Antimicrobial Use Practice and Associated Factors among Hospitalized Adult Patient at Tikur Anbessa Specialized Hospital: Pave the way for Antimicrobial Stewardship.

By: Habtamu Gugsa

A Thesis Submitted to the Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University in Partial Fulfillment of the Requirements for the Degree of Master of Pharmacy in Pharmacy Practice.

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Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Habtamu Gugsa, entitled with "Antimicrobial Use Practice and Associated Factors among Hospitalized Adult Patient at Tikur Anbessa Specialized Hospital:- Pave the way for Antimicrobial Stewardship, Addis Ababa, Ethiopia: Prospective Observational study" and submitted in partial fulfillment of the requirements for Degree of Master of Sciences in Clinical Pharmacy complies with the regulation of the university and meets the accepted standards with respect to originality and quality.

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Abstract

Background: Antibiotic use is frequent in the inpatient context, and approximately 50% of admitted patients receive at least one antibiotic during their hospital stay. Antimicrobials are frequently provided inappropriately to 44–97% of hospitalized patients in developing countries.

Objective: The objective of this study was to assess antimicrobial use practices and associated factors among hospitalized adult patients at Tikur Anbessa Specialized Hospital (internal medicine, surgery, and gynecology/obstetrics wards), Addis Ababa, Ethiopia.

Method: A hospital-based prospective observational study was conducted from September to December 2022. A total of 354 participants were recruited for this study. A semi-structured questionnaire was used to collect the data from medical records and patient interviews. The collected data were entered to SPSS version 26.0 for analysis. Descriptive statistics and logistic regression were used for statistical analysis.

Result: Antibiotic use in 144 (45.7%) patients was considered inappropriate with category IIIA (long duration) being was the most common type of inappropriateness, accounting for 99 (68.7%). According to Define Daily Dose (DDD) measures the total antibiotic consumed per 100 patients per day was 4.71 DDD and based on the WHO antibiotic AWaRe stratification, 298 (62.8%) antibiotics were consumed from the "Watch" and "Reserve" groups**.** Patients whose age between 25 to 34 years were protective to inappropriate antibiotic use practice (AOR=0.24, 95% CI:(0.06–0.89), P = 0.03), marital status of divorced (AOR=5.68, 95% CI:(1.6–19.3),P=0.001) and widowed (AOR=8.91,95%CI:(1.51–52.6),P=0.01), patents who were admitted at internal medicine (AOR=3.53, 95% CI:(1.04-11.9), P=0.04) and surgical ward (AOR=10.8, 95% CI:(3.59–32.9), P=0.001) and patients who were hospitalized for 8 to 14 days (AOR=7.0, 95% CI:(1.59–182.5), P=0.01), for 15 to 21 days (AOR=11.0, 95% CI:(1.2–100.8), P=0.03) and above 22 days (AOR=10.9,95%CI:(1.17–103.0),P=0.03) were determinants of inappropriate antibiotic usage.

Conclusion: Generally, higher consumption and inappropriate antibiotic use were observed among hospitalized adult patients in the study area and need prompt antimicrobial stewardship interventions and stewardship program improvement in the study wards of the Hospital.

Keywords: antimicrobial, stewardship, appropriateness, defined daily dose, Tikur Anbessa Specialized Hospital, Ethiopia.

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List of Acronyms and Abbreviation.

ADE: Adverse Drug Event.

AMR: Antimicrobial Resistance.

AMS: Antimicrobial Stewardship.

AMSP: Antimicrobial Stewardship Programs.

AOR: Adjusted Odd Ratio.

CAP: Community Acquired Pneumonia.

CDC: Centers for Disease Control and Prevention.

CI: Confidence interval.

COR: Crude Odd Ratio.

CSF: Cerebral Spinal Fluid.

DDD: Define Daily Dose.

DOT: Day of Therapy.

GYN/OBS: Gynecology/ Obstetric.

HAI: Hospital Acquired Infections.

HAP: Hospital Acquired Pneumonia.

ICU: Intensive Care Unit.

IDSA: Infectious Diseases Society of America.

IV: Intra Venous.

LMIC: Low- and Middle-Income countries.

MDR: Multi-Drug Resistance.

SAP: Surgical Antimicrobial Prophylaxis.

SSI: Surgical Site Infections.

TASH: Tikur Anbessa Specialized Hospital.

WHO: World Health Organisation.

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1. Background.

1.1. Introduction.

Among all medications, antimicrobials are the most frequently used and misused. Antimicrobial drugs have been widely employed as empirical therapy, definitive therapy, and preventive therapy for the past 50 years [1, 2]. Appropriate antibiotic use means that the patients receive the appropriate drug at the right time with adequate doses and duration for a susceptible pathogen to meet their individual requirements [3]. Antibiotic use is frequent in the inpatient context, and approximately 50% of admitted patients receive at least one antibiotic during their hospital stay. About 20% to 30% of inpatient days of antibiotic therapy are deemed inappropriate [1].

Antimicrobial use in surgical procedures, including gynecologic and obstetric surgeries, is a widely used practice to reduce post-surgical complications [4, 5]. All types of surgeries benefit from surgical antimicrobial prophylaxis (SAP), which is recommended for all clean-contaminated, contaminated, and dirty wounds. Giving the appropriate antimicrobial agent in an adequate dose, timing preoperative prophylaxis appropriately, and maintaining drug levels during the procedure are crucial components of SAP administration [4]. Antibiotic prophylaxis errors are frequent in surgical, obstetrical, and gynecological settings. The typical error in prophylactic antibiotic usage was improper choice, wrong timing, and inappropriate SAP length. Prophylactic antibiotics were given to about 30–50% of surgical patients, and 30–90% of those prescriptions were incorrect. [5].

Uncertainty regarding the differential diagnosis, complicated co-morbidities, a lack of expertise and training, ignorance of local epidemiology and antimicrobial resistance, and incorrect interpretation of microbiological results are some of the causes of inappropriate use of antibiotics. [6, 7]. Various strategies have been used to protect priceless antibiotics from the threat of bacterial resistance. Implementing antimicrobial stewardship (AMS) is one possible strategy to lessen the harmful effects associated with antibiotic use [8]. "The careful and responsible management of something entrusted to one's care" is the definition of stewardship. It was originally applied in the health-care setting as a tool for optimizing antimicrobial use, termed “antimicrobial stewardship”. AMS refers to systematic interventions that are initiated to develop and establish the optimal use of antimicrobials. The primary goals of AMS are optimizing antibiotic use, improving patients' clinical outcomes, reducing antibiotic toxicity or side effects of unnecessary medication, decreasing healthcare expenses, and reducing the overall load of antibiotic resistance [7, 9].

A number of prerequisites must be met for AMS initiatives to be implemented successfully, including sufficient human resources and multidisciplinary participation. Core AMS team members often include an infectious disease physician, a medical microbiologist, and a clinical pharmacist [10, 11].

1.2. Statement of the problem.

Improper antimicrobial use, inadequate diagnosis tests, and failure to finish a treatment course all contribute to an increase in the frequency of antimicrobial resistance (AMR) and other negative effects, especially in developing countries [12, 13]. According to estimates from the World Health Organization (WHO), between 20 and 50% of antibiotics are administered improperly in the community worldwide, about 30.0% of them were used inappropriately. Antimicrobials are frequently provided inappropriately to 44–97% of hospitalized patients in impoverished nations [3]. The prevalence of inappropriate use of antibiotics reported by different countries varied widely. Inappropriate antibiotics use is about 88.8% in Tanzania, 50% in Sudan, 7.9% in Zambia, 58.3% in Nigeria, and 12.5% in Ghana. Poor clinical outcomes, increased hospital length of stay, and increased antimicrobial resistance infection all result from the inappropriate use of antibiotics. AMR infections cause about 700,000 deaths annually, and if nothing is done, that number could rise to 10 million by the year 2050 [14, 15, 16]. In 2017, 10,149 SSIs were reported as complications of 648,512 surgical procedures in 13 European countries. According to the European Centre for Disease Prevention and Control (CDC), 16,049 deaths per year were attributed to SSIs in 2011–2012 [17].

The situation in Ethiopia is not different from the rest of the world, if not worse. Over the past few years, Ethiopia has experienced a noticeable worsening of the antimicrobial resistance issue. An assessment conducted by the Food, Medicine, and Healthcare Administration and Control Authority of Ethiopia showed that inappropriate usage of antibiotics has increased in addition to greater use.[18] And there was no study on antimicrobial use measurement at Tikur Anbessa Specialized Hospital that used both qualitative and quantitative assessment methodologies.

1.3. Significant of the study.

By promoting proper antimicrobial therapy and improving patient clinical outcomes, AMS contributes significantly to current attempts to reduce the harmful effects of antimicrobial use and improve patient care [8]. According to the CDC, monitoring the use of antibiotics in hospitals is essential for identifying prescribing trends, spotting problem regions, and initiating interventions [6]. Additionally, each hospital in Ethiopia should plan the frequency of antimicrobial use surveillance operations at least once a year, according to the AMS practical guidance for hospitals [19]. In order to improve appropriate antimicrobial use and optimize clinical outcomes, it is crucial to analyze and manage the problem of inappropriate antibiotic use.

Therefore, this study measures antimicrobial use practices in the study area in terms of both quality and quantity. The findings of the study will strengthen the appropriateness of antibiotic use, show the current scope of antimicrobial use practice, and provide information about factors associated with antimicrobial use practice in the study area. Additionally, generate valuable data for researchers, antimicrobial stewardship policymakers, the antimicrobial stewardship team of the facility, and health professionals on the appropriate antibiotic use, factors to monitor, evaluate, identify, and which core elements are already in place, the level of implementation, what requires accelerated implementation, and what is missing from the implantation of AMS core elements.

2. Literature review.

The purpose of this chapter is to critically evaluate the available research on the appropriateness of antimicrobial use practices. The literature search was conducted using the electronic databases PubMed, Google Scholar, and the Cochrane Library. Key search terms included 'appropriate antimicrobial', 'appropriateness of antimicrobial, and "antimicrobial use practice'. Studies written in English, not older than ten years, and those based on hospital settings were considered for inclusion in this literature review.

2.1. Appropriateness of antimicrobial use.

Demssie Ayalew et al. conducted a hospital-based prospective follow-up study at the University of Gondar Comprehensive Specialized Hospital in Ethiopia to evaluate the appropriateness of antibiotic use and associated characteristics among hospitalized patients. A total of 664 antibiotics were prescribed for 303 patients. The most common antibiotics prescribed were ceftriaxone + Vancomycin +ampicillin + cotrimoxazole + fluconazole 86 (28.38%). Of all patients, 53 (17.5%) and 250 (82.5%) received empirical antibiotics without culture results simply by clinical evaluation and laboratory investigation, respectively, according to the national guideline. And 167 (55.1%) of patients received antibiotics with an adjusted dose and dosing interval based on renal function, and 82 (27.1%) of patients switched from IV to oral therapy. Only 26 (8.6%) of the patients were receiving the proper antibiotics, according to the current finding [3].

Retrospective cross-sectional research by Getachew Moges et al. at the surgical ward of the Borumeda hospital in north Ethiopia Dessie assessment of antimicrobial prophylaxis and identification of associated risk variables revealed that: Prophylaxis was administered to 188 (82.8%) surgical cases. The most often given antibiotic was ceftriaxone in both preoperative 79 (68.7%) and postoperative 104 (67.5%) prophylaxes. SAP was recommended for 151 (66.5%) patients. One hundred seventy-four (78.4%) of the procedures had appropriate indications. In each case, the time of administration of the initial preoperative dose was absent. Of the patients who received postoperative prophylaxis, 76 (66.7%) received their prophylaxis within 24 hours after surgery [4].

In order to determine the prevalence of SSIs and SAP practice in western Ethiopia, Belayneh Kefale et al. conducted a retrospective cross-sectional study design. Determining the gap in prophylactic surgical antibiotic use among surgically operated patients at Finote Selam General

Hospital revealed that SAP was administered to more than three-fourths of patients (88.6%). Ceftriaxone, metronidazole (45.4%), and ceftriaxone (33.3%) were the most frequently used prophylactic antibiotics. When to use preventative antibiotics before 30 minutes after the incision, 40.6% of antibiotic prophylaxis was administered, while 82.8% of them were given between 30 minutes to 1 hour before the incision and 48 hours' duration of SAP. Of the prescribed antibiotics, 7.2% were inappropriate, and 5.4% of their dosage was inappropriate [5].

Another retrospective analysis conducted in South Africa by Valencia Tamzyn Jacob to investigate the appropriateness of antimicrobial use revealed that 466 patients were hospitalized and 779 antimicrobials were prescribed. 305 (46.2%) of the 660 antimicrobials administered for empiric treatment were adequately prescribed based on medication selection, dosage, and duration. Of the 38 targeted antimicrobials, 36 (94.7%) were prescribed according to the proper dose, and 33 (86.8%) were prescribed according to the correct duration. Only 32 (39.5%) of the 81 antimicrobials administered for postoperative prophylaxis met the criteria for appropriateness in terms of medication choice, dose, and duration [7].

An institution-based prospective observational study was performed in the internal medicine wards of Tikur Anbessa Specialized Hospital, Ethiopia, by Getachew Alemkere et al. to assess the antibiotic use practice and identify predictors of hospital outcome. The results showed that cephalosporin was the most widely prescribed class of drug in all the wards. There was high mortality among patients with systemic bacterial infections in the hospital: 27.13% in the wards and 58.5% in the ICU [8].

A prospective cross-sectional study was conducted by Sileshi et al. to evaluate the appropriateness of ceftriaxone utilization in the medical and emergency wards of Tikur Anbessa Specialized Hospital, Ethiopia, and showed that ceftriaxone prescription rates were found to be very high (58% prevalence). Ceftriaxone use was empiric in 274 (87.3%) cases. Most of the time, ceftriaxone was used inappropriately (87.9%), the greatest proportion of which was attributed to the inappropriate frequency of administration (80.3%), followed by the absence of a culture and sensitivity test (53.2%) [18].

Mohammed Aman and colleagues conducted a cross-sectional study to determine the level of inappropriate antibiotic use among inpatients at Madda Walabu University Goba Referral Hospital in southeast Ethiopia. The results revealed that, for a total of 471 inpatients, 801 antibiotics were prescribed. The three antimicrobials that were most frequently prescribed were cephalosporin, nitroimidazoles, and macrolides, with ceftriaxone being prescribed in 249 (53% of cases), nitroimidazoles in 115 (24.5%), and metronidazole in 123 (26.2%). Of these, 70.0% had received a prescription for a medicine and dosage (dose, frequency, and duration) that were appropriate; however, 142 (30.0%) had received a prescription for the incorrect drug, 56 (12%), the incorrect dosage, 86 (18%), or both [20].

Ina Willemsen et al.'s study to assess the appropriateness of antibiotic therapy at the Amphia hospital in the Netherlands revealed that, of the 938 patients overall, 351 (37.5%) were on antibiotics, and antibiotic therapy was ruled inappropriate in these individuals. More specifically, in 123 patients (13.0%), antimicrobial therapy was unjustified; in 140 patients (14.9%), an incorrect choice was made; and in 88 patients (9.4%), the correct antibiotic was used but it was used incorrectly [21].

A prospective observational study conducted in the internal medicine wards of Tikur Anbessa Specialized Hospital Ethiopia by Theodros Fenta et al. to assess the current practice of antimicrobial utilization and clinical outcomes in the management of adult pneumonia showed that, out of 200 enrolled patients, the treatment approach in almost all patients (99.5%) was empirical and no de-escalation therapy was made even after acquiring culture results. The total duration of antimicrobial therapy was 12.055.09 days. Patients' outcomes were found to be stable (66%), in-hospital mortality (18.5%), and complications (17%) [22].

A cross-sectional point prevalence survey conducted by H. Akhloufi et al. in a Dutch university hospital to determine the prevalence of inappropriate antibiotic use showed that, overall, 90 (29.3%) of the 307 prescribed antibiotics were deemed to be inappropriate antimicrobial drug therapy. More specifically, for 48 (15.6%) prescriptions, there was no indication for antimicrobial therapy, and 25 (8.1%) were an incorrect choice of antibiotic for which a more effective, less toxic, or less expensive alternative agent was available [23].

In a retrospective analysis of antimicrobial prophylaxis and therapy at a university hospital in Switzerland, Alexia Cusini et al. found that 37.0% of the 1270 prescriptions given to 1577 patients—of whom 700 (44.4%) had antimicrobials—were inappropriate. Of these, 958 (75.4%) were for prophylaxis, and 312 (24.6%) were for therapy. The most prevalent traits of ineffective therapies were: lack of an indication (17.5%); improper antimicrobial selection (7.6%); improper medication application (9.3%); and departure from institutional recommendations (8%) [24].

Asnakew Achaw Ayele et al. used a prospective, cross-sectional study to assess the appropriateness of ceftriaxone use in the medical and emergency departments at Gondar University Referral Hospital in Ethiopia. Ceftriaxone was found to be widely used, with a point prevalence of 59%. Ceftriaxone was administered empirically in 79.5% of the instances. More than two-thirds (80.2%) of ceftriaxone use were determined to be improper, with the bulk of unjustified ceftriaxone use resulting from insufficient frequency of administration (78.3%), the absence of a culture and sensitivity test (68.7%), and the length of therapy (47%) [25].

Teklu Gebrehiwot Gebremichael et al. conducted a prospective cross-sectional study on patients who received ceftazidime to assess the appropriateness of ceftazidime use at Ayder Compressive Specialized Teaching Hospital, Mekelle, Ethiopia, and found that 2,084 (70.8%) cases of ceftazidime use were appropriate. Appropriateness of indication was 295 (90.2%), efficacy of ceftazidime usage was 221 (67.6%), appropriate dose of ceftazidime use was 264 (80.4%), and appropriate frequency of ceftazidime use was 230 (70.3%). It was used empirically in 275 people (84.1%) and specifically in 52 (15.9%) [26].

Frehiwot Amare et al. conducted a retrospective cross-sectional study at four government hospitals in Harar town, Ethiopia, to assess the appropriateness of ceftriaxone use. According to the findings, a total of 71 medications were co-administered with ceftriaxone, with metronidazole being the most commonly used, followed by tramadol. According to the findings of the ceftriaxone use evaluation, the majority of 190 (70.1%) were judged to be inappropriate. The incorrect use was caused mostly by the improper indication (indications for which ceftriaxone was not the first-line therapy): 114 (60.0%), followed by the wrong duration: 54 (28.4%) [27].

Rafida Sofi Kamila et al. did a cross-sectional, analytical investigation in Indonesia to determine the proper antibiotic use in patients with community-acquired pneumonia. The results revealed that levofloxacin (28.9%), ceftriaxone (56.7%), ceftazidime (7.8%), meropenem (3.3%), cefixime (1.1%), cefotaxime (1.1%), and azithromycin (1.1%) were the other common antibiotics used for CAP. In 77 prescriptions, the use of antibiotics was deemed suitable (85.6%), while 13 prescriptions were deemed improper (14.4%). Category IIIB (shortened duration) errors made up the majority of errors (11.1%). Five of ninety patients (5.6%) underwent the 30-day readmission period, and one prescription (1.1%) was classified as category IVA (alternating agent is more effective) and two prescriptions (2.2%) as category VI (incomplete medical record) [28].

A hospital-based prospective observational study conducted in Ethiopia at Jimma University Medical Center by Gosaye M. et al. to assess antibiotic use-related problems and their costs among patients hospitalized at the surgical ward indicated that, among 300 participants, antibiotic use-related problems were found in 69.3% of the study participants. Of which 80.28% were surgical antibiotic prophylaxis use-related problems and 52.2% were related to therapeutic antibiotic use. Dose too low was the top ranking of antibiotic use-related problems (32.9%), followed by dose too high (20.7%) [29].

According to Lawless et al.'s single-center retrospective cross-sectional study, which evaluated prescribing practices, adherence to guidelines, and outcomes for patients admitted with CAP, the most frequent prescribing error among 381 patients with low-risk CAP was overusing ceftriaxone. The most frequent mistakes in high-risk CAP were the underdosing of ceftriaxone and failing to provide atypical coverage with azithromycin. In total, 80% of patients were thought to have received improper antibiotic prescriptions. There was no impact on mortality [30].

A Multihospital Cohort Study conducted in the Michigan Hospital Medicine Safety Consortium by Valerie M. et al. to examine predictors and outcomes associated with excess duration of antibiotic treatment showed that, among 6481 general care medical patients with pneumonia, two thirds (67.8% [4391 of 6481]) received excess antibiotic therapy over the shortest effective duration consistent with guidelines (71.8% [3410 of 4747] for CAP and 56.6% [981 of 1734] for HAP). Antibiotics prescribed at discharge accounted for 93.2% of excess duration [31].

Observational research undertaken by Saleem et al. in Lahore, Pakistan, to analyze antibiotic use revealed that 1185 patients were given a total of 2022 medications. Approximately two-thirds of the study population (70.3%) had at least one inappropriate antibiotic administered out of the total prescribed. Overall, 27.2% of patients developed respiratory tract infections, and 62.8% of these received incorrect treatment. Cephalosporin was often prescribed to patients, yet in many situations (67.2%), it was unnecessary. Penicillin was provided to 283 individuals, 201 (71.0%) of whom were given the improper indication, dosage, or both [32].

Additionally, the other retrospective study conducted by Hye-In Kim et al. in Daegu, Korea, among 91 patients to evaluate the efficacy of empiric antibiotic therapy for nosocomial meningitis revealed that extended-spectrum beta-lactam antibiotics plus vancomycin were the most frequently prescribed empirical antibiotics (35/91, 38.6%). 10 (37%) of the 27 patients with cultivated Acinetobacter in their CSF received the incorrect empirical antibiotic therapy. Mortality among the 91 patients was 16.5%, with seven of the 27 patients (or 26.9%) who had cultured Acinetobacter passing away [33].

Tadele Mekuriya's prospective observational study to assess the inappropriateness of antimicrobial use and the associated factors among patients admitted to three hospitals in southwest Ethiopia revealed that a total of 348 antimicrobial-containing orders were prescribed for the 291 patients. Most (80.1%) of the patients had at least one antibiotic usage issue. The most common form of drug therapy problem was 'requires extra drug therapy," which was experienced by 91 (31.3%) of the patients, followed by 'dosage too low," which was experienced by 65 (22.4%) of the patients [34].

2.2. Antimicrobial Consumption.

Mera Ababneh et al. conducted a retrospective cross-sectional study in a 683-bed capacity tertiary care hospital in Northern Jordan to quantify antimicrobial use in the inpatient setting as part of antimicrobial stewardship program surveillance and found that carbapenem, glycopeptides, and piperacillin-tazobactam were the most commonly used antimicrobials in the inpatient setting in both measures DDD and DOT. Internal medicine wards had the greatest antibiotic prescription rate (49.8 DDD/100 admissions), followed by surgery wards (33.2 DDD/100 admissions) and intensive care units (20.6 DDD/100 admissions) [6].

A retrospective study was conducted to measure and compare the five-year antibiotic consumption trends of the two hospitals' medical wards using Defined Daily Dose per 100 bed days (DDD/100-BD) in Eretria Asmara by Nebyu Daniel et al. and showed that benzyl penicillin was the most consumed antibiotic in Hazhaz Zonal Referral Hospital and Orotta National Referral and Teaching Hospital throughout the study period at 87.8 DDD/100-BD and 35.4 DDD/100-BD, respectively. Ceftriaxone and ciprofloxacin were among the most commonly consumed antibiotics in both hospitals [35].

A retrospective study carried out by Eili Y. Klein et al. to identify how patterns of antibiotic consumption in each of the AWaRe categories changed across 76 countries showed that consumption of Watch antibiotics increased by 909%. The increase in Watch antibiotic consumption was greater in low- and middle-income countries (LMICs; 16.5%). The access-to-watch index decreased by 38.5% over the study period globally, with a 46.7% decrease in low- and middle-income countries and a 16.7% decrease in high-income countries, and 37 (90%) of 41 LMICs had a decrease in their relative access-to-watch consumption [36].

Xiaoyuan Qu et al. conducted a retrospective analysis to identify trends, pattern changes, and regional differences in antibiotic consumption in 151 public general tertiary hospitals across China and found that total antibiotic use decreased significantly (P = 0.018) from 75.86 DDD/100 patients in 2011 to 47.03 DDD/100 patients in 2014. Cephalosporin usage grew 6.56-fold from 1.31 DDD/100 patients in 2011 to 8.6 DDD/100 patients in 2014. Narrow-spectrum, broad-spectrum, and combinations with beta-lactamase inhibitor penicillin consumption decreased by 49.32%, 41.23%, and 11.90%, respectively [37].

Andrea Cona et al. conducted a prospective analysis to evaluate antimicrobial consumption and appropriateness one year after the implementation of an antimicrobial stewardship program in an internal medicine department in Milan, Italy, and found that during the "AMS phase," total antibiotic consumption decreased by 11.4% compared to the previous year (67.9 DDD/100 bed days vs. 79.4 DDD/100). Antibiotic usage was consistent during the "follow-up phase" (66.3 DDD/100). In terms of hospital mortality, there is no difference [38].

Tsegaye Melaku et al. conducted a hospital-based cross-sectional study to quantify the amount of antibiotic consumption in outpatient settings at Jimma Medical Centre, an Ethiopian tertiary-care teaching hospital. The overall dosage of antibiotics consumed per day was 5.31 DDD/100 outpatients. Ciprofloxacin was the most often given antibiotic [122 (21.12%)], with a DDD/100 outpatients per day value of 1.13, followed by amoxicillin [68 (11.76%)] with a DDD/100 outpatients per day value of 0.44, and azithromycin [61 (10.55%)] with a DDD/100 outpatients per day value of 0.51. Antibiotics in the "Watch" group had 2.10 DDD/100 outpatients per day on the antibiotic consumption index [39].

2.3. Contributing Factors of Inappropriate Antibiotics Usage and poor clinical outcome.

A hospital-based prospective follow-up study conducted at the University of Gondar Comprehensive Specialized Hospital in Ethiopia to assess the appropriateness of antibiotic use and associated factors among hospitalized patients by Demssie Ayalew et al. showed that patient gender, ethnicity, source of income, and patient belief in prescribed antibiotics were associated factors. Males have used antibiotics five times more appropriately than female patients [AOR = 5.00, 95% CI: 2.00–7.98]; patients who believe that the prescribed antibiotics prevent seriousness used antibiotics more appropriately than those who didn`t understand the use of antibiotics [AOR = 4.21, 95% CI: 1.33–7.35]. Patients who were merchants had 7.29 times more appropriate antibiotic use than patients who were on a monthly salary [AOR = 7.29, 95% CI: 1.34–9.58] [3].

Getachew A. et al. conducted an institution-based prospective observational study in the internal medicine wards of Tikur Anbessa Specialized Hospital, Ethiopia, to analyze antibiotic use practice and identify determinants of hospital outcome. Results showed that digestive disease (AOR = 6.94, 95% CI: 2.24, 21.49), different signs and symptoms of disease (AOR = 2.43, 95% CI: 1.30–4.56), sepsis (AOR = 2.59, 95% CI: 1.12–5.99), and vancomycin use (AOR = 2.60, 95% CI: 1.30–5.21) were independent positive predictors; antibiotic days (>10) (AOR = 0.37, 95% CI: 0.20-0.70) was a negative predictor of mortality [8].

A prospective cross-sectional study was conducted by Sileshi et al. to evaluate the appropriateness of ceftriaxone utilization in the medical and emergency wards of Tikur Anbessa Specialized Hospital, Ethiopia, and showed that the type of therapy with ceftriaxone was found to have a significant association with inappropriate utilization of this drug (p = 0.002) [18].

A prospective observational study was conducted in the internal medicine wards of Tikur Anbessa Specialized Hospital Ethiopia by Theodros Fenta et al. to assess the current practice of antimicrobial utilization and clinical outcomes in the management of adult pneumonia and showed that poor clinical outcome (death and complicated cases) was found to be associated with recent antimicrobial use history (AOR = 2.86, 95% CI: 1.33–6.13), P = 0.007), cancer (AOR = 3.46), and recent recurrent upper respiratory tract infection (AOR = 3.70, 95% CI: 1.02–13.40), P = 0.046) [22].

A prospective, cross-sectional study design was employed to evaluate the appropriateness of ceftriaxone use in the medical and emergency wards of Gondar University Referral Hospital in Northwest Ethiopia by Asnakew Achaw Ayele et al., which showed that factors that were associated with inappropriate use of ceftriaxone in the study population included comorbidity, days of hospital stay, and the presence of co-administered drugs with ceftriaxone. Empiric treatment with ceftriaxone (AOR = 22.57, 95% CI: [4.66-41.47]) and the presence of co-administered drugs (AOR = 4.12, 95% CI: [1.62-8.05]) were significantly associated with its inappropriate use [25].

A retrospective study design done by Hye-In Kim et al. in Daegu, Korea, among 91 patients to assess the adequacy of empiric antibiotic therapy for nosocomial meningitis indicated that seventy-eight patients (85.7%) had infections related to external ventricular drains (EVD). Of the 27 patients who had cultured Acinetobacter in CSF, seven of the 27 patients (26.9%) with cultured Acinetobacter died, and the overall mortality of the 91 patients was 16.5%. The presence of combined septic shock ($p = 0.001$; AOR = 108.4) and a persistent EVD state ($p = 0.021$; AOR = 11.9) was associated with a poor prognosis [33].

2.3. Conceptual Framework.

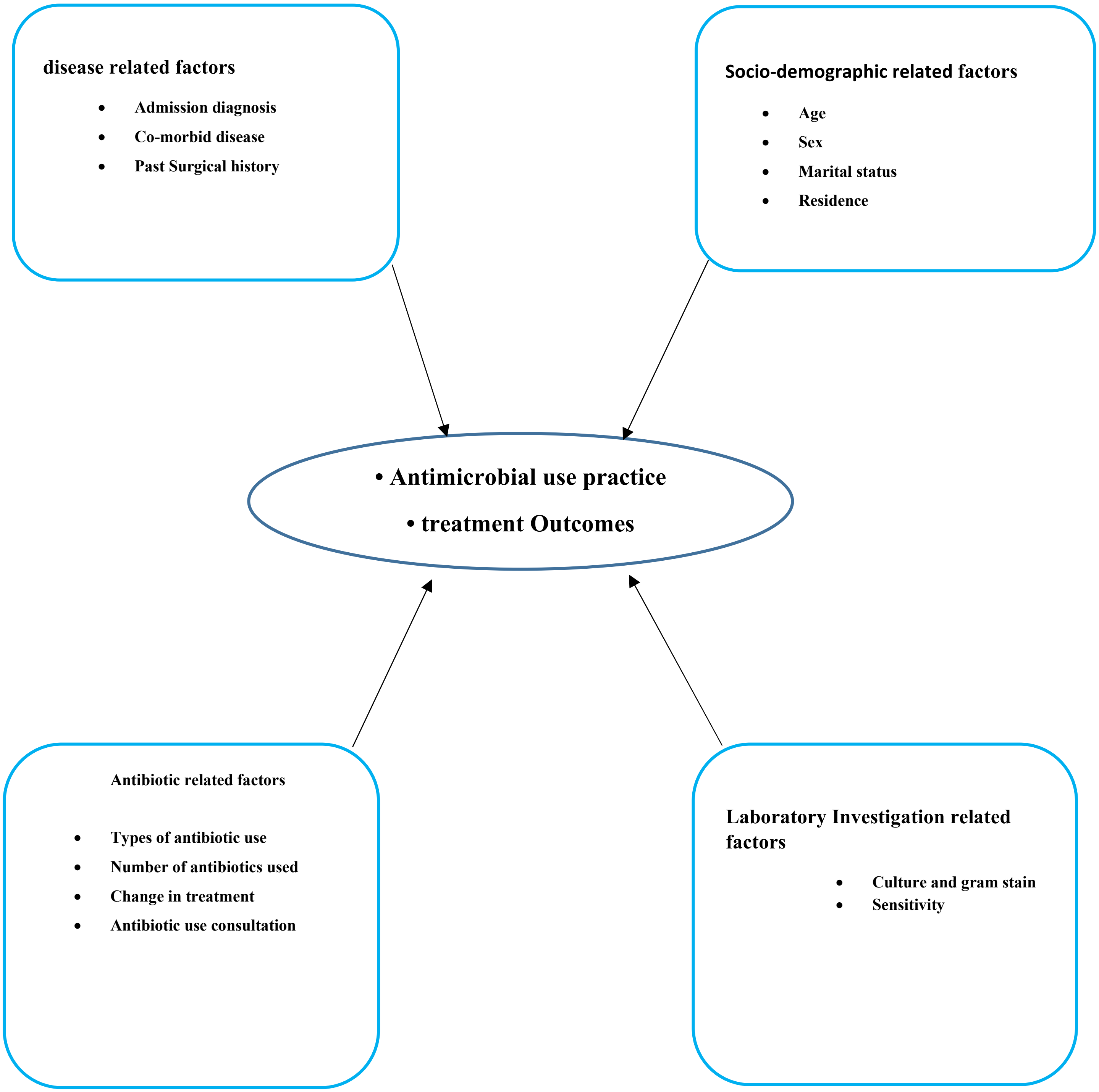


Figure 1: Conceptual frame work that shows the association between antimicrobial use practice and different independent variable of the study conducted at TASH, Addis Ababa, Ethiopia, September 1 – December 30, 2022 (n= 315).

3. Objectives.

3.1. General objective.

- To assess the antimicrobial use practice and its associated factors among hospitalized adult patients at the internal medicine, gynecology/obstetrics, and surgical wards of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

3.2. Specific objectives.

- To assess the antibiotic consumptions among hospitalized adult patients at the internal medicine, gynecology/obstetrics, and surgical wards of Tikur Anbessa Specialized Hospital.
- To assess the appropriateness of antibiotic use among hospitalized adults patients in the three wards of Tikur Anbessa Specialized Hospital.
- To assess the clinical outcomes among hospitalized adult patients at internal medicine, gynecology/obstetrics and surgical wards of Tikur Anbessa Specialized Hospital.
- To identify factors associated with inappropriate antibiotic use among hospitalized adult patients in the three wards of Tikur Anbessa Specialized Hospital.

3.3. Research Questions.

- What are the antibiotic consumptions based on the defined daily dose (DDD/100 patients per day) or Essential Medicine Lists "Access, Watch, and Reserve" classification of antibiotics among adult hospitalized patients in TASH?
- What is the prevalence of inappropriate antibiotic use among adult hospitalized patients in TAHS, Addis Ababa, Ethiopia, during the study period?
- What are the predictors for inappropriate antibiotic use among adult hospitalized patients in TASH, Addis Ababa, Ethiopia?

4. Methods.

4.1. Study Area and Period.

The study was conducted at Tikur Anbessa Specialized Referral Hospital (TASH) from September to December 2022 in Addis Ababa, Ethiopia. TASH is one of the tertiary hospitals in Ethiopia; it was established in 1972 G.C. and is the largest referral hospital in Ethiopia with more than 800 beds to provide tertiary medical, surgical, and gynecological/obstetrical care to 20,000 inpatients and 330,000 outpatients per year. In 1998, TASH was relocated to the teaching hospital of Addis Ababa University College of Health Science by the Federal Ministry of Health. TASH is now the main teaching hospital for both clinical and preclinical training in most disciplines. It is also an institution where specialized clinical services that are not available in other public or private institutions are rendered to the whole nation. TASH has 200 doctors, 379 nurses, 85 pharmacists, and 115 other health professionals dedicated to providing health care services. The hospital also has 950 permanent and contract administrative staff to support hospital activities. In addition, almost all regional and federal hospitals in Addis Ababa are affiliated with TASH as clinical services and training sites. It provides a variety of health care-related services in different departments and units. This study was conducted on internal medicine, surgery, and gynecology/obstetrics wards. These wards comprise 114, 26, and 14 beds, respectively, and 511 patients were admitted to the adult ward between December 2019 and May 2020 [40].

4.2. Study design.

Hospital -based prospective observational study design was used.

4.3. Source and study population.

4.3.1. Source population.

All adult patients admitted to internal medicine, gynecology/obstetrics, and surgical wards of Tikur Anbessa Specialized Hospital.

4.3.2. Study population.

All adult patients admitted to the internal medicine, gynecology/obstetrics, and surgical wards of Tikur Anbessa Specialized Hospital during the study period and those who fulfilled the inclusion criteria were included in this study.

4.4. Sample size determination.

The sample size was determined by using the single population proportion formula with the assumption that 30.1 % of inappropriate antimicrobial use was reported among inpatients attending Madda Walabu University Goba Referral Hospital, southeast Ethiopia [20]. Considering a 95% confidence interval and a 5% marginal error, the desired sample size (n) will be calculated as follows:

$$n = \frac{(Z\ \alpha/2)^2\ p\ (1-p)}{d^2}$$

Where: -

n= required sample size

Z α /2 = Standard normal distribution at 95% confidence interval (Z=1.96 and α=0.05)

d = Margin of error = 5% = 0.05

P = 27.13% is proportion populations reported as death [8].

$$n = \frac{(1.96)^2\ 0.30\ (1-0.30)}{(0.05)^2} = 322$$

Considering 10% (304*0.1= 32.2 ~32) non-response rate, total calculated sample size will be 304+ 30 = **354**

4.5. Sampling procedure.

TASH was selected because it has been implementing antimicrobial stewardship since the antimicrobial stewardship committee was fully established in November 2017 [8]. A simple random sampling technique was employed to select the study participants after getting the list of admitted patients from each ward. Then, by a simple lottery method, the allocated sample of patients was selected. Based on studies conducted in each department, a total of 175, 144, and 236 patients were admitted per month at the internal medicine, surgery, and GNY-OBS departments, respectively [22, 41, 42]. A representative proportional allocation was implemented, and based on that, a total of 105 patients from internal medicine, 87 patients from the surgical ward, and 142 patients from the gynecology-OBS department were recruited for the study.

4.6. Inclusion and Exclusion Criteria.

4.6.1. Inclusion criteria.

- Patients who were admitted to internal medicine, surgery, and gynecology/obstetrics wards.
- Patients who diagnose or develop an infectious disease.
- Patients who need prophylaxis for infectious disease.
- Patients who received at least one systemic antibiotic for treatment and/or prophylaxis during the study period were included.

4.6.2. Exclusion criteria.

- Patients with ages less than 14.
- Patients who were not diagnosed with or developed infections and did not take antibiotics during the study period.
- Patients who took antifungal, antiviral, anthelmintic, antiprotozoal, and anti-tuberculosis drugs.
- Patients who refused to participate in the study were excluded.

4.7. Data Collection instrument.

A semi-structured written questionnaire was used to collect the data on socio-demographic characteristics (age, gender, educational background, etc.), clinical-related factors (admission diagnosis, co-morbidity, past medication history, etc.), and antibiotic-related factors (indication, dosage, frequency, route, duration, etc.). Then outcome-related information was collected with respect to death or morality, complications, and discharge with cure.

4.8. Study variables.

4.8.1. Dependent variable.

- Antibiotics use practices (Indication, Dose Frequency, Route, Duration)
- Treatment outcomes

4.8.2. Independent variables.

- **Socio-demographic characteristics.**
- Age.
- Sex.
- Marital status.
- Occupation.
- Residence.
- **Clinical Factor.**
- Admission diagnosis.
- Duration of the illness.
- Co-morbid disease.
- Past medication history

4.9. Data collection procedure.

A semi-structured questionnaire was prepared in English according to the objectives of the study and the local situation of the study area. The questionnaire was then translated to Amharic and back to English to assure the consistency of the tool. Discrepancies in the translation were resolved by mutual agreement with the main research advisor. The researcher recruited three clinical pharmacists to collect the data and an investigator for supervision. Training was given for one day by the principal investigators on how to use the questionnaire, how to check its completeness, and the ethical principles of privacy, confidentiality, and data management prior to their involvement with data collection, and then data was collected for ninety days.

4.10. Data Quality Control Issues.

The questionnaire was translated into Amharic, and the necessary feedback was offered to the data collectors at the end of each collection. The data quality control issue was addressed by conducting a pre-test among 16 (5%) total samples obtained from patients attending Saint Paul Hospital. Training was given to the data collectors and supervisors on the data collection tool and sampling techniques by the researcher. Supervision was held regularly during the data collection period by the researcher. The collected data was checked on a daily basis for completeness and consistency.

4.11. Data analysis and Processing.

All questionnaires were manually reviewed for completeness and uniformity of responses. The data was cleaned and entered into EPI Info version 3.5.4 before being exported to SPSS version 26 for analysis. Frequencies and percentages of descriptive statistics were used to describe the study participant with respect to the study variables. The presence of a statistically significant association between the independent variables and the dependent variable was assessed using bivariate and multivariate analyses. The strength of the association was presented by the odds ratio and 95% confidence interval. A p value of < 0.25 on the bivariate analysis was considered for the multivariate analysis. Those that had a p-value of < 0.05 on multivariate analyses were considered statistically significant.

According to national and international evidence-based recommendations (including those from the Infectious Diseases Society of America (IDSA) and the most recent Ethiopian standard treatment guideline), the appropriateness of antibiotics was assessed. And classified whether antimicrobial therapy was appropriate using a standard approach that was first reported by Gyssen's et al. and revised by Willemsen and colleagues. This algorithm was chosen because it has been widely used in research all over the world and is a validated method that enables a systematic assessment of all aspects of antimicrobial usage. Gyssen's method, which groups 0-VI categories, illustrates the rationale of antibiotic use [24]. The quantity and types of antimicrobials consumed in this research were measured using the AWaRe classification and the defined daily dose (DDD/100 patients per day) for quantity purposes. These tools for measuring quantity are standardized and recommended by the World Health Organization [43].

4.12. Operational Definition/ definitions of terms.

Antibiotic: An agent or substance that is produced by or derived from a microorganism that kills or inhibits the growth of another living microorganism [43].

Antimicrobial: agents derived from any source (microorganisms, plants, animals, synthetic or semi-synthetic) and that kill or inhibit the growth of microorganisms and especially pathogenic microorganisms [43].

Antimicrobial stewardship: refers to a set of coordinated strategies to improve the use of antimicrobial medications with the goal of enhancing patient health outcomes, reducing resistance to antibiotics, and decreasing unnecessary costs [43].

Appropriate antibiotic use: It is based on Gyssen's categorization, the use of antimicrobial therapy/prophylaxis categorized on category 0 after reviewing the patients' records and the collected data [28].

Category 0: All criteria of antimicrobial therapy/ prophylaxis use are correct.

Category I: Antimicrobial therapy/ prophylaxis is not timely use.

Category II: Antimicrobial therapy/ prophylaxis inappropriate due to improper dose, improper dose interval, and improper route.

Category II A: Antimicrobial therapy/ prophylaxis inappropriate due to improper dose.

Category II B: Antimicrobial therapy/ prophylaxis inappropriate due to improper dose interval

Category II C: Antimicrobial therapy/ prophylaxis inappropriate due to improper route

Category III: Antimicrobial therapy/ prophylaxis inappropriate due to excessive duration and short duration.

Category III A: Antimicrobial therapy/ prophylaxis inappropriate due to excessive duration

Category III B: Antimicrobial therapy/ prophylaxis inappropriate due to short durations

Category IV: Antimicrobial therapy/ prophylaxis inappropriate due to toxicity/ADR, broad spectrum, cost.

Category V: Antimicrobial therapy/ prophylaxis inappropriate due to unjustified indication.

Category VI: The medical record is incomplete or insufficient for categorization.

Cessation of prophylactic antibiotics after surgery: Discontinued of antibiotic prophylactic within 24 hours after surgery aims to reduce patients receiving unnecessary antibiotic treatment [43].

AWaRe classification of antibiotics: AWaRe stands for ACCESS, WATCH and RESERVE. An antibiotic classification system introduced in 2017 by The World Health Organization (WHO) used to promote rational antibiotic use and provide a tool for antimicrobial stewardship activities and monitoring of antimicrobial consumption (Annex 2) [44].

ACCESS group antibiotics: Have activity against a wide range of commonly encountered susceptible pathogens while showing lower resistance potential than antibiotics in Watch and Reserve groups. Widely used as first- or second -choice empiric treatment options for specified infectious syndromes [44].

WATCH group antibiotics: Have higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance. Should be prioritized as key targets of hospital stewardship programs and monitoring [44].

RESERVE group antibiotics: Should be reserved for treatment of confirmed or suspected infections due to multi drug-resistant organisms, and treated as last-resort‖ options. They must be protected and prioritized as key targets of hospital stewardship programs, involving monitoring and utilization reporting, to preserve their effectiveness [44].

Defined daily dose (DDD): Assumed average maintenance dose per day for a medicine used for its main indication in adults as established by the WHO Collaborating Centre for Drug Statistics and Methodology [43]. The values of every antibiotic DDD per 100 inpatients per day are calculated by

$$\frac{\text{DDD of antibiotics}}{(\text{total number of patients})(\text{duration of antibiotics})} * 100$$

Discharge: The formal release of patients from a chronic care after a period of hospitalization if clinical, microbiological and other investigation were well improved.

Dose optimization: it involves "optimization of antimicrobial dosing based on patient's characteristics, causative organisms.

Good clinical outcomes: Clinically cure/ improved Discharged.

Inappropriate antimicrobial use: Antimicrobial inappropriate for several reasons and placed in category I to VI**.** At the same time, it can be placed more than one category [28].

Iv-to-oral switch: If the prescribed IV antibiotic medication convert to oral antibiotic based on patient's clinical and microbiological test improvement will be consider Iv-to-oral switch.

IV to PO conversion inclusion criteria

- Intravenous antimicrobial for > 24 hrs.
- Clinical improvement (Temp. < 37.8^{0}C, O_2 saturation >92%, stable blood pressure, Pulse rate <100 beats / min, respiratory rate, <25 breaths per min.)
- Afebrile for >24 hours (core temperature <38ºC)
- Oral administration of fluids is feasible
- Oral administration of tablets is feasible [22].

Poor clinical outcome: death/ complication

4.13. Ethical issue.

Ethical clearance was obtained from the Addis Ababa University College of Health Science School of Pharmacy Ethical Review Committee. The study was conducted after receiving a letter of ethical approval (ERB/SOP/480/2022). In addition, permission was obtained from the study site. Prior to data collection, written consent was obtained from all study participants, and we informed them that participation is voluntary and they can withdraw themselves from the study at any time. Data were kept anonymous and confidential to avoid possible identifiers such as the names of the participants, and they were used only for research purposes. Only the identification number was used as a reference. The study participants were informed that there was no harm in participating in the study.

5. Result.

5.1 Antimicrobial Quality Measurement Result.

5.1.1 Sociodemographic characteristics of the study participants.

A total of 315 study participants voluntarily consented to be included in the current prospective study at TASH medical, surgical, and gynecology/obstetric wards, yielding a response rate of 89.0 %. The majority of study participants, 98 (31.1%), were between the ages of 25 and 34, with a mean (SD) age of 36.99 (±16.12). More than half of them were female, which accounts for 195 (61.9%). Nearly two-thirds of them were married in those accounts (67.9%). Most of the participants, 260 (82.5%) lived in urban areas (Table 1).

Table 1: Socio demographic characteristics of admitted patients at TASH, Addis Ababa, Ethiopia, September 1 - December 30, 2022 (n = 315).

Variable	**Category**	**Frequency**	**Percent**
Age	14 – 24	73	23.1
	25 - 34	98	31.1
	35 - 44	59	18.7
	45 and above	45	26.9
Gender	Male	120	38.1
	Female	195	61.9
Educational background	Able to read and write	15	4.8
	Unable to read and write	65	20.6
	Primary	70	22.2
	Secondary (grade 9 to 12)	121	38.4
	Diploma and above	44	14.0
Marital status	Single	49	15.6
	Married	214	67.9
	Divorced	13	4.1
	Widowed	39	12.4
Occupation	Civil servant	69	21.9
	Self employed	138	43.8
	Farmer	18	5.7
	House wife	59	18.7
	Student	31	9.8
Residence	Urban	260	82.5
	Rural	55	17.5

5.1.2. Clinical related characteristics of the study participants.

A total of 315 patients were admitted to internal medicine 105 (33.3%), surgical wards 86 (27.3%), and gynecology/obstetric wards 124 (39.4%). At admission, the majority of patients had a diagnosis in the category of other diseases (196 (62.0%)), followed by pneumonia (50 (15.8%), cancer (29 (9.2%), and sepsis (23 (7.3%)). The current study found that the majority of patients, 305 (96.8%), did not change their admission diagnosis. In addition, 111 (35.3%) of them had a history of co-morbid disease. Males were more prevalent than females to have comorbidities, accounting for 62 (57.4%) and 46 (42.6%), respectively. Cardiovascular disease was the most common comorbid disease, accounting for 37 (33.3%), followed by cancer at 25 (22.5%) and diabetes mellitus at 8 (7.2%), and 26 (16.6%) of them had more than one comorbid disease. There were 101 (32.1%) and 71 (22.5%) patients who had previous medication and surgery histories, respectively (Table 2).

Table 2: Clinical related characteristics of hospitalized patients at TASH, Addis Ababa, Ethiopia, September 1- December 30, 2022 (n = 315).

Variable	Category	Frequency	Percent
Admission diagnosis	Pneumonia	50	15.8
	Cancer	29	9.2
	Sepsis	23	7.3
	Tow and above	16	5.1
	Others*	196	62.0
Change in diagnosis**	Yes	10	3.2
	No	305	96.8
Comorbidity	Yes	111	35.3
	No	204	64.7
Type of comorbid diseases	Cardiovascular	37	33.3
	Cancer	25	22.5
	Diabetes mellitus	8	7.2
	HIV	7	6.3
	Renal	6	5.4
	Respiratory	2	1.8
	More than one comorbid disease***	26	16.6
Past medication history	Yes	101	32.1
	No	214	67.9
Past surgical history	Yes	71	22.5
	No	244	77.5
Admission ward	Internal medicine ward	105	33.3
	Surgical ward	86	27.3

	Gynecology/obstetric	124	39.4
Days of hospitalization	1 – 7 days	200	63.3
	8 – 14 days	67	21.2
	15 – 21 days	36	11.4
	22 and above	12	3.8

* = meningitis, cirrhosis, Preeclampsia, spontaneous bacterial peritonitis, Mastoiditis, hernia, ascites, achalasia, eclampsia, glomerulonephritis, Cholelithiasis, Cholesteatoma, UTI, ureteric stone, Pneumonia + sepsis, pneumonia +UTI, neutropenic fever + sepsis, pneumonia + cancer, cancer neutropenic fever.
** = due to poor clinical response, imaging study
*** = cardiovascular + diabetes mellitus, cancer + diabetes mellitus, cardiovascular + renal, cancer + diabetes mellitus, cancer + cardiovascular, cardiovascular +renal+ diabetes mellitus.

5.1.3. Antimicrobial use related characteristic of the study participants.

315 hospitalized patients received a total of 474 antibiotic prescriptions from twelve different antibiotic types during the study period. 284 (90.1%) of the hospitalized patients received their antibiotics intravenously, which is how the majority of patients were treated. The remaining 24 hospitalized patients (7.6%) and 7 (2.2%) were administered via PO and IV, and PO, respectively. Almost all 312 (99%) of the treatment options were judged to be empirical, and de-escalation of therapy was made based on culture and sensitivity data for 3 (1%) patients. The usual dose was prescribed for 308 (97.7%) of the patients, and the dose was optimized for 7 (2.3%) patients based on patient characteristics. In terms of guideline adherence, the prescribed antimicrobial drug was evaluated, and the results revealed that almost all 441 (93%) of the prescribed antimicrobials adhere to the current version of the Ethiopian National Therapeutic Guideline and the Infectious Disease Society of America (IDSA) international guideline. The eligibility of patients for IV (intravenous) to PO (oral) conversion was evaluated, and 29 (9.2%) patients were determined to be eligibled. However, only 15 (4.7%) patients were converted; the reasons for this were the patients' clinical diagnosis and their inability to take oral medication. Eight (53.3%) of the conversions were made at the time of discharge, while 7 (46.7%) were performed between 24 and 48 hours later. The timing of administration and discontinuation of antimicrobial drugs for surgical patients was measured, and the results showed that, among 210 patients, practically all 209 (99.5%) received prophylaxis between 30 minutes and 1 hour before incision. Regarding the discontinuation of prophylactic antimicrobial drugs among 210 patients, more than half (52.8%) were discontinued within 24 hours after surgery. The mean, minimum, and maximum duration of antimicrobial therapy were 5.7 (±SD 2.9) days, 1day, and 30 days, respectively (Table 3).

Table 3: Antimicrobial use related characteristic of admitted patients at TASH, Addis Ababa, Ethiopia, September 1 – December 30, 2022 (n = 315).

Variable	Category	frequency	Percent
Route of drug administration	Po	7	2.2
	IV	284	90.1
	Po and IV	24	7.6
Change in antimicrobial based on culture and sensitivity test	Yes	3	4.8
	No	312	95.2
Use of current version of therapeutic guideline	Yes	441	93.0
	No	33	7.0
Dose optimize based on patient characteristic	Yes	7	2.3
	No	308	97.7
Eligibility of IV to PO conversion	Yes	29	9.2
	No	286	90.8
IV to PO conversion made	Yes	15	4.7
	No	14	4.4
IV to PO Time of conversion	in between 24 to 48 hrs.	7	46.7
	at the time of discharged	8	53.3
Timely administered antimicrobial for prophylaxis	Yes	209	99.5
	No	1	0.5
Prophylactic antimicrobial discontinued within 24 hrs. after surgery	Yes	111	52.8
	No	99	47.3

5.1.4. Patients' clinical outcome

During the study period, the clinical outcomes of the patients were evaluated. The current study's statistical findings revealed that 280 patients (88.9%) had good clinical outcomes and were all discharged. The remaining 35 (11.1%) patients had poor clinical outcomes, with 34 (32.3%) admitted to the internal medicine ward. Among these 32 (10.2%) of these individuals died, and 3 (1%) had clinical complications. Poor clinical outcomes were more common in men than in women, accounting for 22 (62.8%) and 13 (37.2%), respectively (Fig. 2).

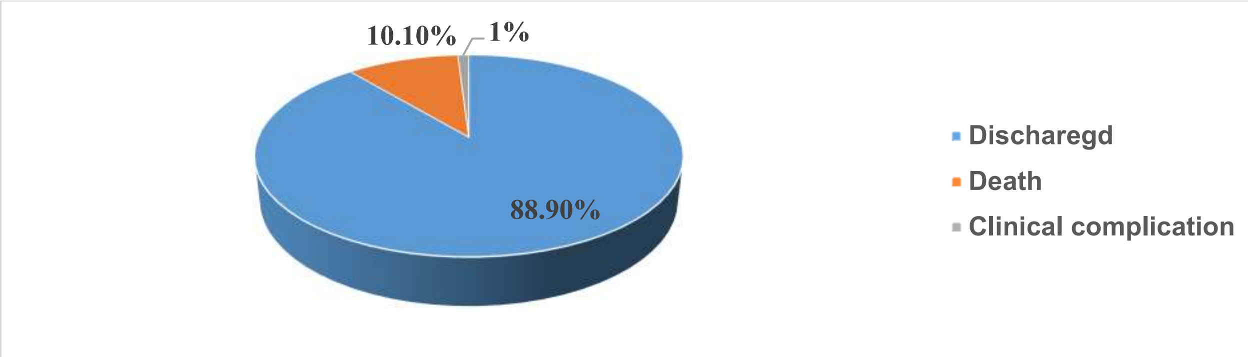


Figure 2: Clinical outcomes of hospitalized patients at TASH, Addis Ababa, Ethiopia, September 1 – December 30, 2022 (n= 315).

5.1.5. Appropriateness of antimicrobial use practice among hospitalized patients.

Antibiotic prescribing practice was classified as 'appropriate' (category 0) or 'inappropriate' (categories I to VI) using Gyssen's method. According to Gyssen's categories, antibiotic use was appropriate (category 0) in 171 (54.3%) hospitalized patients but inappropriate (categories II A, II B, III A, III B, and V) in 144 (45.7%) admitted patients in the current study. Category IIIA (long duration) was the most prevalent inappropriate type, accounting for 99 (68.7%), followed by category IIIB (short duration), 17 (11.8%), category V (inappropriate indication), 13 (9%), and category IIA (inappropriate dose), 8 (5.5 %) (Table 4). The surgical ward was the admission ward with the highest prevalence of inappropriate antibiotic use, accounting for 64 (20.3%). The proportion of patients who used antibiotics appropriately and had positive clinical outcomes was 148 (52.8%), while the remaining 132 (47.2%) patients used antibiotics inappropriately over the study period (Table 5).

Table 4: Quality of antimicrobial use among hospitalized patients according to Gyssen's category at TASH, Addis Ababa, Ethiopia, September 1 – December 30, 2022 (n= 315).

Gyssen's category		**N (%)**
Category 0		171 (54.3%)
Appropriate		**171(54.3%)**
Category II	Category II A	8 (5.5%)
	Category II B	7 (4.8%)
	Category II C	0
Category III	Category III A	99 (68.7%)
	Category III B	17 (11.8%)
Category V		13 (9%)
Category VI		0
Inappropriate		**144 (45.7%)**
Total		**315**
N.B: category 0 = appropriate, category II A= inappropriate dose, category II B = inappropriate interval, category II C = inappropriate route, category III A= long duration, category III B= short duration, category V= inappropriate indication, category VI= incomplete medical records.		

Table 5: cross tabulation showing appropriateness of antibiotic use and patients' clinical outcomes at TASH, Addis Ababa, Ethiopia, September 1, - December 30, 2022 (n=315)

	Appropriateness of antimicrobial			
Patients' clinical outcomes		**Appropriate (n)**	**Inappropriate (n)**	**Total (n)**
	Good outcomes	148	132	280
	Poor outcomes	23	12	35
Total		**171**	**144**	**315**

5.1.6. Factors Associated with inappropriate antibiotics use.

Bivariate analysis was done to find independent variables for inappropriate antimicrobial use with a p-value of less than 0.25. Sociodemographic (age, gender, residence, marital status, occupation) and clinically related characteristics (8 admission ward, day of hospitalization) explanatory variables were identified as possible predictors for further multivariate analysis. Multivariate logistic regression analysis was used to determine independent predictors of inappropriate antimicrobial use. Accordingly, patients with the following four characteristics demonstrated a higher probability of inappropriate use: patients categorized under the age of 25 to 34 years were protective, meaning they were 0.76 times less likely to have inappropriate antimicrobial use as compared with patients younger than 24 years (AOR = 0.24, 95% CI: (0.06–0.89), P = 0.03). Whereas, patients with marital status of divorced or widowed were 5.68 and 8.91 times more likely to have inappropriate antimicrobial use practices as compared with patients who were single (AOR = 5.68, 95% CI: (1.67–19.3), P = 0.001) and (AOR = 8.91, 95% CI: (1.51–52.6), P = 0.01), respectively. In terms of admission wards, patients who were admitted to internal medicine and surgical wards were 3.53 and 10.8 times more likely to have inappropriate antimicrobial use practices as compared with gynecology and obstetrics wards (AOR = 3.53, 95% CI: (1.04–11.9), P = 0.04,) and (AOR = 10.8, 95% CI: (3.59–32.9), P=0.001), respectively. Furthermore, patients who were hospitalized for more than eight days have a highly significant risk of inappropriate antimicrobial use as compared with patients who were hospitalized for less than eight days. The statistical result revealed that patients who were hospitalized for 8 to 14 days, 15 to 21 days, as well as 22 days and above, had odds of (AOR=17.0, 95% CI:(1.59–182.5), P=0.01), (AOR=11.0, 95% CI: (1.20–100.8), P=0.03) and (AOR=10.9, 95% CI:(1.17-103.0), P=0.03) respectively (Table 6).

Table 6: Factors associated with inappropriate antimicrobial use among hospitalized patients at TASH, Addis Ababa, Ethiopia, September 1 – December 30, 2022 (n= 315).

Variable		Antimicrobial use		COR (95% CI)	AOR (95% CI)	P value
		Appropriate (n)	Inappropriate (n)			
Age	14 - 24	48	25	1	1	
	25 - 34	55	43	0.44 (0.23 – 0.84)	0.24 (0.06 – 0.89)	**0.03***
	35 - 44	29	30	0.66 (0.37 – 1.18)	0.53 (0.18 – 1.53)	0.24
	45 & above	39	46	0.87 (0.45 – 1.70)	0.62 (0.23 – 1.71)	0.36
Gender	Male	51	69	1	1	
	Female	120	75	2.16 (1.36 – 3.43)	0.91 (0.43 – 1.91)	0.80
Marital status	Single	22	27	1	1	
	Married	119	95	2.76 (1.14 – 6.67)	4.75 (0.84 - 26.8)	0.07
	Divorced	3	10	1.79 (0.86 – 3.73)	5.68 (1.67 – 19.3)	**0.001****
	Widowed	27	12	7.50 (1.74 – 32.24)	8.91 (1.51 – 52.6)	**0.01***
Residence	Urban	148	112	1	1	
	Rural	23	32	0.54 (0.30 – 0.98)	0.81 (0.36 – 1.81)	0.61
occupational status	Civil servant	38	31	0.99 (0.42 – 2.32)	0.78 (0.19 – 3.10)	0.72
	Self employed	71	67	1.14 (0.52 – 2.50)	1.47 (0.36 – 6.06)	0.58
	Farmer	4	14	4.25 (1.13 – 15.86)	2.06 (0.33 – 12.76)	0.43
	House wife	41	18	0.53 (0.21 – 1.30)	1.26 (0.28 – 5.67)	0.76
	Students	17	14	1	1	
Admission ward	Internal medicine	61	44	1.76 (1.01 – 3.05)	3.53 (1.04 – 11.9)	**0.04***
	Surgical ward	22	64	7.11 (3.82 – 13.22)	10.8 (3.59 – 32.9)	**0.001****
	Gyne/obes	88	36	1		
Day of hospitalization	1 – 7 days	110	90	1		
	8 – 14 days	31	36	10.23(1.30 – 80.22)	17.0 (1.59 – 182.5)	**0.01***
	15 – 21 days	19	17	12.7 (1.56 – 104.1)	11.0 (1.20 – 100.8)	**0.03***
	22 and above	11	1	10.73(1.26 -91.47)	10.9 (1.17 – 103.0)	**0.03***

5.1.7. Predictors of poor outcome in hospitalized patients at TASH.

Since a logistic regression model requires the dependent variable to be stated dichotomously, the clinical outcome was recoded into a good outcome and a poor outcome. Bivariate logistic regression was used to identify independent predictors for poor clinical outcome with a p-value of less than 0.25, and sociodemographic (age, gender, residence) and clinically related (admission diagnosis, past medication history, and day of hospitalization) explanatory variables were selected as potential predictors for further multivariate analysis.

A multivariate logistic regression analysis was used to examine independent factors associated with poor clinical outcomes. Accordingly, the finding demonstrated that patients who were at the age of 45 and above were substantially associated with poor clinical outcome, with odds of 4.86 times as compared with patients who were younger than 24 (AOR = 4.86, 95% CI: (1.41 – 16.7), P= 0.01). Patients who diagnosed sepsis and greater than two diseases during admission were statistically associated with poor clinical outcome with odds of 28.7 and 6.15 times as compared with patients who diagnosed others (AOR = 28.7, 95% CI: (4.73 – 174.7), P = 0.001) and (AOR = 6.15, 95% CI: (1.94 – 40.2), P = 0.05) respectively. Surprisingly, patients who were admitted for more than seven days were less likely to experience a negative outcome, namely mortality and complications, according to the current study. The statistical result shows that patients who were hospitalized for 8 to 14 days, 15 to 21 days, as well as 22 and above, had odds of (AOR = 0.10, 95% CI: (0.01 – 0.89), P = 0.03), (AOR = 0.10, 95% CI: (0.01 - 0.71), P = 0.02) and (AOR = 0.12, 95% CI: (0.01- 0.94), P = 0.04) as compared to those who were admitted for less than 7 days of duration, respectively (Table 7).

Table 7: factors associated with poor clinical outcomes among hospitalized patients at TASH, Addis Ababa, Ethiopia, September 1 – December 30, 2022 (n = 315).

Variable		**Outcome**		**COR (95% CI)**	**AOR (95% CI)**	**P value**
		Good outcome (n)	**Poor outcome (n)**			
Age	14 - 24	68	5	1	1	
	25 - 34	95	3	0.44 (0.15 – 1.33)	1.93(0.35–10.66)	0.44
	35 - 44	44	15	0.19 (0.05- 0.70)	0.44(0.06 – 3.03)	0.41
	45 and above	73	12	2.07 (0.89 – 4.83)	4.86 (1.41 – 16.7)	**0.01***
Gender	Male	98	22	1	1	
	Female	182	13	3.14 (1.51 – 6.51)	2.93(0.94 – 9.11)	0.06
Residence	Urban	240	20	1	1	
	Rural	40	15	0.22 (0.10 – 0.47)	0.47 (0.14- 1.54)	0.21
Admission Diagnosis	Pneumonia	40	10	12.0 (3.58 – 40.1)	4.57 (0.90 – 22.7)	0.06
	Cancer	28	1	1.71 (0.18 – 15.89)	2.16 (0.16 – 27.8)	0.55
	Sepsis	12	11	44.0(12.1 –158.9)	28.7(4.73– 174.7)	**0.001****
	Two and more	8	8	48.0 (11.9 – 193.3)	6.15(1.94 – 40.2)	**0.05***
	Others*	192	4	1	1	
Past medication	Yes	67	34	108.0 (14.5 – 80.6)	83.18(6.06 – 114.0)	**0.001****
	No	213	1	1	1	
Day of hospitalization	1 – 7 days	196	4	1	1	
	8 - 14 days	54	13	0.15 (0.00 – 0.06)	0.10 (0.01- 0.89)	**0.03***
	15 – 21 days	25	11	0.17 (0.04 – 0.62)	0.10 (0.01 -0.71)	**0.02***
	22 and above	5	7	0.31 (0.82 – 1.21)	0.12 (0.01- 0.94)	**0.04***

***** = meningitis, cirrhosis, Preeclampsia, spontaneous bacterial peritonitis, Mastoiditis, hernia, ascites, achalasia, eclampsia, glomerulonephritis, Cholelithiasis, Cholesteatoma, UTI, ureteric stone,

5.2. Quantity Metric Results.

5.2.1. Antibiotics Consumption Metrics Result.

During the study period, a total of 474 antibiotics were prescribed from twelve types of antibiotics for 315 hospitalized patients. Among these, 247 and 227 antibiotics were prescribed for the purposes of prophylaxis and treatment, respectively. The average antibiotic prescribed per patient was 1.5, and the majority of admitted patients, 191 (60.6%), received one antibiotic. The remaining 97 (30.8%), 19 (6%), and 8 (2.5%) patients received two, three, and four antibiotics, respectively. Cephalosporin, penicillin, glycopeptides, carbapenems, fluoroquinolones, macrolides, and cotrimoxazole were the most commonly used antimicrobial classes across the settings. Ceftriaxone was the most prevalent prescribed antibacterial agent overall in the study; it accounts for 152 (32.4%), followed by ampicillin 96 (20.4%), vancomycin 62 (13.2%), and metronidazole 52 (11%). According to DDD measurements, antibiotics were consumed in the study area at a rate of 4.17 DDD/100 patients per day. Meropenem, azithromycin, and ceftazidime were the most commonly used antibiotics in the study area in terms of volume, with 0.59 DDD/100 patients per day, 0.52 DDD/100 patients per day, and 0.47 DDD/100 patients per day, respectively (Table 8).

Table 8: Defined Daily Doses (DDDs) per 100 patients per Day of Antibiotics Subgroups and Substances (in Accordance with the Anatomic Therapeutic Chemical (ATC) Coding System at TASH, Addis Ababa, Ethiopia, September 1 – December 30, 2022 (n= 315).

Antibiotic chemical subgroup	**WHO ATC code**	**Prescribed antibiotics during the study period**							
		Antibiotic type	**Frequency**	**Percent**	**WHO DDD**	**DDD**	**AWaRe group**	**DDD per 100 patient per day**	**DDD per 100 patents per day for Actual user**
Penicillin	J01FA10	Ampicillin	96	20.46	6	150	A	0.36	1.18
	J01CR02	Amoxicillin + clavulanic acid	9	1.91	1.5	117.5	A	0.39	12.5
Cephalosporin	J01DD04	Ceftriaxone	152	32.4	2	751.5	Wa	0.31	0.65
	J01DD02	Ceftazidime	3	0.63	4	75	Wa	0.47	50.00
	J01DE01	Cefepime	49	10.0	4	672	Wa	0.44	2.88
Carbapenems	J0DH02	Meropenem	19	4.05	3	357.3	Re	0.59	9.84
Glycopeptides	J01XA01	Vancomycin	62	13.2	2	639.5	Re	0.31	1.58
Fluoroquinolones	J01MA02	Ciprofloxacin	13	2.34	1	82	Wa	0.31	7.69
Macrolides	J01FA10	Azithromycin	11	2.34	0.3	71.66	A	0.52	15.13
Sulfonamide/ trimethoprim	J01CA04	Sulfamethoxazole + trimethoprim	6	1.27	4	31.92	A	0.16	7.23
Nitroimidazoles	J01XD01	Metronidazole	54	11.0	1.5	483	A	0.31	1.85
Total			**474**	**100**		**3431.3**		**4.17**	**110.53**

Abbreviations: A- Access; Wa, - Watch, Re- Reserve; ATC-Anatomic Therapeutic Chemical.

The internal medicine ward consumed the majority of the antibiotics, accounting for 2643 DDD of the total 3431.3 DDD. The remaining 525.3 DDD and 263 DDD were consumed in the surgery and gynecology/obstetric wards. Cefepime and vancomycin were the most commonly used drugs in the internal medicine ward, with 639.5 DDD and 672 DDD, respectively. Ceftriaxone was the most commonly used antibiotic in the surgical ward, accounting for 292 DDD, whereas ampicillin accounted for 75.5 DDD in the gynecology/obstetric ward during the study period (Table 9).

Table 9: Defined Daily Doses (DDDs) per 100 patients per Day of Antibiotics Subgroups and Substances (in Accordance with the Anatomic Therapeutic Chemical (ATC) Coding System among admission wards at TASH, Addis Ababa, Ethiopia, September 1 – December 30, 2022 (n=315)

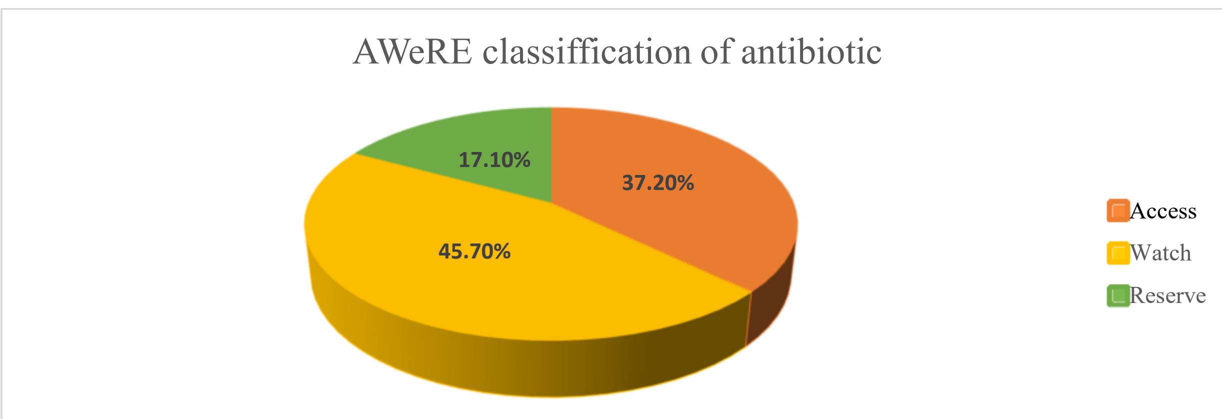
Admission ward	WHO ATC code	Prescribed antibiotics during the study period							
		Antibiotic type	**Frequency**	**Percent**	**WHO DDD**	**DDD**	**AWaRe group**	**DDD per 100 patient per day**	**DDD per 100 patents per day for Actual user**
Internal medicine ward (n = 105)	J01CR02	Amoxicillin + clavulanic acid	2	0.82	1.5	18.7	A	1.19	62.3
	J01DD04	Ceftriaxone	49	20.16	2	391	Wa	0.95	2.04
	J01DD02	Ceftazidime	3	1.23	4	75	Wa	1.42	50.0
	J01DE01	Cefepime	49	20.16	4	672	Wa	1.34	2.88
	J0DH02	Meropenem	19	7.81	3	357.3	Re	1.78	9.84
	J01XA01	Vancomycin	62	25.5	2	639.5	Re	0.93	1.58
	J01MA02	Ciprofloxacin	9	3.70	1	62	Wa	0.95	11.1
	J01FA10	Azithromycin	11	4.52	0.3	71.6	A	1.58	15.1
	J01CA04	Sulfamethoxazole+ trimethoprim	6	2.46	4	31.5	A	0.48	8.33
	J01XD01	Metronidazole	33	13.58	1.5	325	A	0.95	3.03
Total			**243**	**100**		**2643.6**		**11.57**	**166.2**
Surgical ward (n = 86)	J01CR02	Amoxicillin + clavulanic acid	7	6.73	1.5	98.4	A	1.45	17.7
	J01MA02	Ciprofloxacin	4	3.84	1	20	Wa	1.16	25.0
	J01XD01	Metronidazole	12	11.53	1.5	115	A	1.16	8.33
	J01DD04	Ceftriaxone	81	77.88	2	292	Wa	1.16	1.23
Total			**104**	**100**		**525.4**		**4.93**	**34.56**
Gynecology/obstetric ward (n = 124)	J01FA10	Ampicillin	96	75.5	6	150	A	0.91	1.18
	J01DD04	Ceftriaxone	22	17.32	2	70	Wa	0.80	4.54
	J01XD01	Metronidazole	9	7.04	1.5	43	A	0.80	11.1
Total			**127**	**100**		**263**		**2.51**	**16.82**

Abbreviations: A- Access; Wa, - Watch, Re- Reserve; ATC-Anatomic Therapeutic Chemical.

5.2.2. AWaRe Classification of Antibiotics.

From a total of twelve types of antibiotics prescribed, six were in the "Access" category, four in the "Watch" category, and two were in the "Reserve" category. Among the 474 prescribed antibiotics in the Access Group, antibiotic consumption accounted for 176 (37.2%) of total antibiotic consumption. The remaining 217 (45.7%) were prescribed from the watch groups, and 81 (17.1%) were prescribed from the Reserve group of antibiotics (Figure 3). 3431.3 DDD total was consumed throughout the categories of Access, Watch, and Reserve. There were 854 DDDs consumed from the "Access" category, 1580.5 DDDs from the "Watch" category, and 996.8 DDDs from the "Reserve" category. According to DDD/100 patients per day, 1.74 DDD/100 patients per day of antibiotics were consumed from the Access category, 1.53 DDD/100 patients per day from the Watch category, and 0.90 DDD/100 patients per day from the Reserve category.

Figure 3: Antibiotics consumed and their classification based on WHO AWaRe classification at TASH, Addis Ababa, Ethiopia, September 1 – December 30, 2022 (n = 474).



6. Discussion.

According to World Health Organization (WHO), more than two-thirds of antibiotics are used in hospitals and of these antibiotics, about 30% are used inappropriately globally. Antimicrobials are frequently provided inappropriately to 44–97% of hospitalized patients in low- and middle-income countries (LMICs) [3]. The proportions of inappropriate antibiotics utilization across different countries are varied in Africa. Inappropriate antibiotics use is about 88.8% in Tanzania, 50% in Sudan, 7.9% in Zambia, and greater than 10% in other African countries [14, 15, 16]. Reasons for inappropriate antimicrobial use practice in hospitals include uncertainty of differential diagnoses, complex co-morbidities, lack of training and/or experience, lack of knowledge of local epidemiology of antimicrobial resistance, and wrong interpretation of microbiological results. Consequences of excessive or inappropriate antimicrobial use are increased morbidity, mortality, health care costs, drug toxicity and antimicrobial resistance [24, 34].

Antibiotic use was deemed inappropriate in 45.7% of hospitalized patients in the current study, according to Gyssen's algorithm. This means that nearly half of hospitalized patients were given antibiotics that were inappropriate. This degree of inappropriate antimicrobial usage was less than that observed in Australia (80%), Pakistan (70.3%), Gondor Ethiopia (91.4%), and Mizan, Bonga, and Tepi hospitals in Ethiopia (80.1%) [30, 32, 34]. On the other hand, the current study result was higher than the studies conducted in Ethiopia (30.1%), Switzerland (37%), and the Netherlands (37.5%) [20, 21–24]. The difference could be that our study was conducted in a single-center setting with a small sample size of participants. Furthermore, differences in the implementation of AMSP and other infection prevention and control policies among the aforementioned nations could be the source of the discrepancy. Despite this, heterogeneity in systematic approaches to AMS interventions on antimicrobial prescribing practices at the facility and country levels is also a contributing factor to the disparity in optimal antibiotic usage.

According to the current study, the most common type of inappropriate antimicrobial usage was antibiotic duration. According to Gyssen's approach, group IIIA (long duration) accounted for 68.7% of inappropriateness in the current study. The cause could be due to poor adherence to SAP durations, which were extended beyond 24 hours after surgical procedures were completed for patients that underwent surgical procedures. This result was in line with the study conducted at the Michigan Hospital (67.8%). In contrast, inappropriate indication was the most frequent inappropriateness that was reported from the studies conducted in Switzerland and different referral hospitals in Ethiopia, with rates of (25.1%), (31.3%), and (12%), respectively, as compared with our study [20, 24, 28, 31]. Different methods of assessment could be contributing factors to the variance in the categories of inappropriate antibiotic usage. The presence of a high level of inappropriate antibiotic use may be related to the level of implementing the core elements of AMSP, resulting in increased overall health care expenditures, emergency drug resistance, and poor patient clinical outcomes.

In the current study, 474 antibiotics from twelve different categories were prescribed to patients hospitalized in TASH's medical, surgical, and gynecology/obstetric wards. During the study period, 60.6% of hospitalized patients received one antibiotic, while the remaining 39.4% received two or more medicines. This quantity was connected to the recruited patients, and two-thirds of the total admitted patients were admitted to the surgical and gynecology/obstetric wards and given a single antibiotic for prophylaxis. This was of lesser magnitude as compared to the previous studies done in Ethiopia and Switzerland, in which patients who received at least two antibiotics accounted for 48.4% and 74%, respectively [20, 24]. The reason for the discrepancy might be because of variation in the study area. They included patients from the medical ward, the surgical ward, oncology, and patients admitted to the intensive care unit. Furthermore, sample size differences could be one of the reasons they were recruited, with 471 and 1577 sample sizes reported from Ethiopia and Switzerland, respectively [20, 24].

In this investigation, 1.5 antibiotics were prescribed to each patient on average. This result was higher than those of earlier studies in Ethiopia, which found that Jimma Medical Center patients received 1.2 antibiotics per patient while multicenter study participants received 1.1 antibiotics per patient at several referral hospitals in Ethiopia [34, 39]. But lower than the studies conducted at the University of Gondar specialized hospital in Ethiopia and Madda Walabu University Goba Referral Hospital in Ethiopia, which found 2.2 and 1.7 antibiotics per patient, respectively [3, 20]. Variations in the study setting and sample size that have been used and reported in the literature [3, 20, 34, 39] could be the reason for the discrepancy. It is advised that the number of antibiotics given to each patient be maintained as low as possible in order to reduce medication errors, the occurrence of AMR, inappropriate use, and treatment costs. A decrease in the amount of antibiotics administered would be mirrored in a decrease in overall antibiotic usage, implying that infection rates remain consistent over time.

Ceftriaxone, ampicillin, and vancomycin were the most commonly administered antibiotics in the current study. According to our findings, this antibiotic was prescribed at a rate of 32.4%, 20.4%, and 13.2%, respectively. Ceftriaxone and ampicillin were frequently prescribed for patients admitted to surgery and gynecology/obstetrics wards, which was the cause. Our results were different from those of the earlier study carried out in TASH, Ethiopia. In the prior study, vancomycin was frequently administered at a rate of 25% [22]. Similarly, the current study results differ from those published from Ghana, where Metronidazole IV 36.5% and Ceftriaxone 35.3% were the most commonly prescribed antibiotics in the aforementioned country [13].

The study setting, differences in the study area, drug availability, and patient clinical features could all be reasons for variance. In terms of ceftriaxone, this finding was comparable to studies conducted in Ethiopia and Ghana, where rates of 35.7% and 35.3%, respectively, were recorded. However, this figure is lower than that of Pakistani research (78.1%) [13,20,32]. Overuse of a particular antibiotic can result in the development of emergency drug resistance, reduce its efficacy, lead to treatment failure, and raise treatment costs. Therefore, implementing stewardship interventions helps reduce the overuse of a particular antibiotic in the facilities.

The total volume of antibiotics consumed during the study period in the current study was 4.17 DDD per 100 patients per day. This was of lesser magnitude as compared to the studies conducted in Ethiopia, China, Asmara, and across 76 countries. Their findings were that (5.3 DDD/100 outpatients per day), (46.32 DDD/100 inpatients per day), (158.5 DDD/100 patients per day), and (17·2 DDD per 1000 inhabitants per day), respectively [35, 36, 37, 39]. The difference in findings between the current study and the studies completed in the stated nations could be attributed to differences in study design, study area, study time, and treatment methods or prophylaxis procedures employed among hospitals. Other possible explanations for the heterogeneity in antibiotic usage include differences in infection seasonality, infection prevention approaches, and antibiotic use regulation. According to DDD/100 inpatients per day measurements Meropenem, azithromycin, and ceftazidime were the most commonly used drugs in the current study, with 0.59 DDD/100 patients per day, 0.52 DDD/100 patients per day, and 0.47 DDD/100 patients per day, respectively. This differed from the earlier results from Asmara, which found that benzyl penicillin

G was the most commonly consumed antibiotic, with a rate of 35.4 DDD/100 per day. The difference in DDD consumption could be attributed to differences in patient clinical features, antibiotic availability, and hospital structural settings between our country and the aforementioned country [35].

The AWaRe classification is a crucial indicator of the progress being made in the fight against antimicrobial resistance and guarantees that all nations have access to powerful antibiotics. In order to combat the issue of antibiotic resistance, the WHO AWaRe classifications advise placing at least 60% of prescribed antibiotics on the "Access" list rather than the "Watch and Reserve" list. Therefore, the use of "Watch" and "Reserve" lists of antibiotics in the area suggests that there is a relative overuse of antibiotics, which justifies more monitoring. Clinicians should, however, concentrate on the data before prescribing those really important antibiotics included in the "Watch" and "Reserve" groups. Antibiotic consumption was higher in the current study "Watch"; it accounted for 1580.5 DDDs (47%), with 1.52 DDD per 100 patients per day. This result was lower than the 2.10 DDD/100 outpatients per day (50.6%) study in Ethiopia and the 53 DDD per 1000 population per day study in 76 countries [36, 39]. The discrepancy in antibiotic consumption may be caused by variations in how AMSP are implemented, stewardship interventions on antibiotic prescription, and antibiotic monitoring and use policies. Furthermore, our analysis found that "Reserve" antibiotic intake occurred at a rate of 17% in the current study. The excessive consumption of Watch and Reserve antibiotics may be caused by weak stewardship programs, inadequate regulatory capability, diagnostic uncertainty, and a high rate of illnesses with drug-resistant bacteria. Poor conformity to WHO standards according to AWaRe systems, the facility needs to implement evidence-based AMS interventions to modify its antibiotic prescribing practices.

The overall in-hospital mortality rate in the current study was 10.2%, with all of the deaths occurring on the internal medicine ward. This is lower than earlier studies in TASH at the internal medicine ward (27.7%) and (18.5%) [8, 22]. The sample size and clinical features of the study participants may be connected to this difference. We observed a few internal medicine study participants in the current investigation. Additionally, they were tested on individuals with pneumonia and systemic bacterial infections at internal medicine wards, respectively. On the other hand, the findings of the current study were higher than those of studies conducted in Australia and Indonesia. They reported that inappropriate use practices had no effect on mortality [28, 30].

According to a multivariate logistic regression study, patients between the ages of 25 and 34 had a 0.76 times lower likelihood of using antibiotics inappropriately (AOR = 0.24, 95% CI: (0.06-0.89), P = 0.03). Patients with divorced and widowed marital status were more likely to have inappropriate antibiotic use practices (AOR = 5.68, 95% CI: (1.67–19.3), P = 0.001) and (AOR = 8.91, 95% CI: (1.51–52.6), P = 0.01) than single and married patients. Inappropriate antibiotic usage among these populations could be due to differences in attitude, understanding of antibiotic use, and psychosocial behaviors. Patients who were admitted to the surgical and internal medicine wards were more likely to engage in inappropriate antibiotic use practices (AOR = 3.53, 95% CI: (1.04–11.9), P=0.04) and (AOR = 10.8, 95% CI: (3.59–32.9), P=0.001), respectively. The length of the hospital stays, the number of antibiotics provided, the kind of sickness, and adherence to the prophylaxis plan could all be contributing factors. Overall, patients who were hospitalized for more than seven days were significantly associated with inappropriate antimicrobial use practices in the current study. In fact, prolonged hospitalization has a number of negative effects, including the development of hospital-acquired infections, complications, and the misuse of antibiotics. This result did not demonstrate a statistically significant correlation with the research carried out in (Mizan, Bonga, Tepi), and Gondor, Ethiopia. Their studies showed that the following factors were strongly linked with inappropriate antibiotic usage: use of social drugs, prior antimicrobial use, gender, source of income, and ethnicity [3, 34]. The lack of significance could be attributed to participant differences in socioeconomic status, sociocultural practices, knowledge and understanding of proper medication, its treatments, side effects, and concomitant diseases.

According to multivariate logistic regression analysis, patents above the age of 45 (AOR = 4.86, 95% CI: 1.41–16.7), P = 0.01) were more likely to have a poor clinical outcome. One of the possible explanations is that the patients' age is related to chronic diseases, and this group of patients may have distinct comorbidities. Regardless, age has an impact on patients' immune systems and other inflammatory mediators. Patients who were diagnosed with sepsis and more than two disorders at the time of admission had statistically poor clinical outcomes (AOR = 28.7, 95% CI: (4.73–174.7), P = 0.001) and (AOR = 6.15, 95% CI: (1.94–40.2), P = 0.05), respectively. In the current investigation, individuals with a history of medication and those hospitalized for less than seven days were substantially associated with poor clinical outcomes. With the study results that have been reported in the literature [8 and 22], sepsis and patients who had a history of previous medication were likely drivers of poor clinical outcomes.

7. Strength and Limitation.

The main limitation of this study is that the observation was conducted only on 315 admitted patients in a single center, and the outpatient antimicrobial use practice was not included. It might be difficult to generalize due to the small number of study participants. And also because of antibiotic use practice, patients' characteristics and predictors of clinical outcome may vary among hospitals, among inpatients, and among outpatients. The strength of this study is that it evaluates the antimicrobial use practice in different wards and measures both the quality and quantity of antibiotic use practice, additionally classifying the prescribed antibiotics based on the AWaRe classification.

8. Conclusion.

Relatively higher antibiotics consumption was observed among hospitalized adult patients in the study setting. Based on WHO AWaRe system, more than half of the antibiotics prescribed from "Watch" group and "Reserve" group. About half of hospitalized patients had inappropriate antibiotic use. Inappropriate duration of treatment was the most common type of inappropriateness. The age of the patients, marital status, days of hospitalization, and admission ward differences had significant associations with inappropriate antibiotic use. On the other hand, the age of the patients, admission diagnosis, past medication history, and day of hospitalization were significantly associated with poor clinical outcomes. The use of "watch" and "reserve" groups of antibiotics in the study area indicated a relative overconsumption of antibiotics. In general, greater consumption and inappropriate antibiotic usage among hospitalized adult patients in the research area demonstrated the need for immediate AMS interventions and AMSP improvement.

9. Recommendations.

Performing AMS intervention in the study area to change antimicrobial prescribing practice behaviors by providing education and training, restrictions on antibiotics use, developing and updated treatment and surgical prophylaxis guidelines. Additionally, AMSP improvement by identify, which AMSP core element of the facility partially/fully implemented? and develop a stepwise implementation plan suggest for the facility AMS teams.

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11. Annex

Annex 1. Data collection instrument

Section one: demographic characteristics.

s. no	Variable	Category	Response	Skip
101	Age of the patients	----years		
102	Gender of the patient	1. Male 2. Female		
103	Educational background	1. Unable to read and write 2. Able to read and write 3. Primary (grade 1-8) 4. Secondary school (grade 9-12) 5. Diploma and above		
104	Marital status	1. Single 2. Married 3. Divorced 4. Widowed		
105	Occupation	1. Civil servant 2. Self employed 3. Farmer 4. Housewife 5. Student 6. Other specify -------		
106	Residence	1. Urban 2. Rural		
107	Referred from	1. Government institution 2. Private institution 3. Direct admission		

Section two: clinical related variable questions.

s.no	Variable	Choices	Response	Skip
201	Admission diagnosis			
202	Is there change in diagnosis	1. Yes 2. No		
203	Had the patient any preexisted co morbid illness?	1. Yes 2. No		
204	If yes specify co morbid illness	1. Cancer 2. Cardiovascular 3. Renal disease 4. Respiratory disease 5. Diabetes 6. Liver disease 7. HIV		

205	Admission ward	1. Internal medicine 2. Surgical ward 3. Gyne/obes ward		
206	Is there any past medication history?	1. Yes 2. No		
207	Is there any past surgical history	1. Yes 2. No		

Section 3: AMS process measures/indicators related questions.

s.no	Variables	Choices	Response
301	Name of the (empiric/definitive) prescribed antimicrobials.	1. 2. 3. 4.	
302	Dose of the prescribed antimicrobials	1. 2. 3. 4.	
303	Frequency of antimicrobials	1. 2. 3. 4.	
304	Duration of antimicrobials	1. 2. 3. 4.	
305	Rout of administration	1. Po 2. IV 3. IM 4. Others ------	
306	WHO ATC conversion factors	1.-----grams 2. ----grams 3.-----grams 4.	
307	Total days of treatment with antibiotics during hospitalization	----------	
308	Does an antibiotic prescribe according to current version of therapeutic Guidelines /policy and formulary?	1. Yes 2. No	
309	Was that the medication deescalated based on culture and sensitivity?	1. Yes 2. No	
310	Is there IV-to-PO route conversion?	1. Yes	If 2 skip to 314

		2. No	
311	If yes does conversion made based on inclusion/exclusion criteria?	1. Yes 2. No	See operational definition
312	Is the patient eligible to IV to oral based on the inclusion/exclusion criteria?	1. Yes 2. No	
313	After fulfilling eligibility criteria at what time was conversion made?	1. Converted within 24 hr. 2. Converted in between 24-48 hr. 3. Converted in between 48-72 hr. 4. Converted after 72 hr. 5. Converted when the patient discharged	
314	If there is no IV to PO route conversion made specify the reason	1. Patients 'diagnosis/clinical condition (e.g., Endocarditis, meningitis') 2. inadequacy of oral intake 3. absence of adequate oral antibiotic	
315	If yes, specify the reason?	1. Absence of IV medication 2. Patient intolerable for IV medication. 3. Others -------	
316	Does the dose of antibiotics optimize?	1. Yes 2. No/ usual dose	
318	If yes, how was the dose optimize?	1. Based on patient characters 2. Based on site of infection 3. Based on antimicrobial characteristic	
319	Does prophylaxis antimicrobial administer timely 1 hr. before incision	1. Yes 2. No	
320	Does prophylaxis antimicrobial discontinue with 24hrs after surgery	1. Yes 2. No	
321	Is indication for antibiotic treatment documented?	1. Yes 2. No	

Section 4. AMS outcome measure/indicator related question.

S. no.	Variable	Choice	Response	Remark
401	Day of hospitalization by types of infection	---------------days		
402	Total duration of hospitalization with antibiotics?	------------days		
403	Current patient status	1. Good outcome 2. Poor outcome		
404	If the patient has good outcome	1. Clinically cure/ improved 2. Discharged		
405	If the patient has poor outcome	1. Clinically not improved /complications 2. Death during hospitalization		

የአማርኛ ቋንቋ ቅጅ የመረጃ እና የፈቃድ መየቂያ ቅጽ

ውድ የጥናቱ ተሳታፊ ጤና ይስጥልኝ

ይህ ጥናት በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል የፀረ ባክቴሪያ መድኃኒቶች አጠቃቀምና ተያያዥ ጉዳዮች ላይ የሚያተኩር ጥናት ሲሆን ጥናቱ የሚካሄደው የድህረ ምረቃ ተማሪ በሆነው ተማሪ ሀብታሙ ጉግሳ እና በጥናቱ አማካሪ በፕሮፌሰር አለምሰገድ በየነ በአዲስ አበባ ዩኒቨርስቲ ጤና ሳይንስ ኮሌጅ ፋረማሲ ት/ቤት የድሕረ ምረቃ መርሐ ግብር ነው።የጥናቱ ዋና ዓላማ የፀረ ባክቴሪያ መድኃኒቶች አጠቃቀምና ሌሎች ተያያዥ ጉዳዮችን በመዳሰስ የመፍትሔ ሀሳቦችን መጠቆም ነው።

በጥናቱ ላይ የፀረ ባክቴሪያ መድኃኒቶችን የሚወስዱ ታካሚዎች የሚሳተፉ ሲሆን ለተሳታፊዎች ምንም ዓይነት ማበረታቻና ክፍያ የማይኖረው ሲሆን ከጥናቱ በሚገኘው ምክረ ሀሳብ ተጠቃሚ ይሆናሉ ብለን እናምናለን። ጥናቱ የሚካሄደው በቀጥተኛ የህክምና ሂደት ምልከታና በቀጥተኛ ቃለ መጠይቅ ሲሆን የእርስዎ ቀናነትና ትክክለኛ መረጃ ለጥናቱ እጅግ ጠቃሚ ነው። በዚህ ጥናት የእርስዎ ስምና ሌሎች ሚሥጢራዊ መረጃዎች በፍጹም የማይገለጹና በአስተማማኝ ሁኔታ የሚጠበቁ ሲሆኑ የሚሰጡት መረጃም ሚሥጢራዊነቱ የተጠበቀና በሚሥጢራዊ ቁጥሮች (ኮድ) የሚቀመጡ ይሆናሉ ።

በጥናቱ ቢሳተፉ መረጃ ለመስጠት ከሚሰውት ጊዜ በቀር በርስዎ ላይ ምንም ዓይነት የሚያስከትልብዎት አሉታዊ ጉዳት እንደማይኖረው እናረጋግጥልዎታለን። በጥናቱ የሚሳተፉት እርስዎ ፈቃደኛ ከሆኑ ብቻ ስለሆነ ያለመሳተፍም ሆነ ጥናቱን ማቋረጥ ሙሉ መብት አለዎት:: በተጨማሪም መረጃ መስጠት የማይፈልጉት ጥያቄ ካለ ያለመስጠት መብትዎ ተጠበቀ ነው ። ጥናቱን በተመለከተ ለሚኖርዎት አስተያትም ሆነ የጥናቱን ዉጤት ማወቅ ቢፈልጉ በሚከተሉት አድራሻ ማገኘት ይችላሉ።

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Annex 2. AWaRe classification of antibiotics in the EEML*-2020

Group		
Access	Watch	Reserve
1. Amoxicillin	1. Ampicillin + Sulbactam	1. Piperacillin + tazobactam
2. Amoxicillin + Clavulanic Acid	2. Cefuroxime	2. Meropenem
3. Ampicillin	3. Cefixime	3. Meropenem + Vaborbactam
4. Penicillin G. Benzanthin	4. Cefpodoxime Cefotaxime Sodium	4. Ceftazidime + Avibactam
5. Penicillin G. Sodium Crystalline	5. Ceftriaxone	5. Colistin
6. Cloxacillin	6. Ceftazidime	6. Polymyxin B
7. Cephalexin	7. Cefepime	Vancmycin
8. Cefazolin	8. Ceftriaxone + sulbactam	
9. Azithromycin	9. Ciprofloxacin	
10. Clarithromycin	10. Clindamycin	
11. Sulphamethoxazole + Trimethoprim		
12. Nitrofurantoin		
13. Norfloxacin		
14. Gentamicin		
15. Metronidazole		
16. Doxycycline		

* Ethiopian Essential Medicines List,