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Effectiveness of eradication therapy for *Helicobacter pylori* infection in Africa: a systematic review and meta-analysis

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Abstract

Background The effectiveness of *Helicobacter pylori* (*H. pylori*) eradication depends on the treatment protocol. This study investigates the *H. pylori* eradication rate in Africa using the best available evidence from databases.

Methods Databases were searched and results were pooled together. Heterogeneity between studies was assessed using I^2 test statistics. Stata version 13 software was employed to compute the pooled eradication rate. In the subgroup analysis comparison, the finding is considered significant when the confidence intervals did not overlap.

Results Twenty-two studies from 9 African countries with a total population of 2,163 were included in this study. The pooled eradication rate of *H. pylori* was 79% (95% CI: 75%-82%), heterogeneity ($I^2 = 93.02\%$). In the subgroup analysis by study design, a higher eradication rate was reported from observational studies (85%, 95% CI: 79%-90%), compared to randomized control trials (77%, 95% CI: 73%-82%); by the duration of therapy, higher eradication rate was reported in 10-days regimen (88%, 95% CI: 84%-92%), compared to 7-days regimen (66%, 95% CI: 55%-77%); by country, the highest eradication rate was found in Ethiopia (90%; 95% CI: 87%-93%) and the lowest eradication rate was reported in Ivory Coast (22.3%; 95% CI:15%-29%); by type of *H. pylori* test, the highest eradication rate was reported when rapid urease test coupled with histology (88%, 95% CI: 77%-96%), and the lowest eradication rate was reported with histology alone (22.3%; 95% CI:15%-29%). Significant heterogeneity was observed with pooled prevalence ($I^2 = 93.02\%$, $P < 0.000$).

Conclusions In Africa, the first-line therapy showed a variable eradication rate for *H. pylori*. This study demonstrates the necessity to optimize current *H. pylori* treatment regimens in each country, taking into account the antibiotic susceptibility. Future RCT studies with standardized regimens are warranted.

Keywords Africa, Eradication rate, First-line therapy, *H. pylori*

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Background

Helicobacter pylori (H. pylori) is a microaerophilic, Gram-negative, spiral-shaped motile bacterial pathogen that colonizes the gastric mucosa of approximately half of the world's population. *H. pylori* infection is associated with gastritis, peptic ulcer, atrophic gastritis, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma (MALT). The presentation of a range of clinical conditions is primarily determined by bacterial virulence, host genetics, and the individual's lifestyle [1–4]. The prevalence of *H. pylori* infection varies globally, with Africa being the highest infection rate [5]. The bacterium is primarily acquired during early childhood under low socioeconomic conditions and close family contact [6].

According to the Maastricht VI/Florence consensus report 2022, individuals with or without clinical evidence of *H. pylori* infection are recommended to receive first-line eradication therapy to prevent the development of infection-associated complications, such as gastritis and cancer [7]. Moreover, large-scale eradication of *H. pylori* in a population reduced the incidence and mortality of gastric cancer [8]. In light of this, guidelines have been developed as a national or regional first-line eradication protocol that consists of different antibiotic combinations, including triple therapies, bismuth-free therapies (sequential, concomitant, or hybrid regimens), and bismuth-based quadruple therapy [9]. The effectiveness of eradication therapy has been assessed based on the per-protocol analysis and categorized as excellent ($\geq$95% success), good ($\geq$90% success), borderline acceptable (85–89% success), or unacceptable (<85% success) [10]. The presence of *H. pylori* resistance to one or more antimicrobial agents or poor medication adherence increases the likelihood of treatment failure, even with excellent regimens.

H. pylori eradication rate differs in different settings based on the type of regimen employed, duration of therapy, and local antibacterial susceptibility pattern. According to a recent systematic review and meta-analysis, first-line treatment had a 98% global *H. pylori* eradication rate, with a subcontinental success rate of 98% in Asia, 94% in Africa, 94% in Europe, 93% in South America, and 84% in North America. In this report, five African countries with a total of 7 studies comprising 1021 patients were included, Morocco ($n=3$), Egypt ($n=1$), Kenya ($n=1$), Nigeria ($n=1$), and Tunisia ($n=1$) [11].

However, there is no pooled eradication rate consisting of observational and randomized controlled trials for *H. pylori* infection in Africa. However, small-scale studies were reported in different countries in Africa. Therefore, African studies differ in study settings, methodology, and other characteristics. In addition, no systematic review or meta-analysis has been conducted on the eradication rate of *H. pylori* infection in Africa. Therefore, we have undertaken a systematic review to determine the eradication rate of *H. pylori* in Africa using previously published articles.

Methods

Databases and search strategy

PubMed, Google Scholar, Hinari, Scopus, and the Directory of Open Access Journals (DOAJ) were searched to identify potential articles on *H. pylori* eradication in Africa. The search was conducted following PRISMA guidelines and checklists [12], Fig. 1.

Quality assessment

The quality of included studies was assessed by using a revised Cochrane risk-of-bias tool for randomized trials (RoB2) and Risk Of Bias in Non-Randomized Studies-of Interventions (ROBINS-I) (Supplementary files 1 and 2). The authors independently assessed the quality of each study, and a consensus was reached on twenty-two studies conducted in nine African countries.

Data extraction

Data were extracted into a customized Microsoft excel spreadsheet. The characteristics of extracted data in each study include: first author name, year of publication, country of study, study design, number of study participants, characteristics of study participants (naïve or nan-naïve), laboratory methods for *H. pylori* positivity test, number of *H. pylori*-positive participants, *H. pylori* eradication regimen, duration of follow up, laboratory methods for *H. pylori* eradication confirmation, and number of *H. pylori* eradicated individuals. In addition, graphs of the summary of the risk of bias were developed using RevMan 5.3 (Cochrane Informatics and Knowledge Management Department, London, UK).

Data analysis

Statistical analyses were conducted using Stata version 13.0 (StataCorp, LP, college station, TX). The eradication rate values were pooled using the *metaprop* command in Stata. The heterogeneity of the studies was assessed using the I^2 statistic, and significance was declared at $I^2>50\%$ and Q-test ($p<0.10$). Because of high heterogeneity among the studies, the random-effects model (REM) was used to estimate the pooled proportion and 95% CIs using the DerSimonian and Laird methods. The Freeman-Turkey double arcsine transformation was used to avoid missing proportions near or at 0 and 1 from the meta-analysis. Subgroup analysis was done by study design, country, laboratory tests for *H. pylori* infection, eradication regimen, type of regimen analysis, characteristics

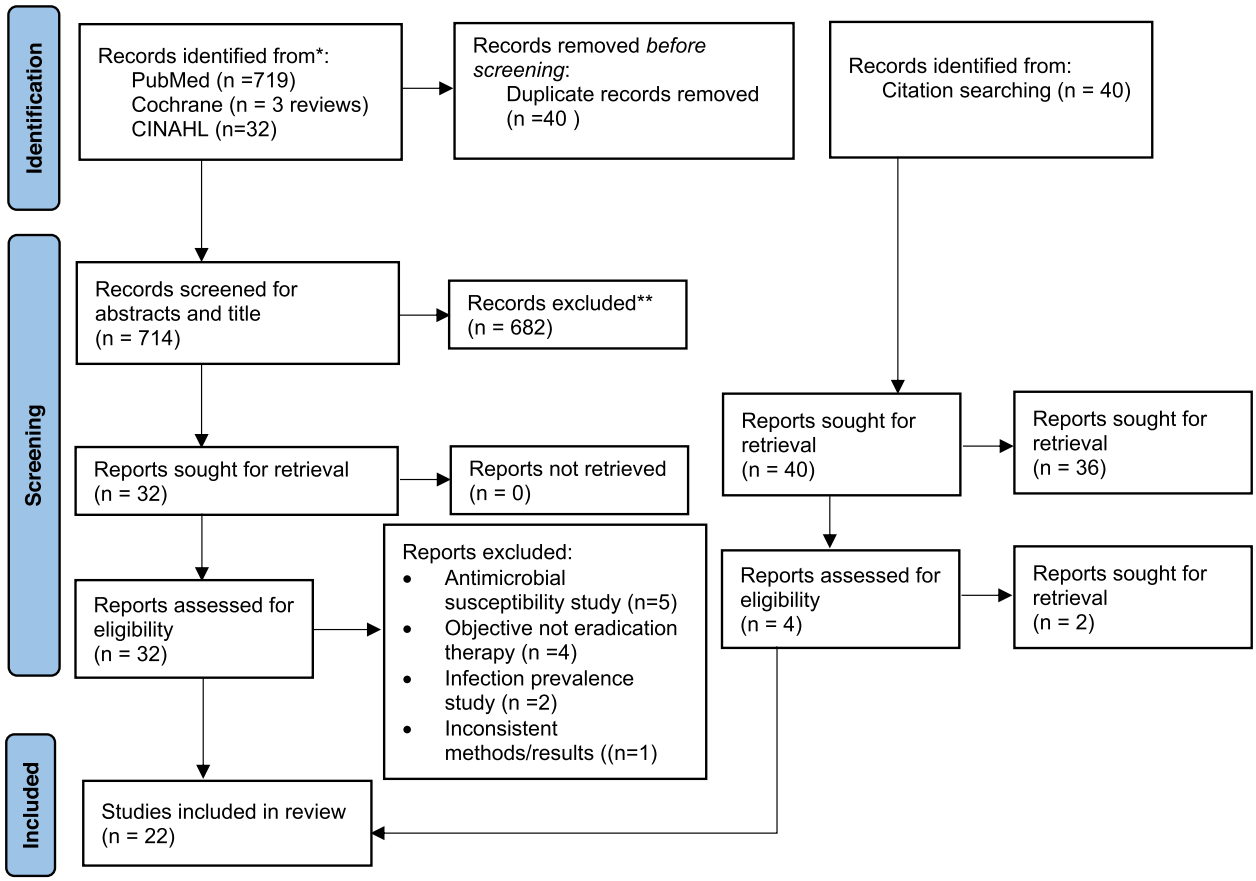

Fig. 1 PRISMA flow chart of studies selection

of the study population, follow-up duration, and tests employed to confirm eradication. The presence of publication bias was tested using Egger's test. Forest plots and tables were constructed to display the individual studies and pooled results.

Publication bias and sensitivity analysis

A funnel plot was drawn to evaluate the potential for publication bias. The funnel plots' gap suggests potential publication bias. In addition, Egger's regression asymmetry tests were used to assess publication bias, with $p < 0.05$ considered to indicate potential publication bias. Finally, sensitivity and leave-one-out analysis were done to evaluate the prime determinant of the pooled eradication rate and to detect the possible causes of heterogeneity between studies.

Results

Characteristics of included studies

Twenty-two studies from nine African countries with a total population of 2,163 met the inclusion criteria of the meta-analysis. These studies were published articles from 1992 to 2020, and the number of articles by country is indicated in Table 1. The detailed characteristics of included studies are presented in Table 2. Among the included studies, 8 were observational, and 14 were randomized control trials (RCT). Except for Abd-Elsalam et al., 2016, all study participants were newly diagnosed cases with gastrointestinal disorder. Twelve

Table 1 Number of articles included in the study by country

Country	Number of articles	Reference
Egypt	7	[13–19]
Morocco	4	[20–23]
South Africa	4	[24–27]
Algeria	2	[28, 29]
Ethiopia	1	[30]
Nigeria	1	[31]
Tanzania	1	[32]
Kenya	1	[33]
Ivory Coast	1	[34]

Table 2 Lists and characteristics of included 22 studies

Authors	Study Type	Country	*H. pylori* Positive	Eradicated	Eradication rate, %	Test method	Regimen	Duration (days)	Outcome measure (weeks)	Confirmed test
Elkhodary et al., 2020 [14]	RCT	Egypt	33	21	63.6	FAT	DLA	7	4	FAT
Farhoud_1 et al., 2020 [15]	RCT	Egypt	30	19	63.3	RUT	LAC	14	6	UBT
Zeriouh_1 et al., 2020 [23]	RCT	Morocco	124	84	67.7	UBT or H	PPI + A	14	6	UBT
Gebeyehu et al., 2019 [30]	PS	Ethiopia	421	379	90.0	FAT	OAC	14	4	FAT
Hassan et al., 2019 [17]	RCT	Egypt	50	31	62.0	FAT	OAC	14	4	FAT
Jaka et al., 2019 [32]	PS	Tanzania	210	145	69.0	FAT	PPICM/A	10	5	FAT
Moubri_1 et al., 2019 [28]	RCT	Algeria	55	39	70.9	C + H + UBT	OAC	7	8	UBT
Moubri et al., 2019 [29]	PS	Algeria	101	79	78.2	C or H + RUT	PPIAC	14	8	UBT
Shehata_1 et al., 2017 [18]	RCT	Egypt	112	106	94.6	FAT + H	OCN	14	6	FAT
Abd-Elsalam et al., 2016[a] [13]	RCT	Egypt	94	83	88.3	FAT	OLDN	14	6	FAT
Hanafy et al., 2016 [16]	PS	Egypt	248	169	68.1	FAT	LAC	14	4	FAT
Abou Saif et al., 2015 [19]	RCT	Egypt	18	17	94.4	FAT	5OA,5OLM	10	4	FAT
Doffou et al., 2015 [34]	RCT	Ivory Coast	64	18	28.1	H	OAM	7	4	H
Onyekwere et al., 2014 [31]	RCT	Nigeria	29	25	86.2	UBT	RAC	10	4	UBT
Benajah_1 et al., 2013 [20]	PS	Morocco	204	156	76.5	RUT + H + C	OAM/C	7	12	UBT
Laving_1 et al., 2013 [33]	RCT	Kenya	45	22	48.9	H	OAC	10	6	FAT
Seddik_1 et al., 2013 [22]	RCT	Morocco	129	116	89.9	H	5OA,OCT	10	10	UBT
Lahbabi et al., 2013 [21]	RCT	Morocco	103	73	70.9	H or PCR	PPIAM	14	12	FAT
Wong et al., 2000 [27]	PS	South Africa	22	19	86.4	H + RUT + UBT	OAC	7	4	H + UBT
Louw_1 et al., 1998_a [25]	PS	South Africa	24	22	91.7	RUT + H	LAC	7	4	RUT + H
Louw_1 et al., 1998_b [26]	PS	South Africa	30	26	86.7	RUT + H + C	PAC	7	4	RUT + H + C
Louw_1 et al., 1992 [24]	RCT	South Africa	17	10	58.8	RUT + C + H	S + B + OA	14	4	RUT + H + C

FAT Fecal antigen test, *RCT* Randomized controlled trial, *PS* Prospective study, *PP* Per protocol, *ITT* Intention to treat, *UBT* Urea breath test, *H* Histology, *RUT* Rapid urease test, *C* Culture, *PCR* Polymerase chain reaction, *OAC* Omeprazole + Amoxicillin + Clarithromycin, *OCM* Omeprazole + Clarithromycin + Metronidazole, *OAM* Omeprazole + Amoxicillin + Metronidazole, *LAC* Lansoprazole + Amoxicillin + Clarithromycin, *PAC* Pantoprazole + Amoxicillin + Clarithromycin, *RAC* Rabeprazole + Amoxicillin + Clarithromycin, *OCN* Omeprazole + Clarithromycin + Nitazoxanide, *OACS* Omeprazole + Amoxicillin + Clarithromycin + Simvastatin, *OLDN* Omeprazole + Levofloxacin + Doxycycline + Nitazoxanide, *DLA* Dexolansoprazol + Levofloxacin + Amoxicillin *OCT* Omeprazole + Clarithromycin + Tinidazole

[a] Study participants were non-naïve

studies used multiple tests to detect *H. pylori,* while 10 employed a single test to declare *H. pylori* infection. Eighteen studies employed a single test, and 4 studies used multiple tests to prove *H. pylori* eradication. The *H. pylori* eradication rates in the qualified studies ranged from 22.3% to 90%.

The eradication rate and the retrieved studies varies with time. Trend analysis is done to explore the time effect of the study using a scatter plot as indicated in Fig. 2. The trend analysis shows that from 2000 to 2010 there is no eradication study and no variability observed with time.

Pooled eradication rate of *H. pylori*

A total of 2,163 people tested positive for *H. pylori* in Africa. Of which 1,659 confirmed eradication following first-line eradication therapy in the period under review. Our meta-analysis revealed pooled eradication rate of 79% (95% CI: 75%-82%), $I^2 = 93.02\%$ (Fig. 3). Moreover, the funnel plot for publication bias supported Egger's regression ($p = 0.672$) test, which showed no significant publication bias (Fig. 4).

Subgroup eradication rate of *H. pylori*

Subgroup analyses were conducted by country, study design, type of analysis, study population, duration of therapy, outcome measures and regimen. The pooled data were from nine countries. In addition, more studies were conducted in Egypt, which showed an eradication rate of 82%, and almost all countries showed a similar eradication rate except Ivory Coast (22.3%) (Table 3).

Discussions

The 22 studies included in our analysis showed the pooled eradication rate in Africa was estimated to be 79% (95% CI: 75–82). This overall eradication rate is lower than reports from Ethiopia (90%), Nigeria (87%), South Africa (86%), Egypt (82%), Morocco (82%), and higher than reports from Tanzania (69%), Kenya (68%) and Ivory Coast (22.3%). These differences might be attributed to methods employed to diagnose *H. pylori*, type of eradication regimen and duration of therapy, local *H. pylori* pretreatment resistance,and drug adherence, as stated by previous reports [35–39].

Trend analysis in *H. pylori* eradication from the 22 studies showed that presence of few studies in the year between 1990s and 2000. There is no relevant study between the year 2000 and 2010. The trend also showed that more publications coming out since 2011. This trend analysis showed that decrease in *H. pylori* eradication rate. Similar studies indicated that decreasing trends of eradication rate for *H. pylori* over the years [40]. On the other hand, *H. pylori* eradication rate consistent in study conducted for a decade [41]. The decrement in eradication rate could be attributed to increasing resistance due to increased antibiotic exposure.

The eradication rate for *H. pylori* varies in different regions of the world. The overall success of eradication depends on the choice of eradication regimen, duration of the treatment, and local and regional antibiotic resistance

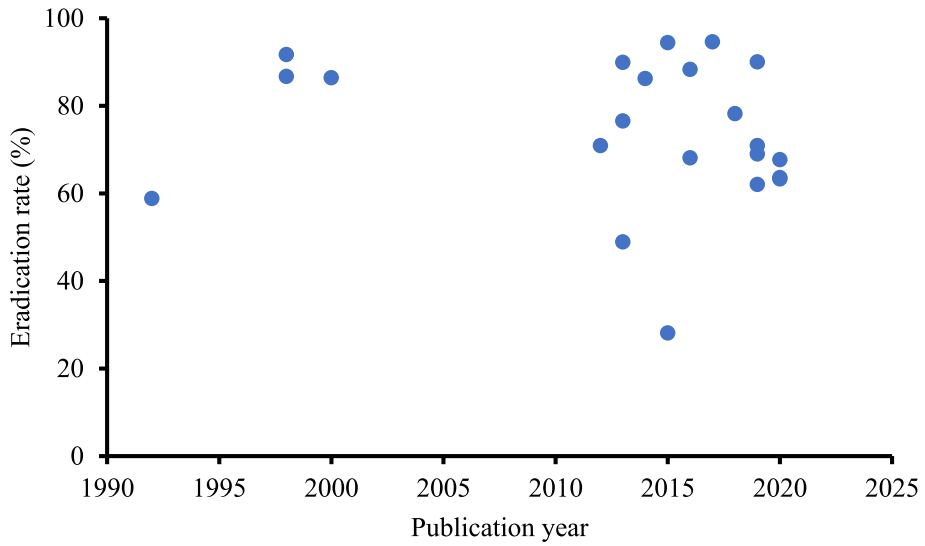

Fig. 2 Trends in *H. pylori* eradication rate in Africa

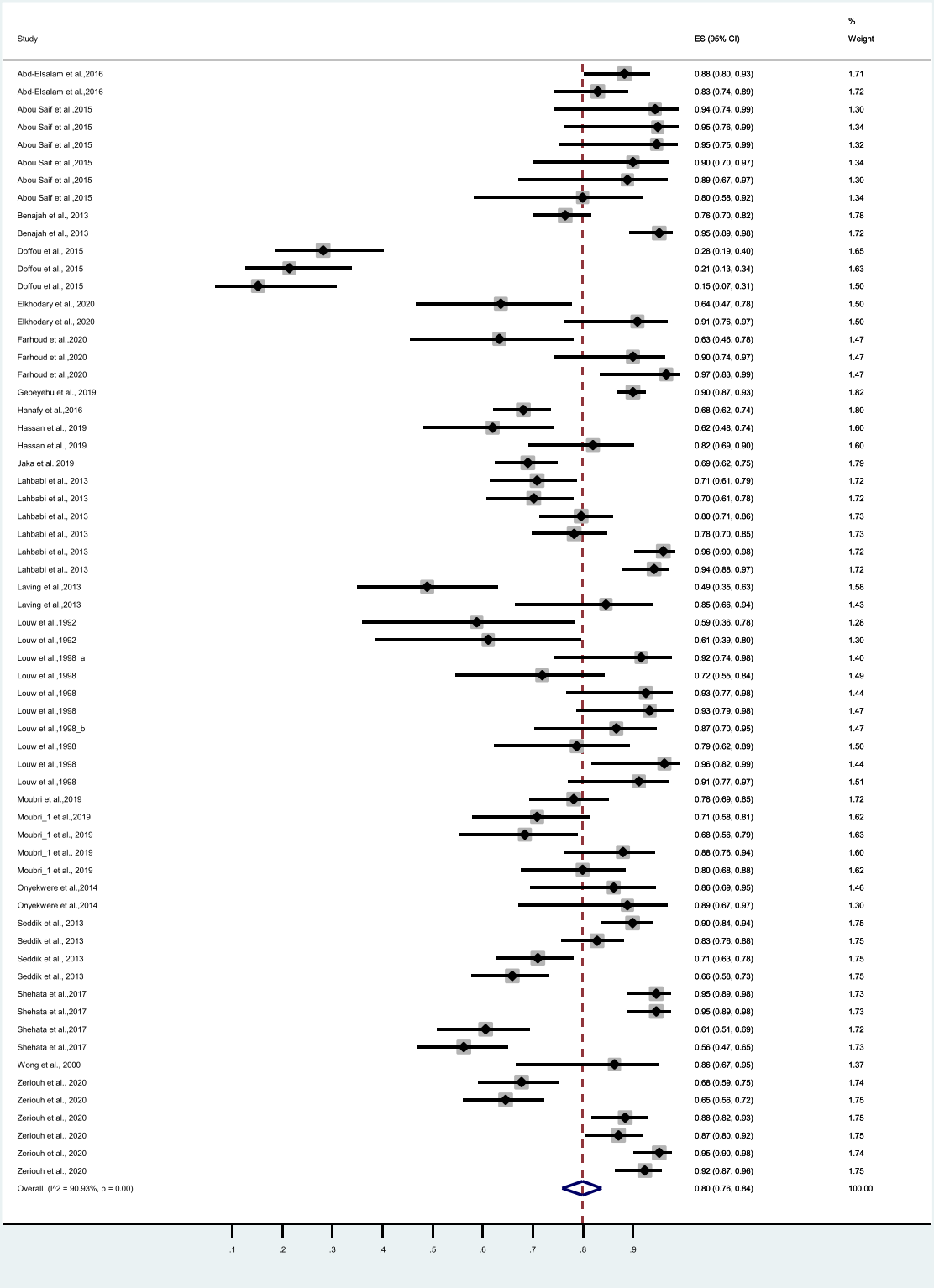

Fig. 3 Forest plots of the pooled eradication rates of *Helicobacter pylori* infection by first-line standard therapy in Africa from 22 studies

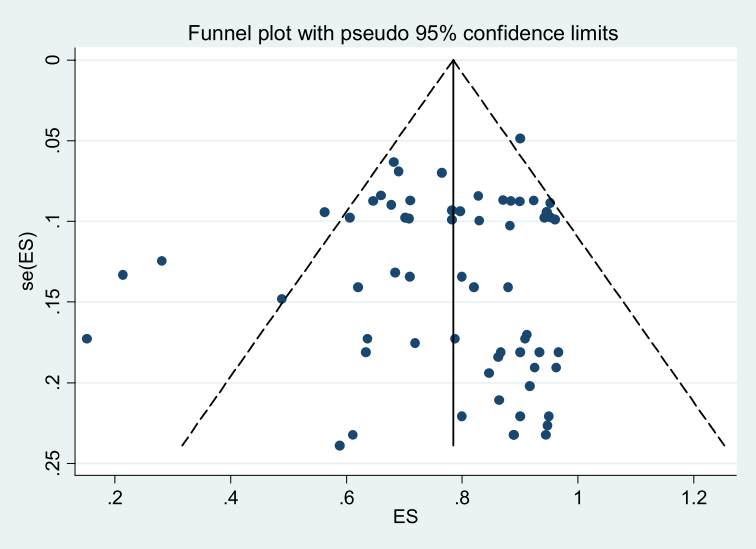

Fig. 4 Funnel plot showing absence of publication bias with no small study effects, $p = 0.672$. Publication bias assessment funnel plot; Egger's regression test ($p = 0.672$)

pattern of *H. pylori*. The World Gastroenterology Organization (WGO), in its 2023 guideline, recommended the minimum acceptable eradication rate greater than 80% on an intention-to-treat basis using PPI-clarithromycin plus amoxicillin in areas where clarithromycin resistance is low or moderate [42]. Determining the national and regional eradication rate is fundamental to establish an appropriate eradication protocol for *H. pylori* infection. Estimating the effectiveness of *H. pylori* eradication is difficult since factors like pretreatment antibiotic resistance have a profound effect [43–46]. Some studies consider distinct *H. pylori* diagnosis or eradication confirmation tests and employ different eradication regimens and/or duration based on the local guideline on the *H. pylori* treatment [47–49]. In the regional context, *H. pylori* treatment in Africa largely depends on an empirical approach despite the highest infection rate in the world [50, 51].

In the subgroup analysis by country, the highest eradication rate of 90% was from Ethiopia, and the lowest was 22.3% from Ivory Coast, as shown in Table 3. The eradication rate depends on the sensitivity and specificity of tests that detect *H. pylori*. The sensitivity and specificity of diagnostic or screening techniques depend on the laboratory techniques employed, personal skill to perform the test, and even the brand of reagents and facility standard. In the study from Ivory Coast, the *H. pylori* pre-and post-eradication detection was based on histological examination of gastric biopsy, which is less sensitive than conventional techniques such as urease test, anti-*H. pylori* antibody test, and PCR detection of bacterial genome. This finding is consistent with studies showing that treatment efficacy varies with *H. pylori* detection techniques [52–55].

This analysis presented the cumulative eradication rate for Africa and identified factors associated with eradication. In addition, the study included a sub-group analysis of differences in study design, country, treatment regimen, type of analysis, duration of eradication therapy, weeks of outcome measure and tests employed for *H. pylori* diagnosis and eradication confirmation. Africa contains 54 countries; however, this study has picked up reports only from 9 countries. Moreover, one-third of data are reported from Egypt. The fact might influence the generalization of our findings. Thus, eradication studies in Africa are so rare that more research must be promoted. There are so many regimen subgroups and result could be difficult to comprehend. But the general finding is that there is not significant variability among the regimen subgroups.

The current study included from observational to randomized control trails whereas the previous systematic review and network meta-analysis included only randomized controlled trials [11]. In Africa there is only very few RCT and only 7 articles are included. As a result, paucity of literature landscape in Africa, the current study has included observational study in addition to RCT. This has given a better understanding of eradication rate in Africa than the previous global meta-analysis. The

Table 3 The subgroup analysis of included studies by country, study design, type of analysis, study population, duration of therapy, outcome measures and regimen from 22 studies in Africa

Subgroup	Eradication rate (%)	95% CI (%)	I^2 (%)
Country			
Egypt ($n=7$)	82	(77–88)	89.85
Morocco ($n=4$)	82	(77–87)	92.2
South Africa ($n=4$)	86	(80–92)	60.17
Algeria ($n=2$)	78	(71–85)	53.33
Ethiopia ($n=1$)	90	(87–93	-
Nigeria ($n=1$)	87	(78–97)	-
Tanzania ($n=1$)	69	(62–75)	-
Kenya ($n=1$)	68	(58–78)	-
Ivory Coast ($n=1$)	22.3	(15–29)	-
Study design			
PS	85	(79–90)	88.76
RCT	77	(73–82)	93.84
Types of analysis			
PP	78	(73–82)	94.18
ITT	81	(76–86)	88.67
Study population			
Naïve	79	(75–82)	93.24
Non-naïve	86	(81–91)	-
Duration of therapy (days)			
14	80	(74–85)	88.73
10	88	(84–92)	83.49
7	66	(55–77)	91.52
Outcome measures (weeks)			
4	78	(71–84)	91.2
6	81	(73–88)	92.7
8	81	(72–88)	69.4
12	84	(76–91)	90.7
H. pylori confirmed test			
FAT	82	(76–87)	90.23
UBT	83	(78–88)	88.5
H	22.3	(16–30)	-
UBT + H	86	(67–95)	-
RUT + H	88	(77–96)	54.44
RUT + H + C	82	(69–92)	69.54
FAT + RUT + H + C	77	(68–85)	59.28
Regimen			
OLDN	86	(80–90)	
5OA, 5OLM	95	(84–100)	
5OA, 5OCM	95	(91–99)	
14OCM	84	(71–95)	
OAM/C	76	(70–82)	
OAM	67	(27–96)	
OAC	66	(50–80)	
OCM	44	(23–67)	
DLA	79	(68–88)	
LAC	81	(69–91)	
5LA, LCT	90	(74–97)	
7LA, LCT	97	(83–99)	
OACS	82	(69–90)	
PPIAM	71	(64–77)	
PPIAC	79	(74–83)	
5PPIA, PPIMC	95	(92–98)	
5OA, OCT	85	(66–94)	
S + B + OA	59	(36–78)	
S + OA	61	(39–80)	
PAC	89	(81–95)	
RAC	87	(76–96)	
5OA, OCT	86	(82–90)	
OCN	95	(91–97)	
PPI + A	66	(60–72)	
5PPI + A, PPI + ACM	88	(84–92)	
OACM	94	(91–97)	

PS Prospective study, *RCT* Randomized control trial, *PP* Per protocol, *ITT* Intention to treat, *FAT* Fecal antigen test, *UBT* Urea breath test, *H* Histology, RUT Rapid urease test, *C* Culture, *OAC* Omeprazole + Amoxicillin + Clarithromycin, *OCM* Omeprazole + Clarithromycin + Metronidazole, *OAM* Omeprazole + Amoxicillin + Metronidazole, *LAC* Lansoprazole + Amoxicillin + Clarithromycin, *PAC* Pantoprazole + Amoxicillin + Clarithromycin, *RAC* Rabeprazole + Amoxicillin + Clarithromycin, *OCN* Omeprazole + Clarithromycin + Nitazoxanide, *OACS* Omeprazole + Amoxicillin + Clarithromycin + Simvastatin, *OLDN* Omeprazole + Levofloxacin + Doxycycline + Nitazoxanide, *DLA* Dexlansoprazole + Levofloxacin + Amoxicillin *OCT* Omeprazole + Clarithromycin + Tinidazole

study suffers from heterogeneity and there is no generalizable finding.

Conclusion

In Africa, the first-line therapy showed variable eradication rate for *H. pylori*. This study demonstrates the need to reassess antibiotic susceptibility in each country and optimize current *H. pylori* treatment regimens. Antibiotic susceptibility of *H. pylori* should be investigated in each nation of Africa. Although gastrointestinal disorders and associated *H. pylori* infections are common problems in Africa, less attention is given to translate the efficiency of eradication and improve the eradication regimen. Future RCT studies with standardized regimens are required.

Abbreviations

CI	Confidence interval
H. pylori	*Helicobacter pylori*
OAC	Omeprazole + Amoxicillin + Clarithromycin
OCM	Omeprazole + Clarithromycin + Metronidazole

OAM	Omeprazole + Amoxicillin + Metronidazole
LAC	Lansoprazole + Amoxicillin + Clarithromycin
PAC	Pantoprazole + Amoxicillin + Clarithromycin
RAC	Rabeprazole + Amoxicillin + Clarithromycin
OCN	Omeprazole + Clarithromycin + Nitazoxacine
OACS	Omeprazole + Amoxicillin + Clarithromycin + Simvastatin
OLDN	Omeprazole + Levofloxacin + Doxycycline + Nitazoxanide
DLA	Dexlansoprazole + Levofloxacin + Amoxicillin
OCT	Omeprazole + Clarithromycin + Tinidazole
PS	Prospective study;
RCT	Randomized control trial
PP	Per protocol
ITT	Intention to treat
FAT	Fecal antigen test
UBT	Urea breath test
H	Histology
RUT	Rapid urease test
C	Culture

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-023-02707-5.

Additional file 1: Supplementary file 1. 'Checklist risk-of-bias assessment for randomized trials (RoB2)'.

Additional file 2: Supplementary file 2. 'Checklist risk-of-bias in non-randomized studies of intervention (ROBINS-I)'.

Additional file 3: Supplementary file 3. Databases and search strategy.

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Authors' contributions
SF: Conceived and designed the study, analyzed data, and drafted the manuscript. SD: interpret the results and review the manuscript. AG: assess methodological quality and review the manuscript. HI and HY: review the manuscript. SF, SD, AG, HE and SS select and evaluate the quality of studies and extract data. All authors revised, edited, and approved the manuscript.

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Availability of data and materials
All data generated or analyzed are included in the result of the manuscript and its supplementary files.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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References

1. Schmidt HM, Ha DM, Taylor EF, Kovach Z, Goh KL, Fock KM, Barrett JH, Forman D, Mitchell H. Variation in human genetic polymorphisms, their association with Helicobacter pylori acquisition and gastric cancer in a multi-ethnic country. J Gastroenterol Hepatol. 2011;26(12):1725–32.
2. Chiarini A, Calà C, Bonura C, Gullo A, Giuliana G, Peralta S, D'Arpa F, Giammanco A. Prevalence of virulence-associated genotypes of Helicobacter pylori and correlation with severity of gastric pathology in patients from western Sicily, Italy. Eur J Clin Microbiol Infect Dis. 2009;28(5):437–46.
3. Rosenstock S, Jørgensen T, Bonnevie O, Andersen L. Risk factors for peptic ulcer disease: a population based prospective cohort study comprising 2416 Danish adults. Gut. 2003;52(2):186–93.
4. Jin G, Lv J, Yang M, Wang M, Zhu M, Wang T, Yan C, Yu C, Ding Y, Li G, et al. Genetic risk, incident gastric cancer, and healthy lifestyle: a meta-analysis of genome-wide association studies and prospective cohort study. Lancet Oncol. 2020;21(10):1378–86.
5. Hooi JKY, Lai WY, Ng WK, Suen MMY, Underwood FE, Tanyingoh D, Malfertheiner P, Graham DY, Wong VWS, Wu JCY, et al. Global Prevalence of Helicobacter pylori Infection: Systematic Review and Meta-Analysis. Gastroenterology. 2017;153(2):420–9.
6. Yuan C, Adeloye D, Luk TT, Huang L, He Y, Xu Y, Ye X, Yi Q, Song P, Rudan I. The global prevalence of and factors associated with Helicobacter pylori infection in children: a systematic review and meta-analysis. Lancet Child Adolesc Health. 2022;6(3):185–94.
7. Malfertheiner P, Megraud F, Rokkas T, Gisbert JP, Liou JM, Schulz C, Gasbarrini A, Hunt RH, Leja M, O'Morain C et al. Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report. Gut. 2022;71(9):1724–62.
8. Chiang TH, Chang WJ, Chen SL, Yen AM, Fann JC, Chiu SY, Chen YR, Chuang SL, Shieh CF, Liu CY, et al. Mass eradication of Helicobacter pylori to reduce gastric cancer incidence and mortality: a long-term cohort study on Matsu Islands. Gut. 2021;70(2):243–50.
9. De Francesco V, Bellesia A, Ridola L, Manta R, Zullo A. First-line therapies for Helicobacter pylori eradication: a critical reappraisal of updated guidelines. Ann Gastroenterol. 2017;30(4):373–9.
10. Graham DY, Lee YC, Wu MS. Rational Helicobacter pylori therapy: evidence-based medicine rather than medicine-based evidence. Clin Gastroenterol Hepatol. 2014;12(2):177-186.e173; Discussion e112-173.
11. Zamani M, Alizadeh-Tabari S, Zamani V, Shokri-Shirvani J, Derakhshan MH. Worldwide and Regional Efficacy Estimates of First-line Helicobacter pylori Treatments: A Systematic Review and Network Meta-Analysis. J Clin Gastroenterol. 2022;56(2):114–24.
12. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.
13. Abd-Elsalam S, Kobtan A, El-Kalla F, Elkhalawany W, Nawasany SE, Saif SA, Yousef M, Ali LA, Soliman S, Mansour L, et al. A 2-week Nitazoxanide-based quadruple treatment as a rescue therapy for Helicobacter pylori eradication: A single center experience. Medicine (Baltimore). 2016;95(24):e3879.
14. Elkhodary NM, Farrag KA, Elokaby AM, El-Hay Omran GA. Efficacy and safety of 7 days versus 10 days triple therapy based on levofloxacin-dexlansoprazole for eradication of Helicobacter pylori: A pilot randomized trial. Indian J Pharmacol. 2020;52(5):356–64.
15. Farhoud NS, Ibrahim OM, Ezzat SE. Efficacy and Cost-effectiveness Comparison of 10-Day, 14-Day Sequential Versus 14-Day Triple Therapies for Treating Helicobacter pylori Infection in Egyptian Patients. J Clin Gastroenterol. 2020;54(9):806–12.
16. Hanafy AS, El Hawary AT, Hamed EF, Hassaneen AM. Impact of Helicobacter pylori eradication on refractory thrombocytopenia in patients with chronic HCV awaiting antiviral therapy. Eur J Clin Microbiol Infect Dis. 2016;35(7):1171–6.
17. Hassan AM, Shawky MAE, Mohammed AQ, Haridy MA, Eid KA. Simvastatin improves the eradication rate of Helicobacter pylori: upper Egypt experience. Infect Drug Resist. 2019;12:1529–34.
18. Shehata MA, Talaat R, Soliman S, Elmesseri H, Soliman S, Abd-Elsalam S. Randomized controlled study of a novel triple nitazoxanide

(NTZ)-containing therapeutic regimen versus the traditional regimen for eradication of Helicobacter pylori infection. Helicobacter 2017;22(5):e12395.
19. Abou-Saif MA, Ahmed AS, Mohammed N. Sequential therapy versus standard triple therapy for Helicobacter pylori eradication. Am J Res Commun. 2015;3:132–46.
20. Benajah DA, Lahbabi M, Alaoui S, El Rhazi K, El Abkari M, Nejjari C, Amarti A, Bennani B, Mahmoud M, Ibrahimi SA. Prevalence of Helicobacter pylori and its recurrence after successful eradication in a developing nation (Morocco). Clin Res Hepatol Gastroenterol. 2013;37(5):519–26.
21. Lahbabi M, Alaoui S, El Rhazi K, El Abkari M, Nejjari C, Amarti A, Bennani B, Mahmoud M, Ibrahimi A, Benajah DA. Sequential therapy versus standard triple-drug therapy for Helicobacter pylori eradication: result of the HPFEZ randomised study. Clin Res Hepatol Gastroenterol. 2013;37(4):416–21.
22. Seddik H, Ahid S, El Adioui T, El Hamdi FZ, Hassar M, Abouqal R, Cherrah Y, Benkirane A. Sequential therapy versus standard triple-drug therapy for Helicobacter pylori eradication: a prospective randomized study. Eur J Clin Pharmacol. 2013;69(9):1709–15.
23. Zeriouh M, Elmekkaoui A, Bouqfar M, Zazour A, Khannoussi W, Kharrasse G, Abda N, Ismaili Z. Non-Bismuth Quadruple Therapy, Sequential Therapy or High-Dose Esomeprazole and Amoxicillin Dual Therapy for First-Line Helicobacter pylori Eradication: A Prospective Randomized Study. Cureus. 2020;12(12):e11837.
24. Louw JA, Zak J, Lucke W, Le Roux E, Jaskiewicz K, Winter T, Lastovica A, Marks IN. Triple therapy with sucralfate is as effective as triple therapy containing bismuth in eradicating Helicobacter pylori and reducing duodenal ulcer relapse rates. Scand J Gastroenterol Suppl. 1992;191:28–31.
25. Louw JA, van Rensburg CJ, Hanslo D, Grundlings HD, Girdwood AH, Marks IN. Two-week course of pantoprazole combined with 1 week of amoxycillin and clarithromycin is effective in Helicobacter pylori eradication and duodenal ulcer healing. Aliment Pharmacol Ther. 1998;12(6):545–50.
26. Louw JA, Van Rensburg CJ, Moola S, Kotze D, Marks IN. Helicobacter pylori eradication and ulcer healing with daily lansoprazole, plus 1 or 2 weeks co-therapy with amoxycillin and clarithromycin. Aliment Pharmacol Ther. 1998;12(9):881–5.
27. Wong BC, Chang FY, Abid S, Abbas Z, Lin BR, Van Rensburg C, Chen PC, Schneider H, Simjee AE, Hamid SS, et al. Triple therapy with clarithromycin, omeprazole, and amoxicillin for eradication of Helicobacter pylori in duodenal ulcer patients in Asia and Africa. Aliment Pharmacol Ther. 2000;14(11):1529–35.
28. Moubri M, Burucoa C, Kalach N, Larras RR, Nouar N, Mouffok F, Arrada Z. Performances of the IDEIA HpStAR Stool Antigen Test in Detection of Helicobacter pylori Infection Before and After Eradication Treatment in Algerian Children. J Trop Pediatr. 2019;65(3):210–6.
29. Moubri M, Kalach N, Larras R, Berrah H, Mouffok F, Guechi Z, Cadranel S. Adapted first-line treatment of Helicobacter pylori infection in Algerian children. Ann Gastroenterol. 2019;32(1):60–6.
30. Gebeyehu E, Nigatu D, Engidawork E. Helicobacter pylori eradication rate of standard triple therapy and factors affecting eradication rate at Bahir Dar city administration, Northwest Ethiopia: A prospective follow up study. PLoS ONE. 2019;14(6):e0217645.
31. Onyekwere CA, Odiagah JN, Igetei R, Emanuel AO, Ekere F, Smith S. Rabeprazole, clarithromycin, and amoxicillin Helicobacter pylori eradication therapy: report of an efficacy study. World J Gastroenterol. 2014;20(13):3615–9.
32. Jaka H, Mueller A, Kasang C, Mshana SE. Predictors of triple therapy treatment failure among H. pylori infected patients attending at a tertiary hospital in Northwest Tanzania: a prospective study. BMC Infect Dis. 2019;19(1):447.
33 Laving A, Kamenwa R, Sayed S, Kimang'a AN, Revathi G. Effectiveness of sequential v. standard triple therapy for treatment of Helicobacter pylori infection in children in Nairobi. Kenya S Afr Med J. 2013;103(12):921–4.
34. Doffou AS, Attia KA, Bathaix MFY, Bangoura AD, Kissy-Anzouan YH, Kouamé HD, Mahassadi KA, N'Da KJ, Kouyaté M, Assi C. The Helicobacter pylori eradication rate in a high prevalence area (West Africa): three triple therapy comparative study. Open Journal of Gastroenterology. 2015;5(12):200.
35. Hu Y, Zhu Y, Lu NH. Novel and Effective Therapeutic Regimens for Helicobacter pylori in an Era of Increasing Antibiotic Resistance. Front Cell Infect Microbiol. 2017;7:168.
36 Bago P, Vcev A, Tomic M, Rozankovic M, Marusić M, Bago J. High eradication rate of H. pylori with moxifloxacin-based treatment: a randomized controlled trial. Wiener klinische Wochenschrift. 2007;119(11–12):372–8.
37. Gumurdulu Y, Serin E, Ozer B, Kayaselcuk F, Ozsahin K, Cosar AM, Gursoy M, Gur G, Yilmaz U, Boyacioglu S. Low eradication rate of Helicobacter pylori with triple 7–14 days and quadriple therapy in Turkey. World J Gastroenterol. 2004;10(5):668–71.
38. Paoluzi OA, Del Vecchio BG, Visconti E, Coppola M, Fontana C, Favaro M, Pallone F. Low efficacy of levofloxacin-doxycycline-based third-line triple therapy for Helicobacter pylori eradication in Italy. World J Gastroenterol. 2015;21(21):6698–705.
39. Di Ciaula A, Scaccianoce G, Venerito M, Zullo A, Bonfrate L, Rokkas T, Portincasa P. Eradication rates in Italian subjects heterogeneously managed for Helicobacter pylori infection. Time to abandon empiric treatments in Southern Europe. JGLD. 2017;26(2):129–37.
40. Kim SE, Park MI, Park SJ, Moon W, Choi YJ, Cheon JH, Kwon HJ, Ku KH, Yoo CH, Kim JH, et al. Trends in Helicobacter pylori eradication rates by first-line triple therapy and related factors in eradication therapy. Korean J Intern Med. 2015;30(6):801–7.
41. Yoon JH, Baik GH, Sohn KM, Kim DY, Kim YS, Suk KT, Kim JB, Kim DJ, Kim JB, Shin WG, et al. Trends in the eradication rates of Helicobacter pylori infection for eleven years. World J Gastroenterol. 2012;18(45):6628–34.
42. Katelaris P, Hunt R, Bazzoli F, Cohen H, Fock KM, Gemilyan M, Malfertheiner P, Mégraud F, Piscoya A, Quach D, et al. Helicobacter pylori World Gastroenterology Organization Global Guideline. J Clin Gastroenterol. 2023;57(2):111–26.
43. Selgrad M, Tammer I, Langner C, Bornschein J, Meißle J, Kandulski A, Varbanova M, Wex T, Schlüter D, Malfertheiner P. Different antibiotic susceptibility between antrum and corpus of the stomach, a possible reason for treatment failure of Helicobacter pylori infection. World J Gastroenterol. 2014;20(43):16245–51.
44. Park CS, Lee SM, Park CH, Koh HR, Jun CH, Park SY, Lee WS, Joo YE, Kim HS, Choi SK, et al. Pretreatment antimicrobial susceptibility-guided vs. clarithromycin-based triple therapy for Helicobacter pylori eradication in a region with high rates of multiple drug resistance. Am J Gastroenterol. 2014;109(10):1595–602.
45. Mahachai V, Thong-Ngam D, Noophun P, Tumwasorn S, Kullavanijaya P. Efficacy of clarithromycin-based triple therapy for treating Helicobacter pylori in Thai non-ulcer dyspeptic patients with clarithromycin-resistant strains. J Med Assoc Thai. 2006;89 Suppl 3:S74-78.
46. Wong WM, Gu Q, Wang WH, Fung FM, Berg DE, Lai KC, Xia HH, Hu WH, Chan CK, Chan AO, et al. Effects of primary metronidazole and clarithromycin resistance to Helicobacter pylori on omeprazole, metronidazole, and clarithromycin triple-therapy regimen in a region with high rates of metronidazole resistance. Clin Infect Dis. 2003;37(7):882–9.
47. Lee SY. Current progress toward eradicating Helicobacter pylori in East Asian countries: differences in the 2013 revised guidelines between China, Japan, and South Korea. World J Gastroenterol. 2014;20(6):1493–502.
48. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2017;112(2):212–39.
49. Coelho LG, Coelho MC. Clinical management of Helicobacter pylori: the Latin American perspective. Dig Dis (Basel, Switzerland). 2014;32(3):302–9.
50. Smith SI, Ajayi A, Jolaiya T, Onyekwere C, Setshedi M, Schulz C, Otegbayo JA, Ndip R, Dieye Y, Alboraie M, et al. Helicobacter pylori Infection in Africa: Update of the Current Situation and Challenges. Dig Dis (Basel, Switzerland). 2022;40(4):535–44.
51. Jaka H, Rhee JA, Östlundh L, Smart L, Peck R, Mueller A, Kasang C, Mshana SE. The magnitude of antibiotic resistance to Helicobacter pylori in Africa and identified mutations which confer resistance to antibiotics: systematic review and meta-analysis. BMC Infect Dis. 2018;18(1):193.
52. Wang YK, Kuo FC, Liu CJ, Wu MC, Shih HY, Wang SS, Wu JY, Kuo CH, Huang YK, Wu DC. Diagnosis of Helicobacter pylori infection: Current options and developments. World J Gastroenterol. 2015;21(40):11221–35.
53. Lee JY, Kim N. Diagnosis of Helicobacter pylori by invasive test: histology. Ann Transl Med. 2015;3(1):10.
54. Lunet N, Peleteiro B, Carrilho C, Figueiredo C, Azevedo A. Sensitivity is not an intrinsic property of a diagnostic test: empirical evidence from

histological diagnosis of Helicobacter pylori infection. BMC Gastroenterol. 2009;9:98.
55. Kocsmár É, Szirtes I, Kramer Z, Szijártó A, Bene L, Buzás GM, Kenessey I, Bronsert P, Csanadi A, Lutz L, et al. Sensitivity of Helicobacter pylori detection by Giemsa staining is poor in comparison with immunohistochemistry and fluorescent in situ hybridization and strongly depends on inflammatory activity. Helicobacter. 2017;22(4):e12387.

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