# **A retrospective clinical evaluation of the quality of antibiotic use in treating ear, nose and throat infections in ambulatory care setting of a teaching hospital in Ghana: Findings and Implications**

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# **Abstract**

**Background:** Ear, nose and throat (ENT) infections are often associated with high levels of morbidity and mortality. Antibiotic overuse and misuse for most ENT infections have been reported, caused by a lack of expertise or uncertainties to distinguish between infection types. This study sought to determine the level of appropriateness of antibiotics for ENT infections and its associated factors in ambulatory care in a teaching hospital in Ghana to guide future policies given rising resistance rates**. Methods:** A retrospective cross-sectional study design was undertaken to audit the quality of antibiotic use in Ho Teaching Hospital, a leading teaching hospital in Ghana, between January 2022 to December 2022. A checklist was designed to extract patient socio-demographic and clinical information from electronic medical records. The main study outcome was the appropriate choice of antibiotics principally in accordance to the Ghana standard treatment guidelines. Descriptive, bivariate and multivariate analysis were performed on the data collected using STATA version 14. **Results:** The electronic medical records of a total of 3,279 patients were extracted. The majority (57.88%, n=1898) of patients were females, median (inter-quartile range) age was 25 (7-42) years. Ear infections were the commonest (66.24%, n=2172) diagnosed ENT infection, followed by throat infections (15.74%, n=516). The most prescribed antibiotic was oral amoxicillin-clavulanic acid together with a topical neomycin-steroid combination (28.00%, n=918), followed by amoxicillin-clavulanic acid alone (18.69%, n=613). The appropriate choice of antibiotic for all ENT infections in accordance with treatment guidelines was 60.11%. Inappropriate use of antibiotics was high when more than one antibiotic and World Health Organisation (WHO) ‘Watch’ group antibiotics were prescribed and ear infections compared to the nose and throat infections were treated. **Conclusion:** The appropriateness of antibiotic use for ENT infections in this hospital was suboptimal. It was predicted by the type of infection, the number of antibiotics prescribed and the WHO AWaRe group. Antimicrobial stewardship interventions such as clinical audit with feedback and clinician education must be enhanced to among other things identify antibiotic use gaps to help reduce unnecessary use of antibiotics for ENT infections.

**Keywords**: Antimicrobial stewardship intervention, Ear, nose and throat infections, ambulatory care

## **1.0 Background**

Drug utilization research is useful in determining the quality and pattern of drug use for pertinent clinical conditions with the intention of identifying any problems and issues associated with medicine use in healthcare systems. This as a result, seeks to provide guidance on potential approaches and policies to enhance appropriate drug use (1, 2). Understanding antibiotic prescribing patterns is critical for antibiotic stewardship (AMS) especially in the ambulatory care setting where antibiotics are mostly prescribed (3). This is especially the case among low- and middle-income countries (LMICs) where up to 95% of total antibiotic use in humans is in ambulatory care (4). However, up to 30%-50% of these antibiotic prescriptions, particularly for upper respiratory tract infections, are unnecessary; fuelling antimicrobial resistance (AMR) (5, 6). AMR results in treatment failure, increased adverse effects and cost to both patients and the healthcare system (7-9). Sub-Saharan African (SSA) countries, including Ghana, appear to have the greatest AMR burden, which needs to be urgently addressed given rising concerns (9). As a result, AMR is increasingly seen as the next pandemic unless active measures are taken to improve appropriate utilisation (10). International initiatives include the development of the Global Action Plan (GAP) by the World Health Organization (WHO) to reduce AMR, translated into National Action Plans (NAPs) which has currently been developed in Ghana, as well as classifying antibiotics into ‘Access’, ‘Watch’ and ‘Reserve’ antibiotics (11-13). The utilisation of ‘Watch’ and ‘Reserve’ antibiotics for common ambulatory infections should be restricted due to their greater resistance potential (14, 15). More recently, this has developed into the WHO AWaRe (Access, Watch and Restrict) antibiotic book giving prescribing guidance, including non-antibiotic choices, for a range of infections seen in ambulatory care (16, 17). The target is to prescribe at least 60% of antibiotics from the’ Access’ list with concerns that the use of ‘Watch’ antibiotics for ambulatory is growing among LMICs, enhancing AMR (14, 18).

Ear, nose and throat (ENT) infections affect both children and adults, often associated with high levels of morbidity including hearing loss and mortality (19). Overall, ENT infections are responsible for the majority of childhood diseases and therefore the major cause of antibiotic prescriptions, even though they are predominantly caused by viruses making their use unnecessary (20). Hearing loss is globally known to be caused by otitis media, an ear infection, which affects more than 42 million people below the age of three (21). Chronic middle ear infections, chronic sinus disorders, chronic coughs, and recurrent pharyngo-tonsillitis are currently some of the ENT diseases resistant to antibiotics (22, 23). Antibiotic overuse and misuse for most ENT infections have been found to be caused by a lack of expertise or willingness to distinguish a viral infection from a bacterial infection (24). Consequently, their management must be improved, including when to prescribe these antibiotics and where needed, these should be avoided, to reduce AMR.

In Ghana, antibiotic misuse has been reported especially for respiratory tract infections (25-27). The compilation and update of the Ghana Standard Treatment Guidelines (STG) alongside the Essential Medicine List are some of the policy strategies of the Ministry of Health to ensure appropriate use of medicines including antibiotics in line with the goals of the Ghana NAP (11, 28). The seventh edition of the Ghanaian STG (2017) covers several ENT infections, outlining parameters for their empirical management with antibiotics including the choice of antibiotic, dose, and frequency. (28). Some notable ENT conditions that may require antibiotic use as part of their management according to the STG include stridor with superimposed bacterial infection, acute epiglottitis, retropharyngeal abscess, pharyngitis, tonsillitis, acute sinusitis and otitis media (acute and chronic). These ENT conditions have also been reported in studies in Ghana as some of the most prevalent ENT disorders (29, 30). Regular auditing and reviewing of antibiotic prescriptions to determine guideline compliance have been identified as an effective AMS approach towards ensuring their rational use (31). With the recent global efforts against the rise of AMR, it is very important that antibiotic use, particularly among ambulatory patients in LMICs, are evaluated to guide future policies and practices (26, 32). Whilst there are published studies that have audited antibiotic use especially for respiratory infections in Ghana, there is currently a scarcity of data on type, pattern and level of rational use of antibiotic use for ENT disorders in ambulatory care settings (25, 33-35). This study sought to address this information gap by determining the level of appropriate use of antibiotics for ENT infections and its associated factors in the ambulatory care settings in Ghana. Previous studies conducted in this hospital reported inappropriate use of antibiotics for general outpatient patients and surgical patients (36, 43). These studies have given baseline data to instigate AMS programs to address the quality gaps in prescribing antibiotics in this leading teaching hospital in Ghana, and this is currently ongoing. There has however never been an audit to specifically assess the appropriate use of antibiotics for ENT conditions in this hospital and beyond to guide policy and practice development.

The findings from this study can be used to design quality improvement AMS programs to improve the future use of antibiotics in ambulatory care in Ghana as part of many funded AMS programs that are currently being implemented in Ghana and other LMICs as part of efforts to implement NAPs.

# **Method**

## **Study design**

A retrospective cross-sectional study was conducted by extracting the medical records of ENT patients of Ho Teaching Hospital (HTH) from January 2022 to December 2022 using the hospital’s electronic database.

## **Study site**

The study was conducted at the ENT clinic of HTH, a 306-bed capacity tertiary health facility located in the Volta Regional capital, Ho, with a staff strength of 1,200 and 14 wards (36). The hospital was chosen for this initial research as it provides several primary clinical care services including surgical, internal medicine, obstetrics & gynecological, child health and public health, pharmaceutical and diagnostic services for patients in the Volta Region. The facility also provides several specialized services as eye, ENT, mental and diabetic care to patients in the municipality and beyond. Consequently, if there are concerns with the prescribing of antibiotics in this setting these will be exacerbated in lower care settings including primary care clinics in this Region and others in Ghana.

## **Study population**

HTH provides services to over 20,000 outpatients and inpatients every month. It is the only tertiary hospital in the Volta Region, one of the 16 administrative regions in Ghana, with a 2021 population of 1,659,040 (37).The ENT department serves approximately 600 outpatient cases every month. Records of ambulatory patients who have visited the ENT clinic within the study period and were prescribed antibiotics were collected and analyzed.

## **Inclusion and exclusion criteria**

Patients of all ages attending the ENT outpatient clinic to whom antibiotics were prescribed during the study period were included.Patients with more than one infection where we could not tell which antibiotic (s) was/ were prescribed for each specific condition were excluded. Patients having conditions other that ENT problems, patients who were admitted and patients who were not prescribed antibiotics for their conditions were excluded. Patients with incomplete medical information relevant to the study were also excluded. However medical records of patients diagnosed with ENT condition with missing data but have antibiotics prescribed for the condition were not excluded.

## **Sample size and sampling technique**

No sampling was done as all patients who attended the ENT ambulatory clinic within the study period were included in this study. An expected annual sample of participants using the Raosoft Inc. online calculator, assuming a 50% appropriateness of antibiotic prescription, an average monthly outpatient attendance of 600, at 90% power and 95% confidence interval, and adding 10% to account for or incomplete data was 2820 patients (38).

## **Data collection**

Data was collected from the hospital's Lightwave Health Information Management System (LHIMS) (an electronic medical record system). The data collection checklist was an adaptation of tools used by similar studies in the hospital setting of other LMICs (2, 39). This approach had been used previously by some of the co-authors (34, 40). The checklist included socio-demographic information including patients’ age, gender and national health insurance (NHIS) status (to assess the influence of payment status on prescribers’ behavior), clinical information (including the principal ENT diagnosis), names of antibiotics prescribed, whether culture and sensitivity test was requested (to assess the proportion of targeted treatments among the ENT infections diagnosed) , number of antibiotics prescribed per patient encounter and the WHO AWaRe category of only systemic antibiotics (comprising of Access, Watch and Restrict antibiotics) prescribed (13). Appropriateness was based on the prescription of the right choice, dose and frequency of antibiotic for the diagnosed ENT condition as was contained in the Seventh Edition of the Ghana Standard Treatment Guideline (STG); whereas overall appropriateness was based the prescription of the right choice, dose, and frequency of the prescribed antibiotics (28). When the condition was not discussed in the Ghanaian STG, international guidelines such as WHO AWaRe antibiotic book, the UK National Institute for Health and Care Excellence guidelines (41) and the American Academy of Otolaryngology-Head and Neck Surgery guideline were used (16, 17, 42).

## **Data handling**

The collated data was coded to safeguard patient identity by removing personal identifiers and password protected to the principal investigator.

## **Data analysis**

The extracted data were entered into a Microsoft Excel sheet before being exported to STATA version 14 (StrataCorp, College Station, TX, USA) for analysis. The appropriateness of prescribed antibiotics based on the prescription of the right choice of antibiotic for the diagnosed ENT conditions in the treatment guideline was the primary study outcome measure. Overall appropriateness was based on guideline compliance based to all three parameters namely choice, dose and frequency of antibiotics prescribed. Age was categorized similar to our previous study (43). Descriptive statistics was used to determine the median age and the proportions of each categorical variable and Chi square test of independence was performed to assess the association between the outcome variable and the various independent variables.A multiple logistic regression analysis was also performed using all statistically significant independent variables from the bivariate analysis (p-value <0.05 at 95% confidence interval) to assess for predictor variables. The crude odd ratio of the outcome variable was adjusted by co-variates which showed statistically significant association with the outcome variable and these included the type of infection, the number of antibiotics, and the WHO AWaRe category of the antibiotics.

**Ethical consideration**

Ethical clearance was obtained from the ethics committees of both the University of Health and Allied Sciences (UHAS-REC A.7 [41]22-23) and the HTH (HTH-REC (32) FC\_2022) prior to the commencement of the study. The collated data were coded to safeguard patient confidentiality by removing personal identifiers and were protected by password accessible to only the principal investigator.

# **Results**

## **Descriptive analysis of socio-demographic and clinical characteristics of patients**

The medical records of a total of 3,279 patients were included in this study. Most of the patients were female (57.88%, n=1898) with a median (inter-quartile range) age of 25 (7-42) years. The majority of the patients (50.63%, n=1660) were between the ages of 0 – 25 years, followed by those in the age category of 26 – 50 years (31.29%, n=1026) with patients above 75 years being the smallest category (2.59%, 85).

The majority of the patients (90.97%, n=2983) were insured. From the medical records, there were no laboratory investigations, particularly culture and sensitivity testing carried out for the patients. Ear infections accounted for a majority (66.24%, n=2172) of the ENT conditions followed by throat infections (15.74%, 516/3279); with mixed ENT infections being the least diagnosed condition (5.55%, 182/3279). Acute/infective otitis externa accounted for a majority (28.06%, n=920) of the principal diagnosis, followed by chronic otitis media (16.35%, n=536) and then acute otitis media (12.44%, n=408) (Figure 1).

A single antibiotic was prescribed for most (49.71%, n=1630) of the diagnosed ENT conditions followed by two antibiotics (42.70%, 1400/3279), and three antibiotics (7.41%, n=243).

Most of the patients (46.78%, n=1534) treated for an ENT condition were prescribed with systemic preparations (oral or intravenous) in combination with topical preparations (nasal drops or ear drops), followed by those prescribed with only topical preparations (28.61%, n=938).

Oral amoxicillin-clavulanic acid in combination with topical preparation of neomycin with a steroid was the most (28.00%, =918) prescribed antibiotic, followed by amoxicillin-clavulanic acid only (18.69%, n=613), and then neomycin plus steroid topical preparations (14.33%, 470/3279) (Figure 2).

The majority of the prescribed antibiotics (57.40%, n=1609) were from the WHO ‘Access’ group, followed by those in the ‘Watch’ group (25.58%, n=717). Appropriateness of antibiotic prescription based on the choice of antibiotics was 60.11% (n=1971) while appropriateness based on dose was 75.72% (2483/3279) and on frequency was 88.23% (n=2893), with overall appropriateness being 37.85% (n=1241) (Table 1). However, as mentioned, there was no culture and sensitivity testing requested (Table 1).

**Table 1:** *Socio-demographic, clinical characteristics of patients and outcome parameters*

|  |  |
| --- | --- |
| **Variable**  | **Total, n (%)** |
| **Age (years) (n= 3279)** |  |
| Mean ± SD | 27.88 ± 22.56 |
| **Age category (years) (n= 3279)** |  |
| 0 – 25 | 1,660 (50.63) |
| 26 – 50 | 1,026 (31.29) |
| 51 – 75 | 508 (15.49) |
| above 75 | 85 (2.59) |
| **Gender (n= 3279)** |  |
| Female | 1,898 (57.88) |
| Male | 1,381 (42.12) |
| **National Health Insurance Status (n= 3279)** |  |
| No | 296 (9.03) |
| Yes | 2,983 (90.97) |
| **Test(s) requested (n= 3279)** |  |
| No | 3,279 (100) |
| Yes | 0 (0) |
| **Type of infection (n= 3279)** |  |
| Ear infection | 2,172 (66.24) |
| Mixed ENT infections | 182 (5.55) |
| Nose infection | 409 (12.47) |
| Throat infection | 516 (15.74) |
| **Number of antibiotics (n= 3279)** |  |
| One | 1,630 (49.71) |
| Two | 1,400 (42.70) |
| Three | 243 (7.41) |
| Four | 5 (0.15) |
| Five | 1 (0.03) |
| **Dosage form (n= 3279)** |  |
| Systemic  | 804 (24.52) |
| Systemic + topical  | 1537 (46.87) |
| Topical | 938 (28.61) |
| **WHO AWaRe category (n= 2803)** |  |
| Access | 1609 (57.40) |
| Access + Watch combination | 477 (17.02) |
| Watch | 717 (25.58) |
| **Appropriateness based on choice (n= 3279)** |  |
| Appropriate | 1,971 (60.11) |
| Inappropriate | 1,308 (39.89) |
| **Appropriateness based on dose (n= 3279)** |  |
| Appropriate | 2,483 (75.72) |
| Inappropriate | 796 (24.28) |
| **Appropriateness based on frequency (n= 3279)** |  |
| Appropriate | 2, 893 (88.23) |
| Inappropriate | 386 (11.77) |
| **Overall Appropriateness (n= 3279)** |  |
| Appropriate | 1,241 (37.85) |
| Inappropriate | 2,038 (62.15) |

**Figure 1.** *Principal diagnosis of ENT conditions (n= 3279)*

NB: Other includes epistaxis, hearing loss, acute nasopharyngitis (common cold), acute/chronic pharyngotonsillitis, acute/chronic pharyngosinusitis, allergic rhinitis, chronic otitis externa, and tinnitus

**Figure 2.** *Type of antibiotics prescribed (n= 3279)*

NB: Others include gentamicin, levofloxacin, metronidazole, cefixime, cefuroxime, chloramphenicol, amoxicillin-clavulanic acid + azithromycin, amoxicillin-clavulanic acid + chloramphenicol, amoxicillin-clavulanic acid + metronidazole, cefuroxime + neomycin + amoxicillin-clavulanic acid, amoxicillin-clavulanic acid + metronidazole + neomycin

## **Association between appropriateness of antibiotic use and patient and clinical characteristics**

Appropriateness of the choice of antibiotic prescription was significantly associated with the type of infection (p <0.001), the number of antibiotics prescribed (p= <0.001) and the WHO AWaRe category (p <0.001) (Table 2).

**Table 2:** *Bivariate analysis between appropriateness of antibiotic use and patient social and clinical characteristics*

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Total, n (%)** | **Appropriateness based on choice** | **P-value** |
|  |  | **Inappropriate, n (%)** | **Appropriate, n (%)** |  |
| **Age category (years) (n=3279)** |  |  |  | 0.061 |
| 0 - 25 | 1660 (50.63) | 637 (38.37) | 1,023 (61.63) |   |
| 26 - 50 | 1026 (31.29) | 411 (40.06) | 615 (59.94) |   |
| 51 - 75 | 508 (15.49) | 217 (42.72) | 291 (57.28) |   |
| > 75 | 85 (2.59) | 43 (50.59) | 42 (49.41) |   |
| **Gender (n=3279)** |  |  |  | 0.191 |
| Female | 1898 (57.88) | 739 (38.94) | 1,159 (61.06) |   |
| Male | 1381 (42.12) | 569 (41.20) | 812 (58.80) |   |
| **National Health Insurance Status (n=3279)** |  |  |  | 0.267 |
| No | 296 | 127 | 169 |   |
| Yes | 2983 | 1181 | 1802 |   |
| **Type of infection (n=3279)** |  |  |  | <0.001\* |
| Ear infection | 2172 (66.24) | 850 (39.13) | 1,322 (60.87) |   |
| Mixed ENT infections | 182 (5.55) | 68 (37.36) | 114 (62.64) |   |
| Nose infection | 409 (12.47) | 250 (61.12) | 159 (38.88) |   |
| Throat infection | 516 (15.74) | 140 (27.13) | 376 (72.87) |   |
| **Number of antibiotics** |  |  |  | <0.001\* |
| One | 1630 (49.71) | 372 (22.82) | 1,258 (77.18) |   |
| Two | 1400 (42.70) | 743 (53.07) | 657 (46.93) |   |
| Three | 243 (7.41) | 187 (76.95) | 56 (23.05) |   |
| Four | 5 (0.15) | 5 (100) | 0 (0) |   |
| Five | 1 (0.03) | 1 (100) | 0 (0) |   |
| **WHO AWaRe category** |  |  |  | <0.001\* |
| Access | 1609 (57.40)  | 281 (17.48) | 1328 (82.52) |   |
| Access + Watch | 477 (17.02) | 264 (55.26) | 213 (44.74) |   |
| Watch | 717 (25.58) | 252 (35.23) | 464 (64.77) |   |

\* = significant at p-value < 0.05 obtained from Chi-Square test

## **Predictors of appropriateness of antibiotic use**

Multiple logistic regression was performed for only variables that showed a significant association with the study outcome from the bivariate analysis. Appropriateness based on choice of antibiotics was 68% less likely for nose infections (aOR= 0.32, CI= 0.26 – 0.41, p <0.001) and 29% less likely for throat infections (aOR= 0.71, CI= 0.55 – 0.92, p= 0.009) compared to ear infections (Table 3). Appropriateness was also reduced by 78% when two antibiotics were prescribed (aOR= 0.22, CI= 0.17 – 0.29, p <0.001) and by 94% when three antibiotics were prescribed (aOR= 0.06, CI= 0.04 – 0.10, p <0.001) compared to when only one antibiotic was prescribed (Table 3). Appropriateness was also predicted by the WHO AWaRe group as appropriateness of antibiotic prescriptions from the ‘Watch’ group 51% less likely (aOR= 0.49, CI= 0.38 – 0.63, p <0.001) compared with prescriptions from the ‘Access’ group (Table 3).

**Table 3:** *Logistic regression between independent variables which showed statistically significant association and appropriateness based on choice*

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **aOR** | **95% CI** | **P-value** |
| **Type of infection (n=3279)** |  |  | <0.001\* |
| Ear infection (R) | 1.00 |  |   |
| Mixed ENT infections | 1.01 | 0.72 – 1.41 | 0.896 |
| Nose infection | 0.32 | 0.26 – 0.41 |  0.009\* |
| Throat infection | 0.71 | 0.55 – 0.92 | 0.245 |
| **Number of antibiotics** |  |  | <0.001\* |
| One (R) | 1.00 |  |   |
| Two | 0.22 | 0.17 – 0.29 | <0.001\* |
| Three | 0.06 | 0.04 – 0.10 | <0.001\* |
| Four | 1.00 |  |   |
| Five | 1.00 |  |   |
| **WHO AWaRe category** |  |  | <0.001\* |
| Access (R) | 1.00 |  |   |
| Access + Watch | 0.76 | 0.54 – 1.06 | <0.001\* |
| Watch | 0.49 | 0.38 – 0.63 | <0.001\* |

\* = significant at p-value < 0.05, aOR = Adjusted Odds Ratio, CI = Confidence Interval, R=Reference variable

# **Discussion**

We believe this is the first study in Ghana that sought to clinically audit antibiotic prescriptions for diagnosed ENT infections at a leading Teaching Hospital to guide future policies. We are aware of studies in Ghana that have assessed compliance with national guidelines in outpatients for specific conditions including community-acquired pneumonia and urinary tract infections but not for ENT infections (6, 25, 34, 44). This is important given the extent of inappropriate prescribing for such infections as well as their impact on morbidity and mortality associated with increasing AMR especially in LMICs (9, 21, 45).

Female gender accounted for the majority of patients who were managed for an ENT condition within the study period whose medical records were extracted. This may be due to the observation of that females are better utilizers of health services compared to their male counterparts. This is in addition to the disparities among the two groups concerning income and educational levels that have been reported in some studies in Ghana and elsewhere (46-48). This though was contrary to other similar studies conducted in Nigeria and India where the majority of patients were male (2, 49).

In our study, ENT infections were diagnosed among all groups but were more predominant among the younger age patient care. those between 0 – 25 years. This may be due to the high prevalence of ENT infections in young people, particularly children (50, 51). The high level of ENT infections among this age group could be due to the internal structures of their ears such as the short eustachian tubes and their immature immune system exposing them to common infections (52).

Approximately half of the study population were managed with one antibiotic namely oral amoxicillin-clavulanic acid alone. This was followed by a combination of neomycin and steroid topical preparations and then oral ciprofloxacin. This is similar to the findings of other studies where penicillins are mostly used for ENT infection management (2, 22). The Ghana STG recommends the use of a single antibiotic for the treatment of ENT infections as it encourages adherence to therapy and reduces exposure to antibiotics, which is a precursor for AMR (28). However, there was still a high rate of prescribing of multiple antibiotics for most of ENT conditions in our study, which may result in increased risk of AMR, high cost of treatment and adverse drug reactions, which need to be avoided going forward (7, 45, 53, 54).

We also found from our study that ear infections were the most common ENT infection reported by patients, followed by throat infections with mixed ENT infections being the least common. Previous studies have also reported similar findings (23, 55). Acute and chronic otitis media accounted for a majority of the ENT conditions treated with antibiotics in our study, which is perhaps not surprising in the absence of any culture and sensitivity testing in our study as this is a major cause of hearing loss in children (21, 50). This finding is similar to other studies which have reported high level of ear infections especially otitis media in the younger population (39, 56).

Typically, ‘Access’ antibiotics are recommended as the first line antibiotic for ENT infections where bacteria are suspected by the WHO and other international guidelines including the Ghana STG due to their efficacy in managing the common ENT infections and the low risk of drug resistance together with their availability and affordability (16, 17). However, our results showed that the majority of antibiotics prescribed were from a combination of the ‘Access’ and ‘Watch’ groups, followed by those in the WHO ‘Watch’ group only. The high usage of ‘Watch’ antibiotics for ENT conditions is a concern as this increases AMR, and this also needs to be urgently addressed going forward (15).

The appropriateness of antibiotic prescriptions based on the choice of antibiotic according to mainly the Ghana STG (2017) was 60.11%, while the overall appropriateness based on choice, dose and frequency was 37.85%. Appropriateness of antibiotic use based on dose and frequency was higher (above 75%). Appropriateness was significantly decreased by the addition of one or more antibiotics to the regimen. We also observed that some ENT conditions whose management does not require the prescription of antibiotics (such as allergic rhinitis) were managed with antibiotics making their prescription inappropriate (20). This is a concern as such unnecessary use of antibiotics drives the increase in AMR development, healthcare cost and antibiotic-associated adverse drug reactions.

The appropriate use of antibiotics for the ENT conditions was associated with the type of infection (P<0.001), the number of antibiotics prescribed (P<0.001) and WHO AWaRe category (P<0.001). Appropriateness was reduced for nose infections (aOR= 0.32, CI= 0.26 – 0.41, p <0.001) and for throat infections (aOR= 0.71, CI= 0.55 – 0.92, p= 0.009) compared to ear infections. The increased inappropriate use of antibiotics for nose infections may be due to poor choice of antibiotics due to the overuse of antibiotics for viral infections and non-infection related-inflammatory disorders of nose and throat such as allergic rhinitis and sore throat. Appropriateness was also reduced when two antibiotics were prescribed (aOR= 0.22, CI= 0.17 – 0.29, p <0.001) and when three were prescribed (aOR= 0.06, CI= 0.04 – 0.10, p <0.001) compared to one antibiotic prescribed as the Ghanaian STG only recommends monotherapy of antibiotics (STG (2017). This shows the overuse of antibiotic for ENT infection which is against the recommendations of treatment guidelines. Appropriateness was further reduced by 51% when antibiotic prescriptions were from the ‘Watch’ group (aOR= 0.49, CI= 0.38 – 0.63, p <0.001) compared to the ‘Access’ group. This is mainly because the current guideline favours the use of antibiotics for common ENT infections from the Access group compared to the Watch group in the AWaRe classification due to low risk of development of AMR with the former compared to the latter.

We are aware of a number of limitations with this study. Firstly, this audit was conducted in only one hospital which was a tertiary facility and therefore may not represent the commonest ENT conditions managed in primary care facilities of low resource settings. However, this hospital and setting was undertaken for the reasons stated. Though patients who missing data on antibiotics prescribed were excluded, this did not affect internal validity due to the large number of medical records of patients that were extracted and analysed. The study was also limited by the clinical details of patients which were neither documented nor easily accessible such as chronic co-morbidities etc. This is common though when undertaking research using patient medical records. Despite these limitations, we believe that the findings from this study will be useful in providing some baseline information of gaps in the appropriate use of antibiotic for ENT conditions in this and neighbouring facilities in Ghana due to the extent of data extracted and the referral status of the facility that allows for collection of diverse ENT conditions.

## **Conclusion and recommendations**

The level of appropriate use of antibiotics for ENT conditions among our study population was suboptimal and was predicted by the type of infection, the number of antibiotics prescribed and the WHO AWaRe category. Going forward, prescribers should be educated and trained regarding guidelines on antibiotic use for ENT conditions, including the Ghanaian STGs and the AWaRe guidelines. Emphasis must be placed on the need to use only ‘Access’ antibiotics when recommended to minimize the risk of AMR development as well as adverse effects. This can be achieved through instigating appropriate ASPs in the clinics. Whilst there was a concern with implementing AMS programs in LMICs due to resource and personnel issues, this is changing through educational and other initiatives throughout Africa, including Ghana. We need to build on these developments to enhance the appropriate use of antibiotics across sectors in Ghana to reduce AMR, which is in line with the Ghanaian NAP.

**List of abbreviations**

AMR – Antimicrobial Resistance

AMS – Antimicrobial Stewardship

ENT – Ear, nose and throat

HTH – Ho Teaching Hospital

LHIMS – Lightwave Health Information Management System

LMIC – Low-and-middle income country

NAP – National Action Plan

NHIS – National Health Insurance Scheme

STG – Standard Treatment Guideline

WHO – World Health Organisation

**Authors’ contribution**

Conceptualization IAS, ID; methodology: IAS, IRD, VB; validation: IAS, IRD, TAA, VB; formal analysis: IAS, IRD, AK, BG, VB; investigation: IAS, IRD; resources: IAS, IRD, VB; data curation: IAS, JK, SA, BG, VB; writing—original draft preparation: IAS, IRD, JK, TAA, BG, VB; writing—All authors; visualization: IAS, JK, TAA, BG, VB; supervision: IAS, JK, VB; project administration: IAS, IRD, SA, AK, BG. All authors have read and agreed to the published version of the manuscript.

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**Declaration of conflicts of interest**

The authors declare that they have no conflict of interest.

**Availability of data:**

The data that support the findings of this study are available from the corresponding author, [IAS], upon reasonable request.

**Ethics approval and consent to participate**

Ethical clearance was obtained from the ethics committees of both the University of Health and Allied Sciences (UHAS-REC A.7 [41]22-23) and the HTH (HTH-REC (32) FC\_2022) prior to the commencement of the study. Administrative approval for data collection was sought from the management of the hospital. Consent to participate was not applicable as patients were not directly interviewed.

**Consent for publication**

Not applicable.

# **References**

1. Joshi U, Banjara H, Hishikar R, Chandrakar R. Prescription pattern of drugs in ENT outpatient department of tertiary care teaching hospital. Int J Basic Clin Pharmacol. 2018;7(9):1688-92. https://doi.org/10.18203/2319-2003.ijbcp20183430

2. Ahmed NJ. The Prescribing Pattern of Medications in Ear, Nose and Throat Outpatient Department of a Public Hospital. Journal of Pharmaceutical Research International. 2021;33(9):21-5. https://doi.org/10.9734/jpri/2021/v33i931221

3. Abuali M, Zivot A, Guerguis S, Valladares E, Aleem S, Gonzalez-Salazar F, et al. Outpatient antibiotic prescribing patterns in pediatric academic and community practices. American Journal of Infection Control. 2019;47(9):1151-3. https://doi.org/10.1016/j.ajic.2019.03.025

4. Duffy E, Ritchie S, Metcalfe S, Van Bakel B, Thomas M. Antibacterials dispensed in the community comprise 85%‐95% of total human antibacterial consumption. Journal of clinical pharmacy and therapeutics. 2018;43(1):59-64. https://doi.org/10.1111/jcpt.12610

5. Kancherla D, Sai MS, Devi HG, Sharma S. A study on prescribing pattern of antibiotics in respiratory tract infections in a tertiary care center. International Journal of Recent Scientific Research. 2015;6(6):4558-63 https://www.recentscientific.com/study-prescribing-pattern-antibiotics-respiratory-tract-infections-tertiary-care-center.

6. Sefah IA, Sneddon J, Essah DO, Kurdi A, Fadare J, Jairoun AA, et al. Evaluation of antibiotic prescribing for ambulatory patients seeking primary dental care services in a public hospital in Ghana: A clinical audit study. JAC-Antimicrobial Resistance. 2022;4(4):dlac079. https://doi.org/10.1093/jacamr/dlac079

7. Butler AM, Brown DS, Durkin MJ, Sahrmann JM, Nickel KB, O’Neil CA, et al. Association of inappropriate outpatient pediatric antibiotic prescriptions with adverse drug events and health care expenditures. JAMA network open. 2022;5(5):e2214153-e. https://doi.org/10.1001/jamanetworkopen.2022.14153

8. Dadgostar P. Antimicrobial resistance: implications and costs. Infection and drug resistance. 2019 Dec 20:3903-10. https://doi.org/10.2147/idr.s234610.

9. Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet. 2022;399(10325):629-55.

10. Gautam A. Antimicrobial Resistance: The Next Probable Pandemic. JNMA: Journal of the Nepal Medical Association. 2022;60(246):225.https://doi.org/10.31729/jnma.7174

11. MOH. Ghana Ministry of Health, Ministry of Food and Agriculture, Ministry of Environment, Science, Technology and Innovation, Ministry of Fisheries and Aquaculture Development. Ghana National Action Plan for Antimicrobial Use and Resistance. 2017 - 2021. . 2018. http://www.moh.gov.gh/wp-content/uploads/2018/04/NAP\_FINAL\_PDF\_A4\_19.03.2018-SIGNED-1.pdf [Accessed on the 15th February, 2024]

12. WHO. Global action plan on antimicrobial resistance - Report by the Secretariat. 2016. https://apps.who.int/gb/ebwha/pdf\_files/WHA69/A69\_24-en.pdf [Accessed on the 15th February, 2024]

13. Sharland M, Gandra S, Huttner B, Moja L, Pulcini C, Zeng M, et al. Encouraging AWaRe-ness and discouraging inappropriate antibiotic use—the new 2019 Essential Medicines List becomes a global antibiotic stewardship tool. The Lancet Infectious Diseases. 2019;19(12):1278-80.https://doi.org/10.1016/s1473-3099(19)30532-8

14. Sharland M, Zanichelli V, Ombajo LA, Bazira J, Cappello B, Chitatanga R, et al. The WHO essential medicines list AWaRe book: From a list to a quality improvement system. Clinical Microbiology and Infection. 2022;28(12):1533-5. https://doi.org/10.1016/j.cmi.2022.08.009

15. Sulis G, Sayood S, Katukoori S, Bollam N, George I, Yaeger LH, et al. Exposure to World Health Organization's AWaRe antibiotics and isolation of multidrug resistant bacteria: a systematic review and meta-analysis. Clinical Microbiology and Infection. 2022;28(9):1193-202. https://doi.org/10.1016/j.cmi.2022.03.014

16. WHO. The WHO AWaRe (access, watch, reserve) antibiotic book. 2022. https://www.who.int/publications/i/item/9789240062382 [Accessed on the 15th February, 2024]

17. Zanichelli V, Sharland M, Cappello B, Moja L, Getahun H, Pessoa-Silva C, et al. The WHO AWaRe (Access, Watch, Reserve) antibiotic book and prevention of antimicrobial resistance. 2023. https://doi.org/10.2471/BLT.22.288614

18. Klein EY, Milkowska-Shibata M, Tseng KK, Sharland M, Gandra S, Pulcini C, et al. Assessment of WHO antibiotic consumption and access targets in 76 countries, 2000–15: an analysis of pharmaceutical sales data. The Lancet Infectious Diseases. 2021;21(1):107-15. https://doi.org/10.1016/s1473-3099(20)30332-7

19. Zaman N, Zaman K, Zaman F, Zaman B. Prescribing Frequency, Trends, And Patterns Of Antimicrobial Therapy In Patients With Acute Tonsillitis: A Review. Bulletin of Pharmaceutical Sciences Assiut. 2022;45(1):299-310. https://doi.org/10.21608/bfsa.2022.239472

20. Cohen R, Haas H, Lorrot M, Biscardi S, Romain O, Le Sage FV, et al. Antimicrobial treatment of ENT infections. Archives de Pédiatrie. 2017;24(12):S9-S16. https://doi.org/10.1016/s0929-693x(17)30512-2

21. Jamal A, Alsabea A, Tarakmeh M. Effect of ear infections on hearing ability: a narrative review on the complications of otitis media. Cureus. 2022;14(7). https://doi.org/10.7759/cureus.27400

22. Dar MA, Kalsi S, Rehman SU. To Evaluate Drug Utilization Pattern Among Ent Patients In A Tertiary Care Hospital Of North Kashmir, Union Territory Of Jammu And Kashmir, India. 2022. http://dx.doi.org/10.20959/wjpps20228-22899

23. Sathiya SB, Panchasara AK, Barvaliya MJ, Jha SG, Tripathi C. Drug utilization pattern of antimicrobial agents in an outpatient department of otorhinolaryngology in a tertiary care hospital: a prospective, cross-sectional study. International journal of basic and clinical pharmacology. 2015;5:65-9. https://doi.org/10.18203/2319-2003.ijbcp20160102

24. Albrecht P. Antibiotic therapy for an ENT specialist. Polish Journal of Otolaryngology. 2018;72(6):1-9. https://doi.org/10.5604/01.3001.0012.4704

25. Ahiabu M-A, Tersbøl BP, Biritwum R, Bygbjerg IC, Magnussen P. A retrospective audit of antibiotic prescriptions in primary health-care facilities in Eastern Region, Ghana. Health policy and planning. 2016;31(2):250-8. https://doi.org/10.1093/heapol/czv048

26. Afriyie DK, Sefah IA, Sneddon J, Malcolm W, McKinney R, Cooper L, et al. Antimicrobial point prevalence surveys in two Ghanaian hospitals: opportunities for antimicrobial stewardship. JAC-Antimicrobial Resistance. 2020;2(1):dlaa001. https://doi.org/10.1093/jacamr/dlaa001

27. Newman P, Opintan J, Sampane-Donkor E. Surveillance of Antimicrobial Drug Resistance in Ghana. Minist Heal. 2015:1-53. https://doi.org/10.2147/idr.s88725

28. STG. Standard Treatment Guideline. 2017. https://www.moh.gov.gh/wp-content/uploads/2020/07/GHANA-STG-2017-1.pdf (7th edition) [Accessed on the 15th February, 2024]

29. Adjeso T, Damah M, Murphy J. Emergency Ear, nose and throat admissions in northern ghana. Postgraduate Medical Journal of Ghana. 2017;6(2):83-5. https://doi.org/10.60014/pmjg.v6i2.120

30. Adjeso T, Dzogbefia M, Dzantor EK. Deep Neck Space Infections in Northern Ghana. 2020. https://doi.org/10.60014/pmjg.v6i2.120

31. Romandini A, Pani A, Schenardi PA, Pattarino GAC, De Giacomo C, Scaglione F. Antibiotic resistance in pediatric infections: global emerging threats, predicting the near future. Antibiotics. 2021;10(4):393. https://doi.org/10.3390/antibiotics10040393

32. Akpan MR, Isemin NU, Udoh AE, Ashiru-Oredope D. Implementation of antimicrobial stewardship programmes in African countries: a systematic literature review. Journal of global antimicrobial resistance. 2020;22:317-24. https://doi.org/10.1016/j.jgar.2020.03.009

33. Idun-Acquah JJ, Opoku MM, Kenu E, Bonful HA. Appropriateness and Factors Associated with Antibiotics Prescription to Outpatients with Respiratory Tract Infection in Tema Polyclinic, Ghana. 2020. http://dx.doi.org/10.21203/rs.3.rs-41132/v1

34. Sefah IA, Essah DO, Kurdi A, Sneddon J, Alalbila TM, Kordorwu H, et al. Assessment of adherence to pneumonia guidelines and its determinants in an ambulatory care clinic in Ghana: Findings and implications for the future. JAC-antimicrobial resistance. 2021;3(2):dlab080. https://doi.org/10.1093/jacamr/dlab080

35. Sumaila A-N, Tabong PT-N. Rational prescribing of antibiotics in children under 5 years with upper respiratory tract infections in Kintampo Municipal Hospital in Brong Ahafo Region of Ghana. BMC research notes. 2018;11:1-5. https://doi.org/10.1186/s13104-018-3542-z

36. Dodoo CC, Orman E, Alalbila T, Mensah A, Jato J, Mfoafo KA, et al. Antimicrobial prescription pattern in Ho Teaching Hospital, Ghana: seasonal determination using a point prevalence survey. Antibiotics. 2021;10(2):199. https://doi.org/10.3390/antibiotics10020199

37. GSS. Ghana 2021 Population and Housing Census. Ghana Statistical Service. 2021. Https://Census2021.Statsghana.Gov.Gh/Gssmain/Fileupload/Reportthemelist/PRINT\_COPY\_VERSION\_FOUR%2022ND\_SEPT\_AT\_8\_30AM.Pdf [Accessed on the 7th February, 2023]

38. Raosoft. Sample size calculator. 2004. http://www.raosoft.com/samplesize.html [Accessed on the 7th February, 2023]

39. Fasunla AJ, Samdi M, Nwaorgu OG. An audit of Ear, Nose and Throat diseases in a tertiary health institution in South-western Nigeria. Pan African Medical Journal. 2013;14(1). https://doi.org/10.11604/pamj.2013.14.1.1092

40. Mustafa ZU, Nazir M, Majeed HK, Salman M, Hayat K, Khan AH, et al. Exploring knowledge of antibiotic use, resistance, and stewardship programs among pharmacy technicians serving in ambulatory care settings in Pakistan and the implications. Antibiotics. 2022;11(7):921. https://doi.org/10.3390/antibiotics11070921

41. NICE. National Institute for Health and care Excellence Guidelines for Ear, Nose and Throat Conditions. https://www.nice.org.uk/guidance/conditions-and-diseases/ear--nose-and-throat-conditions/products?GuidanceProgramme=guidelines [Accessed on the 15th February, 2024]

42. Seidman MD, Gurgel RK, Lin SY, Schwartz SR. American Academy of Otolaryngology—Head and Neck Surgery Foundation Clinical Practice Guidelines: Allergic Rhinitis. Otolaryngology—Head and Neck Surgery. 2014;151(1\_suppl):P24-P. https://doi.org/10.1177/0194599814561600

43. Sefah IA, Nyamadi D, Kurdi A, Bugri AA, Kerr F, Yamoah P, et al. Assessment of the quality of antimicrobial prescribing among hospitalized patients in a teaching hospital in Ghana: findings and implications. Hospital Practice. 2023;51(4):223-32. https://doi.org/10.1080/21548331.2023.2241344

44. Darkwah TO, Afriyie DK, Sneddon J, Cockburn A, Opare-Addo MNA, Tagoe B, et al. Assessment of prescribing patterns of antibiotics using National Treatment Guidelines and World Health Organization prescribing indicators at the Ghana Police Hospital: A pilot study. Pan African Medical Journal. 2021;39(1). https://doi.org/10.11604/pamj.2021.39.222.29569

45. Godman B, Egwuenu A, Haque M, Malande OO, Schellack N, Kumar S, et al. Strategies to improve antimicrobial utilization with a special focus on developing countries. Life. 2021;11(6):528. https://doi.org/10.3390/life11060528

46. Simons K, Bradfield O, Spittal MJ, King T. Age and gender patterns in health service utilisation: Age-Period-Cohort modelling of linked health service usage records. BMC Health Services Research. 2023;23(1):480. https://doi.org/10.1186/s12913-023-09456-x

47. Saeed B, Yawson A, Nguah S, Agyei-Baffour P, Emmanuel N, Ayesu E. Effect of socio-economic factors in utilization of different healthcare services among older adult men and women in Ghana. BMC Health Services Research. 2016;16(1):1-9. https://doi.org/10.1186/s12913-016-1661-6

48. Jatrana S, Crampton P. Gender differences in general practice utilisation in New Zealand. Journal of primary health care. 2009;1(4):261-9. https://pubmed.ncbi.nlm.nih.gov/20690334/

49. Ain M, Shahzad N, Aqil M, Alam M, Khanam R. Drug utilization pattern of antibacterials used in ear, nose and throat outpatient and inpatient departments of a university hospital at New Delhi, India. Journal of Pharmacy and bioallied sciences. 2010;2(1):8. https://doi.org/10.4103/0975-7406.62695

50. Kisembo P, Mugwanya F, Atumanya P, Othin M, Oworinawe R, Kagimu B, et al. Prevalence of ear infections in first year children of primary schools in a Western Ugandan community. African Journal of Biomedical Research. 2018;21(2):117-22. https://pmc.ncbi.nlm.nih.gov/articles/PMC6959216/pdf/nihms-993096.pdf

51. Hullegie S, Venekamp RP, van Dongen TM, Hay AD, Moore MV, Little P, et al. Prevalence and antimicrobial resistance of bacteria in children with acute otitis media and ear discharge: a systematic review. The Pediatric infectious disease journal. 2021;40(8):756. https://doi.org/10.1097/inf.0000000000003134

52. Zeeshan M, Zeb J, Saleem M, Zaman A, Khan A, Tahir M. ENT diseases presenting to a tertiary care hospital. Endocrinol Metab Int J. 2018;6(6):416-8. https://doi.org/10.15406/emij.2018.06.00225

53. Harris AM, Hicks LA, Qaseem A, Physicians HVCTFotACo, Control ftCfD, Prevention\*. Appropriate antibiotic use for acute respiratory tract infection in adults: advice for high-value care from the American College of Physicians and the Centers for Disease Control and Prevention. Annals of internal medicine. 2016;164(6):425-34. https://doi.org/10.7326/m15-1840

54. Smith DR, Dolk FCK, Pouwels KB, Christie M, Robotham JV, Smieszek T. Defining the appropriateness and inappropriateness of antibiotic prescribing in primary care. Journal of Antimicrobial Chemotherapy. 2018;73(suppl\_2):ii11-ii8. https://doi.org/10.1093/jac/dkx503

55. Gupta AS, Ram R, Islam F, Mukherjee S, Ram AK, Bhattacharya S. A study on clinico-epidemiological profile of ear, nose and throat diseases among patients aged 6 to 14 years attending the ENT OPD at MGM Medical College, Kishanganj, Bihar, India. Global J Med Pub Health. 2012;1(4):1-5. DOI: 10.7860/JCDR/2022/47916.16216

56. Kishve SP, Kumar N, Kishve PS, Aarif SM, Kalakoti P. Ear, Nose and Throat disorders in paediatric patients at a rural hospital in India. Australasian Medical Journal. 2010;3(12). https://doi.org/10.4066/AMJ.2101.494