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ORIGINAL RESEARCH

# Risk Factors for Inappropriate Antimicrobial Therapy Among Patients with Hospital-Acquired Infection at Jimma Medical Center: A Prospective Observational Study

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**Background:** Globally, HAIs affect about 2 million people annually and result in 5% to 15% hospitalizations. In low-middle-income countries, antibiotics are improperly prescribed for 44% to 97% of hospitalized patients. A report in Ethiopia revealed that about 66.7% of HAIs are managed inappropriately.
**Objective:** To identify inappropriate antimicrobial therapy (AMT) and its risk factors among patients with HAIs at Jimma Medical Center (JMC).
**Methods:** A prospective observational study was conducted involving 300 patients with HAIs in medical, surgical, and gynecology-obstetrics wards of JMC, from October 2020 to April 2021. Data were collected using data abstraction format. Logistic regression was conducted to assess factors associated with AMT inappropriateness. A p-value <0.05 was considered to declare statistical significance.
**Results:** The overall mean age (± standard deviation) of the participants was 43.2 ± 19.2 years and 183 (61.0%) of them were females. About three-fourths (76.0%) of patients with HAIs were treated inappropriately. Hospital-acquired pneumonia (50.3%) was the most common type of HAI identified in this study. The frequent class of inappropriate AMT was an inappropriate choice, 102 (44.1%), followed by an inappropriate dose, 88 (38.1%), and inappropriate indication, 59 (24.2%). On multivariable logistic regression, patients having culture finding (AOR = 0.32, p = 0.016), taking metronidazole (AOR = 0.25, p = 0.001), and taking vancomycin (AOR = 2.93, p = 0.001) were significantly associated with inappropriate AMT.
**Conclusion:** Inappropriate AMT was identified in about three-fourths of the patients with HAIs. A decrease in the likelihood of inappropriate AMT was identified in patients having culture findings and in those taking metronidazole, whereas taking vancomycin increased the likelihood of inappropriate AMT. Therefore, the authors recommend scaling up the capacity of definitive therapy through culture and sensitivity tests. Furthermore, training of prescribers in the rational use of antimicrobials is also warranted.
**Keywords:** cross infection, anti-infective agents, Jimma Medical Center

## Background

Hospital-acquired infection (HAI) is an infection that occurs during the process of care at a hospital or other health care facility, which was not present or incubated at the time of admission.[1] Hospital-associated pneumonia (HAP), catheter-associated urinary tract infection (CAUTI), blood-stream infection (BSI), surgical site infection (SSI), and skin and soft tissue infections (SSTI) are the most commonly encountered HAIs.[2,3] These infections are diagnosed based on clinical manifestations, physical examination, laboratory, and other diagnostic tests.[4]

More than 90% of HAIs are caused by bacteria, such as *Klebsiella pneumoniae, Staphylococcus aureus, Escherichia coli, Proteus spp*., and *Pseudomonas aeruginosa*. While mycobacterial, viral, fungal, and protozoal agents are other less



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commonly involved etiologies.[2] The common risk factors for HAIs are older and younger age, obesity, immunocompromised medical conditions, smoking, admission to intensive care unit, existing infection, surgical procedures, invasive device utilization, use of immunosuppressants, prolonged hospitalization, excessive and improper uses of broad-spectrum antibiotics, and insufficient application of precautionary measures.[2,3,5,6]

Hospital-acquired infections are a major public health concern worldwide,[7] affecting 100 million patients each year, with an estimated point prevalence range of 3.5–12% and 5.7–19.1% in high and low- and middle-income countries, respectively.[8] In sub-Saharan Africa, the prevalence of HAIs varies from 2% to 49%.[6] Hospital-acquired infections contribute to increased morbidity and mortality, compromise patients' quality of care, prolong hospital stay, increase the cost of health care, increase the emergence of multiple antibiotic resistance microorganisms, an additional financial burden for health care systems, as well as patients and their families, and reduce the chances of treating other medical conditions. Annually, estimated €7 billion direct financial losses and 16 million extra days of hospital stay in Europe, and about US$ 6.5 billion losses in the USA are attributable to HAIs.[8]

Currently, the management of HAIs has become a great challenge and more threatening. This is explained by the fact that emerging multidrug-resistant strains of infectious organisms in hospitals result in reducing the effectiveness of available therapies.[8] Among the emerging drug-resistant bacteria in healthcare settings, penicillin-resistant pneumococci, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant *Staphylococcus aureus* are the most common.[9]

Theoretically, the management of HAIs involves a definitive therapy based on culture and susceptibility findings. However, in most cases, antibiotic treatments in low- and middle-income countries are empirical based on local microbiological backgrounds and their resistance pattern.[2] In principle, the empirical selection of antibiotics should consider the risk factors for multi-drug resistant pathogens and the patient's clinical stability. Furthermore, a broad-spectrum antibiotic is recommended to ensure coverage of most suspected pathogens, including pseudomonas as well as MRSA.[2,10]

The appropriate management of HAIs is crucial for reducing their multi-dimensional impact.[11,12] The rate of management appropriateness varies across countries, healthcare settings, and regions. Globally, despite WHO's efforts to develop and implement strategies to improve the appropriate use of antimicrobials,[13] an estimated 22% to 73% of HAIs treatment is believed to be inappropriate.[14] In low-income countries, 44–97% of antibiotics are prescribed unnecessarily or inappropriately,[15] which contributes enormously to an increased incidence of bacterial resistance and poor treatment outcomes.[12,15] Such data are important for countries to alert and strengthen the antimicrobial stewardship efforts by ensuring the rational use of antimicrobials to improve patient outcomes.[16] Although studies indicate a growing burden of various types of HAIs in Ethiopia,[17,18] there are only a handful of studies on antimicrobial therapy (AMT) appropriateness in these populations. Accordingly, in a study from Zewditu Memorial Hospital, inappropriate HAIs treatment was reported in 66.7% of cases.[17] With this, the present study aimed to assess the inappropriate AMT and its risk factors in patients with HAIs at Jimma Medical Center (JMC) in Southwest Ethiopia.

# Method

## Study Design and Setting

A hospital-based prospective observational study was conducted in JMC from October 2020 to April 2021. JMC is located in Jimma town, Jimma zone, Oromia, South-West of Ethiopia, 352 km from Addis Ababa, the capital. It is the only medical center that serves more than 20 million populations.

## Population

### Source Population

All patients admitted to the medical, surgical, and Gynecology/Obstetrics wards of JMC and diagnosed with HAI during the study period.

### Study Population

All patients admitted to the medical, surgical, and Gynecology/Obstetrics wards of JMC and were diagnosed with HAI during the study period and fulfilled the inclusion criteria.

### Eligibility Criteria

#### Inclusion Criteria

- Patients admitted to the medical, surgical, and Gynecology-Obstetrics wards of JMC and diagnosed with HAI.
- Age >18 years.

#### Exclusion Criteria

- Patients whose medical records were incomplete.
- Readmissions during the study period.
- Patients who declined to participate in the study.

## Sample Size and Sampling Techniques

The sample size was calculated using a single population proportion formula with the following considerations; the proportion of inappropriate management of HAI at Zewditu Memorial Hospital, Addis Ababa, Ethiopia, was 66.7%,[17] a 95% confidence level (α= 5%) with ±5% precision (d). The number of patients with HAIs at internal medicine, gynecology-obstetrics, and surgical ward of JMC in the previous year was 1550, and we assumed this trend was constant across years. After adding a 10% non-response rate, the final sample size was 300. The sample size was allocated accordingly to the proportion of patients admitted to each ward; (830/1550*300) = 166 to internal medicine, (357/1550*300) = 69 to Gynecology-Obstetrics, and (336/1550*300) = 65 to surgical ward). Then, the participants (300 patients) were recruited using a consecutive sampling technique.

## Data Collection Tools and Techniques

The data abstraction tool was developed after reviewing a medical chart of patients with HAIs and various literatures. The tool comprised socio-demographic (age, sex, residence, marital status, and educational status of the patient), clinical characteristics (types of HAIs such as CAUTI, VAP, BSI, and SSI, mean time to develop HAIs, the clinical presentation of HAIs, comorbidity, the reason for admission, the procedure done, previous admission history, presence of the invasive device, and mechanical ventilation), medication-related (antibiotic regimen administered, shifting of the antibiotic regimen, prior antibiotic use, and non-antibiotic drug use), and investigation-related (culture and sensitivity, complete blood count, erythrocyte sedimentation rate, and others) variables. Two data collectors (one clinical pharmacist and one BSc nurse) were trained on the objectives of the study, the data collection tool, and the data collection process. Patient's medical charts and patient interviews were the sources used for extracting the relevant data. For each patient admitted to surgical, internal medicine, and gynecology/obstetrics ward, their medical chart was assessed daily for HAIs diagnosis. The attending physician diagnosed HAIs based on the Centers for Disease Control/National Healthcare Safety Network surveillance definition of healthcare-associated infection and criteria for specific types of infections in the acute care setting.[19] Patients diagnosed with HAIs were primarily assessed for eligibility. Then, all eligible patients were interviewed and their medical charts were reviewed daily throughout the hospital stay. For each patient, antimicrobial treatment appropriateness was assessed using IDSA for HAP,[20] CAUTI,[21] and SSI[22] and Ethiopian standard treatment guideline[23] focusing on the antibiotic choice, indication, dose, frequency of administration, route of administration, and duration of treatment for HAIs.

## Outcome Variable

The primary outcome of the study was AMT appropriateness, while the secondary outcome was the incidence of all-cause in-hospital mortality.

### Outcome Measurement and Validation

Appropriate AMT: is the right choice of antibiotics (including the right indication for use, choice, dose, frequency of administration, route of administration, and duration of treatment) according to IDSA and Ethiopian standard treatment guideline recommendations for treating HAIs.

Inappropriate AMT: any deviation from appropriate AMT of HAIs was considered as inappropriate antimicrobial therapy (AMT). For each detected inappropriate AMT, prescribers were requested for their decision of prescription. If the explanation was scientifically acceptable, the detected inappropriate AMT was not considered as inappropriate. The recorded inappropriate use of AMT was classified based on the standards reported by Gyssens et al, and modified by Willemsen et al, the standard for evaluating antibiotic prescription.[24,25] The classification was as follows:

(A) Inappropriate indication; prescription of antimicrobials without the presence of infectious disease, or prescription of antimicrobials for an infection that does not need antimicrobial treatment.
(B) Inappropriate choice, including the inappropriate spectrum of the antimicrobial agent (too broad, too narrow, not effective), or inappropriate toxicity profile.
(C) Inappropriate dosage,
(D) Inappropriate timing/frequency,
(E) Inappropriate route of administration, and
(F) Inappropriate duration of therapy.

## Data Quality Assurance

Initially, the data collection tool was developed in English, then translated into two dominant local languages (Amharic and Afaan Oromo) and back-translated into English by an independent person to assure its consistency. The tool was pre-tested before starting the actual data collection, and then the necessary adjustment was made. The data were compiled, coded, and checked for completeness and consistency before analysis.

## Data Analysis and Interpretation

The data were coded and entered into Epidata version 4.6.0.5 and exported to the Statistical Package for Social Science (SPSS) version 23.0. Armonk, NY: IBM Corp for data analysis. Categorical variables were presented with frequency and percentage. For continuous data, a normality test was conducted using Shapiro–Wilk's test. Accordingly, all continuous data were parametric and reported with mean ± standard deviation (SD). For all categorical variables, cell adequacy was checked. Bivariate analysis was performed to see the associations between inappropriate AMT and the independent variables. Then, a backward, stepwise multivariate logistic regression [reported with Adjusted odds Ratios (AOR) with 95% Confidence Intervals (95% CI) was performed, including all explanatory variables with a p-value of $<0.25$ on bivariate logistic regression to evaluate factors independently associated with inappropriate AMT. All p-values calculated were two-sided, and the statistical significance threshold was $<0.05$.

## Operational/Term Definition

Empirical treatment: Antibiotic administration before or without identification of sensitive profile of bacterial pathogens.[26]

Comorbidity: The presence of one or more additional conditions co-occurring with HAIs.

Cardiovascular medications: medication classes/drugs used to treat cardiovascular disorders, including angiotensin-converting-enzyme inhibitors, diuretics, beta-blockers, calcium channel blockers, and digoxins.

Analgesics/antipyretics: the group of drugs used to achieve analgesia and/or relief from pain such as tramadol, diclofenac, morphine, pethidine, and paracetamol.

Anti-ulcer: medications used to prevent or treat ulcers such as cimetidine, pantoprazole, omeprazole, and ranitidine.

# Results

## Overview of the Study Participants

A total of 310 patients diagnosed with HAIs were assessed for eligibility. Finally, 300 patients with at least one HAI fulfilling the inclusion criteria were followed and included in the analysis (Figure 1).

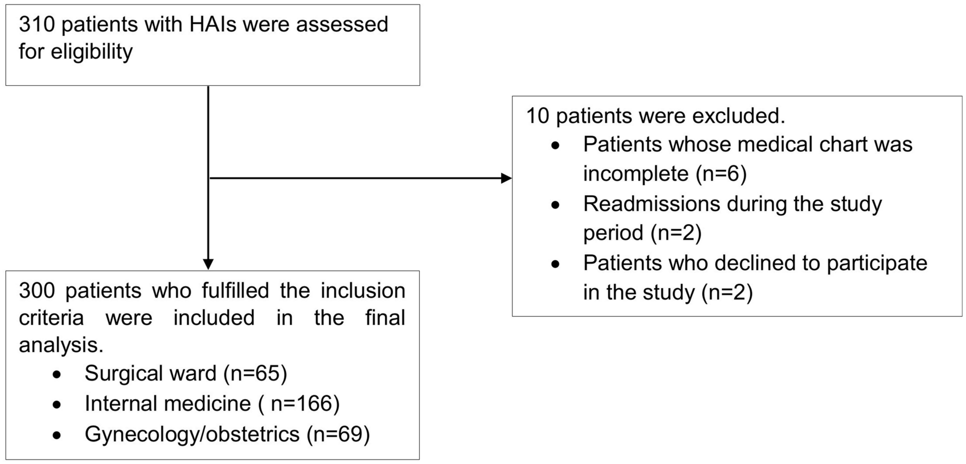


**Figure 1** Patient flow chart of patients with hospital-acquired infection in JMC.

## Socio-Demographic Characteristics

The overall mean (±SD) age of the study participant was 43.2+19.9 years and more than half (61.0%) of them were females. Nearly half of the study participants (49.7%) completed primary school (Table 1).

## Clinical Characteristics of Patients

The most frequent reason for admission was to undergo surgical procedures and care (40.7%). Almost all of the study participants (99.7%) had a peripheral intravenous line inserted and 67.0% of them were catheterized. The most frequently administered non-antibiotic medication classes were anti-pain (56.0%) and anti-ulcer (34.3%). Fever (94.0%) was the most common clinical manifestation of patients with HAIs. Overall, a total of 314 HAIs were diagnosed; fourteen (4.6%) of the total participants had two HAIs. From HAIs, HAP has been diagnosed in 162 (54.0%) participants. The median time to develop HAIs was 5 days (Table 2).

## Pathogens Identified from Patients with Hospital-Acquired Infection

Culture and sensitivity were done for 32 (10.6%) patients; of these, culture was positive in 20 and 11 pathogens were identified. *Escherichia coli* and Coagulase-negative staphylococci (CONS) were the most frequently identified pathogens

**Table 1** Socio-Demographic Characteristics of Patients Diagnosed with HAIs in Medical, Surgical, and Gynecology/Obstetrics Wards of JMC

| Characteristics | | Frequency (%) |
|---|---|---|
| Sex | Male | 117(39.0) |
| | Female | 183(61.0) |
| Age (in years), mean ± SD | | 43.2 +19.9 |
| Residency | Urban | 144(48.0) |
| | Rural | 156(52.0) |
| Marital status | Married | 185(61.6) |
| | Single | 82(27.3) |
| | Widowed | 20(6.6) |
| | Divorced | 13(4.3) |
| Educational status of the patient | Unable to read and write | 31(10.3) |
| | 1–8 | 149(49.7) |
| | 9–12 | 104(34.7) |
| | >12 | 16(5.3) |

**Abbreviation**: SD, standard deviation.


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**Table 2** Clinical Characteristics of Patients with HAIs in Medical, Surgical, and Gynecology/Obstetrics Wards of JMC

| **Characteristics** | | **Frequency (%)** |
|---|---|---|
| Reason for admission | For various surgical procedures and care* | 122(40.7) |
| | Stroke | 31(10.3) |
| | Heart failure | 25(8.3) |
| | Asthma | 19(6.3) |
| | Anemia | 14(4.7) |
| | Kidney disease | 14(4.7) |
| | Chronic obstructive pulmonary disease | 12(4.0) |
| | Hypertensive crisis | 11(3.7) |
| | Other lung diseases | 10(3.3) |
| | Deep Vein Thrombosis | 8(2.7) |
| | Epilepsy | 6(2.0) |
| | Malignancy | 7(2.3) |
| | Meningitis | 6(2.0) |
| | Poorly controlled Diabetes Mellitus | 6(2.0) |
| | Others | 5(2.7) |
| Previous admission in the past 3 months for any reason | | 24(8.0) |
| Peripheral line inserted | | 299(99.7) |
| Catheterized | | 201(67.0) |
| Nasogastric tube inserted | | 62(20.7) |
| Mechanically ventilated | | 55(18.3) |
| Undergone surgery | | 122(40.7) |
| Types of HAI diagnosed | HAP | 151(50.3%) |
| | UTI | 45(15.0%) |
| | SSI | 49(16.3%) |
| | BSI | 41(13.7%) |
| | HAP + UTI | 7(2.3%) |
| | HAP + SSI | 3(1%) |
| | HAP + BSI | 1 |
| | UTI + SSI | 3(1%) |
| Mean time to develop HAIs (Median) | | 5 days |
| Clinical presentation on the diagnosis of HAI | Fever | 283(94.0) |
| | Cough | 172(57.3) |
| | Tachypnea | 167(55.7) |
| | Localized pain | 155(51.7) |
| | Tachycardia | 137(45.7) |
| | Urinary urgency/frequency | 84(28.0) |
| | Discharge from the site of infection | 60(20.0) |
| | Dysuria | 45(15.0) |
| | Headache | 42(14.0) |
| | Swelling at the site of infection | 37(12.3) |
| Laboratory investigation on the diagnosis of HAIs | White blood cell count | 12.3± 5.7×$10^3$ cells/μL |
| | Red blood cell count | 3.9± 1.0×$10^6$ cells/μL |
| | Platelet count | 263.7± 142.1×$10^3$ cells/μL |
| | Erythrocyte sedimentation rate (n=91) | 63.9± 38.6 mm/hr |

**Note**: *Cesarean section, surgery for traumatic brain injury, surgery for benign prostatic hyperplasia, thyroidectomy, and others.
**Abbreviations**: BSI, blood stream infection; HAP, hospital-acquired pneumonia; UTI, urinary tract infection; SSI, surgical site infection; μL, microliters; mm/hr, millimeters per hour.

accounted 4 (20.0%) each, followed by *Enterobacter* 3 (13.6%). *Escherichia coli* resistance to ampicillin was reported in three patient samples, and resistance to cotrimoxazole and nitrofurantoin was captured in two patient samples, each. All of the CONS pathogens were resistant to cloxacillin, doxycycline, penicillin G, and chloramphenicol (Table 3).

**Table 3** Culture and Sensitivity Pattern of Pathogen Identified from Patients with HAIs in Medical, Surgical, and Gynecology/Obstetrics Wards of JMC

| Pathogen | Frequency | Antibiotics to Which Specific Pathogens are Sensitive and Resistant | |
|---|---|---|---|
| | | **Sensitive to** | **Resistant to** |
| *Escherichia coli* | 4 | Imipenem (3), meropenem (3), Gentamicin (1), amikacin (2), chloramphenicol (1) | Ampicillin (3), cotrimoxazole (2), nitrofurantoin (2), gentamicin (1), norfloxacin (1) |
| *CONS (Coagulase-negative staphylococci)* | 4 | Vancomycin (2), imipenem (2), Meropenem (2), nitrofurantoin (2), erythromycin (1) | Cloxacillin (4), doxycycline (4), Penicillin G (4), chloramphenicol (4), erythromycin (3), tetracycline (3) |
| *Enterobacter* | 3 | Nitrofurantoin (1), ampicillin (2) cotrimoxazole (2), gentamicin (2) ceftazidime (1), ceftriaxone (1) norfloxacin (2) | Chloramphenicol (3), ciprofloxacin, (3), cotrimoxazole (3), gentamicin (2), norfloxacin (2) |
| *Klebsiella oxytoca* | 2 | Ampicillin (1), cotrimoxazole (2), gentamicin (2), norfloxacin (2), Imipenem (2), meropenem (2) | Gentamicin (1), tetracycline (1), ciprofloxacin (1) |
| *Citrobacter* | 2 | Amikacin (1), imipenem (1), meropenem (1), nitrofurantoin (1), chloramphenicol (1), tetracycline (1), gentamicin (1) | Ampicillin (2), cloxacillin (2), doxycycline (2), erythromycin (2), penicillin G (2), cotrimoxazole (2) |
| *Acinetobacter* | 2 | Imipenem (1), meropenem (2), amikacin (1), amoxicillin/clavulanic acid (1) | Ampicillin (2), chloramphenicol (2), tetracycline (2), penicillin G (2), oxacillin (2) |
| *Klebsiella pneumonia* | 1 | Ceftazidime, ceftriaxone, cotrimoxazole, norfloxacin, gentamicin | Ampicillin, cloxacillin, doxycycline, erythromycin, oxacillin, penicillin G |
| *Proteus mirabilis* | 1 | Amikacin | Ampicillin, cotrimoxazole, nitrofurantoin, ceftriaxone |
| *Streptococcus pneumoniae* | 1 | Meropenem, imipenem, nitrofurantoin | Augmentin, amikacin, ceftriaxone cefuroxime, ciprofloxacin, norfloxacin, cotrimoxazole gentamicin |
| *Pseudomonas aeruginosa* | 1 | Ciprofloxacin | Oxacillin, penicillin G, nitrofurantoin |
| *Enterobacter aerogenes* | 1 | Imipenem, meropenem | Ceftriaxone, ampicillin, chloramphenicol, gentamicin, nitrofurantoin, doxycycline |

**Note**: The number of times the isolated pathogen-resistant and sensitive to respective antibiotics.

## Management of HAI

The frequently used antibiotics for treatment of HAIs were ceftriaxone (n = 156, 52.0%), metronidazole (n = 156, 52.0%), vancomycin (n = 152, 50.7%), and ceftazidime (n = 126, 42.0%). The overall mean number of antibiotics prescribed per patient was 2.6 ± 1.0. Among medication classes used for comorbidities, anti-pain, 168 (56.0%), anti-ulcer, 103 (34.3%), and cardiovascular medications, 85 (28.3%) were the most frequent (Table 4).

## Antimicrobial Therapy Appropriateness and Other Outcomes

Of the study participants, 228 (76.0%) had at least one AMT inappropriateness, with an average of 1.3 (299/228) inappropriate AMT per patient. Inappropriate AMT was most common in internal medicine (84.3%), followed by surgical (69.2%) and gynecology/obstetrics (62.3%) wards. The change in antibiotic regimen was recorded in 55 (18.3%) of the participant for the management of HAIs. Treatment failure (80.0%) and culture finding (18.20%) were the reasons for changing the regimen. Inappropriate choice, 102 (44.1%), was the most frequent class of inappropriate AMT, followed by inappropriate dose, 88 (38.1%) and inappropriate indication, 59 (24.2%) (Figure 2). The overall mean length of hospital stay following diagnosis of HAIs was 3.8± 1.3 days, and incidence of in-hospital mortality was noted in 53 (17.7%) patients.

**Table 4** Medication Use Profile Among Patients with HAI in Medical, Surgical, and Gynecology/Obstetrics Wards of JMC

| Variables | | | Frequency (%) |
|---|---|---|---|
| Antibiotics used for HAIs | Ceftriaxone | | 156(52.0) |
| | Metronidazole | | 156(52.0) |
| | Vancomycin | | 152(50.7) |
| | Ceftazidime | | 126(42.0) |
| | Cephalexin | | 33(11.0) |
| | Ciprofloxacin | | 16(5.3) |
| | Meropenem | | 15(5.0) |
| | Azithromycin | | 11(3.7) |
| | Gentamicin | | 9(3.0) |
| | Norfloxacin | | 6(2.0) |
| | Doxycycline | | 6(2.0) |
| | Ampicillin | | 5(1.7) |
| | Amoxicillin/clavulanic acid | | 2(0.7) |
| | Erythromycin | | 1(0.3) |
| Number of antibiotics prescribed per patient (mean ± SD) | | | 2.6±1.0 |
| Other medications used for comorbidities | Anti-pain | | 168(56.0) |
| | Anti-ulcer | | 103(34.3) |
| | Cardiovascular medications | | 85(28.3) |
| | Therapeutic iron | | 42(14.0) |
| | Steroids (dexamethasone, prednisolone, hydrocortisone) | | 41(13.7) |
| | Anti-diabetic medications (insulin and/or metformin) | | 33(11.0) |
| | Antiemetic's (Metoclopramide) | | 33(11.0) |
| | Ant-seizure (diazepam and or phenytoin) | | 28(9.3) |
| | Antituberculosis | | 24(8.0) |
| | Antipsychotic/antidepressant (Fluoxetine, haloperidol, valproic acid). | | 10(3.3) |
| | Highly Active Antiretroviral Therapy | | 6(2.0) |
| | Anti-fungal (fluconazole) | | 1(0.3) |
| | Others | Mannitol | 18(6.0) |
| | | Vitamins /minerals | 20(6.7) |
| | | Statins | 11(3.7) |
| | | Warfarin | 11(3.7) |
| | | Heparin | 31(10.3) |
| | | Aspirin | 9(3.0) |

**Abbreviation**: SD, standard deviation.

## Factors Associated with AMT Appropriateness of HAIs

On bivariate logistic regression analysis, admission at internal medicine ward ($p < 0.001$), patients comorbid with cardiac disease ($p = 0.004$), patients with pregnancy complications ($p = 0.010$), patients who underwent surgery ($p < 0.001$), patients who were taking steroids ($p = 0.013$), patients who were taking antipyretics/analgesics ($p = 0.004$), use of ceftriaxone ($p = 0.034$), metronidazole ($p < 0.001$), ceftazidime ($p = 0.006$), vancomycin ($p = 0.001$), and cephalexin ($p = 0.003$) were significantly associated with inappropriate AMT. A total of 19 variables were recruited for multivariate logistic regression and having culture finding (AOR = 0.32, 95% CI: 0.13–0.81, $p = 0.016$), taking metronidazole (AOR = 0.25, 95% CI: 0.13–0.49, $p = 0.001$), and taking vancomycin (AOR = 2.93, 95% CI: 1.57–5.48, $p = 0.001$) were identified as predictors of inappropriate AMT (Table 5).

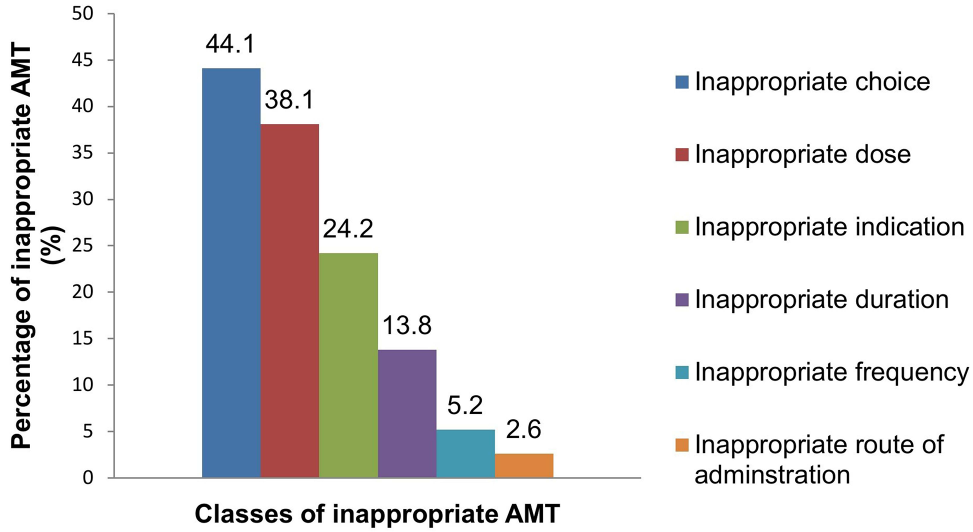


**Figure 2** Classification of AMT inappropriateness in patients with HAIs in medical, surgical, and Gynecology/Obstetrics wards of JMC.

# Discussion

This study was the first of its kind in reporting AMT appropriateness and its potential risk factors for HAIs in JMC. Such findings are a key input to strengthen and implement the institutional antimicrobial stewardship program to optimize appropriate antimicrobial prescription through identifying factors to be tackled as well as showing the status of antimicrobial utilization in patients with HAIs per national/international guidelines.

In the current study, more than three-fourths (76.0%) of patients with HAIs were treated inappropriately according to the international/national guidelines. The frequent class of inappropriate AMT was an inappropriate choice, inappropriate dose, and inappropriate indication accounting for 44.1%, 38.1%, and 24.2%, respectively.

In the present study, the proportion of inappropriate AMT among patients with HAIs was 76.0%, which is corroborated with published evidence in low-income countries, where 44–97% of antibiotics were prescribed unnecessarily or inappropriately.[15] Similar findings were reported from Kyrgyzstan (73.3%)[27] and Pakistan (70.3%).[28] However, the current finding was higher than a report from Barnes-Jewish Hospital in USA (45.2%),[29] Portugal (27.0%),[30] Denmark (20.0%),[31] Switzerland (33.0%),[32] Kenya (46.4%),[33] and Addis Ababa, Ethiopia (66.7%).[17] This discrepancy may be due to differences in ways of assessing and reporting inappropriate AMT across studies and study population characteristics (patients with HAIs vs patients with all types of infection).[17,29–33] Additionally, this difference might be explained by the fact that patients considered in most of the previous studies were treated based on culture findings, while in our study, the treatment was primarily empirical. Furthermore, the difference in the health care system and the availability of drugs may account for this variation.

In the current study, the frequent types of HAI recorded were HAP, SSIs, and UTIs accounting for 50.3%, 16.0%, and 15.3%, respectively. This finding was congruent with a report from Ethiopia,[17] HAP and SSIs in 24.7% and UTI in 19.8% of the cases, in Lithuania,[34] lower respiratory tract infections (32.2%), SSI (32.1%), and UTIs (28.5%), and similarly, in Italy,[3] HAP (31.5%), UTI (21.8%), and SSIs (11.9%) were the frequent HAIs reported. However, unlike the current finding, a study from Europe revealed BSI (45.0%),[35] in Africa, studies from Nigeria[36] and Benin[37] reported UTI as the most frequent HAI, accounting for 45.7% and 48.2%, respectively. In Ethiopia, studies from Addis Ababa (49.4%)[38] and Amhara region (51.1%)[18] reported SSI as the most frequent HAIs. This discrepancy may be due to variations in the implementation of infection control and prevention measures, such as facility-specific hygiene precautions[39] and variations in study population characteristics.

The lack of standard treatment guidelines specific to infections in the present study setup will contribute to a substantial proportion of inappropriate AMT prescriptions. This could be the possible reason for the findings in the present study, where 44.1% of inappropriate selection and 38.1% of incorrect dose were frequently identified as a class of

**Table 5** Bivariate and Multivariate Logistic Regression Analysis to Identify Factors Associated with Inappropriate AMT Among Patients with HAIs

| Variable | | Appropriateness of AMT | | COR (95% CI) | P-value | AOR (95% CI) | P-value) |
|---|---|---|---|---|---|---|---|
| | | Appropriate (n=72) | Inappropriate (n=228) | | | | |
| Admission wards | Internal medicine | 26(36.1%) | 140(61.4%) | 3.26(1.71–6.19) | <0.001 | - | |
| | Surgical | 20(27.8%) | 45(19.7%) | 1.36(0.66–2.79) | 0.400 | - | |
| | Gynecology/obstetrics | 26(36.1%) | 43(18.9%) | 1 | | | |
| Cardiac disease | Yes | 10(13.9%) | 73(32.0%) | 2.92(1.41–6.02) | 0.004 | 2.08(0.95–4.56) | 0.067 |
| | No | 62(86.1%) | 155(68.0%) | 1 | | 1 | |
| Pregnancy complication | Yes | 18(25.0%) | 28(12.3%) | 0.42(0.22–0.82) | 0.010 | - | |
| | No | 54(75.0%) | 200(87.7%) | 1 | | | |
| Mechanical ventilation | Yes | 5(6.9%) | 50(21.9%) | 3.76(1.43–9.84) | 0.007 | 2.69(0.96–7.56) | 0.059 |
| | No | 67(93.1%) | 178(78.1%) | 1 | | 1 | |
| Culture done | Yes | 11(15.3%) | 21(9.2%) | 0.56(0.25–1.23) | 0.150 | 0.32(0.13–0.81) | 0.016 |
| | No | 61(84.7%) | 207(90.8%) | 1 | | 1 | |
| Undergone surgery? | Yes | 45(62.5%) | 77(33.8%) | 0.31(0.18–0.53) | <0.001 | - | |
| | No | 27(37.5%) | 151(66.2%) | 1 | | | |
| Analgesic (s) use | Yes | 51(70.8%) | 117(51.3%) | 0.43 (0.25–0.77) | 0.004 | - | |
| | No | 21(29.2%) | 111(48.7%) | 1 | | | |
| Steroid use | Yes | 3(4.2%) | 38(16.7%) | 4.60(1.38–15.38) | 0.013 | - | |
| | No | 69(95.8%) | 190(83.3%) | 1 | | | |
| Ceftriaxone use | Yes | 62(87.5%) | 172(75.4%) | 0.44(0.21–0.94) | 0.034 | - | |
| | No | 9(12.5%) | 56(24.6%) | 1 | | | |
| Metronidazole use | Yes | 54(75.0%) | 102(44.7%) | 0.27(0.14–0.48) | <0.001 | 0.25(0.13–0.49) | <0.001 |
| | No | 18(25.0%) | 126(55.3%) | 1 | | 1 | |
| Cephalexin use | Yes | 15(20.8%) | 18(7.9%) | 0.33(0.16–0.69) | 0.003 | - | |
| | No | 27(79.2%) | 210(92.1%) | 1 | | | |
| Vancomycin use | Yes | 22(30.6%) | 130(57.0%) | 3.01(1.71–5.30) | <0.001 | 2.93(1.57–5.48) | 0.001 |
| | No | 50(69.4%) | 98(43.0%) | 1 | | 1 | |
| Ceftazidime use | Yes | 20(27.8%) | 106(46.5% | 2.26(1.27–4.03) | 0.006 | - | |
| | No | 52(72.2%) | 122(53.5%) | 1 | | | |

**Abbreviations**: AMT, antimicrobial therapy; AOR, adjusted odds ratio; COR, crude odds ratio; CI, confidence interval.

inappropriate AMT. A similar finding was reported from Addis Ababa, Ethiopia (66.7%),[17] wrong choices of medications account for the higher proportion (53.6%) of inappropriate AMT. The slightly different findings were reported from Kyrgyzstan[27] and Switzerland,[32] where inappropriate indication was the most common reason given for inappropriateness. This might be due to inappropriate initiation of AMT for viral infection and/or without the clear clinical syndrome supporting the bacterial infection.[40] However, an inappropriate indication was the third commonly identified class of inappropriate AMT in the present study.

In our study, inappropriate AMTs were frequently recorded from the internal medicine (84.3%) ward. This might be because a higher proportion of participants in the present study are from the internal medicine ward and these patients have more comorbidities. This is explicated by the pre-existing evidence showing a linear relationship between the number of medical conditions and poor patient care.[41,42]

Various reports have shown that HAIs make a significant contribution to increased mortality.[8,43,44] In the current study, the incidence of all-cause in-hospital mortality in patients with HAIs was 17.7%. This finding is higher than a previous study from Jimma University Medical Center in Ethiopia, which reported 7.5%.[45] This difference might be due to the variation in the study setting, the latter study recruited patients from all hospital wards, while the current study enrolled from three wards. However, a higher result was reported from Serbia, where the death rate in patients with HAIs was 44.4%.[46] This disparity might be due to the difference in the study participants, the study from Serbia recruited patients from the intensive care unit.

Empirical prescriptions were more often inappropriate than evidence-based prescriptions, ie, adjustment of antibiotic therapy based on the findings of blood culture results in optimal antibiotics and reduces unnecessary broad-spectrum antibiotic use.[47,48] This is also supported by the current study, where patients having culture findings had a 68% lower risk of inappropriate AMT use compared with those without it.

The present study showed that metronidazole use in patients with HAIs decreases the risk of inappropriate AMT use by 75.0%, which is in line with a finding from the Netherlands.[24] On the other hand, patients who were taking vancomycin had nearly three times at increased risk of inappropriate AMT use than patients not taking it. This is different from Pakistan,[28] Switzerland,[32] and Maryland[49] studies, where cephalosporin use, penicillin with β-lactamase inhibitors and cephalosporin use, and cefepime or piperacillin-tazobactam use were factors associated with inappropriate use of antibiotics, respectively. This inconsistency might be due to the possibility of variation in the availability, cost, and utilization of antibiotics across the countries.

In general, the present study was able to determine and assess the proportion of AMT appropriateness in patients with HAIs and associated factors. Nevertheless, the authors would like to acknowledge the following limitations. Culture and sensitivity tests were performed for only a small proportion of the participants, thus in most cases, the attending clinicians diagnosed infections based on clinical criteria. Furthermore, the consideration of a single-center and small sample size may have affected the power of the present study.

## Conclusion

More than three-fourths of patients with HAI had inappropriate AMT. Hospital-acquired pneumonia was the most frequently diagnosed HAI, followed by SSI and UTI. A decrease in the likelihood of inappropriate AMT was identified in patients having culture findings and in those taking metronidazole, whereas taking vancomycin increased the likelihood of inappropriate AMT. Therefore, scaling up the capacity of definitive therapy through culture and sensitivity tests is warranted. Furthermore, training of prescribers on the rational use of antimicrobials and adoption of international guidelines for the development of institutional/local treatment guidelines based on the local micro-organism profile might help lessen inappropriate AMT use.

## Abbreviations

AOR, Adjusted Odds Ratio; AMT, Antimicrobial therapy; BSI, Blood Stream Infection; CAUTI, Catheter-Associated Urinary Tract Infection; COR, Crude Odds Ratio; HAP, Hospital-Acquired Pneumonia; IDSA, Infectious Diseases Society of America; JMC, Jimma Medical Center; MRSA, *Methicillin-Resistant Staphylococcus Aureus*; SSI, Surgical Site Infections; SSTIs, Skin and Soft Tissue Infections; USA, United States of America; UTI, Urinary Tract Infections; WHO, World Health Organization.

## Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Ethical Consideration

Ethical clearance and approval were obtained from the Institutional Review Board (IRB) of Jimma University under the reference number of IRB 000193/2020 and all methods were conducted in accordance with the principles of the Declaration of Helsinki. The written informed consent was obtained from the patient before data collection started.

## Consent for Publication

Consent for publication is not applicable in this study.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.


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## Disclosure

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