Helicobacter pylori Infection in Africa: Update of the Current Situation and Challenges

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Keywords

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Abstract

Background: The burden of *Helicobacter pylori* infection (HPI) in Africa remains high with varying levels of prevalence among children and adults reported in different regions of the continent. Persistent and uneradicated HPI could result in gastric cancer, although less severe pathological outcomes have been reported among Africans – the so-called “African enigma.” **Summary:** Analysis of endoscopic findings of the upper gastrointestinal tract demonstrates similarities

with that of patients from the West. Thus, it could be asserted that the true picture of HPI in Africa is yet to be unveiled due to several challenges including inadequate health-care system, lack of treatment guidelines and standardized protocol for diagnosis, and lack of data. This review explores the prevalence, diagnosis, treatment, and health-care system in Africa as it relates to HPI, thus providing an update and highlighting the need for an African HPI guideline. **Key Messages:** There is high prevalence of *Helicobacter pylori* infection (HPI) in Africa with an increasing burden of antibiotic resistance. Various methods including invasive and noninvasive methods are deployed in the diagnosis of HPI in Africa. There is a need for consensus on diagnosis and treatment of HPI in Africa.

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Introduction

Helicobacter pylori infection (HPI) is ubiquitous, with an estimated 50% of the world population infected [1]. The burden of the infection in Africa is high, with a reported prevalence of 70.1% [2]. The pathogen is acquired in childhood and could persist throughout life if not properly treated. Several gastrointestinal pathological outcomes of HPI exist which include peptic ulcer disease, mucosa-associated lymphoid tissue lymphoma, and gastric adenocarcinoma [3]. Prolonged and persistent HPI can result in gastric cancer. Multiple factors including virulence determinants of infecting *H. pylori* strain, genetics of the infected individual, method of diagnosis, and treatment options can facilitate persistent infection and the aforementioned severe outcome. Accurate diagnosis and guided treatment is known to lessen the burden of HPI, as has been reported in developed countries [4]. In Europe, America, and Asia-Pacific region, there are consensus guidelines on diagnosis and treatment of HPI which are reviewed over time by the European *Helicobacter* and Microbiota Study Group, American College of Gastroenterology, and Asia-Pacific Association of Gastroenterology, respectively [5–7]. In Africa, there is no consensus guideline for diagnosis and treatment of HPI. Although several reports from the continent have employed existing invasive and noninvasive methods for diagnosis and different treatment regimens for management and eradication of the disease, the need to harmonize protocols is imperative. Inadequate health-care systems coupled with an increasing number of treatment failures due to antibiotic resistance among other challenges are pervading in Africa. Here, we review the epidemiology, diagnosis, and treatment of HPI in Africa with the view to providing an update that will facilitate a work plan toward initiating a consensus on diagnosis and treatment in the continent.

Epidemiology of HPI

HPI has been a neglected tropic disease in Africa; most other infectious diseases like HIV, malaria, and tuberculosis have more attention in terms of research funding and grants. This microorganism is acquired from childhood through fecal-, oral, or oral-oral route [8, 9]. *H. pylori* was also reported to be isolated from sheep, shepherds, and their families; this finding points to the zoonotic transmission of *H. pylori* [10, 11]. *H. pylori* plays a significant role in the pathogenesis of chronic gastritis, peptic ulcer disease, and gastric cancer [12] which is the

third rated cancer that kills in the world [13, 14]. In Africa, the pathology is not as severe as experienced by infected persons in Europe, Asia, and other continents as erosions are seen as the most prevalent manifestation in patients with dyspepsia; this is termed Africa enigma [11, 15, 16]. There are extra-gastric complications associated with HPI which have been reported such as the negative effect on cognitive function [17], Henoch-Schonlein purpura [18], iron deficiency anemia [19], delay in childhood growth [20], and diabetes mellitus [21–23].

The prevalence of *H. pylori* varies from one geographical location to another; within a country, it is possible to have different prevalences considering the age, level of literacy, diet, and the location. In Nigeria, the prevalence of *H. pylori* as high as 87.8% has been reported in the north [24], while a prevalence rate of 34.2 and 51.4 (adult population), and 36.3 and 42.6% (children population) have been reported in the southeast and south-south geopolitical zones of the country, respectively [25–28]. A prevalence of 6.0 and 28% has been reported in children from north central and southwestern parts of Nigeria, respectively [29]. The high prevalence rate of *H. pylori* has been associated with risk factors such as low socioeconomic status, unclear water source, overcrowding, cigarette smoking, and increased levels of interferon gamma [24, 27, 28]. In other parts of Africa, a 70.8% prevalence rate have been reported in Burundi [30]; 75% in Rwanda 2014, with 20.1% of cases having ulcer, 10% gastric obstruction, and 4.5% malignancy [31]; 70.41% and 93.1% in 2015, respectively, in Togo [32] and Congo Brazzaville [33]; 63.8% in Morocco [34]; 88% in Ghana [35]; and 66.12% in Egypt in 2019 [36]. Furthermore, a prevalence of 64.6% in children with risk factors of overcrowding, patronizing of food vendors, and illiteracy was reported in Egypt [36]. In the Republic of Benin, a 71.5% prevalence rate was reported but was not associated with age, sex, marital status, religion, occupation, or education [37]; 73.2% in Cameroon with a significant association with age, socioeconomic status, alcohol, family history, and nonsteroidal anti-inflammatory drugs and similarly anemia, duodenal ulcer, and chronic gastritis have been reported as common in patients with *H. pylori* infection [38]; and 71.43% prevalence rate was published in Algeria [39]. In a research conducted in Ethiopia, 88.9% *H. pylori* prevalence was reported in male individuals, while 82.8% was in female individuals [40]. These prevalence reports from Africa are higher than reports from other continents. The prevalence of *H. pylori* in Europe (Germany) published in 2018 was said to be 20–40% [41], North America 23.1% [42], Australia 24.6% [43], and 48.8% Asia [44, 45].

Fig. 1. Invasive and noninvasive methods employed in the diagnosis of HPI in Africa. HPI, *Helicobacter pylori* infection; RUT, rapid urease test; UBT, urea breath test; SAT, stool antigen test; FISH, fluorescence in situ hybridization; PCR, polymerase chain reaction.

The possible causes of discrepancies in the prevalence rate across continents have been reported to be due to urbanization with better access to health facilities and portable water [2], host genetic makeup, age and gender, immune response of the host, pathogenicity of the *H. pylori* strains, and environmental factors [46–48]. The complications of HPI in Africa which ranges from erosion, atrophy, ulcers, to cancer (rare) have been reported in many studies where histology and endoscopy have been employed as diagnostic tools [15, 16]. Individuals with habits of smoking and use of alcohol are at greater risk of gastric cancer, while those who consume vegetables, fruits, and vitamins were reported to have an inverse association with gastric cancer [49, 50]. Various studies have reported that HPis are acquired during early childhood, but the symptoms may linger or manifest between the ages of 41–60 years, which is the age range mostly having the highest prevalence [28, 51].

Diagnosis of HPI in Africa

Considering the high burden of HPI in Africa with its associated pathological outcomes, accurate and prompt diagnosis is key to managing, treating, and eradicating

the disease. Several diagnostic approaches of HPI exist which have been broadly categorized into invasive and noninvasive methods [41], as shown in Figure 1. Invasive methods such as endoscopy, histology, and rapid urease test (RUT) are widely in use, and their specificity and sensitivity vary. However, there have been major technological improvements in endoscopy coupled with artificial intelligence that have enhanced diagnosis and turnaround time [52]. Histology has been regarded as a gold standard for the direct detection of *H. pylori* in the mucus, and its accuracy is dependent on the location from which biopsies were obtained and the number of obtained biopsies [3]. RUT has also shown to be reliable in the diagnosis of HPI from biopsies, with a reported 95% sensitivity and about 80–90% specificity [53].

Culture of *H. pylori* from biopsies obtained from endoscopy and stool samples is another method that has been regarded as a gold standard in the diagnosis of HPI and comes with the advantage of being useful in determining the antibiotic susceptibility of *H. pylori* isolates [3]. Another invasive and noninvasive (depending on sample collected) method is serology in which anti-*H. pylori* IgG is detected in serum, whole blood, urine, or saliva. However, the method is less specific as it cannot distin-

Table 1. Various methods used in the diagnosis of HPI in Africa [16, 39, 62–99]

Region/country	Methods								
	endoscopy	histology	RUT	culture	UBT	SAT	serology	molecular	reference
North Africa									
Algeria	✓	✓	✓	✓	✓	✓	NA	✓	[39, 62, 63]
Egypt	✓	✓	✓	NA	✓	✓	NA	✓	[64–66]
Libya	NA	NA	NA	NA	NA	NA	✓	NA	[67–69]
Tunisia	✓	✓	✓	✓	NA	NA	✓	✓	[70–72]
West Africa									
Ghana	✓	NA	✓	NA	NA	NA	NA	NA	[73–75]
Nigeria	✓	✓	✓	✓	✓	✓	✓	✓	[16, 76–79]
Senegal	✓	✓	NA	✓	NA	NA	NA	NA	[80–82]
Central Africa									
Cameroon	✓	✓	✓	✓	NA	✓	✓	NA	[83–86]
East Africa									
Ethiopia	NA	NA	NA	NA	NA	✓	✓	NA	[87, 88]
Kenya	✓	✓	✓	✓	NA	✓	NA	NA	[89–91]
Uganda	✓	✓	✓	NA	NA	✓	✓	NA	[92–95]
Southern Africa									
South Africa	✓	✓	✓	✓	NA	NA	NA	✓	[96–99]

✓, data available; NA, data not available; HPI, *Helicobacter pylori* infection; RUT, rapid urease test; UBT, urea breath test; SAT, stool antigen test.

guish active from inactive infection and has low sensitivity [53, 54]. The use of fluorescence in situ hybridization in the direct detection of *H. pylori* in biopsies has also been reported. Moosavian et al. [55] and Demiray-Gurbuz et al. [56] reported the rapid assessment of clarithromycin susceptibility of *H. pylori* in the biopsies of patients with dyspepsia by using fluorescence in situ hybridization. The stool antigen test (SAT) is a monoclonal or polyclonal antibody approach which has been widely adapted as a noninvasive method in the screening for HPI [57]. However, the monoclonal antibody based tests are superior to the polyclonal. Another noninvasive method for diagnosing HPI is the urea breath test (UBT) which has been referred to as the most accurate noninvasive method. It has also been considered as the best test for epidemiological studies and for assessing the eradication of the bacteria after treatment [58, 59]. The test is based on the hydrolysis of isotope-labeled urea (labeled with ^{14}C) or nonradioisotope-labeled ^{13}C of urease produced by *H. pylori*; the more stable ^{13}C test is preferred [60]. The sensitivity and specificity of the ^{13}C UBT are estimated to be as high as 98.1 and 95.1%, respectively [61].

Several of the aforementioned methods are in use in Africa for the diagnosis of HPI, as shown in Table 1. However, there seems to be no consensus approach that has been adapted by member countries in the continent on the diagnosis of HPI, and poor health infrastructure,

the limited number of health professionals, and poor standard of living limit the routine use of some of the methods in some quarters. Cost-effective and accurate methods are needed to effectively lower the burden of the infection in Africa than developed countries where it has been reported that HPI is on a rapid decline over the past 100 years with concomitant reduction in peptic ulcer disease and gastric cancer associated with *H. pylori* [4]. In Algeria, Moubri et al. [62] in a study used both invasive and noninvasive methods including ^{13}C UBT, monoclonal SAT (*HpStAR*), endoscopy, RUT, histology, and culture for the diagnosis of HPI in children. In another epidemiological study of HPI in symptomatic patients in a tertiary hospital in Algeria, Kasmi et al. [39] reported only the use of endoscopy and histological examination of biopsies in the diagnosis of HPI, for which a prevalence rate of 66.12% was recorded. In Egypt, another North African country, a consensus reached by experts in 2017 on the diagnosis of HPI in the country recommended the use of SAT, which is widely available in Egypt; histological detection of *H. pylori*; and assessment of atrophy; RUT; and UBT. Although prior to this, diagnosis has been mainly based on histology and SAT [64]. In Libya, most studies relied on serological methods for diagnosing HPI using ELISA that assayed for anti-*H. pylori* IgG [67–69]. The approach to the diagnosis of HPI in Tunisia has a combination of endoscopy, serology,

histology, RUT, culture, and polymerase chain reaction (PCR). In a seroprevalence study among blood donors, asymptomatic patients, and control subjects, Mansour et al. [70] reported the use of ELISA, culture, and *cagA* PCR to establish HPI among participants. In other studies, Loghmari et al. [71] and Mansour et al. [72] reported the use of endoscopy, histology, and RUT, and endoscopy, histology, and culture, respectively, in the detection of *H. pylori*. A combination of diagnostic methods is largely used in West Africa. In a retrospective records review of patients attending a public hospital in Accra Ghana between 1999 and 2012, endoscopy and RUT were the sole methods for the diagnosis of HPI [73]. Other studies from Ghana have also reported mainly the use of endoscopy and RUT for the diagnosis of HPI [74, 75, 100]. HPI diagnosis in Nigeria encompasses the use of endoscopy, histology, UBT, SAT, serology, and culture. In the study of Olokoba et al. [101], histology and serology were used in the diagnosis of HPI in patients with dyspepsia in northern Nigeria. In another study in the south-south region of Nigeria, Ray-Offor and Obiorah [102] reported the use of endoscopy and histology in the diagnosis of HPI. Smith et al. [76] in a study compared the use of conventional PCR with other diagnostic techniques for the diagnosis of HPI in patients in Nigeria. Results revealed that PCR using the *glmM* gene was also a reliable test compared to histology and the CLO test. Other studies Smith et al. [103], Onyekere et al. [77], Smith et al. [78], Palamides et al. [16], and Ajayi et al. [79] used SAT, UBT, stool-PCR, UBT and culture from biopsy, and qPCR, respectively, in the diagnosis of HPI in Nigeria. The use of endoscopy, histology, and culture in the diagnosis of HPI has also been reported in Senegal by Breurec et al. [80]; Seck et al. [81]; and Doh et al. [82]. Diagnostic methods of HPI in Central African countries were not in any way different from those used in other parts of Africa. Mabeku et al. [83] in a study in which they compared the diagnostic reliability of serology, SAT, and RUT in the assessment of HPI in patients with gastroduodenal disorders concluded that SAT was a reliable noninvasive method in Cameroon. However, serology is widely reported to have been used for the screening of HPI in dyspeptic patients in primary care settings and other public hospitals in Cameroon [84, 85, 104, 105]. RUT combined with histology [86] and culture [106] has also been used in the diagnosis of HPI in Cameroon. In Ethiopia, an East African country, reports on the diagnosis of HPI are largely based on serology and SAT [87, 88, 107–109]. On the other hand, Kenya, a neighboring country, has reports on the use of SAT [89, 90], endoscopy, RUT, histol-

ogy, and culture [91, 110]. Similarly, in Uganda, SAT [92], endoscopy, histology and RUT [93, 94], serology and SAT [95] have been used in the diagnosis of HPI. In South Africa, several approaches including endoscopy, RUT and histology [96], endoscopy, culture and PCR [97, 98], and endoscopy and histology [99] are used in the diagnosis of HPI.

Health-Care System

H. pylori surveillance, diagnostic, and therapy require health-care resources for optimal management. The African enigma describing dissociation of prevalence between HPIs in Africa and *H. pylori* gastric adenocarcinoma could have its origin in the less developed health-care system in several African countries [111]. Analyses of findings from patients who had upper gastrointestinal endoscopy demonstrated similar findings compared to upper endoscopy trials from industrialized regions suggesting that the grade of diagnostic options determines the diagnostic yield [112].

A survey initiated by the European Society of Gastrointestinal Endoscopy (ESGE) revealed a general shortage of medical and nonmedical personnel in African countries. While in Europe, 1,286–6,645 physicians per million inhabitants are available, in Africa, 14–1,192 medical doctors support the medical system [113]. In parallel, academic and nonacademic training centers for basic or advanced endoscopy exist in only half of African countries [113]. National endoscopy societies are only known to exist in South Africa, Nigeria, Morocco, Ivory Coast, and Burkina Faso. The most frequent indications for upper gastrointestinal endoscopy in Africa are nonvariceal bleeding and infectious diseases such as HPI. The diagnostic test to confirm HPI is influenced by the availability, prevalence and pretest probability of infection, cost, and regional factors such as use of proton pump inhibitors and frequency of use of (over-the-counter) antibiotics. Several guidelines recommend noninvasive tests in dyspeptic patients without alarm symptoms and after eradication treatment such as the ¹³C urease breath test and SAT [5]. In less developed health-care systems, the availability of these tests is low [114]. In addition, recommendation to overcome eradication failure due to increasing resistance rates includes antibiotic susceptibility testing after second eradication failure and also for local resistance prevalence. In several less or least developed regions, no laboratories for HPI SAT are available at present.

Table 2. Reports of outcome of *H. pylori* (clinical Trials) eradication studies in Africa [77, 114, 120-122]

Reference	Subjects	Regime	Country	Failure rate, %	Diagnostic method
Louw et al. [120]	48	Bismuth quadruple therapy (antibiotics included in therapy: metronidazole, second antibiotic either tetracycline or amoxicillin)	South Africa	44	Rapid urease, histology, and culture
Sokwala et al. [121]	120	Esomeprazole-based triple therapy (antibiotics included in therapy: amoxicillin and clarithromycin)	Kenya	7–8	<i>H. pylori</i> SAT
Onyekwere et al. [77]	50	Rabeprazole-based triple therapy (antibiotics included in therapy: Amoxicillin and clarithromycin)	Nigeria	13	UBT
Shehata et al. [122]	224	Nitazoxanide-based triple therapy (antibiotics included in therapy: clarithromycin or metronidazole and clarithromycin)	Egypt	5.5	<i>H. pylori</i>
Kabakambira et al. [114]	299	Omeprazole-based triple therapy (antibiotics included in therapy: amoxicillin and one of clarithromycin/ciprofloxacin/metronidazole or amoxicillin, ciprofloxacin, and doxycycline)	Rwanda	20	<i>H. pylori</i> SAT

HPI, *Helicobacter pylori* infection; RUT, rapid urease test; UBT, urea breath test; SAT, stool antigen test.

Several problems were identified analyzing the low speed of developing health-care structures [114]. In 2015, the Abuja Declaration was published containing a Millennium Development Goal to invest at least 15% of annual budgets into the health sector. No African country has achieved this goal [115]. The most important reasons for limited health-care resources are unstable financial support of public hospitals by the government, underpaid staff in the public health sector with an increased risk for corruption, and a lack of funding resources [116].

Therapy for *H. pylori* and Challenges in Africa

Considering the burden of HPI and its association with gastroduodenal diseases including malignancy, several professional groups have suggested guidelines for treatment. The most recent recommendations on treatment of HPI come from the Maastricht V/Florence Consensus, Toronto consensus conference, and the American College of Gastroenterology (ACG) guidelines [5, 6, 117]. These guidelines have recommended a combination of antisecretory drugs (which ensure stability of the antibiotics) and antibiotics which are effective in the lumen and systematically. The choice of antibiotics should be informed by local resistance patterns; presence of drug allergy, for example, penicillin allergy; previous eradication combinations; and other factors [118]. Treatment of HPI is commenced with first-line eradication therapy which generally offers considerable likelihood of treatment success and should ideally be administered for 14 days. Typ-

ical combinations are a clarithromycin-based triple therapy (PPI with clarithromycin and amoxicillin or clarithromycin and metronidazole) in areas of low clarithromycin resistance (<15%) [5, 117]. An alternative first-line regimen is a bismuth-based quadruple therapy with a PPI, bismuth plus 2 antibiotics (clarithromycin and amoxicillin or metronidazole and tetracycline) [118].

A major challenge however, in both developed and developing countries, is an increased rate of *H. pylori* resistance to antibiotics with recent reports detailing waning efficacy of these combination therapies [119]. Laboratory culture reports show widespread antibiotic resistance of almost 100% to the commonly used antibiotics in some regions like Nigeria [2, 15]. This is driven by indiscriminate use of antibiotics as people can purchase any drug without prescription in most countries in the continent. Even where there are restriction/regulations, enforcement is a major issue. A few reports on outcome of *H. pylori* eradication studies in Africa exist (see Table 2); these are also corroborated by anecdotal data. Varying degrees of eradication failure ranging from 6 to 44% are reported, while some of the studies showed no difference between 7- and 14-day treatment [82, 114, 120, 121]. These differential responses could be attributable to varying bacterial resistance across Africa, patient factors (including genotype), and diagnostic methods employed. An additional challenge is that in cases of treatment failure, endoscopy with biopsy and culture which is ideal is not widely available and/or not affordable. In areas where a resistance rate of over 15% for clarithromycin is recorded, bismuth- or nonbismuth-containing quadruple therapy or concomi-

tant therapy (including 3 antibiotics and a PPI) is recommended [5]. Second-line treatment should be based on the need to carry out an endoscopy. When this approach is requested, culture and standard antimicrobial susceptibility testing should be performed to lead to the more appropriate therapy. When endoscopy is not requested or is not possible, the rationale of the second-line treatment is to drop the empirical use of clarithromycin, due to the high possibility that strains of *H. pylori* resistance to clarithromycin have developed. Recommended second-line therapies include PPI + bismuth + metronidazole + tetracycline or levofloxacin-containing triple (PPI + amoxicillin + levofloxacin) or quadruple (PPI, amoxicillin, levofloxacin, and bismuth) therapy. The use of levofloxacin-containing triple therapy, following the failure of the standard triple therapy, is a reasonable alternative when local fluoroquinolone resistance is <10%. Third-line therapy (after failure of clarithromycin-containing or quadruple regimens) should be guided by culture and antimicrobial susceptibility testing [6]. In this instance, a PPI, amoxicillin, and levofloxacin can be used, if not used before, or in case of high fluoroquinolone resistance, a combination of bismuth with different antibiotics, or a rifabutin-containing rescue therapy is recommended [6]. These options however are either not available or too expensive in our context.

Recommendations and Need for an African Guideline

In summary, there is no treatment regimen which guarantees cure of HPI in 100% of patients; multiple antibiotic regimens have been evaluated for *H. pylori* thera-

py. However, few regimens have consistently achieved high eradication rates. There are also limited data on *H. pylori* antibiotic resistance rates to guide therapy. The treatment regimen that is selected must consider local antibiotic resistance patterns (if known), previous exposure and allergies to specific antibiotics, cost, side effects, and ease of administration. Also in cases of treatment failure, endoscopy with biopsy and culture is ideal, but this is not widely available in many African countries. With the number of studies showing widespread resistance to commonly prescribed antibiotics in Africa, it is time to produce a consensus guideline to guide clinicians on the choice of antibiotic combination for *H. pylori* eradication.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

S.I. Smith contributed to conceptualization of the study; S.I. Smith, A. Ajayi, T. Jolaiya, C. Onyekwere, M. Setshedi, and C. Schulz contributed to manuscript drafting; and all authors read and approved the final version of the article.

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