Indication for antibiotic prescription among children attending primary healthcare services in rural Burkina Faso

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ABSTRACT

We evaluated diagnoses leading to antibiotic use for children <5 years in 48 government-run primary health facilities in Nouna District, Burkina Faso. Among 61,355 visits, 30,975 received an antibiotic (58% pneumonia). Diagnoses not requiring an antibiotic, including malaria, non-bloody diarrhea, and cough without pneumonia, contributed a minority of antibiotic prescriptions.

Keywords: antibiotics; pneumonia; malaria; diarrhea; antibiotic stewardship
INTRODUCTION

Antibiotic consumption can select for resistant organisms at both the individual and community level.\textsuperscript{1,2} Reducing unnecessary antibiotic use may reduce antibiotic consumption without compromising necessary antibiotic use. In regions without diagnostic laboratory facilities, including in many areas of rural sub-Saharan Africa, pediatric antibiotic treatment is guided by clinical symptoms.\textsuperscript{3,4} For example, World Health Organization (WHO) recommends that children with fast breathing and/or chest indrawing pneumonia receive oral amoxicillin, whereas those with a cough and cold only (no pneumonia) should not receive antibiotics.\textsuperscript{5,6} Similarly, WHO recommends antibiotic treatment for children with bloody diarrhea (dysentery) but not for non-dysenteric diarrhea. Here, we used routinely collected data from primary healthcare facilities in rural Burkina Faso to evaluate antibiotic prescription among children under five years of age diagnosed with common childhood illnesses and identify diagnoses with the most potential to reduce unnecessary antibiotic use.

METHODS

Study setting. This study took place in 48 primary health care centers (Centres de Santé et de Promotion Sociale, CSPS) in Nouna District, Burkina Faso.\textsuperscript{7} Nouna District is a rural area of northwestern Burkina Faso that experiences highly seasonal rainfall from approximately July to October.\textsuperscript{8} The high malaria transmission season coincides with the rainy season, when overall healthcare use is typically higher but antibiotic prescriptions are proportionally lower as more diagnoses are due to malaria.\textsuperscript{9} Healthcare in the study area for children under 5 years of age is provided free of charge by the government. The CSPS represents the first level of healthcare available in the healthcare system. CSPSs offer basic preventative and curative care, such as routine vaccinations and antenatal care. These facilities do not typically have access to
diagnostic laboratory facilities, with diagnostic testing limited to rapid diagnostic tests (RDT) for malaria.

**Data collection.** We extracted data from all sick child visits from March-November 2020 at each facility for all children under five years of age. Data were restricted only to first-time visits and we excluded follow-up visits in our analysis. We extracted data from written ledgers issued by the Ministry of Health for recording diagnostic and treatment information, which were entered into a custom-made electronic data capture form. We included information on the date of the visit, the child’s age and sex, diagnosis, and treatment. We focused the analysis on the most commonly diagnosed infections and infectious symptoms, including pneumonia, malaria, diarrhea, fever, and cough. When available, malaria is diagnosed via RDT. Because RDT stockouts are common, malaria is diagnosed symptomatically when RDTs are not available. All other diagnoses are made following WHO community management of childhood illness algorithms, although the accuracy of these diagnoses is not captured in the dataset. We categorized diagnoses as mutually exclusive categories, including: pneumonia; dysentery without pneumonia; malaria without pneumonia or dysentery; non-bloody diarrhea without dysentery pneumonia, or malaria; fever without pneumonia, malaria, non-bloody diarrhea, or dysentery; cough without pneumonia, dysentery, malaria, non-bloody diarrhea, or fever; and all other diagnoses excluding the previous categories.

**Data analysis.** We calculated the proportion of each major diagnosis that received an antibiotic prescription overall and by antibiotic (including amoxicillin/penicillin, erythromycin, and cotrimoxazole) and corresponding binomial confidence intervals account for clustering at the CSPS level using a nonparametric bootstrap. We then calculated the prevalence ratio of an
antibiotic being prescribed for children with each diagnosis versus pneumonia as the reference category using a modified Poisson model, adjusting for the child’s age and sex and season of the visit, with standard errors adjusted for clustering at the CSPS level using a Huber-White robust standard error. All analyses were conducted in Stata version 15.1 (StataCorp, College Station, TX).

RESULTS

Of 61,355 visits, 30,975 (50.5%) received an antibiotic prescription. Antibiotic prescription was more common in the dry season compared to the rainy season (57.1% versus 42.9% of visits receiving an antibiotic; Table S1). Of all antibiotic prescriptions, 23,554 (76%) were associated with pneumonia, malaria, diarrhea, dysentery, fever, and cough. The majority of the remaining antibiotic prescriptions were primarily for skin conditions (Table S2).

The majority of pneumonia and dysentery diagnoses received an antibiotic prescription (97.1% and 91.9%, respectively; Figure 1). Amoxicillin was the most commonly prescribed antibiotic for pneumonia, whereas metronidazole and ciprofloxacin were commonly prescribed for dysentery (Figure 1). Antibiotics were prescribed for 7.3% of malaria diagnoses, and malaria-only diagnoses were significantly less likely to receive an antibiotic prescription compared to pneumonia (Table S3). However, given the frequency of malaria diagnosis, 1,462 antibiotic prescriptions were given for malaria diagnoses without pneumonia (approximately 5% of all antibiotic prescriptions). Approximately 1 in 5 (20.0%) non-bloody diarrhea diagnoses received an antibiotic prescription, most of which were ciprofloxacin (14.9% of non-bloody diarrhea diagnoses). Pneumonia diagnoses were responsible for the majority of antibiotic prescriptions (Figure S1), and pneumonia diagnoses were significantly more likely to receive an antibiotic prescription than other diagnoses (Table S3).
DISCUSSION

We document that the majority of antibiotic prescriptions among children attending primary care facilities in Nouna District are dispensed for pneumonia diagnoses. Pneumonia is the leading cause of childhood mortality, and treatment is based on WHO-recommended treatment classification. Childhood pneumonia can have viral or bacterial etiology but distinguishing between viral and bacterial pneumonia requires sophisticated diagnostic facilities that many children in regions with high pneumonia burden do not have access to. As non-severe pneumonia cases may be self-limiting and viral in nature, recent studies have evaluated whether antibiotics are necessary for mild pneumonia without danger signs.\textsuperscript{10–12} Although most cases of non-severe pneumonia recover without antibiotics, the proportion recovered after 4 days was slightly higher with use of amoxicillin than without in randomized controlled trials.\textsuperscript{10,11} The majority of antibiotic prescribing in the current study was appropriate given the pneumonia diagnosis, as antibiotics are indicated for pneumonia. However, the diagnostic accuracy of pneumonia in this setting is unknown, and improvements in pneumonia diagnosis may reduce antibiotic consumption.

Malaria diagnoses were uncommonly prescribed an antibiotic. Amoxicillin, which was the most commonly prescribed antibiotic overall and for malaria, does not have anti-malarial properties. The WHO does not recommend routine antibiotic treatment for uncomplicated malaria. Pneumonia and malaria can present with similar clinical signs, including fever, which often results in diagnosis and treatment for both conditions. Previous analyses have shown that while concomitant diagnosis is common, true overlap in disease is rare.\textsuperscript{13} Primary healthcare facilities in the study area have RDT capability for diagnosing malaria, but do not typically have
x-ray facilities for pneumonia diagnosis. An improvement in diagnostics for pneumonia could reduce unnecessary antibiotic treatment if children are misdiagnosed as having pneumonia.

WHO guidelines recommend antibiotic treatment for dysentery, with ciprofloxacin recommended as first-line treatment as they are presumed to be due to *Shigella* spp. In the study area, dysentery presenting with mucus is presumed to be amoebiasis (*Entamoeba histolytica*), and is prescribed metronidazole. In this analysis, approximately half of antibiotic prescriptions for dysentery were metronidazole. *E. histolytica* is a relatively uncommon cause of childhood diarrhea in other settings in the Sahel, and it is possible that the current classification system is overcalling amoebic dysentery. Etiologic studies of diarrhea in this setting may be useful for clinical decision-making to better understand the most common causes of diarrhea in these children to guide treatment decisions. Although the WHO does not recommend antibiotic treatment for non-bloody diarrhea, studies have shown that it is common in multiple settings. In the present study, approximately 1 in 5 non-bloody diarrhea cases were antibiotic treated, which may represent an opportunity to reduce antibiotic prescription.

Routinely collected healthcare surveillance data have inherent limitations that must be considered. Although we were able to rapidly collect data on thousands of child visits in the study area, these data are subject to misclassification. If data are entered incorrectly in ledgers, diagnosis and treatment data could be misclassified. In the absence of laboratory diagnostic facilities, diagnoses themselves may be misclassified. RDT stockouts are not uncommon, and in the absence of an available RDT malaria diagnoses are made symptomatically. Similarly, although the goal is to follow WHO algorithms for diagnosis of pneumonia, in practice they are not always followed. We did not have data on RDT stockouts, which malaria diagnoses were made symptomatically versus with an RDT, or quality of the pneumonia diagnoses. Data were not prospectively collected specifically for the purposes of this study, and thus we have limited information on co-presenting symptoms that may drive
treatment decisions and the accuracy of diagnoses. Data were collected in one district of northwestern Burkina Faso and may not be generalizable outside of the region. Despite these limitations, these data represent real-world diagnostic and treatment decisions based on currently available infrastructure in primary healthcare facilities in a rural area of Burkina Faso. These data offer insight into treatment decisions made under real-world conditions.

These data demonstrate that the majority of pediatric antibiotic prescriptions in this area of Burkina Faso were due to a pneumonia diagnosis, with a minority of prescriptions due to diagnoses for which antibiotic use is not indicated, including malaria and non-bloody diarrhea. Interventions to reduce the use of antibiotics for non-indicated diagnoses may reduce overall antibiotic consumption.
**Funding.** This work was supported by the Bill and Melinda Gates Foundation (OPP1187628) Grant made to institution to support parent study; article processing charges.

**Conflicts of interest.** None to report. BFA reports grants from NIH / National Institute of Allergy and Infectious Diseases and Task Force for Global Health / NTD Support Center; travel support from Bill & Melinda Gates Foundation; advisory board fees from NIH/ National Institute of Allergy and Infectious Diseases and Task Force for Global Health / NTD Support Center; travel support from Bill & Melinda Gates Foundation, outside submitted work. MB reports travel support from Bill & Melinda Gates Foundation, outside the submitted work. TL reports grants from National Eye Institute and NTD Support Center/Task Force for Global Health; travel support from Bill & Melinda Gates Foundation, outside submitted work. CO reports research grants to support ongoing work, made to institution from National Institute of Child Health and Development and National Eye Institute; and travel support from Bill & Melinda Gates Foundation. AS reports grants from National Institute of Child Health and Development; travel support from Bill & Melinda Gates Foundation, outside submitted work.
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FIGURE LEGEND

Figure 1. Percentage of each major infectious diagnosis receiving an antibiotic prescription, overall (A) and by specific antibiotic, including amoxicillin (B), cotrimoxazole (C), erythromycin (D), ciprofloxacin (E), and metronidazole (F). Dots represent point estimates and bars indicate exact binomial 95% confidence intervals.
A. All antibiotic classes

- Cough
- General fever
- Non-bloody diarrhea
- Malaria
- Dysentery
- Pneumonia

0 25 50 75 100

% of diagnoses

B. Amoxicillin

- Cough
- General fever
- Non-bloody diarrhea
- Malaria
- Dysentery
- Pneumonia

0 25 50 75 100

% of diagnoses

C. Cotrimoxazole

- Cough
- General fever
- Non-bloody diarrhea
- Malaria
- Dysentery
- Pneumonia

0 25 50 75 100

% of diagnoses

D. Erythromycin

- Cough
- General fever
- Non-bloody diarrhea
- Malaria
- Dysentery
- Pneumonia

0 25 50 75 100

% of diagnoses

E. Ciprofloxacin

- Cough
- General fever
- Non-bloody diarrhea
- Malaria
- Dysentery
- Pneumonia

0 25 50 75 100

% of diagnoses

F. Metronidazole

- Cough
- General fever
- Non-bloody diarrhea
- Malaria
- Dysentery
- Pneumonia

0 25 50 75 100

% of diagnoses