Predictors of antibiotics prescription for febrile patients: A health facility-based survey in the Greater Accra region of Ghana

Michael Mireku Opoku
University of Ghana School of Public Health
Harriet Affran Bonful (harriet.bonful@gcpharm.edu.gh)
Ghana College of Pharmacists https://orcid.org/0000-0003-0069-3241
Kwadwo Ansah Koram
University of Ghana Noguchi Memorial Institute for Medical Research

Research article

Keywords: Predictors, Antibiotic Prescription, febrile, facility-based, Ghana

Posted Date: July 1st, 2019

DOI: https://doi.org/10.21203/rs.2.10739/v1

Abstract

Introduction Frequent or/and misguided prescription of antibiotics are important facilitators of the emergence and spread of antibiotic resistance. In the absence of the implementation of effective interventions to control antibiotic use, its consumption may quadruple. Antibiotic stewardship interventions must be appropriately targeted to enhance the proper use of antibiotics. The objective of this study was to determine the predictors of prescribing antibiotics to febrile patients who seek care in health facilities within the Greater Accra region of Ghana. Methods Secondary data obtained from a review of medical records of 2,519 febrile patients at the outpatient department of 6 health facilities in 3 municipalities during the baseline survey of a quasi-experiment in 2016, were used. In addition, sociodemographic data on the prescribers who saw the patients were obtained. The primary outcome was prescription of any antibiotic. Predictor variables included patients' demographics, symptoms, laboratory investigations, diagnoses and prescribed medicines. Binary and multivariable logistic regression analyses were used to determine the predictors of antibiotics prescription. Clustering was adjusted for in all the analyses. Results The prevalence of antibiotics prescription was 70.1% (95% CI: 67.7-72.4). Prescribers with 6 to 9 years and 10 or more years of practice experience were 3 (95% CI: 1.99, 4.44) and 1.6 (95% CI: 1.12, 2.27) times more likely to prescribe antibiotics, respectively ($p < 0.001$). IMCI training was associated with a 2.3 (95% CI: 1.54, 3.53, $p < 0.001$) times higher odds of antibiotic prescribing. Patients aged 5 years or more were 60% less likely to be prescribed antibiotics compared with those under 5 years (AOR=0.40, 95% CI: 0.32, 0.51; $p<0.001$). Patients referred for laboratory investigations were 29% less likely to be prescribed with antibiotics than those not referred. Presenting to the outpatient clinic with cough was associated with a 3.5 (95% CI: 2.54, 4.92) times higher odds of antibiotics prescribing. Conclusion Prescription of antibiotics to febrile patients was high. Promoting laboratory testing can potentially reduce irrational antibiotics prescribing. Prescribing antibiotics for children under five and the prescribing practices of experienced prescribers should be targeted with interventions.

Introduction

Antibiotic resistance is a major global health challenge. Frequent or misguided consumption of antibiotics are critically important facilitators of the emergence and spread of antibiotic resistance [1, 2]. Higher consumption is not only associated with antibiotic resistance at the individual level but also at the community, national and regional levels, with implications for all patients [2]. A study of the global consumption pattern of antibiotics found that antibiotic consumption increased by 65% between 2000 and 2015 [3]. This study further estimates that antibiotic consumption will quadruple by 2030, if no new policy interventions are implemented.

Developing countries contribute disproportionately more to the increasing trend of antibiotic consumption than developed countries [3, 4, 5]. Owing to the poor availability of data, antibiotic use in these countries is not optimally understood [6]. In African communities, high and inappropriate use of antibiotics have been shown to be widespread [6, 7, 8]. The prevalence of antibiotics prescription in Africa has been

estimated to be 50% [4]. A comparable point prevalence (51.4%) was determined by an antibiotic-use-survey at a teaching hospital in Ghana [10]. These are high considering the standard recommended by the World Health Organization (WHO) for the region, which is 20-26.8% [11]. Inappropriate prescription of antibiotics has also been established among prescribers in other parts of Ghana [11, 12, 13]. The phenomenon is driven by patients demands, poor quality laboratory services, pressure from pharmaceuticals promotional activities, and health worker factors such as non-adherence and lack of access to institutional guidelines and lack of knowledge [14, 15].

Interventions that have been introduced to reduce irrational prescription of antibiotics in Ghana include the Standard Treatment Guidelines (STG) and Essential Medicines List (EML), provision of training and supervision for health care providers and mass education of the public [17]. The success of these interventions will result in delays in the progression of bacterial resistance, and a reduction in hospital visits, medical costs and potential side effects [17, 18, 19]. Monitoring the prescription of antibiotics is necessary for the successful implementation of these interventions [16, 20]. As useful as measuring antibiotics prescription is, linking it to patient, prescriber and clinical factors is crucial to identifying the determinants of the undesirable prevailing patterns [21]. However, fewer studies are focused on determinants of antibiotic use in sub-Saharan Africa. This linking will help in appropriately targeting local antibiotic-stewardship interventions to enhance the proper use of antibiotics. Additionally, this knowledge will be key to informing the policy changes necessary for reversing the increasing trend of antibiotic consumption at all levels.

To these ends, the objective of this study was to determine the predictors of prescribing antibiotics for febrile patients who seek care in health facilities within the Greater Accra region of Ghana using secondary data.

Methods

Study area

Data for this study were obtained from the baseline survey of a quasi-experimental study, which sought to develop and assess the effectiveness of a one-way text messaging intervention on health providers' adherence to malaria case management guidelines. The study was conducted in Ga South, La Dade-Kotopon and La-Nkwantanang Madina municipalities in the Greater Accra region from October to December 2015. The cross-sectional survey collected data in 6 health facilities, 2 in each of the 3 municipalities. As at the time of the study, Greater Accra was one of 10 administrative regions in Ghana with 16 administrative units (including municipalities).

In Ghana, the lack of a National Antibiotic policy until recently, the lack of a national system for surveillance of the consumption of antibiotics, weak medicines regulatory regime and poor adherence to practice standards have been identified as contributing to high use of antibiotics [22]. A study conducted in the Ghana estimated that 14% of children under 5 reported having had fever within the 2 weeks preceding the survey. The proportion of children who had diarrhoea 2 weeks preceding the survey was

12%. In the Greater Accra region, the prevalence of fever was 10.7%. Care was sought from a health facility for 33.7% of all the children in the region aged 25 to 49 months and 39.0% took antibiotics [23].

Data collection

The secondary data contained the medical records of 2,519 febrile OPD patients, at least six months or older, who did not present with any danger signs at the out-patient department (OPD) of the six health facilities. Available information included their demographic characteristics, symptoms, laboratory results of five investigations (blood film microscopy, malaria rapid diagnostic test, full blood count, urine and stool routine examinations), diagnoses and medicines prescribed.

The dataset also contained information on the 82 prescribers who saw the febrile patients. Prescriber variables included prescriber's age, profession, years of practice and training on integrated management of childhood illnesses (whether or not prescriber had ever been trained).

Data extraction tools were used to collect data from febrile OPD patients records in the primary study. Records of patients who were pregnant, had danger signs or visited the health facility for review were excluded. Further to that, prescribers who saw the patients on the visits selected for inclusion in the study were interviewed using a structured questionnaire. Details on the methodology of the primary study is available elsewhere [24].

Data management and analysis

The data obtained were validated and analysed using Stata Version 14.

Diagnoses included in this study and described as diagnoses of interest were those which had a prevalence of at least 5%.

The outcome variable, prescribing of antibiotics, was derived based on whether or not at least 1 antibiotic was prescribed for the patient. A prescribed medicine was considered an antibiotic if it was so classified by the WHO Anatomical Therapeutic Chemical classification [25]. Categorical variables were checked for accuracy (including errors and outliers) using frequencies and continuous variables were checked using histograms. To adjust for clustering, unique identifiers for each patient folder and for the municipalities were chosen as primary sampling units and stratum identifiers, respectively. Chi square tests were used to examine each categorical variable for differences in antibiotic prescription between the sub-categories. Simple binary logistic regression was used to estimate unadjusted odds ratios for all the independent variables. The variables which were significantly associated with antibiotic prescribing ($p< 0.05$) were used to fit a multivariable logistic regression model. Although sex of patient was not significant in the crude analysis it was included in the multivariable model because it was considered a potential confounder. The predictors in the adjusted model were checked for multicollinearity. Adjusted Wald test was used to determine the significance of multilevel categorical variables in the model. Statistical significance was set at $p< 0.05$. Cluster-Robust standard errors were estimated for all models.

Results

A total of 2,519 valid records of patients, who had received care at the selected health facilities in Accra, were used for the study. Table 1 presents a summary of the characteristics that are descriptive of the patterns of prescribing antibiotics by prescribers at the health facilities, during the period of the records were taken. The frequency of prescribing antibiotic was 70.1% (95% CI: 67.7% - 72.4%). Half of the patients (51.6%), whose records were reviewed, were attended to by Physician Assistants, while 42.3% were attended to by Medical Doctors. Of the 1766 prescriptions that had antibiotics prescribed, approximately half (49.2%) were written by physician assistants, 43.9% by medical doctors and 5.7% by nurse prescribers. Regarding the number of years they had been practising, 31.4% of the patients were seen by prescribers who had been practising for less than 3 years, a little over a third (37.7%) had been practising for 3 to 5 years, and 30.9% had been practising for 6 years or more. The majority of the prescriptions with antibiotics were written by prescribers who had been practising for 3 to 5 years (37.4%), while 79.4% of the prescriptions with antibiotics were written by prescribers who had never been trained on integrated management of childhood illnesses (IMCI). 87.9% of the prescriptions without antibiotics were written by those with no training on IMCI ($p<0.001$).

Table 1: Cross-tabulation of antibiotics prescription and the characteristics that are descriptive of prescribing patterns among prescribers

The chi-square output showing the association of antibiotic prescription with study location, and patients' age and symptoms are presented in Table 2a. There was a statistically significant difference in antibiotics prescription based on municipality, age and symptoms, including cough, dizziness, difficulty in swallowing, watery stool, general body pain and nasal congestion ($p < 0.05$). Other variables including abdominal pains, bitter taste in mouth, convulsions, loss of appetite, dyspnoea, fatigue, headache, lethargy, joint pains, nausea, rigor, dysuria, sore throat and vomiting were not significantly associated with antibiotic prescribing ($p > 0.05$). Table 2b shows a cross-tabulation of antibiotics prescription and clinical factors. The chi-square test showed that laboratory investigations, pneumonia, acute respiratory tract infection (ARTI), typhoid fever, urinary tract infection and skin diseases were associated with antibiotic prescribing ($p < 0.05$). Diagnoses which were not significantly associated with antibiotic prescribing from the chi-square analyses were malaria, diarrhoeal diseases, anaemia, ear infection, eye infection, enteritis, trauma and tonsillitis. The laboratory investigations included blood film for malaria parasites or malaria rapid diagnostic test (90.8%), full blood count or haemoglobin (82%), urine routine examination (13.2%) and stool routine examination (0.8%). More patients were treated without laboratory investigations (56%; 95% CI: 52.9% - 59.0%) than otherwise (44%; 95% CI: 41.0% - 47.1%). Results of the multivariable logistic regression analysis (Table 3a) identified the following as significant non-clinical predictors of antibiotic prescription: prescriber's profession, prescriber's years of practice, prescriber's training in IMCI, location of facility (municipality) and age of patient. Compared to prescribers who had practised for less than 3 years, those who had 6 to 9 years of practice experience and those who had practiced for 10 years or more had 3 times (AOR=2.97; 95% CI: 1.99-4.44) and 1.6 times (AOR=1.60; 95% CI: 1.12-2.27) higher odds of prescribing antibiotics, respectively. Prescribers who had ever been trained on IMCI had 2.3 times greater odds of prescribing antibiotics than those who had never been trained (AOR= 2.33; 95% CI: 1.54-

3.53). After adjusting for all the other covariates, children aged 5 years or above were 60% (AOR=0.40; 95% CI: 0.32-0.51) less likely to be prescribed antibiotics than those under 5. Table 3a: Binary and multivariable logistic regression of factors associated with antibiotic prescribing The significant clinical predictors as identified from the multivariable logistic regression (Table 3b) include laboratory investigation, symptoms including cough, dizziness, difficulty in swallowing, watery stool, and diagnoses including urinary tract infection, typhoid fever, and skin disease. Patients who presented with cough were 3.54 times more likely to be prescribed antibiotics than those who did not cough (AOR= 3.54; 95% CI: 2.54-4.92). Patients for whom laboratory investigations were requested were 29% (AOR= 0.71; 95% CI: 0.57-0.89) less likely to be prescribed antibiotics than those for whom laboratory investigations were not requested. Sex of patient, symptoms including general body pains, nasal congestion and diagnoses including ARTI and pneumonia were not significant predictors of antibiotic prescribing ($p<0.05$). Table 3b: Binary and multivariable logistic regression of factors associated with antibiotic prescribing The most prevalent diagnosis among the patients was ARTI (Figure1). The diagnoses not found to be significantly associated with antibiotic prescription were malaria, diarrhoeal diseases, anaemia, ear infection, eye infection, enteritis, trauma and tonsillitis (Table 3b). Figure 1: Bar chart showing the prevalence of diagnoses of interest. ARTI, Acute Respiratory Tract Infection; UTI, Urinary Tract Infection

Discussion

We aimed to determine the predictors of antibiotic prescription for febrile patients. The predictive factors were prescriber's profession and years of practice, age of patient, presenting symptoms including cough, watery stool, dizziness, difficulty in swallowing, laboratory tests, diagnoses including typhoid fever, urinary tract infection and skin disease. A high prescription of antibiotics for febrile patients was observed. The prevalence of prescribing antibiotics, which was 70.1% (95% CI: 67.7-72.4) was higher than was found among febrile patients in Zambia [26]. An important difference observed between the 2 studies which could explain the difference in prevalence is that a higher proportion of the febrile patients (74.6%) underwent diagnostic testing in the Zambian study than in the present study (44%). Studies in Uganda [27], Cameroon [28] and Switzerland [29] have shown that laboratory testing reduces the odds of antibiotic prescribing. Indeed, our findings showed that when laboratory investigations were requested prior to prescribing, patients were less likely to be prescribed with antibiotics. This was observed despite the laboratory tests requested not including culture test or any non-malaria point-of-care testing for infections. Advocating for the increased use of point-of-care tests for infections could improve the control of antibiotic prescribing. Despite the scarcity of resources, it must be considered that the ultimate cost of overprescribing antibiotics outweighs the cost of the optimal use of laboratory services. In addition to being a high rate of prescribing antibiotics for febrile patients, owing to low malaria testing rates, the prevalence of prescribing antibiotics in our study is higher than has been reported by other studies in Ghana, and other developing countries [9, 22, 28]. A critical difference between our study and these other studies is that only febrile patients were included in the former. This suggests that the prevalence of antibiotic prescribing among the sub-population of febrile patients is higher than among the general population of patients. The higher use of antibiotics among febrile patients is unjustified and must be

addressed as these infections are mostly caused by viruses [30, 31]. The observation that neither ARTI nor pneumonia is significantly associated with antibiotic prescribing seems progressive (Table 3b). In other studies, respiratory tract infection has been shown to be predictive of antibiotic prescribing [24, 31, 32]. The finding in our study is suggestive of prescribers appreciating that these diseases are more likely to be caused by viruses rather than bacteria [33, 34] or that using antibiotics to treat these diseases provides no clear benefit [35, 36]. This understanding may be translated to the treatment of febrile illnesses at large, since these principles apply generally but were not reflected in the findings. Cough is often associated with respiratory infection of one kind or the other. It seems paradoxical that it was found to be significantly associated with antibiotic prescribing whilst ARTI was not. Accordingly, a patient who presents with cough is likely to be prescribed an antibiotic, irrespective of whether ARTI or pneumonia is diagnosed. This raises the question of whether prescribers treat symptoms rather than the diseases they diagnose. Another related observation is that patients who present with watery stool are likely to be treated with antibiotics though same cannot be said when diarrhoea is diagnosed. Further studies are required to investigate this practice. That prescribers with more than 5 years of practice experience are more likely to prescribe antibiotics than those with less experience is at variance with a study conducted in Italy [40] but similar to another study in Canada [41]. Our finding may be because of the fear medical doctors develop after a while of practice about their patients returning to them with similar symptoms following an initial visit [21, 39, 40]. Less experienced prescribers may uphold the seeming theoretical ideals of rational use of medicines, less encumbered by the practical challenges of inadequately treated diseases and the associated patient dissatisfaction. Over time, prescribers may prefer treating as many likely causes of a set of symptoms in the face of overwhelming workload, inadequate human resources and poorly resourced laboratories [41, 42]. It must be pointed out that at the time of the study, review of the STG was overdue by a year [46]. At instances of diagnosis uncertainty, more experienced prescribers may depend on their experience which may be more focused on the individual needs and expectations of their patients rather than the public health interest [43]. The prescribing practices of more experienced prescribers must be targeted by antibiotic stewardship interventions. Though inadequate training of prescribers has been shown to worsen antibiotic prescribing [42] we found that those not trained on the IMCI have lower odds of prescribing antibiotics. This appears to suggest that IMCI training may be counterproductive for controlling high antibiotic prescribing. It is noteworthy that IMCI is relevant in the management of childhood illnesses but our study included adults. That notwithstanding, it must be pointed out that one approach recommended by IMCI is the active involvement of patients or caregivers in deciding on treatments [47]. This approach, however, has been suggested as influencing high antibiotic prescribing [48]. During IMCI trainings, it may be necessary to point this out and address the tendency for higher use of antibiotics. Thus, integrating IMCI training with responsible use of antibiotics may be worthwhile. Regarding age, we found that patients aged 5 years or more had lower odds of being prescribed antibiotics. A similar observation was made in Cameroon [28]. Children under five, as a result of having less developed immune systems are more susceptible to infections than older people. As a result, prescribers are more likely to manage illnesses of children in this age group with antibiotics than in older age groups. Also, the higher rate of mortality among children under 5 may condition prescribers to prefer erring cautiously by prescribing antibiotics given that treatments are usually done empirically. This

is occasioned by the resource constraints of the health facilities and relatively expensive diagnostic tests. This trend is worrying considering that high antibiotic consumption has been linked with the development of metabolic diseases in later life [49]. To the best of our knowledge this is the largest study on antibiotic prescribing in Ghana. The relatively large sample size allowed for the inclusion of several predictors in the assessment. It is our expectation that even small but relevant differences were detected if they existed. One limitation of this study is that the period of the data collection was short (3 months). As such, seasonal variations in antibiotic prescribing was not accounted for. Another limitation of this study is the assumption that all documented actions were carried out. Similarly, all undocumented actions were assumed not to have been taken. This may have introduced misclassification bias but was considered more acceptable than direct observation which may have caused prescribers to vary their usual prescribing habit. Also, behavioural factors were not assessed.

Conclusion

The predictors of antibiotic prescription for febrile patients were prescriber's profession and years of practice; age of patient; some presenting symptoms which included cough, watery stool, dizziness, difficulty in swallowing, laboratory tests; some diagnoses including typhoid fever, urinary tract infection and skin disease. In contrast, ARTI and pneumonia were not significantly associated with antibiotic prescription.

The rate of antibiotics prescription for febrile patients is high. To reduce this, advocacy for the increased use of laboratory testing prior to prescribing antibiotics is key. Also, more experienced prescribers and treatment for children under five should be targeted with interventions aimed at reducing antibiotic prescribing. IMCI training appears to be counterproductive for controlling antibiotic prescribing. There is the need to emphasize Responsible use of antibiotics during IMCI training.

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Abbreviations

ARTI – Acute Respiratory Tract Infection

EML – Essential Medicines List

IMCI – Integrated Management of Childhood Illnesses

OPD – Outpatient department

STG – Standard Treatment Guidelines

WHO – World Health Organization

Declarations

Ethics Approval and Consent to Participate

Ethical approval for the primary study was given by the Ethics Review Committee of the Ghana Health Service. Permission was further sought from the Greater Accra Regional Health Administration, the Municipal Health directorates of the study sites and the management of Health facilities and prescribers. Informed consent was obtained from all the prescribers who saw the patients whose records were used.

Consent for publication

All medical superintendents of the six health facilities and the prescribers were adequately informed about the study and they consented to the publication of the research study findings. Adequate information about the original study was also placed at vantage points in all health facilities during the data collection period.

Availability of Data and Material

The dataset is not publicly available. However, it can be accessed after a reasonable request has been sent to the corresponding author.

Competing Interests

The authors declare that they have no competing interests.

Funding

Funding for the original study was obtained from the German Academic Exchange Service Project as part of funding for the PhD project of the corresponding author.

Authors' Contributions

HAB and MMO conceptualised the study under the supervision of KAK. HAB assisted MMO in the analysis phase. Interpretation was done by MMO, HAB and KAK. The initial manuscript was written by MMO. HAB made inputs. All the authors reviewed and approved the final manuscript for publication.

Acknowledgements

We would like to acknowledge the owner of the data-set (Dr Harriet Affran Bonful) for granting access to the dataset. We are grateful to Dr. Adolf Kofi Awua for reviewing and proof reading the manuscript.

Figures

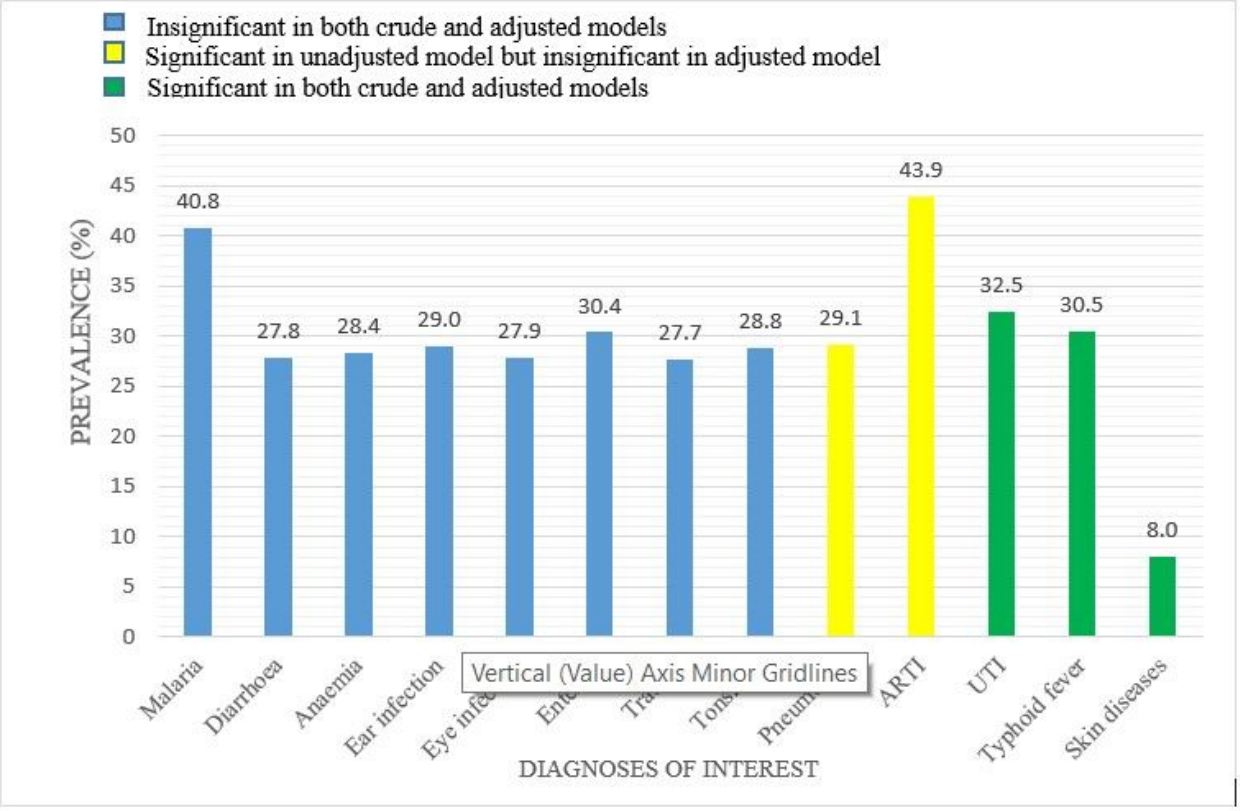

Figure 1: Bar chart showing the prevalence of diagnoses of interest. ARTI, Acute Respiratory Tract Infection; UTI, Urinary Tract Infection

Figure 1

Supplementary Files

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- supplement1.docx