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Antibiotic prescribing practices for patients with fever in the transition from presumptive treatment of malaria to 'confirm and treat' in Zambia: a cross-sectional study

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Abstract

OBJECTIVES To evaluate antibiotic use among patients presenting to primary healthcare facilities with febrile illness in Zambia.

METHODS We analysed data from a 2011 nationwide cross-sectional health facility survey of routine malaria case management in Zambia. Patient consultation observation and medical record charts were used to calculate the proportion of febrile patients who were prescribed antibiotics, stratified by symptoms, health workers' diagnosis and malaria test results. Logistic regression was used to identify factors affecting antibiotic prescribing behaviour.

RESULTS Of 872 patients presenting with fever, 651 (74.6%) were tested for malaria. Among those tested, 608 (93.4%) had analysable results; 230 (37.8%) had positive results. Antibiotics were prescribed to 69/230 (30.0%), 247/378 (65.3%) and 132/221 (59.7%) of those who tested positive, negative and those 'not tested', respectively. Furthermore, antibiotics were prescribed to 36/59 (61.0%) and 242/322 (75.1%) of those diagnosed with diarrhoea and upper respiratory tract infection (URTI), respectively. Among patients prescribed any antibiotic, concurrent antimalarial prescribing occurred in 66/69 (95.6%), 32/247 (12.9%) and 19/132 (14.4%) for those with positive results, negative results and 'not tested', respectively. Respiratory symptoms, diagnosis of URTI, malaria or skin disease and level of health care in the health delivery system were associated with antibiotic prescribing.

CONCLUSIONS Testing positive for malaria or receiving a malaria diagnosis was associated with reduced antibiotic prescribing, while testing negative, not being tested or a diagnosis of URTI resulted in higher rates of antibiotic prescribing. There is a need for improving diagnostic capacity for non-malaria causes of febrile illness at healthcare delivery points and limiting antibiotic use to patients with definite bacterial infections.

keywords antibiotic, prescribing, fever, malaria, Zambia

Introduction

Malaria, acute respiratory infections and diarrhoea rank among the top ten causes of morbidity and mortality in the developing world [1, 2]. These diseases commonly manifest with fever and differentiating them poses a diagnostic challenge. A substantial proportion of febrile illnesses in malaria endemic areas is not due to malaria infection [3] and where there are limited diagnostic capabilities for malaria, most episodes of these fevers are attributed to malaria [4, 5]. The resulting misdiagnosis of malaria leads to overuse of antimalarials while denying non-malarial febrile illnesses appropriate treatment.

Recently, sustained investment in malaria control interventions in most countries in malaria endemic regions has markedly reduced the incidence of parasitologically confirmed malaria [6]. With fewer parasitologically confirmed malaria cases, the proportion of non-malaria fevers will increase and thus the need for the healthcare providers to treat alternative causes of febrile illnesses. To ensure that appropriate treatment is given to patients with a febrile illness, WHO now recommends universal testing for malaria in such patients and prescribing an antimalarial only upon confirmation of malaria [7].

Most countries in malaria endemic regions have introduced malaria testing capabilities at primary healthcare facilities (PHCs), mainly as malaria rapid diagnostic tests (mRDTs). Worldwide, up to 77% of patients with fever received a blood test in 2011 [6]. The increased availability of malaria testing facilities has resulted in improved management of patients with febrile illness, confirmed malaria cases receiving an effective antimalarial and reduced inappropriate antimalarial prescriptions for those with a negative test [8]. However, the availability of mRDTs has resulted in increased prescribing of antibiotics for patients with fever and a negative malaria test [9]. Therefore, the introduction of malaria diagnostics coupled with changes in treatment guidelines recommending prescribing an antimalarial only to confirmed malaria cases could potentially reduce antimalarial usage while promoting overuse of antibiotics.

In recent years, Zambia has invested in malaria control using integrated vector control, increased availability of malaria diagnostics and artemisinin-based combination therapy (ACT). By 2009 malaria diagnostic services, mostly mRDTs, were available at over 90% of PHCs [10]. Furthermore, malaria treatment guidelines were revised to include treating for malaria only when there was a positive test result [11]. Reduction in both malaria incidence at PHCs and ACT usage has been demonstrated as these interventions were implemented [12, 13]. With the declining malaria incidence and increased availability of malaria diagnostics at most PHCs, many patients with fever will likely test negative for malaria and healthcare providers will need to consider alternative diagnoses and treatments. PHC services are accessible mostly through public (government and religious mission) facilities in urban and rural areas, while the private-for-profit sector provides health services for a minority of the population mostly in the urban areas. Diagnosis and treatment of malaria and other common cause of febrile illnesses is provided free of charge at the former while the latter charges variously. Both public and private health facilities are required to follow the national malaria diagnosis and treatment guidelines.

Understanding how healthcare providers manage patients with febrile illness, both when malaria is parasitologically confirmed and when tests are negative, in regard to antibiotic use is important. Hence, this study aims to examine healthcare providers' antibiotic prescribing practices for patients with febrile illness who were tested and those not tested for malaria in Zambia.

Methods

Study design

This is a secondary data analysis of a larger nationwide cross-sectional survey previously completed by the National Malaria Control Programme as routine monitoring and evaluation of malaria case management in areas with varying levels of malaria transmission. The survey was conducted in March and April of 2011. The study design and implementation of the health facility survey is given elsewhere [14, 15]. In summary, the sampling frame consisted of health facilities (HFs) from both private and public sectors, in all the provinces in Zambia, as compiled by the Ministry of Health [16]. The HFs were stratified into four groups according to the level of healthcare services provided: hospital ($N = 107$), urban health centre ($N = 428$), rural health centre ($N = 1042$) and health post ($N = 266$). Forty-two HFs were then randomly selected from each stratum for a total of 168 HFs, but only 148 (88.1%) HFs were surveyed. Of the surveyed HFs, 110/148 (74.3%) were government, 18 (12.2%) not-for-profit mission facilities, 13 (8.8%) private-for-profit and 7 (4.7%) were company operated for their employees. Overall, 111/148 (75.0%) HFs had malaria diagnosis capacity, either as mRDTs 72/111 (70.0%), microscopy 7/111 (6.3%) or both 32/111 (28.8%).

In the primary survey, each selected HF was surveyed over one working day and all patients attending the HF (considered as a cluster) on that particular day were considered eligible. If the expected patient attendance was fewer than 10 on the survey day for any particular HF, all eligible patients were recruited while a subset was chosen by systematic sampling if greater than 10. Patient eligibility criteria included the following: visiting the outpatient section of the HF for consultation with a healthcare provider and seeking health care for the first time for the current illness. Patients visiting the HF for follow-up visit for chronic illness or routine services such as antenatal and under five were excluded. From the 148 HFs surveyed, 1393 participants were recruited and observed during consultation with a healthcare provider although only 1290 (92.6%) completed the study. Patients from hospitals were obtained from the hospital-affiliated health centres (HAHCs) where outpatient attendees were seen.

Data collection

Data were obtained by observing patient–health worker interactions during a medical consultation, from patient-held health records and by direct exit interview with the patient or caregiver. The patients' chief complaint or symptom reported, patients' use of medications for current illness prior to visiting HF, physical assessments, diagnoses made, and investigations requested and/or performed, and drugs prescribed by the health worker were all recorded.

Variables and measurements

The primary outcome was the proportion of patients with suspected malaria that was prescribed a systemic antibiotic, stratified by patients' chief complaint reported to the health worker, health worker diagnosis of the patients' illness and malaria test results.

'Suspected malaria' was defined as patient with a history of fever (temperature ≥37.5°C or complaint of fever at exit interview) attending the HF for the first time for the current illness during the exit interview. Any patient prescribed an antimalarial for treatment was placed in the antimalarial group for purposes of analysis.

The health workers' diagnosis was the diagnosis indicated by the health worker in the patient-held clinical record and captured by the survey team in the primary study. This study did not re-evaluate the appropriateness of the health workers' diagnosis.

An antibiotic was counted as prescribed if it was systemic, that is topical preparations were excluded. All patients who were prescribed a systemic antibiotic were placed in the antibiotic group for analysis, even if they had also received an antimalarial drug.

Ear, nose and throat (ENT) diagnoses included pharyngitis, otitis media and sinusitis. These were analysed separately from other upper respiratory tract infections (URTIs), which were most likely viral infections such as the common cold.

Data management and statistical analysis

In the primary survey, all data were double-entered by two independent clerks into Microsoft Access. The two data sets were then compared and discrepancies corrected by referring to the source documents. For this study, 872 records of patients with fever were extracted from the database for analysis using STATA (version 11, College Station, TX, USA).

Descriptive statistics as proportions and their 95% confidence intervals (CI) are reported. When calculating CIs around observed proportions, cluster design was accounted for by specifying the health facility as the primary sampling unit. All analyses were weighted unless specified. We used the weighting factor as defined in the primary data set. As patients were first selected from different strata, stratum estimates were combined into an overall estimate as a sum of the weighted means or proportions from each stratum. Details are presented in Littrell *et al.* [14]. Pearson's chi-square test was used to evaluate differences in the proportion prescribed antibiotics among groups of patients. All tests were two-tailed and a *P*-value of ≤0.05 was considered statistically significant. Unadjusted odds ratios (OR) were derived in bivariate logistic regression to identify covariates associated with antibiotic prescribing. The covariates included age categorised as children aged less than 5 years (under-fives) and 5 years and above (older patients), patients' chief symptoms reported to the health worker, duration of symptoms, health workers' diagnosis, malaria test result, type of health worker and level of healthcare delivery in the health system. To obtain adjusted ORs, a multivariate model was fitted; all covariates with $P \leq 0.15$ in bivariate logistic regressions were included in an initial model. The importance of each of the covariates in the multivariate model was tested using the Wald statistic. Those found not to be statistically significant were removed. Lastly, to select the final model, the variables whose $P > 0.15$ in the bivariate logistic regressions were then added one at a time and their effect on the outcome was assessed using the Wald statistic. Only those that improved the model were retained. The Hosmer and Lemeshow goodness-of-fit test was used to assess the overall multivariate model.

Ethical considerations

Ethical clearance and authorisation for this survey was provided by the University of Zambia Research Ethics Committee and by the Ministry of Health. Individual consent was obtained from both the health worker and patient or caretaker to be observed during the consultation and for the exit interview.

Results

Participants and causes of health facility visitation

Of the 1290 records for patients who completed the exit interview, 872 (72.2%) met the criteria for suspected malaria, ranged from 213/353 (62%) at hospital to 251/308 (74.9%) at UHCs (Table 1). A total of 737/872 (84.5%) consultations occurred at government-owned health facilities, while 46 (5.3%) occurred in the private-for-profit sector. Of health workers with pre-service medical training, nurses and clinical officers together

Table 1 Number of consultations by type of healthcare provider and level of care

	n	%
Proportion of patients with suspected malaria by level of care		
Hospital (*N* = 353)	213	61.7
Urban health centre (*N* = 308)	221	74.9
Rural health centre (*N* = 363)	251	72.2
Health post (*N* = 266)	187	72.6
All (1290)	872	72.2
Number of consultations among patients with suspected malaria by type of health facility (*N* = 872)*		
Government owned*	737	84.5
Mission owned	89	10.2
Private-for-profit	46	5.3
Number of consultations among patients with suspected malaria by health worker cadre (*N* = 872)*		
Medical officer (doctor)	38	4.3
Clinical officer	295	33.8
Nurse	284	32.6
Environmental health technologist	75	8.6
Classified daily employee†	180	20.6

*Unweighted.
†A health worker with no prior formal clinical training initially employed to perform functions other than clinical work.

performed 579/872 (66.4%) of consultations, while medical doctors evaluated less than 5% of the patients. A health worker cadre without formal pre-service medical training (classified daily employees) performed consultations for about 180/872 (20%) of the patients.

Participants were predominantly female among the older patients (232/435, 59.7%) compared to under-fives (212/437, 48.8%) (Table 2). Overall, 501/865 (55.1%) had symptoms for more than 48 h with minor differences between the age groups (Table 2). Although cough with or without difficulty breathing was the most common symptom, a higher proportion of under-fives 350/437 (80.0%) reported this symptom compared to 259/435 (64.1%) of older patients. Similarly, diarrhoea was reported in over twice the proportion of under-fives compared to older patients: 29.1% *vs.* 13.4%.

Overall, respiratory tract infections and malaria were the most frequent diagnoses made by health workers. While there was no difference in proportions of malaria diagnosed between the two age groups, URTI, pneumonia and diarrhoea were two to three times more frequently diagnosed in under-fives than older patients. Ear, nose and throat (ENT) problems, although less frequent, were more often diagnosed in older patients 22/435 (7.3%) than under-fives 7/437 (2.1%). Skin infections and/or allergic conditions were more frequently diagnosed among under-fives than older patients.

Antibiotic prescribing for patients with fever

Of the 872 patients with suspected malaria, 470 (53.9%) were prescribed at least one antibiotic, and among these, 446/470 (94.9%) were prescribed a single antibiotic, 23/470 (4.9%) two antibiotics and 1/470 (0.2%) received three antibiotics. Penicillin and amoxicillin, cotrimoxazole and erythromycin were commonly used, being prescribed in 279 (57.9%), 98 (21.3%) and 35 (9.3%), respectively. The rest included metronidazole, doxycycline, gentamicin, chloramphenicol, quinolones and cephalosporins (cephalexin, cefuroxime and ceftriaxone), together accounting for slightly over 10%.

The majority of patients with respiratory (391/609; 64.2%), diarrhoea (105/195; 53.8%) or ENT complaints (133/194; 68.5%) were prescribed at least one antibiotic regardless of age (Table 3). Similarly, the majority of patients diagnosed with URTI (242/322; 75.1%), ENT infections (25/29; 86.2%) and non-diarrhoea (36/59; 61.0%) were prescribed an antibiotic. Regardless of age, all patients diagnosed with pneumonia were prescribed an antibiotic, while only a third of patients diagnosed with malaria received an antibiotic. Among patients with dermatologic problems, 17/21 (80.9%) of under-fives compared to 3/9 (33.3%) older patients were prescribed an antibiotic.

The frequency of prescribing for each type of antibiotic varied according to patient age and health workers' diagnosis (Table 4). Oral penicillins, amoxicillin and penicillin V, and cotrimoxazole were the commonly used antibiotics, together accounting for over 65%, among the 470 patients prescribed at least one antibiotic. However, among those diagnosed with malaria, 38/70 (54.3%) of older patients and 26/70 (37.1%) of under-fives were prescribed amoxicillin, while 24/70 (34.4%) of under-fives compared to 14/70 (20.0%) were prescribed cotrimoxazole. While amoxicillin was commonly used for both age groups among those diagnosed with URTI, cotrimoxazole was prescribed more for under-fives 38/139 (27.3%) compared to 17/103 (16.5%) older patients. Among those diagnosed with pneumonia, there were minor differences in the proportions prescribed either penicillins or erythromycin, but 5/37 (18.6%) of under-fives compared to 1/17 (5.9%) were prescribed cotrimoxazole. Among patients with non-bloody diarrhoea, cotrimoxazole (10/28; 22%) and penicillins (8/28; 29.6%) were commonly prescribed in under-fives, while metronidazole (6/8; 75%) was prescribed for older patients. Notably, doxycycline was not prescribed for any under-fives and sparingly prescribed for older patients.

Table 2 Characteristics of patients with 'suspected malaria' *

	Age group		
Characteristic	<5 years *N* = 437 *n* (%, 95% CI)	≥5 years *N* = 435 *n* (%, 95% CI)	All *N* = 872 *n* (%, 95% CI)
Gender (*N* = 872)			
Female	212 (48.8,42.3–55.4)	232 (59.7, 53.0–66.2)	444 (54.2,49.4–58.9)
Symptoms excluding fever†			
Cough/difficult breathing	350 (80.0, 74.5–84.6)	259 (64.1, 57.4–70.2)	609 (72.2,67.9–76.1)
Vomiting	140 (33.9, 28.0–40.4)	174 (43.0, 36.2–50.0)	314 (38.4, 33.9–43.1)
Ear, nose, throat problems	109 (28.5, 22.8–35.2)	85 (25.5, 19.7–32.3)	194 (27.1, 22.9–21.7)
Diarrhoea	132 (29.1, 23.6–35.1)	63 (13.4, 9.7–18.3)	195 (21.4, 17.9–25.3)
Other	57 (9.9, 6.6–14.6)	63 (15.9, 11.2–22.2)	120 (12.9, 9.9–16.7)
Duration of illness (*N* = 856)			
≤2 days	195 (45.7, 39.2–52.3)	160 (42.0, 35.2–49.1)	355 (43.9, 39.1–48.7)
>2 days	235 (54.3, 47.7–60.8)	266 (58.0, 50.9–64.8)	501 (56.1, 51.3–60.9)
Health worker's diagnosis†			
Malaria	193 (46.1, 39.7–52.1)	209 (49.8, 43.2–56.8)	402 (48.0, 43.2–52.7)
URTI‡	191 (44.3, 37.9–50.9)	131 (27.5, 22.0–33.8)	322 (36.0, 31.6–40.7)
Pneumonia	37 (8.4, 5.8–12.6)	17 (4.1, 2.1–8.1)	54 (6.4, 4.4–9.0)
Diarrhoea§	45 (11.1, 7.7–15.6)	14 (3.7, 1.9–7.3)	59 (7.5, 5.4–10.2)
ENT¶	7 (2.1, 0.8–5.7)	22 (7.3, 4.2–12.4)	29 (4.7, 2.9–7.5)
Dermatologic problem**	21 (3.1, 1.9–5.7)	9 (0.9, 0.3–5.7)	30 (2.0, 1.2–3.4)
Other††	33 (7.2, 4.5–11.3)	55 (9.5, 6.4–14.0)	88 (8.3, 6.2–11.2)

*'Suspected malaria' defined as patient with a history of fever (temperature ≥37.5°C or complaint of fever at exit interview) attending the HF for the first time for the current illness.
†Percentages add to more than 100% as some patients had more than one symptom or diagnosis indicated.
‡Non-pneumonia infections of respiratory tract.
§Non-bloody diarrhoea.
¶ENT = ear, nose and throat. Included diagnoses such as tonsillitis, pharyngitis, sinusitis and otitis media.
**Skin infections and allergies. Infections or septic lesions were common in under-fives.
††Included urinary tract infections, worm infestations, non-communicable disease, for example hypertension, diabetes mellitus, arthritis, gynaecological problems, asthma, anaemia, musculoskeletal and dental caries/cavities.

Blood testing for malaria and antibiotic prescribing patterns

Among the patients who met the criteria for suspected malaria, health workers requested or performed a malaria blood test for 651/872 (74.7%) during the consultation, while 221 (23.3%) were not tested. Among the tested patients, 608/651 (93.4%) had complete test results at exit interview (Figure 1). An mRDT was used in 549/608 (90.3%) and microscopy in 47 (7.7%), while 12 (2.0%) were tested with both.

Among patients with available malaria blood test results, 230/608 (37.8%) had a positive test. Antimalarial prescribing, singly or in combination with an antibiotic, occurred in 227/230 (98.7%), 70/378 (18.5%) and 57/221 (25.8%) of patients with a positive test, negative test and those not tested, respectively. Antibiotics were prescribed for 215/378 (56.9%) and 113/221 (51.1%) of patients with negative blood tests and among those not tested, respectively, compared to 3/230 (1.3%) of patients with positive test results. There were statistically significant differences in proportions between positive test *vs.* negative tests ($P < 0.001$) and positive tests *vs.* 'no test' ($P = 0.001$) but not between negative blood results *vs.* 'no test' ($P = 0.280$). Concurrent prescribing of antimalarials was lowest among patients with a negative test compared to those with positive blood tests.

Predictors of antibiotic prescribing

Level of care in the health delivery system, health worker cadre, symptoms reported by the patient, health workers' diagnosis and malaria test results were all statistically significant determinants of antibiotic prescribing in the unadjusted logistic regressions (Table 5). Compared to hospitals, patients at RHCs and HPs were 2.6 ($P < 0.001$) and 1.7 ($P = 0.032$) times less likely, respectively, to be prescribed an antibiotic. Additionally, compared to medical doctors, nurses were four times less

Table 3 Proportions of patients prescribed antibiotics by symptom and health workers' diagnosis

	Age (years)		
	<5 *n*/N (%, 95% CI)	≥5 *n*/N (%, 95% CI)	All *n*/N (%, 95% CI)
Symptom			
Cough/difficult breathing	227/350 (64.8, 59.1–69.8)	164/259 (63.3, 57.1–69.2)	391/609 (64.2, 60.2–68.0)
Vomiting	62/140 (44.3, 36.2–51.4)	76/174 (43.7, 36.2–51.4)	138/314 (43.9, 38.4–49.6)
ENT problems	75/109 (68.8, 59.2–77.3)	58/85 (68.2, 57.2–77.9)	133/194 (68.5, 61.5–75.0)
Diarrhoea	74/132 (56.1, 47.2–64.7)	31/63 (49.2, 36.4–62.1)	105/195 (53.8, 46.6–61.0)
Other	40/57 (70.2, 56.6–81.6)	26/63 (41.3, 29.0–54.4)	66/120 (55.0, 45.6–64.1)
Health workers' diagnosis			
Malaria	70/193 (36.5, 27.1–40.3)	70/209 (33.5, 27.1–40.3)	140/402 (34.8, 30.2–39.7)
URTI	139/191 (72.8, 65.9–78.9)	103/131 (78.6, 70.6–85.3)	242/322 (75.1, 70.1–79.8)
Pneumonia	37/37 (100)	17/17 (100)	54/54 (100)
ENT	6/7 (85.7, 42.1–99.6)	19/22 (86.3, 65.1–97.1)	25/29 (86.2, 68.3–96.1)
Diarrhoea *	28/45 (62.2, 46.5–76.2)	8/14 (57.1, 28.9–82.3)	36/59 (61.0, 47.4–73.4)
Dermatologic diseases†	17/21 (80.9, 58.1–94.5)	3/9 (33.3, 7.5–70.1)	20/30 (66.7, 47.2–82.7)
Other‡	14/33 (42.2, 25.5–60.8)	25/55 (45.4, 32.0–59.4)	39/88 (44.3, 33.7–55.3)

*Non-bloody diarrhoea only.
†Skin infections and allergies. Infections or septic lesions were commoner in under-fives.
‡Included urinary tract infections, worm infestations, non-communicable disease, for example hypertension, diabetes mellitus, arthritis, gynaecological problems, asthma, anaemia, musculoskeletal and dental caries/cavities.

likely to prescribe an antibiotic ($P = 0.012$). Cough and ENT complaints were significantly associated with increased antibiotic prescribing, while vomiting had an inverse effect. Patients diagnosed with URTI, ENT and dermatological problems were 3.4, 5.9 and 3.5 times more likely to receive an antibiotic, respectively. However, a diagnosis of malaria reduced the odds of a patient receiving an antibiotic by 76% ($P < 0.001$). A negative malaria test and non-performance of a malaria test both increased the odds of an antibiotic being prescribed compared to positive results. Although not statistically significant, older patients were 1.4 times less likely to receive an antibiotic, while longer duration of symptoms increased the odds of a patient receiving an antibiotic by 11%.

In adjusted logistic regression, only level of health care, symptom of respiratory system, diagnosis of malaria, URTI and dermatology conditions were significantly associated with receiving an antibiotic. Adjusting for the health worker cadre, patients attending RHCs and HPs were 2.6 and 1.7 times less likely to receive antibiotics, respectively. Respiratory symptoms, diagnosis of URTI, dermatologic problem and ENT all increased the odds of antibiotic prescribing. By contrast, a malaria diagnosis reduced the odds of antibiotic prescribing by 62% ($P = 0.001$) after adjusting for malaria test results. There were no statistically significant interactions.

Discussion

In this nationwide malaria case management survey, a higher proportion of patients with suspected malaria who tested negative for malaria and those not tested for malaria were prescribed an antibiotic compared to those who tested positive for malaria. Furthermore, the study revealed a high level of adherence to malaria treatment guidelines by health workers as only 13% of fever patients with a negative test result were prescribed an antimalarial compared to 94% of those with a positive test result.

A major proportion of fevers at outpatient departments were due to non-malaria causes as most febrile patients tested negative for malaria. This is similar to findings in similar settings [3, 17, 18]. Therefore, with the availability of quick and simple-to-perform malaria tests at point of care, the most significant task for the health workers is to determine alternative causes of these non-malaria fevers. The deployment of malaria diagnostic capacity at PHCs is thus useful for the identification of non-malaria fevers. This will be beneficial in two ways: (i) reduction in use of ACTs and (ii) correct evaluation of patients with febrile illness [19, 20], thus allowing for the evaluation and identification of causes non-malaria fevers. Failure to correctly treat the latter group of patients, i.e. those with non-malaria fevers, only increases their chance of poor clinical outcomes. Crump *et al.* [4] demonstrated

Table 4 Proportions of patients with a named health workers' diagnosis that was prescribed the named antibiotic by age group*

	Malaria		URTI		Pneumonia		Diarrhoea		ENT		Dermatologic		Other	
Antibiotic	<5 years N = 70 *n* (%)	≥5 years N = 70 *n* (%)	<5 years N = 139 *n* (%)	≥5 years N = 103 *n* (%)	<5 years N = 37 *n* (%)	≥5 years N = 17 *n* (%)	<5 years N = 28 *n* (%)	≥5 years N = 8 *n* (%)	<5 years N = 6 *n* (%)	≥5 years N = 19 *n* (%)	<5 years N = 17 *n* (%)	≥5 years N = 3 *n* (%)	<5 years N = 14 *n* (%)	≥5 years N = 25 *n* (%)
Penicillin V	3 (4.3)	1 (1.4)	17 (12.2)	8 (7.8)	4 (11.8)	2 (11.6)	2 (4.4)	0	1 (16.7)	4 (21.0)	0	0	2 (14.3)	2 (8.0)
Amoxicillin	26 (37.1)	38 (54.3)	66 (47.4)	68 (66.0)	12 (34.2)	6 (35.3)	6 (25.2)	0	1 (16.7)	7 (36.8)	5 (29.4)	1 (33.3)	5 (35.8)	5 (20.0)
Injectable penicillin	4 (5.7)	0	0	0	9 (24.5)	3 (17.6)	0	0	0	5 (26.3)	5 (29.4)	1 (33.3)	0	1 (4.0)
Cotrimoxazole	24 (34.3)	14 (20.0)	38 (27.3)	17 (16.5)	5 (18.6)	1 (5.9)	10 (19.8)	1 (12.5)	2 (33.0)	0	1 (5.9)	0	4 (28.5)	0
Erythromycin	7 (10.1)	7 (5.7)	10 (7.2)	5 (4.8)	5 (13.5)	2 (11.8)	1 (2.2)	1 (12.5)	0	1 (5.2)	0	0	2 (14.3)	1 (4.0)
Metronidazole	4 (5.7)	4 (5.7)	5 (3.6)	1 (0.9)	1 (2.8)	1 (5.9)	11 (44.2)	6 (75.0)	1 (16.7)	0	0	1 (33.3)	0	4 (16.0)
Doxycycline	0	5 (7.1)	0	2 (2.4)	0	1 (5.9)	0	0	0	0	0	0	0	6 (24.0)
Other†	2 (2.8)	3 (4.3)	3 (2.2)	3 (1.9)	3 (8.1)	1 (5.9)	0	0	1 (16.7)	2 10.5)	0	0	1 (7.1)	10 (40.0)

*Analysis restricted to those patients prescribed at least one antibiotic; some percentages are more than 100% as some patients were prescribed more than one antibiotic.

†Cephalexin, ciprofloxacin, cefuroxime, chloramphenicol, nalidixic acid, cefotaxime, gentamicin.

that bacteraemia with typical and atypical organisms and viraemias accounted for most illnesses in patients with severe febrile diseases despite the majority of them being labelled as having had clinical malaria.

Nearly all patients who tested positive for malaria received an antimalarial. However, 30% were also prescribed an antibiotic suggesting that health workers were not entirely confident that a positive malaria test implied malaria alone, that is that they were concerned that there might also be a bacterial cause of the fever. As patients with uncomplicated malaria are unlikely (relative to those with severe malaria) to have a concurrent systemic bacterial infection such as bacteraemia, these antibiotic prescriptions were most likely inappropriate. Conversely, a negative test result or non-performance of a test resulted in an antibiotic being prescribed in at least 60% of patients suggesting that health workers considered bacterial infections as alternative causes of fever. Similar health worker antibiotic prescribing practices have been reported elsewhere; high rates of antibiotic prescribing when malaria test was negative or not tested and low prescribing rates when the test was positive [8, 9]. Nevertheless, 60% is high and demonstrates a tendency for health workers to overuse antibiotics for illnesses that do not require such drugs. Although there is limited understanding of the aetiology of non-malaria febrile illnesses locally, evidence from similar settings suggests that over 70% of malaria-negative febrile illnesses are not bacterial infections [3, 18]. Additionally, Chanda *et al.* demonstrated that more than 40% of non-malaria febrile illnesses among under-fives, in settings where the current study was conducted, were due to acute respiratory infections (non-pneumonia) [12] which are often due to viral infections and do not require antibiotic treatment.

Except for ENT, pneumonia and some dermatologic diseases, most antibiotics were prescribed for patients diagnosed with URTI, non-bloody diarrhoea and malaria. This shows an overuse of antibiotics for illnesses that do not require antibiotics. Even though most URTIs are viral in nature and antibiotics offer no benefits, the bulk of the antibiotics prescribed in this study were for patients with cough or who received a diagnosis of URTI. Although this practice has been reported in other settings [21], there is little evidence that that withholding antibiotics in such patients results in development of serious respiratory complications [22, 23], nor does prescribing antibiotics help in the resolution of the cough and sputum production [24, 25]. Furthermore, a study in Tanzanian children aged up to 10 years who presented with a febrile illness found that nasopharyngeal and URTI were mostly viral in nature and did not warrant antimicrobial therapy [18].

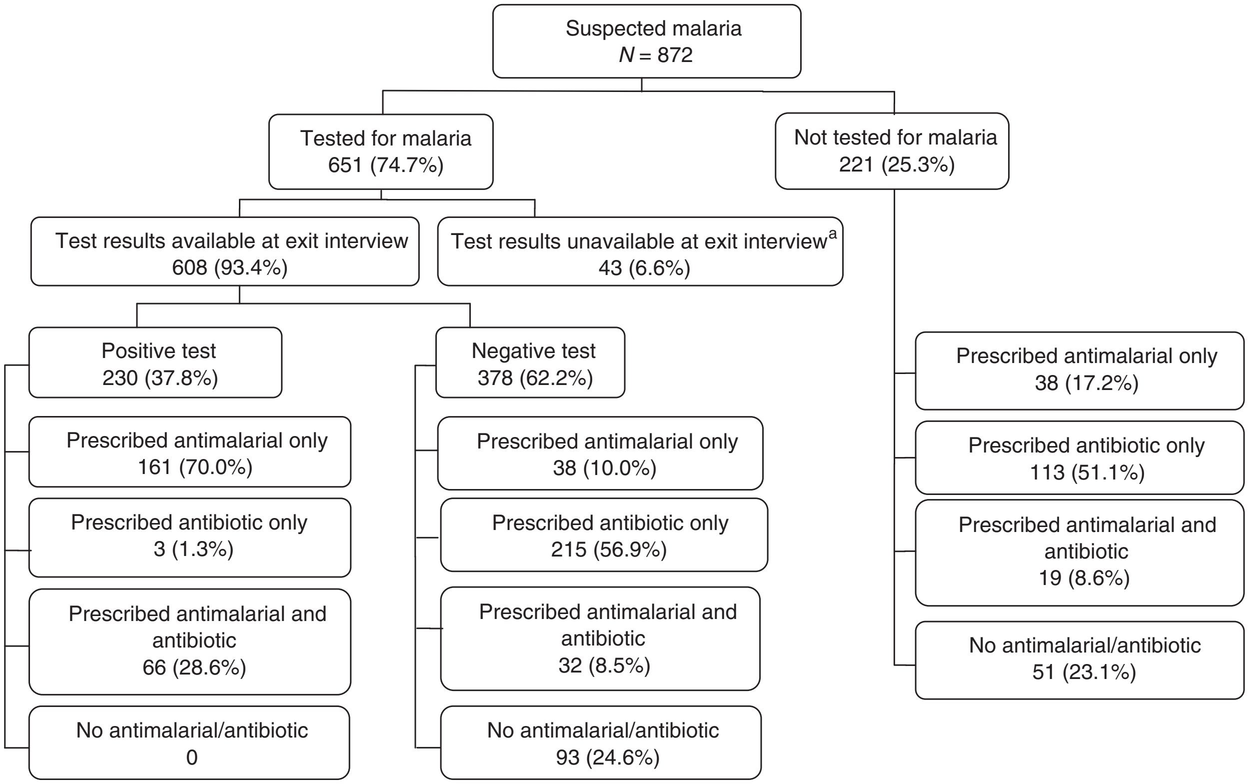

Figure 1 Antibiotic and antimalarial prescribing among patients with suspected malaria. [a]Health workers requested a malaria test but surveyors could not obtain the result for various reasons. Excluded from analysis.

More than 70% of acute non-bloody diarrhoea episodes are caused by viral organisms, especially rotavirus and norovirus [26, 27]. As such, use of antibiotics, such as metronidazole, cotrimoxazole and amoxicillin as seen in the current study, confers limited benefits but serves to select for resistant bacterial pathogens. Studies in similar settings have reported comparable health worker practices for patients with acute non-bloody diarrhoea [28, 29].

Among important independent determinants of prescribing an antibiotic for febrile patients were a negative malaria test and a diagnosis of URTI in bivariate regression. These are related in that URTI would present with fever but is likely to test negative for malaria unless there is co-infection. Health workers in this study seemed to have held this view and ascribed a significant proportion of fevers to URTI. However, the majority of the patients receiving this diagnosis were prescribed at least one antibiotic. Except for a few patients who had tonsillitis, pharyngitis or otitis media (illnesses which might require antibiotics), most of the antibiotic prescriptions in this study were unnecessary [24]. URTIs, which are often due to viral infections, are known to be a strong predictor of antibiotic prescribing in primary healthcare settings [30]. The greatest burden of inappropriate or overuse of antibiotics in this study occurs in patients with respiratory symptoms or URTI as they represented the majority of patients. Interventions targeted at improving the management of this group of patients therefore would potentially result in a great reduction in antibiotic prescriptions.

Patients attending RHCs and HPs were 2–3 times less likely to be prescribed an antibiotic. Similarly, health workers other than doctors and clinical officers were less likely to prescribe an antibiotic. After adjusting for the type of health worker, patients attending at lower level PHCs were less likely to receive antibiotics. Studies have shown that lower ranking healthcare providers demonstrate better adherence to guidelines compared to medical officers. Medical officers feel they have latitude to decide what to prescribe and not adhere to guidelines or policies [31]. Additionally, patient profile at hospital level may have been different from those at lower levels; hospitals serve as referral centres and are likely to deal with severely ill patients or those that have already been

Table 5 Determinant of antibiotic prescribing among patients with suspected malaria: crude and adjusted ORs

Explanatory variable	Crude OR (95% CI)	*P*-value	Adjusted OR*(95% CI)	*P*-value
Level of health care				
Hospital	1		1	
Urban health centre	1.07 (0.68–1.70)	0.762	0.76 (0.42–1.36)	0.356
Rural health centre	0.39 (0.25–0.61)	<0.001	0.20 (0.10–0.45)	<0.001
Health post	0.59 (0.36–0.96)	0.032	0.35 (0.17–0.74)	0.005
Health worker cadre				
Medical officer (doctor)	1		1	
Clinical officer	0.74 (0.24–2.29)	0.605	1.45 (0.37–5.69)	0.595
Nurse	0.24 (0.18–0.74)	0.012	0.92 (0.23–3.72)	0.911
Environmental health tech	0.39 (0.11–1.30)	0.127	1.94 (0.39–9.52)	0.415
Classified daily employee	0.47 (0.15–1.44)	0.190	3.59 (0.86–15.53)	0.077
Duration of symptoms				
≤48 h	1			
>48 h	1.11 (0.75–1.64)	0.592	–	–
Patient age				
<5 years	1			
≥5 years	0.7 (0.54–1.17)	0.249	–	–
Symptoms (No/Yes)†				
Cough/difficult breathing	3.68 (2.35–5.76)	0.001	3.59 (2.08–6.20)	<0.001
Vomiting	0.54 (0.36–0.80)	0.002	1.07 (0.66–1.73)	0.783
ENT problems	2.43 (1.5–3.91)	0.001	1.58 (0.91–2.74)	0.102
Diarrhoea	1.10 (0.71–1.70)	0.666	–	–
Other	0.87 (0.48–1.56)	0.640	–	–
Health workers' diagnosis† (No/Yes)				
Malaria	0.24 (0.16–0.36)	0.001	0.38 (0.21–0.67)	0.001
URTI	3.39 (2.21–5.21)	0.001	1.99 (1.15–3.41)	0.013
ENT	5.86 (1.38–24.8)	0.016	5.27 (0.87–32.1)	0.071
Diarrhoea	1.78 (0.91–3.52)	0.093	1.66 (0.59–4.63)	0.330
Dermatological diseases	3.52 (1.27–9.76)	0.016	5.17 (1.57–17.0)	0.007
Other	0.52 (0.28–0.99)	0.046	0.64 (0.29–1.41)	0.272
Malaria test				
Positive	1		1	
Negative	4.08 (2.49–6.69)	0.001	1.14 (0.59–2.21)	0.693
Not tested	2.31 (1.35–3.96)	0.002	1.04 (0.53–2.06)	0.894

†Reference group was patients without the named symptom or health workers' diagnosis.

treated with antimalarials. This might influence the decision to prescribe antibiotics to patients with fever. However, the patients from hospitals in this study were recruited from outpatient departments and were likely to have a similar profile as patients from lower PHCs. Factors not measured in this study but shown to influence antibiotic prescribing could also explain the high rates of antibiotic prescribing seen in this study. These include prescribers' perception of the patients' desire for an antibiotic [32], large volumes of patients to be assessed [33, 34] patients' or parents' expectations and demands for an antibiotic [35].

Although patient age did not seem to influence antibiotic prescribing, 10% more under-fives compared to older patients who tested negative for malaria or were not tested were prescribed an antibiotic. Studies in comparable settings have shown similar practices [3, 36]. Health workers may have had a higher index of suspicion of bacterial infection in younger patients for whom they were unwilling to neglect to treat.

The major limitation was that the study did not confirm the health workers' diagnosis either by re-examination of the patients or performing tests to ascertain the aetiology of the fever. Therefore, the appropriateness of the decision to prescribe antibiotics could not be assessed. Furthermore, we did not establish the availability of drugs such as paracetamol and oral rehydration solution, which, if unavailable, could potentially induce a health worker to prescribe an antibiotic for fever and diarrhoea. Observations of doctor–patient interactions could potentially result in prescribers changing their behaviour relative to what they would normally do. However, at least one study has demonstrated that health workers do not change their practices when being observed [37]. Another limitation was the lack of a diagnostic capacity to distinguish viral from bacterial infections and thus a reliance on clinical diagnoses for all infections except malaria. The strength of this study includes nationwide representation, and thus, the results could be generalised and serve as baseline once interventions to reduce antibiotics usage are implemented.

Conclusions

Testing positive for malaria or receiving a diagnosis of malaria reduced antibiotic prescribing while testing negative, not being tested or receiving a diagnosis of URTI resulted in higher tendency to prescribe antibiotics. The high tendency of antibiotic prescribing negates the potential benefits accrued from reduced antimalarial usage and contributes to the emergence of antimicrobial resistance which results in increased direct and indirect cost of health services [38]. To enhance appropriate use of drugs, there is immediate need to define the epidemiology of causes of non-malaria febrile illnesses among outpatients and developing RDTs for bacterial infections could potentially reduce unnecessary antibiotic prescribing.

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