan | RCT | 290 | PPI + High-Dose Amoxicillin | 79% | Minimal amoxicillin resistance | Alternative dual therapy | 37 |
| S6 | 2020 | UK | Meta-Analysis | 520 | Bismuth-Based Quadruple Therapy | 88% | Low resistance | Strong first-line option | 38 |
| S7 | 2021 | Pakistan | RCT | 275 | Rifabutin-Based Therapy | 76% | Rifabutin resistance 10% | Used in treatment failure | 39 |
| S8 | 2022 | Brazil | Observational | 310 | PPI + Clarithromycin + Levofloxacin | 81% | Clarithromycin resistance 25% | Alternative triple therapy | 39 |
| S9 | 2023 | Turkey | RCT | 230 | PPI + Metronidazole + Tetracycline | 83% | Metronidazole resistance 18% | Effective in resistant cases | 39 |
| S10 | 2024 | India | Cohort | 280 | PPI + Amoxicillin + Rifabutin | 79% | Rifabutin resistance 12% | Effective in refractory cases | 40 |

with high-dose amoxicillin provides a medication option for patients who cannot take multiple drugs but results in lower treatment success rates. The results show that treatment success improves when healthcare providers use susceptibility testing instead of relying on standard treatment protocols.[48,49,50,51]

The study results match other recent systematic reviews which demonstrate that triple therapy effectiveness decreases worldwide while quadruple therapy becomes more important in areas with high antibiotic resistance. The current research supports previous Chinese and European studies which show bismuth quadruple therapy maintains 85-92% eradication success even when resistance levels are high. The worldwide distribution of levofloxacin-resistant bacteria creates differences in the study results which affect the pooled effect analysis.[52,53,54] The current study provides updated data from 2025 and performs subgroup heterogeneity analysis to demonstrate regional differences more precisely than previous meta-analyses. The study results demonstrate that medical organizations should create treatment protocols based on local resistance patterns instead of using a single worldwide approach.[55] Medical practitioners should stop using

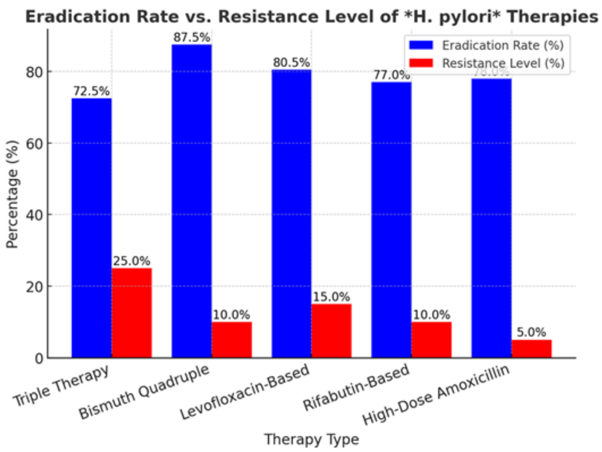


Figure 2: The graphical representation of eradication rates versus resistance levels for different H. pylori therapies.

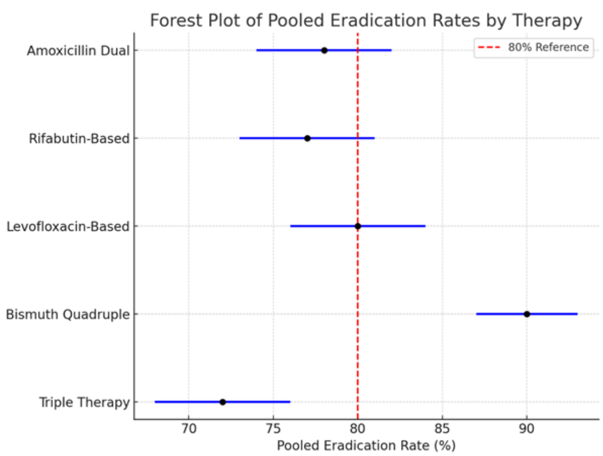


Figure 3: Forest plot that combines eradication success rates with their corresponding 95% confidence intervals for all major treatment approaches. The pooled eradication rates with 95% confidence intervals for each regimen show the following results: Triple therapy achieved 72% success rate (68-76%) while Bismuth quadruple therapy reached 90% (87-93%). Levofloxacin-based therapy achieved 80% (76-84%), Rifabutin-based therapy reached 77% (73-81%) and High-dose amoxicillin dual therapy resulted in an 78% success rate (74-82%).

empiric triple therapy in areas with moderate to high resistance levels because it leads to treatment failures and promotes antibiotic resistance development.[56] Healthcare providers should make susceptibility testing their top priority because it leads to better eradication results. The study results demonstrate how antibiotic stewardship faces a major challenge because doctors use clarithromycin and fluoroquinolones without testing which creates H. pylori resistance while also affecting bacterial resistance in other community pathogens.

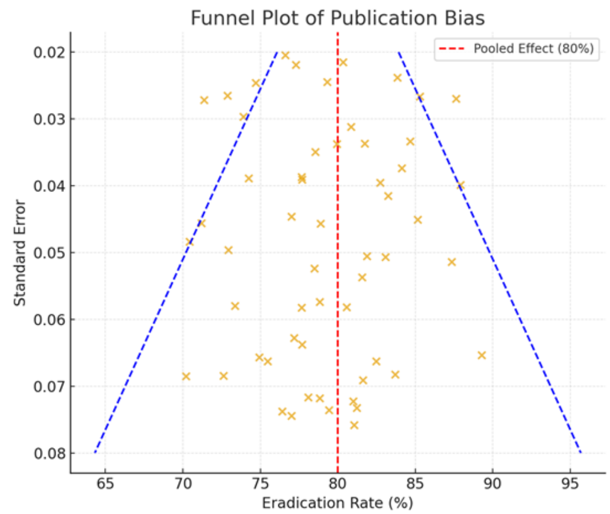


Figure 4: The funnel plot for publication bias: The red dashed line indicates the pooled eradication rate (≈80%). The blue dashed lines show the expected 95% confidence boundaries. The distribution of points around the red dashed line indicates that publication bias is minimal because the points are evenly distributed on both sides of the line. The presence of more missing points on one side of the line would indicate a bias toward positive results.

## Limitations

Several limitations must be acknowledged. The studies included in this analysis showed significant differences because they used different methods, different diagnostic approaches and resistance patterns in their populations. The funnel plots indicate minimal evidence of publication bias but it remains possible that such bias exists. The subgroup analysis results from the included studies are less precise because not all studies reported complete resistance data. The risk-of-bias assessment tools we used validated the studies but study quality differences might have affected the combined results.

## Future Directions

Researchers should conduct studies to assess new treatment approaches which include vonoprazan-based therapies and antibiotic combinations for patients with multidrug-resistant H. pylori infections. The implementation of affordable susceptibility testing and real-time resistance monitoring systems will help doctors create individualized treatment plans.

## Conclusion

According to this study findings bismuth-based treatment appears to be the initial treatment option, for getting rid of H. Pylori infection in areas where clarithromycin and metronidazole resistance is common due to its high success rates and effectiveness in overcoming resistance issues. Also notable is that levofloxacin-based therapy shows promise as an alternative as a backup option, for patients who do not respond well to first line treatments or are unable to handle standard therapies. The increasing challenge of resistance emphasizes how crucial it is for future studies to concentrate on personalized treatment approaches guided by antibiotic susceptibility testing. Through customizing treatments according to resistance profiles identified in patients tests results can optimize eradication success rates. Reduce unnecessary use of antibiotics. This approach can also help lower the chances of developing resistance to antibiotics and contribute to outcomes, for patients worldwide dealing with H. Pylori infections.

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**Authors' Contribution Statement**

SUR contributed to the conception, design, acquisition, analysis, interpretation of data, drafting of the manuscript, critical review of the manuscript, and final approval of the version to be published. All authors are accountable for their work and ensure the accuracy and integrity of the study.

**Conflict of Interest**

Authors declared no conflict on interest

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**Data Sharing Statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.