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REVIEW

Recommendations and Adjuvant Therapies to Mitigate Clarithromycin-Resistant *Helicobacter pylori*-Associated Infections in Africa

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Abstract: *Helicobacter pylori*, (*H. pylori*) is responsible for approximately 90% of the global burden of non-cardiac gastric cancer. In Africa, first-line therapy combines antimicrobials (*eg*, amoxicillin and clarithromycin) with proton pump inhibitors (PPIs), whereas second-line therapies (levofloxacin-based triple therapy, sequential non-bismuth quadruple therapy, or bismuth-based quadruple therapy) combine antimicrobials (amoxicillin, clarithromycin, nitroimidazole, levofloxacin, or tetracycline) with PPIs and bismuth compounds. Antimicrobial-resistant *H. pylori* strains have been widespread worldwide and clarithromycin-resistant *H. pylori* strains (CRHp) are emerging as a seven-fold risk of treatment failure when using a clarithromycin-based regimen. Efficient prevention, detection, and treatment of CRHp-associated infections have become imperative in Africa and should be in accordance with the reality of the African continent. In this mini-review, we briefly highlighted the problem of the emergence of CRHp isolates in Africa and provided recommendations and adjuvant therapies for the successful prevention, detection and treatment of CRHp-associated infections in Africa. The recommendations included the implementation of prevention measures, standardized antimicrobial susceptibility testing methods, strengthening the surveillance, and promoting antimicrobial stewardship, while phytotherapy and probiotics were discussed as potential adjuvant therapies to conventional antimicrobial treatments. While awaiting the full implementation of these measures, the treatment of *H. pylori* infections should be based on the guidelines of the AHMSG First Lagos Consensus.

Keywords: antimicrobial resistance, Africa, gastric infection, clarithromycin resistance, global priority pathogens

Introduction

Helicobacter pylori, (*H. pylori*) is responsible for approximately 90% of the global burden of non-cardiac gastric cancer[1] and has been classified as a class 1 carcinogen, with a higher incidence of cancer than human papillomavirus, hepatitis B virus, and hepatitis C virus.[2]

Significant progress has been made in the management of *H. pylori* infection, and regimens for the eradication of *H. pylori* infection are frequently chosen empirically based on regional bacterial resistance patterns, local recommendations, and drug availability. In Africa, first-line therapy combines antimicrobials (*eg*, amoxicillin and clarithromycin) with proton pump inhibitors (PPIs), whereas second-line therapies (levofloxacin-based triple therapy, sequential non-bismuth quadruple therapy, or bismuth-based quadruple therapy) combine antimicrobials (amoxicillin, clarithromycin, nitroimidazole, levofloxacin, or tetracycline) with PPIs and bismuth compounds.[3]

Antimicrobial-resistant *H. pylori* strains have massively spread worldwide. In this regard, the World Health Organization (WHO) classified in 2017 clarithromycin-resistant *H. pylori* (CRHp) isolates as high-priority pathogens

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for which new antibiotics are urgently needed.[4] The resistance of *H. pylori* to clarithromycin is associated with a seven-fold risk of treatment failure when using a clarithromycin-based regimen.[5] Recently, in 2025, we conducted a systematic review and meta-analysis, reporting a pooled prevalence of CRHp of 27% (95% CI: 22, 33) in Africa.[6] We found a pooled prevalence of CRHp in Africa that is similar to the patterns observed in Europe,[7,8] while being slightly lower than those reported in the Asian continent.[8,9] Mutations in 23S rRNA are responsible for clarithromycin resistance, with A2143G and A2142G being the most common 23S rRNA mutations in CRHp strains isolated in Africa.[6]

Due to limited investments, resources, and healthcare infrastructure, efficient prevention, detection, and treatment of CRHp-associated infections are crucial in Africa. These efforts must be adapted to the continent's specific realities. Therefore, this mini-review aims to provide recommendations and alternative therapies for the detection and management of CRHp-associated infections in Africa.

Recommendations

The Importance of Prevention

The WHO states that the prevention of infections should be the primary weapon to improve health and reduce the need for antimicrobial therapy.[10] Therefore, preventing *H. pylori* infection is one of the best strategies for decreasing the morbidity and mortality rates associated with *H. pylori* infection (Figure 1). Individual and collective prevention strategies should focus on improving hygiene practices, sanitation, and drinking water quality, as *H. pylori* infections are usually associated with poor sanitation and unclean water supplies.[11] Public health authorities should continue to recommend frequent and correct handwashing,[12] provide safe tap water, and help communities efficiently disinfect boreholes and well water. Direct patient contact is a major risk factor for *H. pylori* infection among hospital workers.[13,14] Therefore, African medical staff should continue to work according to the hygiene guidelines for healthcare facilities. Moreover, because several samples of raw vegetables, meats, ready-to-eat meals, and dairy products have been reported to carry *H. pylori* strains,[15,16] it is imperative to adhere to food safety best practices for the processing and storage of food products.

Implement Standardized Methods to Efficiently Detect Clarithromycin-Resistant *H. pylori*

A significant number of bacteriology laboratory in Africa lacks the capacity to culture *H. pylori* and to perform antimicrobial susceptibility testing (AST) on *H. pylori* strains. However, when resources and infrastructure permit, it is recommended to perform AST on the *H. pylori* strains that are detected in order to provide targeted treatment with antimicrobials that are sensitive.

In addition, we reported that the agar dilution method, considered the gold standard for AST for *H. pylori*, was used in only 10% of studies conducted in Africa.[6] In contrast, the Kirby-Bauer disc diffusion method, which is regarded as an unreliable AST method for detecting CRHp, was the most commonly used phenotypic method on the continent (22

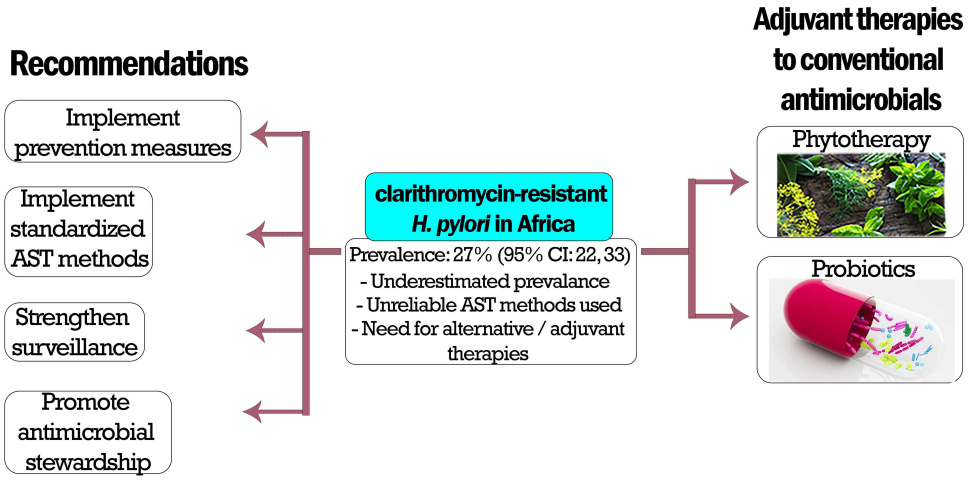

Figure 1 Summary of some recommendations and promising adjuvant therapies to mitigate the CRHp in Africa.

studies out of 62, or 35%).[6] This highlights the urgent need to implement standardized microbiological methods for resistance detection to improve the accuracy and reliability of surveillance data (Figure 1).

Strengthening Surveillance to Combat Clarithromycin-Resistant *H. pylori*

In several African regions, tracking *H. pylori* resistance is hindered by limited infrastructure, inadequate resources, and uneven data-collection practices.[17–19] Current data on CRHp tend to be fragmented and are based on a narrow set of studies, which leaves gaps in the overall understanding of resistance patterns across the African continent.[5,20]

Basic antimicrobial susceptibility testing methods, such as the agar dilution and E-test, offer cost-effective and accessible means for detecting antimicrobial resistance in *H. pylori* strains. These techniques remain particularly relevant in low-resource settings, where advanced molecular diagnostics are often not feasible due to cost, infrastructure limitations, and logistical challenges. Moreover, the utility of DNA sequencing technologies for routine susceptibility testing remains limited, as not all genetic mutations associated with resistance are fully characterized.

However, when resources and infrastructure permit, advanced molecular techniques can provide valuable complementary insights that enhance surveillance efforts. The integration of advanced DNA sequencing technologies, including whole-genome sequencing (WGS), could significantly improve monitoring of *H. pylori* resistance[21,22] (Figure 1). These approaches might allow for precise identification of genetic alterations linked to resistance and offer a clearer view of the underlying mechanisms. DNA sequencing technologies can unravel the detailed genetic makeup of *H. pylori* strains, facilitating the detection of resistance-related mutations and monitoring of how these mutations evolve over time. A key example of this is stool testing using next-generation sequencing (NGS). This method has an additional advantage in that there is no need for endoscopy or gastric biopsy.[23–25] Despite the high cost, complex logistics, and limited access to sequencing facilities in Africa, NGS holds promise for future research applications aimed at significantly improving the monitoring of *H. pylori* antimicrobial resistance.

Incorporating these diagnostic techniques into surveillance efforts would enhance the accuracy and depth of data regarding CRHp.[22] Consequently, these approaches would enable better-informed treatment strategies, a clearer understanding of resistance trends, and more effective public health interventions. Strengthening the capacity to use these tools locally could play a crucial role in managing CRHp more effectively and bolster the continent's response to *H. pylori* resistance.

Promoting Antimicrobial Stewardship

According to the WHO, promoting antimicrobial stewardship has become a key strategy in addressing antimicrobial resistance. For *H. pylori*, antimicrobial stewardship should be implemented at the levels of public health authorities, patients, and healthcare professionals (Figure 1). Therefore, optimal drug regimens should be used, and treatment duration should be strictly respected. Regarding antimicrobial stewardship, the Maastricht VI/Florence consensus[26] recommends conducting AST prior to prescribing first-line treatment. As *H. pylori* AST cannot be performed in most African laboratories, treatment recommendations established by the First Lagos Consensus Statement of the African *Helicobacter* and Microbiota Study Group (AHMSG) in 2024[3] should be strictly respected. According to the First Lagos Consensus Statement of the AHMSG, the first-line treatment includes (amoxicillin + clarithromycin + PPI), whereas the salvage therapies include (amoxicillin + clarithromycin + nitroimidazole + PPI), or (levofloxacin + amoxicillin + PPI), or (tetracycline + metronidazole + bismuth subcitrate or subsalicylate + PPI).[3]

Public health authorities need to continually update their national/regional guidelines and educate physicians according to the latest *H. pylori* infection treatment consensus guidelines. In addition, every therapy should be preceded by formal patient counseling regarding the therapy, potential side effects, and importance of completing the entire course.[27–30]

Exploring Adjuvant Therapies to Conventional Antimicrobial Treatments

Several other options, including prophylactic *H. pylori* vaccines, phage therapy, and antimicrobial photodynamic therapy,[30–33] have emerged as promising adjuvant or alternative treatments for *H. pylori* infections. However, this review primarily focuses on phytotherapy and probiotics, which appear to be more readily accessible and applicable for use in

conjunction with conventional antimicrobial treatment on the African continent and have been actively studied by African research groups.

Phytotherapy as a Promising Weapon to Tackle Antimicrobial-Resistant *H. pylori* Infection

Phytotherapy offers promising potential in tackling antimicrobial resistance and various phytochemicals from classes including alkaloids, phenols, coumarins, and terpenes have demonstrated their antibacterial potential against drug-resistant pathogens.[31]

Several herbal preparations and compounds have demonstrated antibacterial activity, either alone or in combination with clarithromycin (Figure 1). Several herbal extracts from *Pistacia lentiscus, Brassica oleracea, Glycyrrhiza glabra, Camellia sinensis, Cinnamomum cassia, Allium sativum, Castella tortuosa, Ibervillea sonorae, Ambrosia confertiflora, Pelargonium sidoides* roots and *Nigella sativa* demonstrated good in vitro and in vivo antibacterial activities against *H. pylori*.[32–35] Georgian propolis extracts demonstrated antimicrobial properties against the reference *H. pylori* ATCC 43504 and clinical *H. pylori* strains, with MICs ranging from 31.3 to 125.0 µg/mL,[36] whereas a flavonoid-rich extract of *Glycyrrhiza glabra*, GutGard®, showed MICs ranging from 32 to 64 µg/mL.[37] Moreover, the addition of licorice to the triple clarithromycin-based regimen resulted in a significant increase in *H. pylori* eradication rates.[38] In addition, *Pelargonium graveolens* oil, chrysin (extracted from *Passiflora caerulea* flowers), artemisone, and aurasperone A (extracted from *Aspergillus niger*) demonstrated synergistic activity when combined with clarithromycin.[39,40] Furthermore, extracts from *Mirtus communis, Teucrium polium, Achillea millefolium*, and *Thymus vulgaris* have been shown to decrease the occurrence of 23S rRNA mutations in *H. pylori* strains. If additional and appropriate research is conducted, phytotherapy could significantly help tackle drug-resistant *H. pylori* strains and reduce the morbidity and mortality rates associated with *H. pylori* infections.

The Importance of Probiotics

Another key solution for tackling *H. pylori* infections is the use of probiotics (Figure 1). Probiotics are live microorganisms that confer health benefits to the host when administered in adequate amounts. Many studies have assessed the use of probiotics as a single therapy in *H. pylori* treatment and reported that probiotics probably diminish the bacterial load but do not completely eradicate *H. pylori* bacteria. Therefore, probiotics should not be recommended as a single treatment for *H. pylori* infections.[41,42] A large number of studies have supported the significant beneficial use of probiotics as adjuvant therapy in standard eradication protocols, and both single-strain and pooled-strain preparations of probiotics such as *Lactobacillus* spp., *Bifidobacterium* spp., and *Saccharomyces* spp. have been reported to significantly increase *H. pylori* eradication rates and decrease antimicrobial-related adverse effects such as diarrhea, nausea, vomiting, constipation, and abdominal pain.[41,43–45] Moreover, the pooled-probiotic preparations (*ie, Bifidobacterium-Lactobacillus* or *Bifidobacterium-Lactobacillus-Saccharomyces*) in combination with conventional regimen therapy would have a greater beneficial effect in enhancing the eradication rates and decreasing the antibiotic-related effects than single-probiotic preparations.[46] Some authors have reported the capacity of probiotics to significantly increase the eradication success. For example, Zhang et al[47] mentioned overall eradication rates of the probiotic group (*Lactobacillus* spp., *Bifidobacterium* spp.) and the control group of 82.31% versus 72.08%, respectively, whereas Fakhry et al[44] reported, 81.04% versus 71.19%, respectively. Furthermore, it has been shown that probiotics as adjuvants should be administrated before eradication treatment, throughout the eradication treatment, and also for more than 2 weeks after the eradication treatment to have optimal beneficial effects.[48]

Conclusion

In this mini-review, we briefly highlighted the problem of CRHp in Africa and provided recommendations and promising adjuvant therapies for the effective prevention, detection, and treatment of CRHp-associated infections on the continent. The importance of prevention, implementing standardized methods to efficiently detect CRHp, strengthening surveillance to combat resistance, promoting antimicrobial stewardship, and exploring adjuvant therapies such as probiotics and phytotherapy (both currently being studied by African researchers) were discussed. Additionally, the need for continuous education,

training, and investment was emphasized as essential to successfully address these challenges and improve outcomes across the continent. The lack of robust clinical trials evaluating phytotherapy and probiotic therapies in African populations also underscores the need for further research in this area. While awaiting the full implementation of these measures, the treatment of *H. pylori* infections should initially follow the guidelines of the AHMSG First Lagos Consensus.

Abbreviations

AST, antimicrobial susceptibility testing; CRHp, clarithromycin-resistant *Helicobacter pylori*; MIC, minimum inhibitory concentrations; NGS, next-generation sequencing; PPI, proton pump inhibitors; WGS, whole-genome sequencing; WHO, World Health Organization.

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Disclosure

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