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ABSTRACT

Background: \textit{Helicobacter pylori} (\textit{H. pylori}) infection and chronic dyspepsia represent significant medical burdens in the developing world. An accurate assessment of the prevalence of chronic dyspepsia, as well as of the effectiveness of population-based screening and eradication of \textit{H. pylori} are warranted.

Objectives: We determined the prevalence of \textit{H. pylori} and chronic dyspepsia within the general adult population in a region of eastern Uganda. Independent predictors of \textit{H. pylori} infection were assessed. Finally, we evaluated the efficacy of standard triple therapy on \textit{H. pylori} eradication.

Methods: Of 400 randomly selected adult residents in eastern Uganda, 376 were administered a validated, chronic dyspepsia questionnaire and provided a stool sample for \textit{H. pylori} testing. \textit{H. pylori}-positive participants were given standard triple therapy and monitored for medication adherence. The efficacy of triple therapy on \textit{H. pylori} eradication was determined by fecal antigen testing after treatment. Log-linear and logistic regression analyses identified predictors of \textit{H. pylori} positivity and eradication failure.

Results: \textit{H. pylori} prevalence within the study population was 48%. The prevalence of chronic dyspepsia was 87%. The presence or severity of dyspepsia did not predict \textit{H. pylori} infection. However, a higher level of education was an independent predictor of \textit{H. pylori} infection. Standard triple therapy resulted in ~90% eradication. Missing at least four doses of any of the triple therapy medications over the 14-day course predicted eradication failure.

Conclusions: In our study population, chronic dyspepsia did not predict \textit{H. pylori} infection, though clinical suspicion for this prevalent pathogen should nonetheless remain high. Population-based screening and adherence to triple therapy are effective at eradicating \textit{H. pylori} within this region.

1. Introduction

\textit{Helicobacter pylori} (\textit{H. pylori}) is one of the world's most successful pathogens, affecting approximately half of the global population \cite{1}. Its success in part relies on its ability to establish chronic infection and persist within the hostile environment of the human stomach \cite{2}. Classified as a human carcinogen \cite{3}, \textit{H. pylori} remains the most significant and modifiable risk factor for the development of gastric cancer, one of the leading global causes of cancer-related deaths \cite{4}. While treatment regimens over the past few decades have significantly improved global eradication rates \cite{5}, \textit{H. pylori} remains a ubiquitous pathogen that contributes to significant morbidity and mortality worldwide \cite{1}.

In particular, \textit{H. pylori} disproportionately affects the developing world and remains a leading cause of disability adjusted life years (DALY) in low-income countries \cite{6}. The “test-and-treat” strategy that guides management of \textit{H. pylori} infection \cite{7} assumes the ability to accurately diagnose \textit{H. pylori} through invasive or non-invasive means, which may not exist or be readily accessible in countries with limited testing capacity. In addition, the predictive value of these diagnostic tests is dependent on the prevalence of \textit{H. pylori} within the population, which is often unknown or inferred from limited studies. Moreover, most studies
determine the regional prevalence based on symptomatic residents presenting to a hospital or health center [8, 9, 10]. If we consider that most chronically infected patients exhibit few if any symptoms [11] and take into account the limited access to health care facilities in underserved or rural areas, it stands to reason that the reported prevalence of *H. pylori* within the general population has been inaccurately assessed in the developing world.

Central to the effective management of *H. pylori* infection is a heightened clinical suspicion for its variable, and often mild, symptomatic presentation [11]. *H. pylori* remains a common cause of chronic dyspepsia, a complex set of gastrointestinal symptoms that accounts for frequent health care visits and substantial costs [12]. Indeed, recent guidelines emphasize the importance of testing for and treating *H. pylori* when managing chronic dyspepsia [13]. It remains to be seen, however, whether these guidelines effectively translate to the developing world. Studies demonstrate that the prevalence of dyspepsia on the African continent is highly variable [14, 15, 16]. However, most if not all studies in the developing world directly correlating active *H. pylori* infection to dyspepsia have focused on patients presenting to a hospital or health care setting [8, 10, 17, 18, 19, 20, 21], and the true prevalence of *H. pylori* and its correlation with dyspepsia within the general population is not known. The empiric treatment of chronically dyspeptic patients with inconsistent regimens to eradicate *H. pylori* often replaces the recommended “test-and-treat” strategy, contributing to antibiotic resistance and limiting efficacy [22].

The medical and economic burden of chronic dyspepsia in the developing world cannot be mitigated, therefore, without accurately determining the prevalence of *H. pylori*, identifying patients at risk of *H. pylori* infection, establishing a relationship between chronic dyspepsia and *H. pylori* infection, and evaluating treatment efficacy. The objectives of this study were multiple. We first aimed to determine the prevalence of *H. pylori* and chronic dyspepsia among residents of the Namutumba district in eastern Uganda. Given the variable symptomatology of *H. pylori* infection, we investigated whether chronic dyspepsia predicted *H. pylori* infection. Finally, we assessed the efficacy of standard triple therapy for *H. pylori* eradication.

## 2. Materials and methods

### 2.1. Ethical considerations

All study participants provided written informed consent. This study was approved by the Institutional Review Board at the Washington University in St. Louis School of Medicine (U.S.A.; IRB # 201807047), and by the Ugandan National Council of Science and Technology (UNCST) and The AIDS Support Organization (TASO; Uganda; Protocol # TASOREC/002/18-UG-REC-009). This study was retrospectively registered in ClinicalTrials.gov (TRN: NCT04525664, registered 24 August 2020 – Retrospectively registered, https://clinicaltrials.gov/ct2/show/NCT04525664), and the objectives and hypotheses proposed as part of the study protocol that was approved by the ethical committees remained consistent throughout the study. The authors confirm that all ongoing and related trials for this drug/ intervention are registered. This study adheres to CONSORT guidelines.

### 2.2. Study design

To determine the prevalence of *H. pylori* within this region, we conducted a cross-sectional study within a randomly selected population of eastern Uganda. Since the prevalence of *H. pylori* within the general adult population in this region was not known, we calculated our sample size (n) based on previous data suggesting a regional prevalence of dyspepsia of approximately 50% [14]:

\[
n = \left( z^2 \cdot p \cdot (1 - p) \right) / d^2
\]

where *n* is the sample size, *z* is the level of confidence according to the normal standard distribution corresponding to 95% confidence (*z* = 1.96), *p* is the estimated prevalence of *H. pylori* within this region (which was unknown but based on the prevalence of dyspepsia [14]), and *d* is the margin of error, which we set at 0.05. Based on this equation [23], our calculated sample size was 384 participants. Accounting for an approximate 5% dropout rate, we set out to enroll 400 participants for the study.

To assess the efficacy of standard triple therapy on *H. pylori* eradication, we treated all consenting *H. pylori*-positive participants with triple therapy and determined their *H. pylori* infection status after treatment, using fecal *H. pylori* antigen testing. Given ethical limitations that precluded us from randomizing and treating *H. pylori*-positive participants with a placebo, this aspect of the study could not be placebo-controlled. In addition, it has been shown that the spontaneous clearance of *H. pylori* infection is low (<5%) [24] and that the clearance rate significantly decreases after the first decade of life [25]. As a result of these ethical limitations and epidemiological findings, along with the relatively low risk of adverse effects from standard triple therapy, we believed that the risk of not treating *H. pylori*-positive participants or potentially losing this group to follow-up outweighed the benefit of including a placebo treatment group.

### 2.3. Exclusion criteria

Any participants unwilling or unable to provide informed consent, less than 18 years of age, or who had used proton pump inhibitors and/or antibiotics within the past month were excluded. Participants could withdraw from the study at any point and for any reason.

### 2.4. Data collection and management

400 adult residents (aged 18 or older) of the Namutumba District in eastern Uganda were randomly selected between October 2018 and May 2019 using the lot quality assurance sampling (LQAS) method [26]. Briefly, data collectors received a list of all households within a particular village from village leaders. From that list, households were selected through random sampling. An adult from each randomly selected household was approached by the study team and asked to participate in the study. If a household had multiple adults, one adult was randomly selected from the household and asked to participate in the study.

Of the 400 participants identified, 376 participants met inclusion criteria, provided informed consent, and completed a questionnaire conducted by a research study member, in either English or the local dialect, Lusoga. All participants providing informed consent were administered a survey questionnaire, which also included the Short-Form Leeds Dyspepsia Questionnaire [27] (SFLDQ). Participants also agreed to provide a stool sample for fecal *H. pylori* antigen testing (OnSite™ *H. pylori* Antigen Rapid Test; CKT Biotech, Poway, CA), and the reported sensitivity and specificity of this test, per the package insert, were 96.7% and 93.8%, respectively. Participants positive for *H. pylori* by fecal antigen testing were offered standard triple therapy, consisting of clarithromycin (500 mg per os twice daily), amoxicillin (1 g per os twice daily), and omeprazole (40 mg per os twice daily) for 14 consecutive days. A study member met with each participant on standard triple therapy every 3–5 days to inquire about any side effects and to assess for adherence to the treatment regimen through pill counts. Missed doses were recorded by the study member for each participant on standard triple therapy. One month following the completion of their treatment regimen, participants answered a follow-up questionnaire and repeated a fecal *H. pylori* antigen test. Those who were still positive for *H. pylori* after repeat fecal antigen testing were referred to a clinic for an additional 14 days of salvage quadruple therapy, consisting of tetracycline (500 mg per os four times daily), metronidazole (250 mg per os four times daily), bismuth subsalicylate (525 mg per os four times daily), and omeprazole (40 mg per os twice daily). Participants with chronic dyspepsia scores of 8 or greater, as determined by the SFLDQ, and who were negative for *H. pylori* by fecal antigen testing, were offered daily omeprazole (20 mg) for one month. Their overall symptomatic improvement was reassessed by a research study member one month after the completion of the omeprazole regimen.
2.5. Dyspepsia severity assessment

All consenting participants completed a questionnaire, which included the SFLDQ [27]. Based on the summed total score from the SFLDQ (out of 32), participants were categorized as either having no dyspepsia (score of 0), mild dyspepsia (score of 1–8), moderate dyspepsia (score of 9–15), or severe dyspepsia (score >15). Participants who were negative for *H. pylori* and had a dyspepsia score of 8 or greater were offered daily omeprazole (20 mg) for one month. Dyspepsia scores for participants who tested positive for *H. pylori* were calculated before standard triple therapy and one month after completion of the treatment regimen.

2.6. Modeling dyspepsia severity as a function of age

The probability of dyspepsia as a function of age among *H. pylori*-positive participants (Supplemental Figure 1C) was based on multinomial and ordinal logistic regression models, using the R packages mnet and MASS. Treating the severity of dyspepsia (i.e., none, mild, moderate, or severe) as ordinal categorical data, the model used no dyspepsia as the baseline, and the logarithm of the ratio of the probability for different levels of dyspepsia was modeled by a linear function of age (Supplemental Table 1).

2.7. Statistical analyses

All statistical analyses were done using the R 4.0 statistical package. Log-linear models were used to study the relationship between *H. pylori* status and categorical baseline characteristics (Table 1). The relationships between chronic dyspepsia, dyspepsia severity, the components of the SFLDQ (Table 2) and *H. pylori* infection were determined by logistic regression models. Predictors of *H. pylori* eradication failure (Table 3) were modeled and tested by log-linear models. Dyspepsia scores among *H. pylori*-positive participants before and after treatment (Figure 3) were compared using the Wilcoxon sign rank test. For all analyses, *p* < 0.05 was considered statistically significant.

3. Results

3.1. Prevalence of *H. pylori* within the Namutumba District

Of the 400 adult participants contacted for the study, 376 (94%) met the inclusion criteria, completed the survey questionnaire, and provided a stool sample for fecal *H. pylori* antigen testing. The majority of excluded participants declined to complete the survey questionnaire and/or to provide a stool sample (Figure 1). Table 1 shows the baseline characteristics for the study population.

At baseline, *H. pylori*-positive and *H. pylori*-negative participants were similar in most of the demographic and socioeconomic factors analyzed. Of note, a formal education (primary education or above) was predictive of *H. pylori* positivity (*p* = 0.02). While there was a trend toward higher NSAID use among *H. pylori*-positive participants, the difference was not statistically significant (*p* = 0.081).

The point prevalence of *H. pylori* within this study population was 181 of 376 participants (48%; Figure 1). The magnitude of *H. pylori* cases varied regionally within the Namutumba District, with the Namutumba sub-county accounting for the highest number of cases and the Nabweyo sub-county recording the fewest number of cases (Figure 2A). When controlling for the number of participants sampled from each sub-county, the prevalence of *H. pylori* ranged from 22% to 68%, with the Namutumba sub-county again representing the highest density of *H. pylori* cases within the district (Figure 2B). No statistically significant differences in *H. pylori* prevalence were observed between any of the sub-counties (not shown).

3.2. Dyspepsia among *H. pylori*-positive and –negative participants

*H. pylori* infection is a common cause of chronic dyspepsia. Given the prevalence of *H. pylori* within this population and the variable symptomatology associated with *H. pylori* infection [11, 28], we investigated whether the presence or severity of chronic dyspepsia predicted *H. pylori* positivity. To quantify the degree of dyspepsia within our study population, we assigned each participant a dyspepsia score based on the SFLDQ, a questionnaire to quantitatively categorize dyspepsia severity [27] that has been validated among African patients [29]. Of the 376 participants, 326 (86.7%) reported some degree of dyspepsia (SFLDQ score >0; Figure 1 and Supplemental Figure 1A). Most dyspeptic participants reported mild dyspepsia (SFLDQ score 1–8), with similar proportions reporting moderate (SFLDQ score 9–15) and severe dyspepsia (SFLDQ score >15). In our study population, neither the presence nor severity of chronic dyspepsia predicted *H. pylori* infection (Table 2 and Supplemental Figure 1). In addition, individual components of the SFLDQ also did not predict *H. pylori* infection (Table 2). Interestingly, however, the probability of being free of dyspepsia (i.e., SFLDQ score of 0) increased with age among *H. pylori*-positive participants, while the probability of having severe dyspepsia was largely unchanged as a function of age (Supplemental Figure 1C). Within our study population,
Table 2. Presence and severity of chronic dyspepsia according to H. pylori infection status.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>H. pylori-positive (n = 181)</th>
<th>H. pylori-negative (n = 195)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspepsia score, median (IQR)</td>
<td>8 (10)</td>
<td>7 (9)</td>
<td>0.1858</td>
</tr>
<tr>
<td>Dyspepsia, n (%)</td>
<td></td>
<td></td>
<td>0.8204</td>
</tr>
<tr>
<td>None</td>
<td>23 (12.7)</td>
<td>27 (13.8)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>76 (42.0)</td>
<td>89 (45.6)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>48 (26.5)</td>
<td>45 (23.1)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>34 (18.8)</td>
<td>34 (17.4)</td>
<td></td>
</tr>
<tr>
<td>Indigestion, n (%)</td>
<td></td>
<td></td>
<td>0.3098</td>
</tr>
<tr>
<td>Not at all</td>
<td>50 (27.6)</td>
<td>72 (36.9)</td>
<td></td>
</tr>
<tr>
<td>Less than once a month</td>
<td>11 (6.1)</td>
<td>13 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Between once a month and once a week</td>
<td>46 (25.4)</td>
<td>37 (19.0)</td>
<td></td>
</tr>
<tr>
<td>Between once a week and once a day</td>
<td>39 (21.5)</td>
<td>36 (18.5)</td>
<td></td>
</tr>
<tr>
<td>Once a day or more</td>
<td>35 (19.3)</td>
<td>37 (19)</td>
<td></td>
</tr>
<tr>
<td>Heartburn, n (%)</td>
<td></td>
<td></td>
<td>0.6043</td>
</tr>
<tr>
<td>Not at all</td>
<td>53 (29.3)</td>
<td>71 (36.4)</td>
<td></td>
</tr>
<tr>
<td>Less than once a month</td>
<td>17 (9.4)</td>
<td>16 (8.2)</td>
<td></td>
</tr>
<tr>
<td>Between once a month and once a week</td>
<td>44 (24.3)</td>
<td>38 (19.5)</td>
<td></td>
</tr>
<tr>
<td>Between once a week and once a day</td>
<td>40 (22.1)</td>
<td>40 (20.5)</td>
<td></td>
</tr>
<tr>
<td>Once a day or more</td>
<td>27 (14.9)</td>
<td>30 (15.4)</td>
<td></td>
</tr>
<tr>
<td>Regurgitation, n (%)</td>
<td></td>
<td></td>
<td>0.3217</td>
</tr>
<tr>
<td>Not at all</td>
<td>86 (47.5)</td>
<td>104 (53.3)</td>
<td></td>
</tr>
<tr>
<td>Less than once a month</td>
<td>25 (13.8)</td>
<td>19 (9.7)</td>
<td></td>
</tr>
<tr>
<td>Between once a month and once a week</td>
<td>31 (17.1)</td>
<td>23 (11.8)</td>
<td></td>
</tr>
<tr>
<td>Between once a week and once a day</td>
<td>27 (14.9)</td>
<td>31 (15.9)</td>
<td></td>
</tr>
<tr>
<td>Once a day or more</td>
<td>12 (6.6)</td>
<td>18 (9.2)</td>
<td></td>
</tr>
<tr>
<td>Nausea, n (%)</td>
<td></td>
<td></td>
<td>0.5252</td>
</tr>
<tr>
<td>Not at all</td>
<td>91 (50.3)</td>
<td>111 (56.9)</td>
<td></td>
</tr>
<tr>
<td>Less than once a month</td>
<td>18 (9.9)</td>
<td>18 (9.2)</td>
<td></td>
</tr>
<tr>
<td>Between once a month and once a week</td>
<td>35 (19.3)</td>
<td>30 (15.4)</td>
<td></td>
</tr>
<tr>
<td>Between once a week and once a day</td>
<td>30 (16.6)</td>
<td>25 (12.8)</td>
<td></td>
</tr>
<tr>
<td>Once a day or more</td>
<td>7 (3.9)</td>
<td>11 (5.6)</td>
<td></td>
</tr>
</tbody>
</table>

H. pylori: Helicobacter pylori.

3.3. Efficacy of triple therapy on H. pylori eradication and dyspepsia severity

To determine the efficacy of triple therapy on H. pylori eradication, all participants who tested positive for H. pylori, regardless of the presence of dyspepsia, underwent 14 days of standard triple therapy treatment (see Methods). Of the 181 participants who were positive for H. pylori, 171 (94.4%) began triple therapy. Nine participants were lost to follow-up prior to starting treatment, and one participant declined treatment (Figure 1). Participants undergoing treatment met with study team members three to five times during their 14-day regimen to assess for symptoms, adverse reactions, and medication compliance. As defined by the ethical standards of the study, all participants who tested positive for H. pylori had to be offered standard triple therapy (see Materials and Methods). Symptoms experienced during the treatment regimen are listed in Supplemental Table 2. No adverse events were reported.

Approximately one month after completing treatment, participants met with study team members to complete a follow-up questionnaire and to submit a stool sample for fecal H. pylori antigen testing. Of the 171 participants who underwent treatment, 165 (96.4%) filled the follow-up questionnaire and submitted a stool sample at the completion of the study. Five participants who completed treatment were lost to follow-up and did not complete a follow-up questionnaire or undergo repeat fecal antigen testing. One participant refused to complete the follow-up questionnaire and did not provide a stool sample after completing triple therapy (Figure 1).

Of the 165 H. pylori-positive participants who completed therapy and post-treatment testing, 148 were negative by fecal antigen testing at the completion of the study, for an eradication efficacy of 89.7% (Figure 3A). Seventeen participants (10.3%) were still positive, and these participants underwent a mean score of 1.7 after therapy (Figure 3B). Of various risk factors analyzed, only participants who missed four or more doses of their medications during the course of the triple therapy regimen were significantly more likely to fail H. pylori eradication (p = 0.0415; Table 3).

4. Discussion

Although H. pylori is regarded as an ubiquitous pathogen, an accurate determination of its prevalence in the developing world, particularly on the African continent, has been hampered by a lack of data or by limited studies focusing on symptomatic individuals presenting to a health care
Adult residents of Namutumba district asked to participate in study (n = 400)

- Excluded (n = 24):
  - Declined to answer questionnaire/H. pylori fecal antigen testing (n = 21)
  - Lost to follow-up (n = 2)
  - Currently being treated for H. pylori (n = 1)

Study participants (n = 376)

H. pylori prevalence = 48%

- Dyspepsia positive/H. pylori negative (n = 168)
  - Dyspepsia score 1 - 7 (n = 77)
    - Lost to follow-up (n = 1)
    - No treatment; reassess symptoms in 1 month (n = 76)
  - Dyspepsia score ≥8 (n = 91)
    - Lost to follow-up (n = 9)
    - Daily omeprazole for 1 month (n = 82)
    - Reassess symptoms (n = 90)

- Dyspepsia positive/H. pylori positive (n = 158)
  - Lost to follow-up (n = 1)
  - Triple therapy (clarithromycin, amoxicillin, omeprazole) for 14 days (n = 157)

- Dyspepsia negative/H. pylori positive (n = 23)
  - Lost to follow-up (n = 5)
  - Declined follow-up (n = 1)

- Dyspepsia negative/H. pylori negative (n = 27)
  - No further follow-up

Figure 1. Study design. Flow diagram of the study design.

These estimates are often used to extrapolate the prevalence within the general population and may not account for inadequate access to health care and limited use of health resources in these countries [32, 33]. This study determined the prevalence of H. pylori within the general population of a rural district of eastern Uganda by fecal antigen testing, an accurate, non-invasive, convenient, and inexpensive method for diagnosing H. pylori infection [34, 35, 36, 37]. The sensitivity and specificity of our antigen test kit have been reported as 96.7% and 93.8%, respectively. Though these results have not been independently validated, they are consistent with previous literature [38, 39]. Forty-eight percent of participants in the Namutumba district tested positive for H. pylori, a prevalence that is slightly lower than the reported prevalence in other African countries [1], including the neighboring Democratic Republic of Congo [40], though consistent with the reported prevalence in Kenya [41]. Of note, this prevalence was higher than that reported for symptomatic patients presenting to a hospital in western Uganda [10], which ranged from 29.9% to 37.4%, depending on the method of detection. However, those studies relied on detection of H. pylori in symptomatic patients presenting to a health care facility, which may have underestimated the true burden of disease within the community.

The reasons for the variation in regional H. pylori prevalence within the Namutumba district are unclear. The Namutumba sub-county had the highest prevalence and serves as an economic hub for the region, where residents from neighboring sub-counties converge to conduct business and sell goods and services. As such, the Namutumba sub-county represents a peri-urban environment that may promote the spread of H. pylori. This could also explain the finding that having a primary level of education or above significantly correlated with H. pylori positivity, which appears to contradict previous findings [10, 42, 43] but has been reported [8, 44]. Those living and working in a more urban setting such as the Namutumba sub-county may have attained a higher level of education compared to residents in more rural, less densely populated areas and who are predominantly subsistence farmers that may not have obtained a formal education. Regardless, the regional variation in H. pylori prevalence identified in this study can allow public health officials to target certain “hot spots” within the district and to focus efforts on detection and eradication of H. pylori.
Despite the prevalence of chronic dyspepsia and \( H. pylori \) within our study population, chronic dyspepsia did not predict \( H. pylori \) infection, in accordance with previous studies [11, 45]. We found that the majority of \( H. pylori \)-positive participants experienced mild or no dyspepsia, as assessed by the SFLDQ, highlighting \( H. pylori \)'s variable and often mild symptomatology. Interestingly, the probability of being free of dyspepsia increased with age among \( H. pylori \)-positive participants, while the probability of experiencing severe dyspepsia was largely unchanged with respect to age. While the age of exposure or recurrent exposures to \( H. pylori \) were not assessed in this study, we would speculate that most of the \( H. pylori \)-positive participants have been chronically harboring \( H. pylori \) [46, 47], and our data would suggest that their dyspeptic symptoms wane over time. Whether the severity of dyspepsia is a result of more chronic \( H. pylori \) infection within this population remains to be seen, as the degree of gastritis was not endoscopically or histologically determined in \( H. pylori \)-positive participants. Nonetheless, the mild nature of symptoms may not have prompted infected participants to seek medical care, emphasizing the need for high clinical suspicion within this population. Based on our findings, if we estimate that approximately half of the Namutumba district harbors \( H. pylori \), then we must acknowledge that a significant percentage of this population carries pre-neoplastic gastric lesions [48] and is at risk of developing gastric cancer [49].

The efficacy of \( H. pylori \) eradication in our study population using a standard triple therapy regimen was 89.7%, in contrast to data showing a trend for declining cure rates (<80%) with standard triple therapy over the past two decades [50, 51, 52]. Current guidelines recommend the choice of therapy based on regional rates of antibiotic resistance [7]. Indeed, the rate of clarithromycin resistance within this region is not known, and the choice of standard, 14-day triple therapy was based on cost and availability. Within this study population, standard triple therapy was relatively effective and well tolerated. Moreover, the triple therapy regimen significantly improved dyspepsia among \( H. pylori \)-positive participants. Importantly, we noted that the likelihood of not eradicating \( H. pylori \) was significantly higher in participants who missed at least four doses during their treatment regimen. We did not ascertain whether those who failed treatment were colonized with \( H. pylori \) strains resistant to amoxicillin and/or clarithromycin. While it is established that poor compliance with therapy significantly reduces eradication efficacy [53], the reasons for decreased compliance within our study population are unclear, though treatment failure did not seem to be associated with level of education, medication side effects, or the use of other medications during the treatment regimen. A small minority of participants experienced an increase in dyspepsia one month after completing therapy and successfully eradicating \( H. pylori \). The reasons for this are currently unclear. Some have suggested that the symptomatic gain for \( H. pylori \)-induced dyspepsia may take 6–12 months to achieve [54]. If these participants had been followed for a longer time period (>1 month), it is possible that this dyspepsia would have improved, as has been previously reported [55a]. Finally, these participants may have been experiencing dyspepsia from other causes unrelated to \( H. pylori \) infection, including functional dyspepsia.

4.1. Strengths and limitations of study

The strengths of this study are multiple. To our knowledge, this is the first study that determined active \( H. pylori \) infection within a general
adult population in sub-Saharan Africa. We identified hot spots for 
*Helicobacter pylori* positivity that can guide public health officials in targeting their prevention and treatment efforts. Most *H. pylori*-positive participants had mild to no dyspeptic symptoms, and chronic dyspepsia did not predict *H. pylori* infection. These findings highlight the need for heightened clinical suspicion for this common pathogen. We also found that standard triple therapy was highly effective at eradicating *H. pylori* among medication-compliant participants, compared to eradication rates reported in other global regions [50, 51, 52]. The reasons for this are unclear and warrant further study, given that this study did not obtain detailed information about prior antibiotic exposure within this study population. This study had several limitations. Rates of antibiotic resistance within this region were not determined [22, 53, 54, 55b]. In addition, comorbidities were not explicitly asked in the questionnaire, though it is worth mentioning that the vast majority of participants were not taking prescribed medications at the time of the study and did not have established care with a health care provider. A recent health survey found malaria and human immunodeficiency virus (HIV) infection to be the most common comorbidities in Uganda [56], though the association between these diseases and chronic dyspepsia have not been directly investigated. Given limited endoscopic and diagnostic resources within the Namutumba district, the prevalence of underlying gastric pre-neoplastic lesions was not assessed in *H. pylori*-positive residents. Similarly, the causes for dyspepsia in *H. pylori*-negative participants were not endoscopically investigated. It is possible that the observed prevalence of dyspepsia among *H. pylori*-negative participants could be in part explained by gastroesophageal reflux disease (GERD), for example, which would not be distinguished by the SFLDQ alone. However, though the prevalence of chronic dyspepsia within this population may appear high, this may be largely driven by the significant proportion of participants reporting mild dyspepsia. If we only consider the prevalence of moderate and severe dyspepsia, this may be more in line with rates of dyspepsia in prior population-based studies [15, 29].

5. Conclusions

A population-based screening of a sub-Saharan African region found that *H. pylori* was prevalent, but dyspeptic symptoms in themselves did not predict who was infected with *H. pylori*. This study highlights that clinical suspicion for *H. pylori* within this population should nonetheless remain high, given the observed prevalence of *H. pylori* among all those with dyspepsia, including many with relatively mild or no dyspeptic symptoms. A previous study looking at dyspepsia in this region found that out of nine randomly selected health centers in the Namutumba District, none of the health centers had the capacity to test for *H. pylori*, and only two of the nine health centers prescribed appropriate triple therapy for clinically significant dyspepsia [14]. Moreover, unlicensed pharmacies provide approximately 40% of all healthcare to people in the Namutumba District [57]. Though diagnostic kits for *H. pylori* are relatively inexpensive [37], instituting government-level policies to make these tests widely available and providing a standard of care for management of dyspeptic patients prior to empiric antibiotic usage would be a more effective method to appropriately manage *H. pylori* infection and limit antibiotic resistance. This study illustrates the effectiveness of population-based screening and eradication of *H. pylori* in sub-Saharan Africa. More importantly, it can serve as a template for future studies on the cost effectiveness of these measures for gastric cancer prevention in a resource-limited setting.

Declarations

Author contribution statement

Yang Jae Lee, M.D.; Ibrahim Ssekalo; Rauben Kazungu: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Timothy S. Blackwell: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data.

Peter Muwereza: Conceived and designed the experiments.

Yuefeng Wu; José B. Sáenz: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.
Declaration of interest statement
The authors declare no competing interests.

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