



WHO Guideline Adherence and AWaRe Antibiotic Use in Severe Childhood Pneumonia in Ethiopia: Associations with Treatment Outcomes

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Highlights

- 46.1% of children received WHO-recommended treatment based on drug selection alone
- Gentamicin and ampicillin were underdosed in 94.5% and 62.4% of cases, respectively
- 43.6% of children received at least a *Watch* antibiotic
- WHO guidelines rely on older studies with limited data from sub-Saharan Africa
- Current antibiotic use may contribute to increasing antimicrobial resistance

Journal Pre-proof

WHO Guideline Adherence and AWaRe Antibiotic Use in Severe Childhood Pneumonia in Ethiopia: Associations with Treatment Outcomes

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ABSTRACT

Background: Pneumonia remains a leading cause of childhood mortality in sub-Saharan African countries. The World Health Organization (WHO) recommends a combination of ampicillin or benzylpenicillin with gentamicin for severe pneumonia in children aged 2–59 months. Real-world adherence to these guidelines remains limited.

Methods: We conducted a retrospective observational study at St. Luke Hospital in Woliso, Ethiopia, including all children aged 2–59 months admitted with severe pneumonia between May 2021 and April 2024. Antibiotic prescriptions were evaluated for adherence to WHO guidelines and categorized using the WHO AWaRe classification. Clinical outcomes were analyzed based on adherence status using univariate and multivariate analyses.

Results: Among 427 patients, 46.1% received guideline-adherent treatment, based on drug selection alone. Gentamicin and ampicillin were underdosed in 94.5% and 62.4% of cases, respectively. Overall, 43.6% of children received at least one antibiotic from the Watch group. In adjusted analyses, adherence to WHO guidelines was associated with longer duration of oxygen therapy (0.7 days, 95% CI: 0.1-1.3, $p = 0.02$) but showed no significant association with mortality or treatment failure.

Conclusions: Adherence to WHO guidelines was suboptimal, particularly regarding antibiotic dosing. These findings underscore the need for improved antimicrobial stewardship and further evaluation of guideline implementation in Ethiopia.

Keywords: Severe childhood pneumonia, WHO guideline adherence, antibiotics, Sub-Saharan Africa, gentamicin, antimicrobial resistance

INTRODUCTION

Lower respiratory tract infections (LRTIs) are the leading infectious cause of death in children under five, particularly in high-burden regions such as the Horn of Africa. According to the Global Burden of Disease (GBD) study, in 2021, LRTIs were responsible for an estimated 502,000 deaths worldwide in this age group, including 261,000 in sub-Saharan Africa, where the mortality rate was 151.2 per 100,000 children under five. Ethiopia is among the most affected countries, with an estimated 13,500 deaths in 2021 and a mortality rate of 84.5 per 100,000, more than forty times higher than that of high-income countries (1).

Although the burden of LRTIs among children under five in Ethiopia is decreasing, with a 23.9% reduction in mortality between 2019 and 2021 (1), antimicrobial resistance (AMR) is rising, threatening to undermine this progress. High resistance rates among common pathogens have prompted national health institutions to launch targeted initiatives aimed at containing AMR (2). A study conducted in the Amhara region in northern Ethiopia reported an overall AMR prevalence of 59.9%, with *Klebsiella pneumoniae* and *Streptococcus* species, both commonly associated with LRTIs, showing resistance rates of 78.5% and 54.8%, respectively (3).

The inappropriate use of antibiotics plays a major role in the development of AMR (4). In 2023, an observational study in Southern Ethiopia found that only 49% of children diagnosed with severe pneumonia were treated in accordance with current World Health Organization (WHO) guidelines (5,6). Similarly, a study conducted in Sudan between 2009 and 2010 reported only 18.8% adherence to WHO guidelines in the treatment of severe pneumonia in children (7). In Kenya, adherence to pediatric pneumonia treatment guidelines at Garissa Provincial General Hospital was 27.7% (8).

In 2014, the WHO revised its guidelines for the classification and treatment of pneumonia in children aged 2 to 59 months. These updated guidelines redefined the criteria for severe pneumonia and introduced new recommendations for first-line antibiotic therapy. Severe pneumonia is diagnosed based on the presence of at least one of the following clinical signs: central cyanosis or oxygen

saturation below 90%, severe respiratory distress (such as grunting or very severe chest indrawing), inability to drink, persistent vomiting, convulsions, lethargy or unconsciousness, stridor in a calm child, or signs of severe malnutrition (9,10). The recommended first-line treatment is a combination of ampicillin (50 mg/kg every 6 hours) or benzylpenicillin (50,000 units/kg every 6 hours) with gentamicin (7.5 mg/kg once daily) for a minimum of five days. Ceftriaxone is recommended only as a second-line treatment when first-line therapy fails (6).

These recommendations align with the WHO's Access, Watch, and Reserve (AWaRe) classification of Essential Medicines List. Benzylpenicillin and gentamicin are categorized as Access antibiotics, recommended for first-line use due to their effectiveness and narrower spectrum. In contrast, ceftriaxone is classified in the Watch group, which includes broader-spectrum agents with a higher potential to drive antimicrobial resistance and should therefore be used more cautiously (11,12).

This study aims to evaluate adherence to the WHO's 2014 revised guidelines for the treatment of severe childhood pneumonia at a referral hospital in Woliso, Oromia, Ethiopia, and to assess the impact of adherence on patient outcomes.

METHODS

Study Design, Population, and Data Source

This retrospective observational study was conducted at St. Luke Hospital in Woliso, a town located in the South West Shoa Zone (SWSZ) of the Oromia Regional State, Ethiopia. Approximately 40% of the population in the SWSZ is under 15 years of age, with around 68% residing in remote rural settlements, 18% in rural villages, and 14% in Woliso Town, the zone's largest urban center, which has a population of 53,065 (13).

The study population included all children aged 2 to 59 months who were admitted to and either discharged from or died in the Pediatric Ward of St. Luke Catholic Hospital between May 1, 2021, and April 30, 2024, with a diagnosis of severe pneumonia. Children were excluded if they had a known Human Immunodeficiency Virus (HIV) infection, were already receiving antibiotic therapy

at the time of admission for an indication other than pneumonia, or had a confirmed or suspected diagnosis of another severe bacterial infection, such as sepsis or meningitis. Data were retrospectively extracted from patient medical records that met the inclusion and exclusion criteria, using discharge diagnoses for case identification.

Definition of Adherence and Outcomes

Adherence to WHO guidelines was defined as the administration of either ampicillin or benzylpenicillin in combination with gentamicin as first-line treatment, regardless of dosage. First-line therapy was defined as any antibiotic regimen initiated within 48 hours of the first prescription. Additionally, first-line prescribed antibiotics were categorized according to the WHO AWaRe (Access, Watch, and Reserve) classification to assess the distribution of antibiotic use.

The outcomes assessed in this study included in-hospital mortality or a combined outcome (referred to other hospital, self-discharge, in-hospital mortality), the number of days of hospitalization, the number of days during which the patient required oxygen therapy, and treatment failure. Treatment failure was defined as a switch in the antibiotic regimen that occurred after at least 48 hours had elapsed since the initiation of first-line therapy (14).

Clinical and Laboratory Variables

Clinical variables were based on the WHO-defined signs of severe pneumonia, which include central cyanosis or oxygen saturation below 90%, severe respiratory distress such as grunting or severe chest indrawing, inability to drink, persistent vomiting, convulsions, lethargy or unconsciousness, stridor in a calm child, and signs of severe malnutrition. In addition, the study recorded whether the child had a clinical diagnosis of measles and whether they were documented as HIV-exposed at birth. HIV status was determined using three different rapid antibody tests: One Step, First Response, and Uni-Gold.

Biochemical variables included malaria status and complete blood count (CBC) results. Malaria infection was diagnosed through microscopy of Giemsa-stained blood films. CBCs were performed using Sysmex and Mindray analyzers at the hospital's laboratory.

Statistical Analysis

Descriptive statistics were used to summarize the study variables. Continuous variables were reported as means and standard deviations, while categorical variables were presented as frequencies and percentages. Patient outcomes were compared between children treated in adherence to WHO guidelines and those who were not. For comparisons involving categorical variables, the chi-square test or Fisher's exact test was applied, as appropriate. For continuous variables, comparisons were conducted using Student's t-test. Associations between adherence to WHO guidelines and outcome measures were further evaluated using multivariable regression models, applied when a significant association was observed in univariate analyses. Multivariable logistic regression was used for binary outcomes, and linear regression was applied for continuous outcomes. Covariates that demonstrated a statistically significant association ($p < 0.20$) in univariate analyses were included in the multivariable models. A reduced model approach was used by retaining only those variables that remained statistically significant in the multivariable analysis. To evaluate whether children with severe acute malnutrition influenced the results, we repeated all multivariate models excluding this subgroup. Statistical significance was set at $p < 0.05$. All analyses were performed using R software (version 4.3.2 for Windows).

Ethical Considerations

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki, as revised in October 2024. The Ethical Committee of St. Luke Catholic Hospital and College of Nursing and Midwifery approved the study (reference number 1238/2025), which included a waiver of informed consent because of the retrospective nature of the investigation.

RESULTS

During the observation period, 441 children aged 2–59 months were hospitalized with a diagnosis of severe pneumonia. Fourteen patients were excluded: 12 due to concurrent ongoing therapy, and 2 due to suspected or confirmed severe bacterial infections other than pneumonia. A total of 427 patients

were included in the analysis: 170 (39.8%) females and 257 (60.2%) males, with a mean age of 15.7 \pm 13.2 months.

Table 1 presents patients' characteristics, symptoms at presentation, and outcomes for the overall sample and sorted by sex. No significant differences were detected between sexes. The most commonly reported symptom was severe respiratory distress, which was observed in 331 (77.5%) children, followed by central cyanosis or oxygen saturation $<90\%$ in 313 (73.3%), and inability to drink in 109 (25.5%). There were 9 deaths (2.1%) and 6 cases (1.6%) of self-discharge during hospitalization. A higher proportion of males required oxygen therapy compared to females (78.2% vs 68.8%, $p = 0.03$).

Overall, 196 children (45.9%) received a first-line antibiotic regimen in accordance with WHO guidelines. Detailed antibiotic regimens are shown in Table 2. The most frequently used regimen was ampicillin plus gentamicin in 196 patients (45.9%), followed by ceftriaxone alone in 163 patients (38.2%), and ampicillin alone in 43 patients (10.1%). Of the 642 antibiotics prescribed, 448 (69.8%) belonged to the Access group and 194 (30.2%) to the Watch group, according to the WHO AWaRe classification. A detailed breakdown of antibiotic prescriptions by AWaRe category is presented in Table S1 (Supplementary Material). Overall, 186 children (43.6%) received at least one antibiotic from the Watch group. We found a high proportion of incorrect gentamicin dosing, which was correctly prescribed in only 8 children (4%). In 189 cases (94.5%), the prescribed dose was lower than recommended. Ampicillin was prescribed at the recommended dose (200 mg/kg/day) in 91 cases (37.4%). The dosages of the prescribed antibiotics are detailed in Table S2 (Supplementary Material).

When comparing patients treated in accordance with WHO guidelines to those treated with non-adherent regimens, we found that the former were younger (mean age 10.5 vs. 14.3 months, $p < 0.001$), more frequently presented with severe malnutrition (9.2% vs. 2.2%, $p = 0.001$), had higher proportions of treatment failure (14.3% vs 7.4%, $p = 0.02$), required longer oxygen therapy (3.2 vs. 2.2 days, $p = 0.002$), and had a longer duration of hospitalization (6.5 vs. 5.6 days, $p = 0.007$). Table

3 shows baseline characteristics, clinical features, outcomes, and blood test results according to adherence to WHO guidelines.

Multivariable analysis of adherence to WHO guidelines and clinical outcomes

In the multivariable logistic regression using a reduced model approach, the association between adherence to WHO guidelines and treatment failure was no longer statistically significant (OR 1.9, 95% CI 0.9 to 3.8, $p = 0.08$). However, severe malnutrition, stridor in a calm child, and severe respiratory distress remained independently associated with treatment failure. Severe malnutrition was associated with more than threefold increased odds of treatment failure (OR 3.5, 95% CI 1.2 to 9.0, $p = 0.01$), as were stridor in a calm child (OR 3.3, 95% CI 1.0 to 9.8, $p = 0.03$) and severe respiratory distress (OR 3.2, 95% CI 1.2 to 11.1, $p = 0.03$). These results are presented in [Table 4](#).

In the linear regression model evaluating duration of oxygen therapy, adherence to WHO guidelines was associated with a modest but statistically significant increase of 0.7 days ($\beta = 0.7$, 95% CI 0.1 to 1.3, $p = 0.02$). Severe malnutrition was the strongest predictor, associated with an increase of 3.4 days ($\beta = 3.4$, 95% CI 2.0 to 4.8, $p < 0.001$). Severe respiratory distress was also associated with increased oxygen therapy duration ($\beta = 0.7$, 95% CI 0.05 to 1.5, $p = 0.04$).

Regarding length of hospital stay, adherence to WHO guidelines showed a positive association, but it did not reach statistical significance ($\beta = 0.5$, 95% CI -0.16 to 1.12, $p = 0.10$). Severe malnutrition was the only variable significantly associated with prolonged hospitalization, with an average increase of 5.6 days ($\beta = 5.6$, 95% CI 4.3 to 7.0, $p < 0.001$). Results of the multivariable linear models for oxygen therapy and hospital stay are shown in [Table 5](#).

Sensitivity analysis in multivariate models, excluding children with severe acute malnutrition, yielded similar results ([Table S3, supplementary materials](#)).

DISCUSSION

The main findings of this study can be summarised as follows. First, only 45.9% of children aged 2–59 months diagnosed with severe pneumonia were treated according to WHO-recommended antibiotic regimens, and 43.6% received at least one Watch antibiotic as first-line treatment. Second, both ampicillin and gentamicin were incorrectly prescribed in most cases, predominantly at doses lower than recommended. Third, guideline adherence, based on drug selection alone, was associated with a longer duration of oxygen therapy, but not with mortality, treatment failure, or length of hospital stay; this should be interpreted cautiously given the high frequency of subtherapeutic dosing.

Our findings on adherence to WHO guidelines align with a previous study from Jinka Town, South Omo Zone, Southern Ethiopia, which reported that 49% of children with severe pneumonia were treated according to WHO recommendations (5), as well as with a study from South Uganda showing only 24.9% adherence to national guidelines (15). Our study confirms these findings in a larger sample from a geographically and culturally distinct region of Ethiopia, suggesting that suboptimal adherence is a widespread issue. Several factors may contribute to this low adherence, including clinician-related factors such as training, experience, or clinical judgment, and system-level barriers such as the limited availability of recommended antibiotics, or perceived complexity and limited applicability of the guidelines in real-world settings (16). Children with severe acute malnutrition were more often treated in accordance with WHO guidelines, possibly because national protocols for malnutrition recommend gentamicin and ampicillin, aligning with WHO pneumonia treatment and reinforcing adherence in this group (17). This finding may also reflect clinician-level clustering, as St. Luke Hospital has a clinician specifically dedicated to the care of malnourished children.

Current WHO recommendations are based largely on two randomized controlled trials (RCTs) published in 2002 and 2008, which compared the efficacy of penicillin plus gentamicin with chloramphenicol in treating severe pediatric pneumonia (6,18,19). Since then, there has been a lack of high-quality trials evaluating alternative regimens. In 2015, a multicenter non-inferiority RCT found no significant difference in treatment failure between children with chest indrawing pneumonia

(without other severe signs) treated with oral amoxicillin versus those treated with intravenous benzylpenicillin (20). An RCT found that the combination of injectable amoxicillin plus gentamicin was not inferior to ampicillin plus gentamicin (21). A new trial (NCT04041791), recently completed in Kenya, is evaluating multiple antibiotic regimens (ampicillin plus gentamicin, ceftriaxone, and amoxicillin-clavulanic acid), as well as different approaches to nutritional support and fluid administration, including nasogastric feeding and intravenous fluids (22). No other ongoing randomized controlled trials on antibiotic treatment for childhood pneumonia in sub-Saharan countries were identified through searches of major trial registries, including ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP), and ISRCTN.

Our study also found that gentamicin was prescribed at lower-than-recommended doses in 94.5% of cases. This may reflect prescribers' concerns about potential side effects associated with aminoglycosides (23), and raises important questions about the universal recommendation of gentamicin for all children with severe pneumonia. Subtherapeutic dosing appears to be common in clinical practice. One study reported that 63% of children receiving gentamicin at 5 mg/kg/day had subtherapeutic serum concentrations, compared to 47 percent of those receiving 7 mg/kg/day (24). A pharmacokinetic study in children aged 1–14 years concluded that 7.5 mg/kg/day is more appropriate for achieving therapeutic targets (25).

Ampicillin was also underdosed in our cohort, with 62.4% of prescriptions falling below WHO recommendations. One simulation-based study found that 85.7% of *Streptococcus pneumoniae* strains were susceptible to ampicillin when administered at 150 mg/kg/day in four divided doses (26). A retrospective study comparing injectable penicillin alone to penicillin plus gentamicin found no difference in mortality among children with chest-indrawing pneumonia (27). Similarly, in adults with community-acquired pneumonia, ampicillin use did not increase mortality risk compared to ceftriaxone (28). These findings suggest that penicillin-only regimens may be sufficient in selected cases and warrant further evaluation in prospective studies, such as the aforementioned trial (22)

currently underway. Widespread underdosing may also drive AMR by exposing pathogens to subtherapeutic antibiotic levels.

Adherence to WHO guidelines, based on drug selection alone, was associated with a longer duration of oxygen therapy, a finding that contrasts with previous research from Southern Ethiopia, which did not find a correlation with outcomes (5). However, when adjusted for key covariates, no significant association was found between adherence and other outcomes such as death, self-discharge, referral, treatment failure, or hospital stay. The retrospective design of this study does not allow for definitive conclusions about causality. The counterintuitive association between guideline adherence and longer oxygen therapy likely reflects several factors. First, most children classified as adherent received subtherapeutic doses, particularly of gentamicin, which may have diluted the expected benefits of adherence and contributed to prolonged illness. Second, important variables such as vaccination status, comorbidities, or presence of fever were not available and may have influenced outcomes (29). Third, adherence may have clustered among particular clinicians or patient groups, such as children with severe acute malnutrition, who were also more likely to receive prolonged oxygen support regardless of underlying severity. Notably, a sensitivity analysis excluding malnourished children showed similar results. Fourth, local AMR patterns may have attenuated the effectiveness of both guideline-adherent and non-adherent regimens, as *Klebsiella pneumoniae*, a major cause of childhood pneumonia deaths in Ethiopia, shows high resistance to gentamicin and ceftriaxone (30). Finally, although underdosing and implementation challenges are likely major contributors, we cannot exclude the possibility that the WHO-recommended regimen itself may be less effective than alternative therapies in this setting. For example, a single-center cross-sectional study in Addis Ababa found that treatment with ceftriaxone plus azithromycin was associated with fewer poor treatment outcomes (31). Taken together, these findings likely reflect challenges in real-world guideline implementation rather than the ineffectiveness of the guidelines themselves. Importantly, they highlight the urgent need for prospective, context-specific studies in sub-Saharan Africa, where

pneumonia remains a leading cause of childhood mortality but where few, and often outdated, data exist to evaluate antibiotic efficacy in the context of rapidly rising AMR.

The most frequently prescribed antibiotic outside of WHO guideline recommendations was ceftriaxone, likely reflecting clinician preference, as no supply issues with gentamicin or ampicillin were reported during the study period. A systematic review identified *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, and *Haemophilus influenzae* as the major causative agents of pneumonia in Ethiopia, with an overall ceftriaxone resistance rate of 46%, ranging from 8% for *S. pneumoniae* to 88% for *S. aureus*. For the same pathogens, ampicillin resistance ranged from 45% in *S. pneumoniae* to 100% in *K. pneumoniae* (based on three isolates), while gentamicin resistance ranged from 0% in *S. pneumoniae* (based on a single isolate) to 64% in *K. pneumoniae* (32). The high frequency of ceftriaxone use is concerning, given local resistance patterns, as it is a WHO Watch antibiotic whose overuse can accelerate resistance and undermine first-line Access drugs such as ampicillin and gentamicin.

This study has several limitations. Its retrospective design limits causal inference and relies on the completeness and accuracy of existing clinical records. Important variables such as vaccination status, comorbidities, fever, and prior antibiotic use were not consistently documented. In addition, microbiological confirmation of causative pathogens was not available, limiting our ability to directly assess the role of antimicrobial resistance. A key limitation is that adherence was defined based on antibiotic selection rather than dosing, even though underdosing, particularly of gentamicin, was common. This likely introduced misclassification bias, diluting any true associations between adherence and outcomes such as mortality or treatment failure. In other words, the “adherent” group may not represent optimal WHO guideline-based care, but rather a mixture of appropriately and inadequately treated children. This limitation may also explain why adherence was associated with longer oxygen therapy but not with improved survival: our classification did not capture whether children received therapeutic dosing. As only four children in our cohort received treatment fully

adherent to WHO guidelines in both drug choice and dosing, it was not possible to conduct a meaningful comparison with this subgroup. As a single-center study, the findings may not be generalizable to other settings in Ethiopia or neighboring countries. Finally, the relatively small number of deaths may have reduced the statistical power to detect significant differences in mortality between groups. Despite these limitations, this study has several important strengths. First, it provides data from a geographically underrepresented region of Ethiopia, where pneumonia-related mortality is high and evidence on antibiotic adherence and antimicrobial resistance is limited. Second, our sample size is larger than in previous analyses on this topic, allowing for the use of adjusted models to better account for potential confounding. Third, the study addresses clinically relevant and practical challenges in the management of severe childhood pneumonia, with potential to inform clinical practice, guide future research, and improve patient care in similar settings.

CONCLUSION

Adherence to WHO guidelines for the treatment of severe pneumonia was suboptimal, particularly with regard to gentamicin and ampicillin dosing. Future studies should critically evaluate whether gentamicin is truly necessary for all children with severe pneumonia and explore the barriers that contribute to low-dose prescribing. Adherence to WHO guidelines, without accounting for dosing accuracy, was associated with a longer duration of oxygen therapy. However, this finding should be interpreted with caution due to limitations in study design and the high proportion of subtherapeutic dosing, which may have influenced outcomes. These findings underscore the need for improved antibiotic stewardship and context-specific implementation of treatment guidelines in Ethiopia. Strengthening stewardship is critical to optimize outcomes and preserve the effectiveness of first-line Access antibiotics amid rising resistance.

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Availability of data and material: Data available upon reasonable request.

Authors' contributions: ALV and EH conceptualized and designed the study. ALV designed the data collection instruments. EF and MAC collected data. ALV was responsible for the analysis and interpretation of data. ALV drafted the manuscript. CA, AP, EH performed a critical revision of the manuscript and gave a significant contribution in their field of expertise. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Ethics approval: This study was conducted in accordance with the ethical principles of the Declaration of Helsinki, as revised in October 2024. The Ethical Committee of St. Luke catholic Hospital and College of Nursing and Midwifery approved the study (reference number 1238/2025), which included a waiver of informed consent because of the retrospective nature of the investigation.

Declaration of competing interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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TABLES AND FIGURES

Table 1: Sample characteristics divided by sex and total sample.

	F (n = 170)		M (n = 257)		TOT (n = 427)	p-value
	NoM	N (%)	NoM	N (%)		
Baseline characteristics						
Age in months, mean (SD)	170	15.1 (13.1)	257	16 (13.3)	15.7 (13.2)	0.5
Comorbidity	170	20 (11.8)	257	34 (13.2)	54 (12.65)	0.7
Referred from other Hospital	170	22 (12.9)	257	31 (12.1)	53 (12.4)	0.8
HIV exposed at birth	48	4 (8.3)	55	1 (1.8)	5 (4.8)	0.2
Clinical characteristics						
Severe respiratory distress	170	137 (80.6)	257	194 (75.5)	331 (77.5)	0.2
Central cyanosis or SpO ₂ < 90%	170	118 (69.4)	257	195 (75.9)	313 (73.3)	0.1
Inability to drink	170	48 (28.2)	257	61 (23.7)	109 (25.5)	0.3
Persistent vomiting	170	20 (11.8)	257	25 (9.7)	45 (10.5)	0.5
Severe acute malnutrition	170	12 (7.1)	257	11 (4.3)	23 (5.4)	0.2
Stridor in a calm child	170	9 (5.3)	257	10 (3.9)	19 (4.45)	0.5
Lethargy or unconsciousness	170	3 (1.8)	257	3 (1.2)	6 (1.4)	0.6
Convulsions	170	1 (0.6)	257	5 (1.9)	6 (1.4)	0.2
No WHO severe defining symptoms	170	13 (7.6)	257	9 (3.5)	22 (5.15)	0.06
Therapy and outcome						
WHO-adherent therapy*	170	88 (51.8)	257	142 (55.3)	197 (46.1)	0.5
Improved	170	160 (94.1)	257	240 (93.1)	400 (93.7)	1
Referred to other Hospital	170	4 (2.4)	257	8 (3.1)	12 (2.8)	
Self-discharge	170	2 (1.2)	257	4 (1.6)	6 (1.4)	
Deaths	170	4 (2.4)	257	5 (1.9)	9 (2.1)	0.7
Treatment failure [#]	170	21 (12.4)	257	24 (9.3)	45 (10.5)	0.3
Oxygen therapy	170	117 (68.8)	257	201 (78.2)	318 (74.5)	0.03
Oxygen days, mean (SD)	117	2.8 (2.6)	201	2.6 (2.8)	2.7 (2.7)	0.7
Hospitalization days, mean (SD)	170	6.2 (3.9)	257	6 (3.1)	6.1 (3.4)	0.6
Blood test results						
Hb in g/dl, mean (SD)	159	11.3 (1.6)	245	11.2 (1.7)	11.2 (1.6)	0.4
WBC/mm ³ , mean (SD)	159	13932.6 (7168.7)	245	13996.3 (6600.6)	14445 (12019)	0.9
PTL/mm ³ , mean (SD)	159	407094 (165937.5)	244	405508.2 (1735305.7)	406133 (171463)	0.9
Malaria blood film positive	81	2 (2.5)	108	3 (2.8)	5 (2.6)	1

* First-line antibiotics as per WHO guidelines (ampicillin or benzylpenicillin + gentamicin), regardless of dose

[#] Failure was defined as a switch in antibiotic regimen occurring ≥48 hours after treatment initiation.

Abbreviations:

Hb, Haemoglobin

HIV, Human Immunodeficiency Virus

NoM, Number of measurements

PTL, Platelet Count

SD, Standard Deviation

SpO₂, Saturation of Oxygen

WBC, White cells blood count

WHO, World Health Organization

Table 2: First-line antibiotic treatments used.

Antibiotic schemes	Frequency (percentage)
Ampicillin + Gentamicin	196 (45.9)
Ceftriaxone alone	167 (39.1)
Ampicillin alone	43 (10.1)
Ampicillin+ Azithromycin	6 (1.4)
Ceftriaxone + Azithromycin	4 (0.9)
Ceftriaxone + Gentamicin	4 (0.9)
Ceftriaxone + Vancomycin	2 (0.5)
Amoxicillin alone	2 (0.5)
Azithromycin	2 (0.5)
Ceftriaxone + Metronidazole	1 (0.2)

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Table 3: Baseline, clinical characteristics, and outcomes by adherence to the revised WHO guidelines. Adherence was defined as first-line antibiotics according to WHO (ampicillin or benzylpenicillin + gentamicin), regardless of dose.

	Therapy not adherent (n = 231)		Therapy adherent (n = 196)		p-value
	NoM	N (%)	NoM	N (%)	
Baseline characteristics					
Female sex	231	89 (38.5)	196	81 (41.3)	0.5
Age in months, mean (SD)	231	19.1 (14.3)	196	11.5 (10.5)	<0.001
Comorbidity	231	29 (12.6)	196	25 (12.8)	1
Referred from other Hospital	231	30 (13.0)	196	23 (11.7)	0.7
HIV exposed at birth	50	2 (4)	53	3 (5.7)	0.7
Clinical characteristics					
Severe respiratory distress	231	174 (75.3)	196	157 (80.1)	0.2
Central cyanosis or SpO ₂ < 90%	231	172 (74.5)	196	141 (71.9)	0.5
Inability to drink	231	62 (26.8)	196	47 (24.0)	0.5
Persistent vomiting	231	26 (11.3)	196	19 (9.7)	0.6
Severe acute malnutrition	231	5 (2.2)	196	18 (9.2)	0.001
Stridor in a calm child	231	7 (3.0)	196	12 (6.1)	0.1
Convulsions	231	3 (1.3)	196	3 (1.5)	0.8
Lethargy or unconsciousness	231	5 (2.2)	196	1 (0.5)	0.1
No WHO severe defining symptoms	231	11 (4.8)	196	11 (5.6)	0.7
Outcome					
Improved	231	217 (93.9)	196	183 (93.4)	0.8
Referred to other Hospital	231	5 (2.2)	196	7 (3.6)	
Self-discharge	231	4 (1.7)	196	2 (1.0)	
Deaths	231	5 (2.2)	196	4 (2.0)	1
Treatment failure*	231	17 (7.4)	196	28 (14.3)	0.02
Oxygen therapy	231	173 (74.9)	196	145 (74.0)	0.8
Oxygen days, mean (SD)	273	2.2 (1.6)	145	3.2 (3.6)	0.002
Hospitalization days, mean (SD)	231	5.6 (2.8)	196	6.5 (4.0)	0.009
Blood test results					
Hb in g/dl, mean (SD)	222	11.3 (1.7)	182	11.2 (1.6)	0.5
WBC/mmc, mean (SD)	222	13834.9 (7318.4)	182	14137.5 (6176.5)	0.7
PTL/mmc, mean (SD)	221	392162.9 (167872.1)	182	423098.9 (174687.9)	0.07
Malaria blood film positive	111	3 (2.7)	79	2 (2.6)	1

* First-line antibiotics as per WHO guidelines (ampicillin or benzylpenicillin + gentamicin), regardless of dose.

Abbreviations:

Hb, Haemoglobin

HIV, Human Immunodeficiency Virus

NoM, Number of measurements

PTL, Platelet Count

SD, Standard Deviation

SpO₂, Saturation of Oxygen

WBC, White cells blood count

WHO, World Health Organization

Table 4: Association between treatment failure (dependent variable) and adherence to WHO guidelines using a multivariate regression model. Failure was defined as a switch in antibiotic regimen occurring ≥ 48 hours after treatment initiation.

Independent variables	OR	95% CI	p-value
Adherence to WHO guidelines*	1.9	0.9-3.8	0.08
Age in months	1.0	1.0-1.0	0.5
Severe malnutrition	3.5	1.2-9.0	0.01
Stridor in a calm child	3.3	1.0-9.8	0.03
Severe respiratory distress	3.2	1.2-11.1	0.03

* First-line antibiotics as per WHO guidelines (ampicillin or benzylpenicillin + gentamicin), regardless of dose.

CI, confidence interval

OR, odds ratio

WHO, World Health Organization

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Table 5: Association between oxygen therapy duration and hospitalization in days (dependent variables) and adherence to WHO guidelines using multivariate linear regression analyses.

Dependent variable: oxygen therapy duration in days				
Independent variables	Beta-Estimates	SE	95% CI	p-value
Adherence to WHO guidelines*	0.7	0.3	0.1-1.3	0.02
Age in months	-0.01	0.01	-0.03--0.01	0.4
Severe acute malnutrition	3.4	0.7	2.0-4.8	<0.001
Stridor in a calm child	-0.3	0.6	-1.5-1.0	0.7
Severe respiratory distress	0.7	0.4	0.05-1.5	0.04
Dependent variable: hospitalization in days				
Adherence to WHO guidelines*	0.5	0.3	-0.16-1.12	0.1
Age in months	-0.0	0.01	-0.02-0.02	0.7
Severe acute malnutrition	5.6	0.7	4.3-7.0	<0.001
Stridor in a calm child	-0.5	0.8	-2.0-0.9	0.5
Severe respiratory distress	0.2	0.4	-0.5-0.9	0.6

* First-line antibiotics as per WHO guidelines (ampicillin or benzylpenicillin + gentamicin), regardless of dose.

CI, confidence interval

SE, standard error

WHO, World Health Organization

Declaration of Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

WHO Guideline Adherence and AWaRe Antibiotic Use in Severe Childhood Pneumonia in Ethiopia: Associations with Treatment Outcomes

Background

- WHO recommends AMP/PenG + GM for severe pneumonia (ages 2–59 months)
- Real-world adherence to these guidelines remains limited
- The WHO AWaRe classification categorizes antibiotics based on recommended use

Methods



INCLUSION CRITERIA

- Children (aged 2–59 months)
- Diagnosed with severe pneumonia
- St. Luke Hospital, Woliso, Ethiopia
- May 2021 - April 2024

EXCLUSION CRITERIA

- HIV infection
- On antibiotics for another illness
- Other severe bacterial infection



ADHERENCE DEFINITION: based on drug selection alone (AMP/PenG + GM)



OUTCOMES

- mortality
- combined outcome (referral, self-discharge, death)
- length of hospital stay
- need for and duration of O₂
- treatment failure (switch of antibiotics \geq 48h after starting)

Results



441 children diagnosed with severe pneumonia → 14 excluded

427 included, 39.8% female, mean age of 15.7 ± 13.2 months



- 46.1% received guideline-adherent treatment (drug selection only)
- GM underdosed in 94.5% of cases
- AMP underdosed in 62.4% of cases
- 43.6% received at least one Watch antibiotic (mostly ceftriaxone)



- Adherence was associated with longer O₂ (+0.7 days, 95% CI 0.1–1.3)
- No association with other outcomes

Conclusions

Adherence to WHO guidelines was low, especially regarding dosing, highlighting the need for stronger antimicrobial stewardship and better guideline implementation in Ethiopia

AMP: ampicillin; AWaRe: Access, Watch, and Reserve; GM: gentamicin; HIV: human immunodeficiency viruses; O₂: oxygen therapy; PenG: benzylpenicillin;
WHO: World Health Organization

