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Yang Jae Lee
Washington University School of Medicine in St. Louis

Gautam Adusumilli
Washington University School of Medicine in St. Louis

Francis Kyakulaga
Uganda Christian University

Peter Muwereza
Makerere University

Rauben Kazungu
Makerere University

See next page for additional authors

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Authors
Yang Jae Lee, Gautam Adusumilli, Francis Kyakulaga, Peter Muwereza, Rauben Kazungu, Timothy Scott Blackwell, Jose Saenz, and Moonkyung Cho Schubert

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Survey on the prevalence of dyspepsia and practices of dyspepsia management in rural Eastern Uganda

Yang Jae Lee a, e, *, Gautam Adusumilli a, e, Francis Kyakulaga b, Peter Muwereza c, e, Rauben Kazungu c, Timothy Scott Blackwell Jr. a, Jose Saenza d, Moonkyung Cho Schubert d, e

a Washington University School of Medicine, USA
b Uganda Christian University, USA
c Makerere University School of Public Health, USA
d Charlie Norwood Veterans Affair Medical Center, USA
e Empower Through Health, USA

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ABSTRACT

Aim: To investigate the current prevalence and management of dyspepsia in rural Eastern Uganda.

Methods: Residents older than 18 years of age across 95 study sites in Namutumba District, Eastern Uganda were surveyed. Each respondent was administered a questionnaire about dyspepsia and pertinent health-seeking behaviors. Health workers at 12 different clinics were also assessed on their competence in managing dyspepsia. Proportion-based analysis was used to determine self-reported outcome variables reported in this study, including: prevalence of dyspepsia; breakdown of symptoms; initial diagnosis location; management strategies; and appropriate medication usage.

Results: 397 residents (average age of 41.2 years) participated in this study (54.4% males, 45.6% females). 57.9% self-reported currently having dyspepsia, of average duration 4.5 years. Of this subset, 87% reported experiencing epigastric pain, and 42.2% believed that ulcers were “wounds in the stomach.” Only 3% of respondents had heard of Helicobacter pylori (Hp). Respondents varied in their management of dyspepsia, with frequent eating (39.1%), doing nothing (23.9%), and taking Western medicine (20%) being the most common strategies. The diagnosis of “peptic ulcer disease” was made by a health worker in 64.3% of cases, and 27% of cases were self-diagnosed. Notably, 70.3% of diagnoses at formal health centers were based on clinical symptoms alone and only 22.7% of respondents received treatment according to Ugandan Ministry of Health guidelines. Among the 12 health care workers surveyed, 10 cited epigastric pain as a common symptom of “ulcer,” although only two reported having heard of Hp. Only two out of 12 clinics had the capability to prescribe the triple therapy as treatment for presumed Hp.

Conclusion: There is a high incidence of dyspepsia in Eastern Uganda, and current management strategies are poor and inconsistent, and may contribute to antibiotic resistance. Further studies are needed to investigate the causes of dyspepsia to guide appropriate management.

1. Introduction

Dyspepsia refers to pain or discomfort, centered in the upper abdomen, for which patients seek medical care [1]. Dyspepsia is a common clinical symptom with many possible underlying causes, requiring extensive differential diagnosis. The approach to further evaluate is based on the clinical presentation, the patient’s age, and the presence of alarm symptoms or signs. Helicobacter pylori (Hp) is a bacterium commonly implicated in infection manifesting dyspepsia symptoms. Testing for Hp is recommended in patients without alarm features or age <55, years prior to endoscopy if there is no suspected organic disease [2].

Infection with the Gram-negative bacterium Hp can result in significant gastric pathology, including gastritis, peptic ulcer disease, dyspepsia, gastric mucosa-associated lymphoid tissue (MALT), and gastric adenocarcinoma [3].

Clinical manifestations can be variable, and most patients infected with Hp are asymptomatic. Regardless, Hp contributes to significant

* Corresponding author.
E-mail address: jaelee@wustl.edu (Y.J. Lee).

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morbidity and mortality, with a worldwide prevalence of about 50 percent [4]. Infection is better managed in developed countries, where prompt routine diagnosis and treatment are widely accessible, but it remains an important cause of disability adjusted life years (DALYs) in the developing world [5]. Hp infection has been shown to be highly correlated with socioeconomic status, educational level, and geographical location [4].

In 1994, the International Agency for Research on Cancer classified Hp as a human Class I carcinogen [6]. It has been assumed that Hp is endemic to many regions of Africa, in particular sub-Saharan Africa, though the reported incidence of gastric cancer in African populations has been relatively low. The reasons for this “African paradox” are subject to debate, though it may simply be the result of poor detection and limitations in diagnosis, as Agha et al shows [7].

Internal medicine remains a neglected field in global health, particularly in the developing world. Guidelines for the management of gastroenterological conditions are often developed from clinical studies conducted in resource-rich countries and may not translate to effective diagnosis and management strategies in the developing world. To diagnose infection with Hp, an upper endoscopy, urea breath test, stool antigen test, or serology is recommended. However, it is unrealistic for rural populations in the developing world to have access to any of these methods, with a study even calling diagnosis of gastric cancer at Uganda’s National Referral Hospital “a dream.” [8] Global guidelines for this prevalent pathogen should therefore be adapted in a regional and resource-specific manner.

Most rural health facilities in the sub-Saharan Africa including in Uganda are not equipped for diagnosing and managing chronic dyspepsia and its common cause, infection with Hp, or its associated complications [8]. Untreated chronic dyspepsia generates a significant medical and economic burden. Further, Hp infection disproportionately affects impoverished populations in developing countries [3]. If we consider the global burden of Hp and its endemicity in sub-Saharan Africa, Hp infection is a likely and under-diagnosed underlying cause for chronic dyspepsia in this region of the world. As a result, a pressing need exists for assessing the current prevalence and practices for managing chronic dyspepsia at the community and health facility levels. In addition, it is essential to identify potential limitations in the implementation of appropriate treatment in resource-limited countries. A previous study showed that in a non-randomized sample of patients getting endoscopies in Southwest Uganda, the rate of gastric cancer and gastritis are relatively high [9]. However, our observational study was the first to identify the prevalence of dyspepsia in a low-resource community and assess the current practices by regional health-care providers in the management of chronic dyspepsia.

Namutumba is a district in rural Eastern Uganda with a population of 252,557 [10]. Less than 15% of adults in this district have completed their secondary school education, and 40.5% of the adult population is illiterate. The most common water source in the region is groundwater from a borehole (71.9%), and the vast majority of the population are subsistence farmers (93.8%). Namutumba District was selected as our study site because of these poor economic and health indications, which limits in diagnosis, as Agha et al shows [7].

2. Methods

2.1. Study population

This study was conducted over the course of four weeks in Namutumba District in Eastern Uganda. Ninety-five study sites in the district were selected through a random number generator using the lot quality assurance sampling (LQAS) method. The health facilities were chosen randomly from a government list of health facilities in Namutumba District, and the health workers to be interviewed were selected at random from a roster at the given health facility. Only respondents over the age of 18 were eligible to participate.

2.2. Study design

In each of the study sites, local residents were selected through LQAS methodology and administered a survey relating to dyspeptic symptoms. Through this random sampling, the prevalence of self-reported dyspepsia in rural Eastern Uganda was found. The respondents who did not have symptoms suggestive of dyspepsia were not asked further questions, but those who confirmed dyspeptic symptoms were asked further questions (Study Tool 1).

Uganda’s healthcare system functions on a referral basis. In ascending order of size and available equipment, Uganda’s health facility levels are Village Health Teams, Health Center II’s, Health Center III’s, Health Center IV’s, Regional Referral Hospitals, and National Referral Hospitals [11]. Village Health Teams and frontline health workers who provide diagnoses and prescriptions to patients at various levels of health facilities were sampled to gauge their knowledge of dyspepsia and to find if they have the diagnostic tools and medicines to treat dyspepsia (Study Tool 2).

2.3. Methods of recruitment

The study was explained to the local council chairperson in the selected areas. Households were chosen randomly, and each household was asked for a list of all people over 18-years old in the home. Then, a person on each household list was selected at random to be administered the questionnaire.

2.4. Inclusion criteria

All individuals at the community level in the selected study sites and over 18 years were eligible for the study. All frontline health workers at the selected health facilities who diagnose and treat patients were eligible for the study.

2.5. Data collection

Research assistants, local people with good knowledge of English and Lusoga, the local language, were present at each interview. Research assistants were trained on the use of the questionnaire, obtaining consent, explaining confidentiality, and managing data. Informed consent was obtained before the start of each structured questionnaire.

2.6. Data management system

The research assistants entered data for the study into Epi-info on a password-protected computer. Backups were made on a regular basis and stored in a secure location. Consent forms and questionnaires were filed in a locked cabinet when not in use.

2.7. Quality control

Investigators validated a random sample of cases to ensure that the information was accurately captured. Investigators checked 10 percent of records in the database, comparing them to the original questionnaires.

2.8. Sample size justification

LQAS was used to determine the sample size. Traditional random sampling methods are time-consuming, but LQAS methodology, initially developed in industry for quality control, enables the utilization of small sample sizes in health surveys [12,13]. Community health workers were already trained and experienced in the utilization of LQAS methods for health surveys, thus facilitating data collection. 19 locations in each of the five supervision areas in Namutumba District was chosen utilizing a
random number generator. In each of the locations, one man between the ages of 18 and 40, one man over the age of 40, one woman between the ages of 18 and 40, and one woman over the age of 40 will be randomly sampled. In total, 380 interviews will be conducted. Sample size of 19 provides an acceptable level of error for making management decisions at 92%. Consent and Confidentiality.

Before beginning the questionnaire, all participants were asked for verbal consent after an explanation of the study. If the participants met the inclusion criteria, written consent was obtained. In cases where the participants were illiterate or wary of signing any written documents, an impartial witness was present to sign the consent form as an agent authorized by the participant.

All personally identifiable information was kept confidential. The interviews took place at a time and place of the participants’ choice. All data from the interviews were stored in a password-protected laptop, and all paper copies were kept in a locked cabinet.

2.9. Intellectual property rights

The participants were told the purpose of the study. It was also explained to them that participating in the study would carry no direct financial or medical benefit to them.

2.9.1. Ethical approval

The study team received Institutional Review Board approval from The AIDS Support Organization (TASO). The District Health Officer of Namutumba District also provided letters of support for the project.

2.9.2. Statistical analyses

Proportion-based analysis was used to determine the outcomes of this study, including: prevalence of dyspepsia; breakdown of symptoms; initial diagnosis location; management strategies; and appropriate medication usage. We first evaluated the differences in the respondents’ knowledge of dyspepsia, then transitioned to health-seeking behaviors of the respondents.

Of the respondents who visited a conventional health center, we determined the proportion who were diagnosed by each type of diagnostic test, as well as the proportion who received each medication or combination of medications. Appropriateness of medications and their duration of prescription was then determined through the same proportion-based analyses. These analyses were then repeated for respondents who visited an alternative health center.

Finally, healthcare workers’ knowledge of dyspepsia, including its causes and symptoms were evaluated. This data, along with each health worker’s knowledge of ulcer prevention strategies, was represented by percentages to exemplify the proficiency of health workers in the region.

3. Results

3.1. Participant demographics

The average age of surveyed respondents (54.4% males, 45.6% females) was 41.2 years, 57.9% of whom reported having symptoms of dyspepsia, with an average duration longer than 4.5 years.

3.2. Respondents’ concept of dyspepsia and personal management strategies

The 230 respondents self-reporting dyspepsia cited experiencing chronic epigastric pain (200; 87.0%), heartburn (67; 29.1%), nausea (31; 13.5%), backache (9; 3.9%), and bloating (5; 2.2%). Note that each participant was allowed to cite multiple symptoms.

The perception of dyspepsia among respondents was variable with: 70 stating that they were wounds in the stomach (30.4%), 60 reporting no knowledge of it (26.1%), 23 stating that it was abdominal pain (10.0%), 19 stating that it was sores (8.3%), 15 stating that it was disease (6.5%), and 43 reporting another perception of it (18.7%). Notably, only 7 participants (3%) indicated any knowledge of H. Pylori or mentioned it during the interview.

Participants varied in their management strategies of dyspepsia. There was also considerable variability in the perception of whether the treatment strategy was successful at alleviating symptoms. Further, “ulcers” were the local catch-all term for dyspepsia. A majority of participants (67.8%) believed their management relieved their symptoms (Fig. 1).

Of the 230 participants, 90 (39.1%) reported eating on time as their management strategy, 46 (20.0%) reported taking Western medicine, 17 (7.4%) reported eating on time and taking Western medicine, 22 (9.6%) reported taking herbal medicine, and notably 55 (24%) reported doing nothing. Western medicine was defined as any medicine with a certified FDA brand name or generic counterpart. Herbal medicine was defined as any plant-based medicine, irrespective of effectiveness.

Despite these findings, only 75 respondents (32.6%) reported that they thought “ulcers” could be cured. The remaining 155 participants reported believing that dyspepsia is incurable (32.2%) or did not know whether it could be cured (35.2%). Most respondents, 164 out of 230 (71.3%), thought that “ulcers” could be fatal.
3.3. Health-seeking behaviors

Approximately one fourth of respondents either self-diagnosed their “ulcer” status (52; 22.6%) or were diagnosed by a community member who was not a health worker (10; 4.3%). The majority (64.3%) were diagnosed by a certified health worker, defined as any health care provider at a define health center or non-governmental organization (NGO) private facility.

Regardless of the initial diagnosis, 175 (76.1%) respondents eventually sought help from some type of health center or NGO private facility, and the stratification of facilities where medical aid was sought, along with the diagnostic methods, is depicted in Fig. 2. Of the 175 respondents who were diagnosed at health centers, 123 (70.3%) were diagnosed with “ulcers” through clinical symptoms alone, without the use of established invasive (upper endoscopy) or non-invasive (serology, urease breath test, fecal antigen) diagnostic means.

3.4. Medications: conventional health centers

Of the 175 respondents who visited a conventional health center, 170 were given medication (97.1%). Fig. 3a and b highlight the frequency of prescribed medicines and for how long the medication regimen was typically recommended.

Notably, participants rated the effectiveness of medications in alleviating their symptoms similarly, whether they were prescribed for 1–6 days (86.7% positive), 7–14 days (81.4% positive), or >14 days (83.3% positive).

Treatment appropriateness for H. Pylori peptic ulcers was stratified into five categories: quadruple therapy (US standard of care); 11 concomitant triple therapy (Ugandan standard of care); one antibiotic and one proton pump inhibitor (PPI); only antibiotics; and, only PPIs. Quadruple therapy consisted of amoxicillin, metronidazole or an analogue, omeprazole or another proton pump inhibitor analog, and another antibiotic. Triple therapy consisted of the initial three drugs in quadruple therapy without the extra antibiotic. Only 75 respondents could be classified accurately because the remaining 95 who received medication reported that they took unknown drugs or did not have their prescription handbooks with them (Fig. 4). Of these 75 participants, 3 were given quadruple therapy (4.0%), 22 were given triple therapy (29.3%), 26 were given one antibiotic and one PPI (34.7%), 12 were given only antibiotics (16.0%), and 12 were given only PPIs (16.0%).

Collectively, only 22.7% of respondents received a minimum of triple therapy of the appropriate duration (>7 days) to treat their dyspepsia. It is worth noting that ~10% of the respondents were inappropriately given anti-malarial medicine (Coartem or Tinidazole) in addition to other drugs (not shown).

3.5. Medications: informal health centers (e.g. local drug shops)

Similar treatment regimens were observed if the patients went to informal health centers. Forty-two of 230 respondents (18.3%) reported seeking help at these centers, and 61.9% of these respondents were initially diagnosed there. Of these 42 respondents, 26 were given medications that they were able to remember. Eleven respondents were given medications that they reported as “unknown,” implying that 26% of patients who were managed at an alternative health center could not recall or were unaware of their medication regimen (Fig. 5).

The appropriateness of treatment for the 26 respondents reporting known medications was stratified into the same categories used for the conventional health centers. Two additional categories for exclusively herbal medicine or exclusively antimalarial medicine, that did not apply to Fig. 4, are included (Fig. 6). Of the 26 participants, none received...
Fig. 3. (a) Prescribed medications and (b) recommended duration of usage at conventional health centers.

Fig. 4. Treatment appropriateness in conventional health centers based on standard of care and duration of treatment.

*Note: PPI = Proton Pump Inhibitor
quadruple therapy, 7 received triple therapy (26.9%), 5 received one antibiotic and one PPI (19.2%), 1 received only antibiotics (3.8%), 3 received only PPI (11.5%), 7 received herbal medicine (26.9%), and 3 received anti-malarial medicine (11.5%). Notably, only one participant out of 26 (3.8%) received a minimum triple therapy of the appropriate duration.

3.6. Proficiency of healthcare centers and workers

In an additional survey, 12 healthcare workers at different sites were asked questions to evaluate their knowledge of dyspepsia diagnosis and treatment, as well as the resource availability at their site. All 12 healthcare workers believed that peptic and duodenal ulcers were synonymous with dyspepsia. Two of the 12 healthcare workers were VHTs.
Healthcare worker understanding of symptoms and causes of dyspepsia. (community health workers), and thus were excluded from the medicine prescription questions. Only two healthcare workers reported having heard of Hp, with only one healthcare worker familiar with diagnostic methods specific to Hp. Dyspepsia was diagnosed at nine centers via self-reported symptoms and at a district hospital via a stool antigen test. The other two centers did not report on their diagnostic method.

To evaluate proficiency of training, each worker was asked to list all symptoms they thought indicated dyspepsia and the most common causes of ulcers (Table 2) (see Table 1). Ten of 12 (83.3%) healthcare workers cited epigastric pain as a symptom characteristic of dyspepsia. Another finding of note, though not included in Table 2, was that 10 of 12 healthcare workers believed that dyspepsia could be fatal.

With respect to treatment, nine of the 10 healthcare workers reported on medicine availability. PPIs were present at six of the nine sites, metronidazole at five, amoxicillin at four, and magnesiam at seven. Only two of the nine reporting sites could prescribe the appropriate triple therapy. The workers at only two sites, those with the triple therapy medications available, prescribed the appropriate treatment. In a follow-up response, two workers reported that treatment is available at their site 0–33.3% of the time, four reported 33.3–66.7% of the time, and four reported 66.7–100% of the time. On average, treatment is available at these 10 sites only 58.7% of the time.

Each healthcare worker was then requested to list suggestions that they give to patients for the prevention of ulcers (Fig. 7).

4. Discussion
This study highlighted the prevalence of dyspeptic symptoms among the residents of Namutumba District, Eastern Uganda and emphasized its chronic nature. Very few residents, and surprisingly few health care providers, were aware of Hp as a possible etiology of chronic dyspepsia. The diagnosis of “ulcers” in patients with dyspepsia was mostly reported as being done by a health worker, but over a quarter of respondents reported being diagnosed by a community member or by themselves. The majority of diagnoses by healthcare workers were based on clinical presentation alone, without the use of any established invasive or non-invasive diagnostic tests.

Our results showed that medications were prescribed to 97.1% of respondents who visited a conventional health center, and less than a quarter received triple therapy for Hp eradication, despite most health care providers denying any knowledge of Hp as a possible etiology. Over one-third of triple therapy given at formal health centers were inadequate, based on either an inappropriate duration of treatment or insufficient dosage of one or more components of triple therapy. These shortcomings increase the risk for antibiotic resistance among circulating Hp strains. At informal health centers such as local drug shops, treatment appropriateness was further reduced to ~4%. These low rates, while alarming, may be explained partly by the fact that only two out of nine health centers had sufficient resources to prescribe the triple therapy and that treatment was available only about half of the time. Although ten of twelve health care workers surveyed had not heard of Hp, all had a concept of ulcers that included at least one characteristic symptom, such as epigastric pain. Finally, nearly all health care workers believed that ulcers were caused by delayed food intake or stress, demonstrating limited knowledge of the disease.

Data collection in this study was bolstered through the collaboration with local university graduates in an effort to build rapport with local residents. This allowed for efficient communication and a reliable gathering of information. Questions within the surveys were designed not to be leading or convoluted, keeping in mind the education levels of local populations. Finally, we randomized the selection of villages and health centers, allowing a fair representation of the population. This study was limited by the nature of its scope as an observational study, without any interventions to determine the prevalence of Hp among those reporting dyspeptic symptoms. As a result, the specific cause of dyspepsia (“ulcers”) in these residents remains undetermined. Finally, a notable proportion of medications were listed as unknown by respondents, resulting in their exclusion from the analysis on medication and likely skewing the data towards medications already frequently encountered by these populations.

If we extrapolate the high prevalence of uninvestigated dyspepsia, as determined in this study, this would imply that one in two residents are presumably suffering from “ulcers or ulcer-like symptoms.” This is significantly higher than the global pooled prevalence of 21% reported by Ford et. al in a 2014 meta-analysis [14]. Their reported 95% confidence interval of 25.3%–33.9%, even when using the broadest definition of dyspepsia, is still notably less than the prevalence in our study sample. In Asian populations, it was found that the prevalence of uninvestigated dyspepsia ranged from 8 to 30 %, again noticeably lower than our results [15]. A meta-analysis conducted in 2017 reported a greater than 70% prevalence of residents living with Hp in six out of eight African countries [16]. Even though Uganda was not included in this analysis, the Democratic Republic of Congo, a country bordering Uganda, was found to have a Hp prevalence of 77.4%. Equally alarming was the low rate of appropriate therapy in formal health centers, a phenomenon further exacerbated by lack of dyspepsia knowledge in informal health centers such drug shops. Healthcare workers in this study generally regarded peptic ulcers as synonymous with dyspepsia, although a few reported less common causes such as genetics or unknown causes. Healthcare workers were generally found to be knowledgeable about symptoms of dyspepsia, listing characteristic symptoms such as epigastric pain, heartburn, nausea, bloating, and vomiting. However, four workers also listed headache – not typically found in dyspepsia – as a symptom. More

Table 1
Demographics of study participants. Age (years), Gender, and Self-reported prevalence of dyspeptic symptoms for 397 participants in Namutumba District, Uganda. Self-reported duration of dyspepsia for 230 participants who reported having dyspepsia. Note that 193 participants did not fill out the field for gender.

|                | Mean  | SD   | Range  |
|----------------|-------|------|--------|
| Age            | 41.2  | 15.9 | 18–98  |
| Gender         | 111 males, 93 females |
| Self-reported prevalence of ulcer | 230 yes, 167 no (total 397 participants) |
| If yes, self-reported duration of ulcers (months) | 55.7  | 52.9 | 0.5–600 |

* SD = standard deviation.

Table 2
Healthcare worker understanding of symptoms and causes of dyspepsia.

| Cited symptom of dyspepsia | Number of Healthcare Workers (%) |
|---------------------------|----------------------------------|
| Heartburn                | 7 (58.3%)                        |
| Epigastric Pain           | 10 (83.3%)                       |
| Nausea                   | 4 (33.3%)                        |
| Bloating                 | 4 (33.3%)                        |
| Headache                 | 4 (33.3%)                        |
| Vomiting                 | 4 (33.3%)                        |
| Diarrhea                 | 4 (33.3%)                        |
| Loss of Appetite         | 3 (25.0%)                        |

| Cited cause of dyspepsia | Number of Healthcare Workers (%) |
|-------------------------|----------------------------------|
| H. Pylori               | 1 (8.3%)                         |
| Stress                  | 4 (33.3%)                        |
| Delayed Meals           | 8 (66.7%)                        |
| Genetics                | 2 (16.7%)                        |
| Alcohol                 | 1 (8.3%)                         |
| Don’t know              | 1 (8.3%)                         |
importantly, the lack of knowledge related to the diagnosis and therapy of \textit{Hp} was concerning. This study replicates findings of multiple previous studies in Africa about general knowledge of bacterial diseases being low among healthcare workers [17,18]. When we consider the inconsistent practices for the management of chronic dyspepsia, coupled with a limited knowledge of possible etiologies and appropriate \textit{Hp} eradication regimens, it stands to reason that this population could be at risk of antibiotic resistant infection.

Dyspepsia can arise from many different causes, including the use of NSAIDs [19]. Inappropriate prescription of NSAIDs for various illnesses, as is commonly seen in Uganda, can cause or exacerbate dyspepsia. Further, inconsistent use of antibiotics leads to antibiotic resistance with potentially grave implications [20].

The therapeutic strategy of treating with antibiotics and PPIs before testing, which is common in Uganda and many other low-resource countries, must be scrutinized. The lack of studies detailing the benefits of the treat-before-test strategy in a low resource setting illustrates negligence in the field of Internal medicine [21]. In global health, certain acute diseases that cause rapid mortality receive most of the resources while chronic diseases receive a very small amount of resources [22]. The likelihood that \textit{Hp} infection progresses to gastric adenocarcinoma if the dyspepsia is causally linked to \textit{Hp} is 1–3% while less than 1% of those affected with \textit{Hp} develop mucoid-associated lymphoid tissue (MALT) lymphoma [23]. Given the large burden of dyspepsia in Eastern Uganda, it would be essential to assess the prevalence of \textit{Hp}, especially if a significant proportion of patients are at risk of developing pre-neoplastic lesions. Much of sub-Saharan Africa vastly lacks the ability to manage cancers, and most health centers have limited capacity to diagnose, much less treat them.13 Nonetheless, dyspepsia significantly affects quality of life [24,25,26]. Thus, the principal causes of dyspepsia in Eastern Uganda need to be investigated with a more stratified and consistent evaluation. If the dyspepsia epidemic in Eastern Uganda is mainly caused by \textit{Hp}, there is a dire need to develop and implement more effective \textit{Hp} diagnosis and eradication strategies. Future studies should determine the precise causes of dyspepsia symptoms in rural Eastern Uganda, as well as examine the emergence of antibiotic resistant \textit{Hp}.

Declarations

\textbf{Author contribution statement}

Yang Jae Lee: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Gautam Adusumilli, Timothy Scott Blackwell Jr, Jose Saenz: Analyzed and interpreted the data; Wrote the paper.

Francis Kyakulaga: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data.

Peter Muwerez: Conceived and designed the experiments.

Rauben Kazungu: Performed the experiments.

Moonkyung Cho Schubert: Conceived and designed the experiments; Wrote the paper.

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\textbf{Competing interest statement} 

The authors declare no conflict of interest.

\textbf{Additional information} 

No additional information is available for this paper.

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