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Inappropriate Antibiotics Use and Its Associated Factors among Patients with Hospital-Acquired Infection in the Medical and Surgical Ward of Wollega University Referral Hospital, Nekemte, Western Ethiopia: A Prospective Cross-Sectional Study

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Abstract

Background: A hospital-acquired infection is an infection that arises during a patient's hospital stay, typically 48–72 hours after admission, and was not present or incubating at the time of admission. In low- and middle-income countries, antibiotics are improperly prescribed. Ethiopia is one of the countries where the healthcare system is not yet developed, and a report revealed that about 76% of HAIs are managed inappropriately.

Objective: To assess inappropriateness of antibiotics use and its associated factors among patients with hospital-acquired infection in the medical and surgical wards of Wollega University Referral Hospital, Western Ethiopia.

Methods: A cross-sectional study was conducted in the medical and surgical wards of Wollega University Referral Hospital from June 1, 2023, to August 31, 2023. All patients who developed hospital-acquired infections were included using a consecutive sampling technique. The data were entered into Epidata version 4.2.0 and exported to SPSS version 21.0 for analysis. Multivariable logistic regression was performed to identify factors associated with antibiotics therapy appropriateness, and the adjusted odds ratio (AOR) was used to assess the strength of the association between the outcome and independent variables, where statistical significance was declared at a p-value less than 0.05.

Results:A total of 294 patients with HAIs participated in the study. The overall mean age (± standard deviation) of the patients was 43.88 ± 15.14 years. The number of patients with HAIs who were treated inappropriately was 230 (78.2%). Hospital-acquired pneumonia (52.0%) was the most prevalent HAI. The most common type of inappropriate antibiotic use was inappropriate choice (137/294, 46.6%). Patients having self-medication practice (AOR=6.767, 95% CI: 1.951-23.473, P=0.003), taking anti-emetics (AOR=7.43, 95% CI: 1.594- 34.645, P=0.01), and taking 4-6 drugs (AOR=5.337, 95% CI: 1.208-23.569, P=0.027) were significantly associated with antibiotics use related problems.

Conclusion and Recommendation: This study identified that patients with HAI had a high rate of inappropriate antibiotic use, but this decreased when they received ceftazidime and vancomycin, took two or fewer antibiotics, switched from intravenous to oral medication, and stayed in the hospital for 20 days or less. Therefore, the development of local treatment guidelines might be used to optimize appropriate antibiotic use among patients with HAI.

Introduction

A hospital-acquired infection (HAI) is an infection that develops throughout treatment at a hospital for 48–72 hours but was not present at the time of admission (1, 2). The most common predisposing factors among patients with HAIs are older age, immunocompromised medical conditions, prolonged hospitalization, inappropriate use of antibiotics, prior antibiotic use, surgery, and other underlying patient conditions (3–7). The most frequent HAIs include hospital-associated pneumonia (HAP), catheter-associated urinary tract infections (CAUTI), bloodstream infections (BSI), surgical site infections (SSI), ventilator-associated pneumonia (VAP), and skin and soft tissue infections (SSTI). These infections are determined based on clinical signs, physical examination, and laboratory results (8). Almost 90% of HAIs are brought on by bacteria such as Klebsiela pneumonia, S. aureus, E.coli, Proteus spp., and P. aeruginosa (7).

Hospital-acquired infections are significant public health problems that affect 2 million people annually (9, 10), and results from studies indicate that each year, 100 million patients are affected around the world (11). HAI

prevalence in sub-Saharan Africa ranges from 2% to 49%, with patients in intensive care units ranging from 21.2% to 35.6% (3). Increased morbidity and mortality, compromised patient care, lengthened hospital stays, higher healthcare costs, and an increase in the growth of antibiotic-resistant microbes are all effects of HAI (3, 4). Inappropriate antibiotic practice arise when antibiotics are used inappropriately, which has an impact on patient health outcomes and can potentially lead to bacterial resistance (12).

In 2019, the CDC estimates that each year, antibiotic-resistant infections result in the deaths of more than 35,000 Americans (13). In Greece, the current Antimicrobial resistance levels in HAIs with limited treatment options were €73 million in hospitalization costs (14). A published study conducted in England indicated the attributable costs for resistant infections compared to susceptible infections in high-income and upper- and middle-income economies were high (2). The estimated AMR would cost the world up to 100 trillion USD by 2050 (15). Similarly, evidence from Ethiopia showed multidrug-resistant strains, inappropriate antibiotic use, and self-antibiotic prescription were 59.7%, 49.2%, and 43.3%, respectively. The reasons for inappropriate antibiotic use were the wrong indication, the wrong duration, and improper discontinuation of antibiotics (16). The inappropriate use of antibiotics in hospitals increases resistance, morbidity, and mortality (17).

In Serbia, surgical antibiotic prophylaxis (SAP) for more than 1 day was recommended for 71.4% of patients (18). In Ghana, SAP was administered for longer than one day to 88.4% of patients (19). In Cameroon, the majority of prescribed antibiotics were empirical (20). In Northeast Ethiopia, 48.6% of SAPs were inappropriate in the timing of administration (21). In Tikur Anbessa Specialized Hospital, 88.9% of patients received antimicrobial prophylaxis for more than 24 hours after surgery (22). Antibiotics are inappropriately given to 44% to 97% of hospitalized patients in LMIC, which significantly increases bacterial resistance. Inappropriate antibiotic use, diagnostic uncertainty, prevalence of self-medication, and a lack of diagnostic resources are the causes of improper antibiotic use and prescribing errors (5, 19).

In hospitals, increasing multidrug-resistant strains of infectious organisms are diminishing the efficacy of current medicines, making the management of HAIs a significant concern. The treatment of HAIs requires a definitive therapy. Nonetheless, antibiotic treatments are empirical in LMIC (5). In Africa, the absence of budget lines for ASP activities and the lack of systems aimed at pathogen identification and antibiotic susceptibility for optimal use of antibiotics were reported (23). Additionally, barriers to improving antibiotics prescribing were prohibitively expensive, limited availability, the resistance of antimicrobials, and limited diagnostic capabilities (24). However, ASP efforts in LMIC have been constrained in terms of their resources, feasibility, and effectiveness (25).

The lack of administration standards for presumptive and prophylactic antibiotic use is unclear in LMIC. This is a significant problem because of the widespread overuse of antimicrobial drugs and the possible emergence of AMR (26, 27). Therefore, this study aimed to assess inappropriate antibiotics use and its associated factors among hospitalized patients with HAI in the medical and surgical wards of Wollega University Referral Hospital, Nekemte town, Western Ethiopia.

Methods and materials

Study Area and Period

This study was conducted in the medical and surgical ward of Wollega University Referral Hospital (WURH), located 330 kilometers west of Addis Ababa, the capital of Ethiopia. The hospital has several wards, including medical, surgical, emergency medicine, and ART. It has about 300 beds in total. WURH employs a variety of

healthcare professionals: 27 general practitioners, 37 medical laboratory scientists, and 45 pharmacists. Annually, the hospital serves approximately 74,692 patients in total, with about 13,440 receiving chronic care. Over the past year (from April 1, 2022, to March 31, 2023), there were 1,345 patients with HAIs in the internal medicine and surgical wards at WURH. Currently, WURH provides clinical services such as inpatient care, laboratory services, pharmacy services, and others. Data were collected from June 1 to August 31, 2023.

Study Design: A hospital-based prospective cross-sectional study was employed.

Source Population: All patients who developed HAI in the medical and surgical ward of WURH

Study Population: All patients who developed HAI in the medical and surgical ward of WURH who fulfilled the inclusion criteria during the study period

Inclusion Criteria

- All patients with confirmed HAIs after 48 hours of admission
- Age ≥18 years

Exclusion Criteria

- Patients with incomplete medical records.
- Readmissions during the study period.
- Patients who are severely ill and can't give information

Sample Size Determination and Sampling Techniques

Sample Size Determination

The sample size was determined using a single population proportion formula with the following assumption taken into account: P is the proportion of antimicrobial use-related problems, which was 0.76 in the previous study conducted at Jimma (5). Z is the level of confidence of 1.96 with a 95% confidence interval and a 5% margin of error (d). The number of patients with HAIs in the internal medicine and surgical wards of Wollega University Referral Hospital in the past 1-year (from April 1, 2022, to March 31, 2023) was 1345.

$$\text{Sample size (n)} = \frac{[(Z\ \alpha/2)^2 \text{ x } p\ (1\text{-}p)]}{d^2} = \frac{(1.96)^2 * 0.76(1\text{-}0.76)}{(0.05)^2}$$

$$= \frac{(3.8416)*(0.1824)}{0.0025}$$

$$= \frac{0.70071}{0.0025} = \mathbf{280}$$

By adding 10% to the follow-up rate**: 308**

Sampling Techniques

The sample size was proportionally allocated based on the percentage of patients admitted to each ward: (445/1345*308) = 102 for the surgical ward and (900/1345*308) = **206** for internal medicine. Then, **294** patients were recruited using a consecutive sampling technique.

Dependent variables: Inappropriate antibiotics use in the medical and surgical ward

Independent variables

Socio-demographic factors: age,sex**,** religion**,** annual income, educational status, residence, marital status, occupation

Disease-related factors: reason for admission, length of hospital stay

Drug-related factors: current medication, polypharmacy

Hospital and patient-related factors: self-medication, lack of diagnostic tests

Data Collection Tools and Techniques

The data abstraction was developed after reviewing a medical chart of patients with HAIs and various literature (5, 28-31). Four pharmacists collected the data after receiving training for two days on the data collection process. Each patient's medical chart was assessed daily for HAI diagnosis. The attending physician diagnosed HAIs based on the Centers for Disease Control/National Healthcare Safety Network surveillance definition of HAIs and criteria for specific types of infections in the acute care setting (1). For each patient, AMT appropriateness was assessed using Infectious Disease Society of America (IDSA) antimicrobial prophylaxis and therapeutic guidelines for Hospital-Acquired Pneumonia (32), Ventilator-Associated Pneumonia (32), Catheter Associated Urinary Tract Infections (33), Skin and Soft Tissue Infection (34), WHO recommendations for Surgical Site Infections (35) and, Ethiopian Standard Treatment Guidelines (ESTG) 2020 (36).

Outcome Measurement and Validation

Appropriate Antibiotics Therapy: is the right choice of antibiotics (the right indication for use, choice, dose, frequency of administration, route of administration, and duration of treatment) according to IDSA and ESTG recommendations for treating HAIs.

Inappropriate Antibiotics Therapy: This refers to the irrational use of medication that deviates from the appropriate antibiotics therapy for treating hospital-acquired infections (37).

The recorded inappropriate use of Antibiotic therapy was classified based on the standards reported by Gyssens and modified by Willemsen as the standard for evaluating antibiotic prescription (38, 39).

(A) Inappropriate indication; prescription of antibiotics without the presence of infection

(B) Inappropriate choice, inappropriate spectrum antibiotics, or inappropriate toxicity profile

(C) Inappropriate dosage

(D) Inappropriate timing/frequency

(E) Inappropriate route of administration and

(F) Inappropriate duration of therapy

A panel of different multidisciplinary staff (Physicians, Pharmacists, Nurses, laboratory technologists, and Surgeons) was selected and organized based on their clinical experience and specialties. Each member was asked to review the literature, evaluate the evidence, and determine the appropriateness of antibiotics use among patients with hospital-acquired infections, along with evidence consistent with each recommendation of the IDSA 2016 guidelines for HAIs and the STG 2020 guidelines. The panel members reviewed all patients' information from questionnaires and Epidata software. Discrepancies were discussed and resolved, and all panel members were in agreement with the final decision on antibiotics appropriateness and inappropriateness of use recommendations for HAI patients.

Data Quality Assurance

The data collection tools were prepared in English and translated into Afaan Oromoo; then back-translated to English to ensure consistency. Data was collected by trained data collectors. Training was given to data collectors on the objective of the study and the process of data collection for two days. Before the actual data collection process, 5% of study participants were pre-tested in Nekemte Specialized Hospital. Based on feedback from the pre-test, the questionnaires were revised, and necessary modifications were made. The collected data were checked by the supervisor and principal investigator for completeness and accuracy. The data was compiled, coded, and checked for completeness and consistency before analysis. Finally, data analyses began after the completion of the cleaning process.

Data Analysis and Interpretation

The data were coded and entered into Epidata version 4.2.0 and exported to the Statistical Package for the Social Sciences version 21.0. Categorical variables were presented with frequency and percentage. For continuous data, a normality test was conducted using Shapiro–Wilk's test. All continuous data were parametric and reported with mean ± standard deviation. For all categorical variables, cell adequacy was checked. The logistic regression model was used to analyze the association between dependent variables and the independent variable. Variables with a p-value less than 0.25 in bivariate logistic regression were entered into a multivariate logistic regression model. An adjusted odds ratio with a 95% CI was used to assess factors significantly associated with inappropriate antibiotics use. The statistical significance threshold was declared at a P-value <0.05.

Operational Definition

Access groups: are a core set of antibiotics that have activity against a wide range of susceptible pathogens and are recommended as first- or second-choice empiric treatment options (40).

Antimicrobials are agents that destroy or inhibit the growth of microorganisms (36).

Antimicrobial drug therapy problems occur when antimicrobials are used inappropriately, which has an impact on patient health outcomes and potentially leads to bacterial resistance (41).

Antimicrobial stewardship refers to a set of coordinated strategies to improve the use of antimicrobial medications to enhance patient health outcomes, reduce resistance to antibiotics, and decrease unnecessary costs(22).

Bloodstream infection: patient with any of the following signs and symptoms: fever (>38 °C), Chills, hypotension, and at least one positive blood culture not related to contamination (42).

Cather-associated urinary tract infection: infection of the urinary tract after the patient had an indwelling urinary catheter that had been in place for >2 days on the date of the event, with urine cultures ≥ 10^5 CFU/ml and catheter urine ≥ 10^2 CFU/ml or pyuria (≥ 10 WBC) (42).

Hospital-associated pneumonia: respiratory symptoms with at least two of the following appearing during hospitalization: cough, purulent sputum, and a new infiltrate on chest radiograph consistent with infection (42).

Surgical site infection: any purulent discharge, abscess, or spreading cellulitis at the surgical site during the month after the operation (42).

Suspected diagnosis: diagnosis made by the judgment of physicians without adequate evidence of laboratory findings, imaging, and clinical manifestations (43).

Reserve group: antibiotics reserved for treatment of confirmed or suspected infections due to multidrug-resistant organisms (40).

Ventilator-associated pneumonia: this is pneumonia that develops after more than 48 hours of mechanical ventilation on the date of the event (44).

Watch group: critically important antimicrobials for high-risk selection of bacterial resistance and recommended for a limited number of specific infectious diseases (40).

Ethical consideration and consent to participate

Before starting the study, ethical approval was obtained from the Ethical Review Committee (RERC Minutes number: 1034/2023), Institute of Health Science, Wollega University. Additionally, permission was secured from the Department of Pharmacy and the hospital's medical director to carry out the research. **Written informed consent was obtained from all study participants and/or their legal guardians** after providing detailed information about the purpose of the study and potential risks, including the time required for the interview. For participants who could not read or write, verbal informed consent was obtained. Confidentiality was maintained by using code numbers instead of personal names. Patients were informed of the reasons for their selection and assured that refusing to participate would not affect their access to treatment. They were also told they could withdraw from the study at any time.

Results

Socio-demographic characteristics of study participants

Of the 308 patients with HAIs screened, 294 eligible participants were enrolled, giving a 95.5% response rate. A total of 14 patients were excluded: in the medical ward, 4 declined participations, 3 had incomplete medical charts, and 2 were readmissions; in the surgical ward, 2 were critically ill, 2 were readmissions, and 1 declined participation.

The mean age of participants was 43.88 ± 15.14 years, with the largest proportion, 123 (41.8%), falling within the 35–54-year age range. Females accounted for 149 (50.7%) of the study population, while 255 (86.7%) were married. More than half, 153 (52.0%), resided in rural areas. Regarding religion, 196 (66.7%) identified as Protestant. Over half of the participants, 158 (53.7%), reported an average monthly income between 1,500 and 6,000 Ethiopian birr. In terms of education, 93 (31.6%) had attained tertiary education, and the most common occupation was farming, reported by 62 (21.1%) of the participants.

Table 1
Socio-demographic characteristics of patients who developed Hospital-acquired infection in medical and surgical Wards of WURH, June –August, 2024

Variables	Category	Frequency	Percentage
Patient's Sex	Male	145	49.3%
	Female	149	50.7%
Age Category	18–34	90	30.6%
	35–54	123	41.8%
	≥ 55	81	27.6%
Marital status	Single	32	10.9%
	Married	255	86.7%
	Divorced	3	1.0%
	Widowed	4	1.4%
Religions	Orthodox	42	14.3%
	Protestant	196	66.7%
	Muslim	35	11.9%
	Adventist	8	2.7%
	Wakefata	13	4.4%
Educational status	Can’t read or write	19	6.5%
	Non-formal education	22	7.5%
	Primary education (1–8 grade)	76	25.9%
	Secondary education (9–12 grade)	84	28.6%
	Tertiary education (diploma and above)	93	31.6%
Occupation	Farmers	62	21.1%
	Merchant	32	10.9%
	Employed	55	18.7%
	Unemployed	17	5.8%
	House wife	61	20.7%
	Students	40	13.6%
	Private employee	11	3.7%
	Others*	16	5.4%
Income category	< 1500	74	25.2%

Others*: Daily laborer, Driver, Tailor, Retired

Variables	Category	Frequency	Percentage
	1500–6000	158	53.7%
	> 6000	62	21.1%
Current Residence	Rural	153	52.0%
	Urban	141	48.0%
Others*: Daily laborer, Driver, Tailor, Retired			

Clinical characteristics of study participants

Among the HAIs diagnosed, hospital-acquired pneumonia 153 (52.0%) and surgical site infections 58 (19.7%) were the most common, with 23 participants (7.8%) experiencing two HAIs. The mean time to develop HAIs was 5.8 ± 1.8 days. The leading reasons for hospital admission were infectious diseases 116 (39.5%), respiratory disorders (84, 28.6%), and cardiovascular disorders 83 (28.2%). All participants had a peripheral intravenous line, and 192 (65.3%) were catheterized. The most frequent clinical manifestations were fever 283 (96.3%) and cough 168 (57.1%). Over half of the participants 166 (56.5%) had three comorbidities, and 116 (39.5%) had been hospitalized once in the past year. The mean length of hospital stay was 15.72 ± 4.40 days, and the majority of patients 277 (94.2%) showed clinical improvement.

Table 2
Clinical characteristics of patients with Hospital-acquired infection in medical and surgical wards of WURH, 2023 (N = 294)

Characteristics	Category	Frequency	Percentages
Reason for admission	Infectious disease	116	39.5%
	Respiratory disorders	84	28.6%
	Cardiovascular disorders	83	28.2%
	Hematologic disorders	65	22.1%
	Soft tissue injury	53	18%
	Kidney disease	40	13.6%
	Gastrointestinal disorders	35	11.9%
	Urologic and biliary tract disorders	52	17.7%
	Diabetes mellitus	15	5.1%
	Others*	25	8.5%
Previous admission in the past 3 months	Yes	36	12.2%
	No	258	87.8%
Number of hospitalizations in the last year	Never	8	2.7%
	One times	116	39.5%
	Two times	86	29.3%
	More than three times	84	28.6%
Invasive device use	Peripheral line inserted	294	100.0%
	Nasogastric tube inserted	64	21.8%
	Catheterized	192	65.3%
	Mechanically ventilated	50	17.0%
Clinical presentation on the diagnosis of HAIs	Fever	283	96.3%
	Cough	168	57.1%
	Tachypnea	165	56.1%
	Tachycardia	151	51.4%
	Localized pain	131	44.6%
	Discharge from the site of infection	74	25.2%
	Swelling at the site of infection	71	24.1%

Others*: Electrolyte imbalance disorder, neurologic & psychiatric disorder, fungal infection

Characteristics	Category	Frequency	Percentages
	Headache	69	23.5%
	Urinary urgency	60	20.4%
	Dysuria	57	19.4%
	Hematuria, Nausea, Vomiting	15	5.1%
Number of comorbidities	2	54	18.4%
	3	166	56.5%
	4	51	17.3%
	5	21	7.1%
	≥ 7	2	0.7%
Overall Hospital stay (days)	≤ 20	251	85.4%
	≥ 21	43	14.6%
Overall clinical outcome of patients	Improved	277	94.2%
	Left against medical advice	9	3.1%
	Referral	6	2.0%
	Death	2	0.7%

Others*: Electrolyte imbalance disorder, neurologic & psychiatric disorder, fungal infection

Practice of surgical antibiotics prophylaxis and consequences of HAI

The most common surgical procedures were upper and lower gastrointestinal tract surgeries 25 (25%), followed by urological procedures 19 (19%). Most participants, 250 (85%), were classified as low-risk (score 0–2) according to the Charlson comorbidity index. Although exact costs of antimicrobial-resistant HAIs are difficult to measure, the direct treatment costs were calculated from patient and government perspectives, considering self-payers, free care, and insurance coverage. Among participants, 188 (63.9%) were self-payers, 18 (6.1%) received free care, and 88 (29.9%) were insured. The estimated mean direct medical cost due to HAIs was 8,099.17 ± 2,209.67 Ethiopian Birr.

Table 3
Types of surgery and other determinants among Hospital-acquired infection in medical and surgical wards of Wallaga University Referral Hospital, 2023 (N = 294)

Variables	Category	Frequency	Percentages
Undergone surgery	Yes	97	34.0%
	No	197	67.0%
Discipline of surgery	Upper and lower GIT	25	25.8%
	Urology	19	19.6%
	Skin and deep tissue	18	18.6%
	Biliary Tract	7	7.2%
	Hernia repair	5	5.2%
	Head and neck	5	5.2%
	Breast	4	4.1%
	Others*	14	14.4%
Cost Types	Self payer	188	63.9%
	Free	18	6.1%
	Insurance	88	29.9%
Charlson comorbidity index score	0–2	250	85.0%
	3–4	38	12.9%
	≥ 5	6	2.0%
Laboratory investigation on the diagnosis of HAIs	White Blood Cell	$16.6 \pm 3.7\times10^3$cells/ml	
	Red Blood Cell	$4.1 \pm 0.8\times10^6$ cells/ml	
	Platelet Count	$347 \pm 128\times10^3$cells/ml	
	Erythrocyte Sedimentation Rate	50 ± 13.5mm/hr	
	Neutrophils%	81.03 ± 5.43	

Others* Other organ or space infection, Soft tissue injury, Reproductive infection

Time of antibiotics prophylaxis among HAI Patients who underwent surgery

Among the 294 patients, 97 (34.0%) received preoperative antimicrobial prophylaxis, of whom 96 (32.7%) also received postoperative prophylaxis. For preoperative administration, 49 (50.5%) received it within 2 hours before surgery, 44 (45.4%) within 1 hour, and 7 (7.2%) within 30 minutes. Regarding postoperative prophylaxis, 41 (42.7%) patients received it for more than 72 hours, 34 (35.4%) for 48 hours, and only 21 (21.9%) for 24 hours or less.

Treatments of HAI and medication information of participants

During hospitalization, the most commonly administered medication classes were analgesics 219 (74.5%), anti-ulcer drugs 192 (65.3%), and cardiovascular medications 94 (32.1%). Antibiotics used to treat HAIs included Vancomycin 170 (57.8%), Ceftazidime 159 (54.1%), and Metronidazole 141 (48%), with therapeutic purposes accounting for 183 (62.2%) of antibiotic use. Nearly three-fourths of patients (74.8%) had antibiotic exposure within 3 months prior to admission, and the majority (78.6%) received three or more antibiotics during their hospital stay, with a mean exposure of 3.49 ± 1.14. The average number of drugs per patient was 7.87 ± 1.84, with 76.5% using seven or more drugs. Self-medication was reported in 178 patients (60.5%), mainly due to cost-cutting 66 (37.1%) and long delays in health facilities 49 (27.5%). Of all prescribed antibiotics for HAIs, 577 (73%) were from the Watch group and 213 (27%) from the Access group.

Table 4
Treatments and Medication Information among Patients with HAI in Medical and Surgical Wards of WURH, 2023 (N = 294)

Variables	Category	Frequency	Percentage
Antibiotics used for HAIs	Vancomycin	170	57.8%
	Ceftazidime	159	54.1%
	Metronidazole	141	48%
	Ceftriaxone	136	46.3%
	Ciprofloxacin	39	13.3%
	Cefepime	35	11.9%
	Amoxicillin/clavulanic acid	33	11.2%
	Cloxacillin	11	3.7%
	Norfloxacin	7	2.4%
	Azithromycin	6	2.0%
	Piperacillin Tazobactam	3	1.0%
	Cephalexin	3	1.0%
	Meropenem	2	0.7%
	Amoxacillin	1	0.34%
Medications used for comorbidities	Antipain	219	74.5%
	Antiulcer	192	65.3%
	Cardiovascular medications	94	32.1%
	Steroids	79	26.9%
	Antiemetics (Metoclopramide)	74	25.2%
	Antidepressant	61	20.7%
	Therapeutic Iron	60	20.4%
	Antimalaria	58	19.7%
	Heparin Therapy	24	8.2%
	Salbutamol	23	7.8%
	Warfarin	18	6.1%
	Antidiabetic	16	5.5%
	Statins	16	5.5%
	Antiseizure	15	5.1%
	Others*	53	18.0%

Variables	Category	Frequency	Percentage
Indications for antibiotic use	Therapeutics	183	62.2%
	Prophylaxis and therapeutics	111	37.8%
History of antibiotics exposure in the past 3 months	Yes	220	74.8%
	No	74	25.2%
Total drugs used	≤ 3	12	4.1%
	4–6	57	19.4%
	≥ 7	225	76.5%
Total Antibiotic used	≤ 2	63	21.4%
	≥ 3	231	78.6%
Self-Medication History	Yes	178	60.5%
	No	116	39.5%
Reasons for self medication	Cost-cutting	66	37.1%
	Long delays in health facility	49	27.5%
	Busy day's program	46	25.8%
	Easy access from nearby facility	9	5.1%
	Easy access from friends or neighbor	8	4.5%

Others* *Anti-constipation, Antipsychotic, Mannitol, Vitamins, TAT, Antifungal drugs*

Appropriateness of antibiotics use among Hospital-acquired infection

Among the 294 study participants, **230 (78.2%)** experienced at least one antibiotics therapy problem, with inappropriate antibiotics use most common in the **internal medicine ward (67%)** followed by the **surgical ward (33%).** Conversion from intravenous to oral therapy was performed in **135 (45.9%)** participants. The most frequent antibiotics use-related problem was **inappropriate choice** (137, 46.6%), followed by delayed intravenous-to-oral conversion (45/135, 33.3%) and **inappropriate dosing** (92, 31.3%). The mean time for intravenous -to-oral conversion was **5.20 ± 4.56 days**. The overall mean hospital stay due to HAIs was **9.26 ± 3.31 days**, and in-hospital mortality occurred in **2 (0.7%)** patients.

Table 5
Types of inappropriate antibiotics use for patients with Hospital-acquired infection in medical and surgical wards of WURH, 2023 (N = 294)

Types of Antibiotics use-related problems	Category	Frequency	Percentage
Inappropriate Choice **(N = 294)**	Yes	137	46.6%
	No	157	53.4%
Late to change IV to PO **(N = 135)**	Yes	45	33.3%
	No	90	66.7%
Inappropriate Dose **(N = 294)**	Yes	92	31.3%
	No	202	68.7%
Inappropriate Duration **(N = 294)**	Yes	61	20.7%
	No	233	79.3%
Inappropriate Indication **(N = 294)**	Yes	54	18.4%
	No	240	81.6%
Inappropriate Frequency **(N = 294)**	Yes	19	6.5%
	No	275	93.5%
Inappropriate Route of administration **(N = 294)**	Yes	7	2.4%
	No	287	97.6%

Factors associated with antibiotics inappropriateness among Hospital-acquired infections

In the multivariate logistic regression analysis of 16 variables, several factors were significantly associated with inappropriateness of antibiotics use. Patients with a history of self-medication were 7 times more likely to experience antibiotics use inappropriately (AOR = 6.767, 95% CI: 1.951–23.473, p = 0.003). Use of ceftriaxone and metronidazole (AOR = 0.024, 95% CI: 0.001–0.840, p = 0.040) and ceftazidime and vancomycin (AOR = 0.004, 95% CI: 0.000–0.207, p = 0.006) was associated with a lower likelihood of inappropriate antibiotics use. Conversely, patients taking anti-emetics were 7 times more likely to have antibiotics use related problems (AOR = 7.430, 95% CI: 1.594–34.645, p = 0.011), whereas those receiving anti-seizure medications were less likely to experience inappropriate use of antibiotics (AOR = 0.009, 95% CI: 0.000–0.334, p = 0.011).

Patients who underwent intravenous-to-oral conversion were less likely to practice inappropriate use of antibiotics (AOR = 0.265, 95% CI: 0.073–0.965, p = 0.044). Taking 4–6 drugs increased the likelihood of inappropriate antibiotics use fivefold compared with ≤ 3 drugs (AOR = 5.337, 95% CI: 1.208–23.569, p = 0.027), while using ≤ 2 antibiotics reduced the risk (AOR = 0.225, 95% CI: 0.063–0.795, p = 0.021) compared with ≥ 3 antibiotics. Finally, patients with a hospital stay of ≤ 20 days were less likely to experience inappropriate antibiotics use than those hospitalized for ≥ 21 days (AOR = 0.127, 95% CI: 0.019–0.870, p = 0.036).

Table 6
Bivariate and Multivariate logistic regression analysis to identify factors associated with inappropriate antibiotics use among patients with HAI at WURH, 2023

Variables	Category	Appropriateness of Antibiotics use		COR(95%CI)	P-value	AOR(95%CI)	P-value
		Appropriate (n = 64)	Inappropriate (n = 230)				
Self Medication History	Yes	31(48.4%)	147(63.9%)	**1.885** (1.078–3.298)	**0.026**	**6.767** (1.95-23.473)	**0.003**
	No	33(51.6%)	83(36.1%)	1		1	
Antibiotic use in past 3 months	Yes	42(65.6%)	178(77.4%)	**1.79**3 (0.983–3.271)	**0.057**	0.938 (0.281–3.133)	0.918
	No	22(34.4%)	52(22.6%)	1			
Nasogastric tube inserted	Yes	21(32.8%)	43(18.7%)	0.471(0.254–0.874)	**0.017**	1.734 (0.505–5.955)	0.382
	No	43(67.2%)	187(81.3%)	1		1	
Undergone Surgery	Yes	34(53.1%)	66(28.7%)	**0.355** (0.201–0.627)	**0.001**	-	-
	No	30(46.9%)	164(71.3%)	1		1	
Catheterized	Yes	46(71.9%)	146(63.5%)	0.68 (0.37–1.249)	**0.214**	1.027 (0.05-20.895)	0.986
	No	18(28.1%)	84(36.5%)	1		1	
Ceftriaxone and Metronidazole	Yes	34(53.1%)	90(39.1%)	**0.567** (0.325–0.991)	**0.046**	**0.024** (0.001–0.84)	**0.040**
	No	30(46.9%)	140(60.9%)	1		1	
Ceftazidime and Vancomycin	Yes	28(43.8%)	130(56.5%)	**1.671** (0.956–2.922)	**0.071**	**0.004** (0.00-0.207)	**0.006**
	No	36(56.3%)	100(43.5%)	1		1	
Anti-pain	Yes	55(85.9%)	164(71.3%)	**0.407** (0.19–0.87)	**0.020**	0.125 (0.012–1.265)	0.078
	No	9(14.1%)	66(28.7%)	1			
Anti-ulcer	Yes	37(57.8%)	155(67.4%)	**1.508** (0.855–2.66)	**0.156**	2.067 (0.647–6.601)	0.221
	No	27(42.2%)	75(32.6%)	1		1	

Anti-emetics	Yes	6(9.4%)	68(29.6%)	**4.058** (1.671–9.851)	**0.002**	**7.43** (1.594–34.645)	**0.011**
	No	58(90.6%)	162(70.4%)	1		1	
Anti-seizure	Yes	6(9.4%)	9(3.9%)	**0.394** (0.135–1.151)	**0.089**	**0.009** (0.00-0.334)	**0.011**
	No	58(90.6%)	221(96.1%)	1		1	
IV to PO conversion	Yes	42(65.6%)	93(40.4%)	**0.356** (0.199–0.635)	**0.000**	**0.265** (0.073–0.965)	**0.044**
	No	22(34.4%)	137(59.6%)	1		1	
Post-operation antibiotics duration	≤ 24 hours	11(17.2%)	10(4.3%)	**0.303** (0.101–0.906)	**0.033**	0.41(0.10–1.69)	0.220
	48 hours	12(18.8%)	23(0.1%)	**0.639** (0.241–1.696)	0.368	0.83 (0.23–2.99)	0.771
	72 hours	11(17.2%)	33(14.3%)	1		1	
Total drugs	≤ 3 drugs	5(7.81%)	7(3.04%)	**0.340** (0.103–1.123)	**0.077**	0.406 (0.250–4.766)	0.392
	4–6 drugs	15(31.3%)	42(18.3%)	**0.596** (0.322–1.102)	**0.099**	**5.337** (1.208–23.57)	**0.027**
	≥ 7 drugs	44(68.8%)	181(78.7%)	1		1	
Total Antibiotics	≤ 2 antibiotics	22(34.4%)	40(17.4%)	**0.402** (0.217–0.746)	**0.004**	**0.225** (0.063–0.795)	**0.021**
	≥ 3 antibiotic	42(65.6%)	190(82.6%)	1		1	
Overall Hospital Stay	≤ 20 days	58(90.6%)	193(83.9%)	**0.540** (0.217–1.342)	**0.185**	**0.127** (0.019–0.870)	**0.036**
	≥ 21 days	6(9.4%)	37(16.1%)	1		1	

Discussion

Inappropriate use of antibiotics are among the major challenges for the healthcare system (45). This study attempted to address inappropriate antibiotics use and factors associated with hospital-acquired infections at Wollega University Referral Hospital. In this study, 78.2% of hospital-acquired infections were treated inappropriately. The most frequent types of inappropriate antibiotics use were inappropriate choice, too late to change intravenous to oral, inappropriate dose, and inappropriate duration, accounting for 46.6%, 33.3%, 31.3% and 20.7%, respectively.

This study revealed that the proportion of inappropriate antibiotics use among patients with HAIs was 78.2%. This finding was lower compared to the study findings from China (86.97%) (46), Italy (79.8%) (29), and Mizan Tepi (80.1%) (47). The difference might be due to the study setting; the study from China enrolled patients from all Chinese hospitals, in Italy, two hospitals in Southern Italy, in three units, and in Mizan Tepi, patients were recruited from three hospitals, respectively.

However, it was higher than a report from Japan (38.0%)(48), Pakistan (70.3%) (17), Vietnam (30.8%) (49), Jimma (75.7%) (28), and Dilla (70.74%) (50). The study population and the hospital setting may have contributed to this discrepancy. In Japan, 820 patients were recruited from multicenters; in Pakistan, 1185 patients were enrolled from 2 private hospitals and 2 public hospitals; in Vietnam, 5104 patients were recruited from multicenters. Furthermore, the study population's high access variability to antimicrobial drugs and patients' treatment based on culture results, which differed from this study in which the primary therapy was empirical, may have contributed to the difference.

As per the present findings, the most frequent types of HAIs identified were HAP (52.0%), SSI (19.7%), and UTI (16.3%), respectively. This was almost similar to the study reported from Nepal (51), where HAP (53%), SSI (15.4%), and UTI (12.8%) were the most frequent HAIs reported. This finding was also consistent with reports from Ethiopia on SSI and pneumonia (24.7%), followed by UTI 19.8% (43). In Italy(4), pneumonia (29.6%), UTI (19.1%), and SSI (13.3%), and Serbia (31), SSIs (20.0%) were the most common HAI. The high prevalence of HAP, SSI, and UTI may be attributed to factors such as prolonged hospital stays, invasive procedures, inadequate infection prevention practices, and limited adherence to antimicrobial prophylaxis protocols. To reduce the burden of HAIs, hospitals should strengthen infection prevention and control measures, including strict hand hygiene, proper sterilization of surgical instruments, and routine surveillance of HAI incidence.

According to the current study, the inappropriate choice of antibiotics accounts for 46.6%. This was similar to a study finding reported from Jimma (28), where wrong choices of medications account for 44.1%. However, the current study finding was different from a study reported from Addis Ababa, which showed that wrong choices of medications account for 53.6. This study also revealed that the longer duration accounts for 19%, which was similar to the current study's 20.7% (43). %. The discrepancy might be due to the patients from Addis Ababa were recruited from 4 wards (medical, pediatrics, gynecology and obstetrics, and surgical) with 410 patients. To address inappropriate antibiotics therapy choices and prolonged durations, hospitals should strengthen clinical decision-making support systems that integrate local resistance patterns and treatment guidelines into prescribing workflows. Establishing multidisciplinary antimicrobial stewardship teams—including physicians, pharmacists, and microbiologists—can facilitate case-by-case review of antimicrobial prescriptions. Regular prescriber training and audit-feedback sessions should be conducted to reinforce evidence-based prescribing practices. Furthermore, implementing stop/review dates for antimicrobial prescriptions in medical records can help ensure timely discontinuation or adjustment, thereby minimizing unnecessary exposure and reducing resistance risk.

This study found that delayed switching from intravenous (IV) to oral (PO) antibiotics accounted for 33.3% of inappropriate antibiotics use therapy, which is substantially higher than the 9% reported in Switzerland (52) and slightly higher than the 25.8% reported in Jimma (28). The difference may be attributed to variations in study settings, clinical protocols, and prescribing practices related to IV-to-PO conversion. Hospitals should adopt clear IV-to-PO conversion protocols that specify clinical stability criteria and timelines for switching. Prescribers should be trained to assess patient readiness for PO therapy early and consistently. Integration of electronic medical record alerts or pharmacist-driven reminders can prompt timely conversion. Regular audits of IV-to-PO switching

practices, with feedback to prescribers, will further promote adherence and improve antimicrobial stewardship outcomes.

The current study found that 42.7% of patients received postoperative surgical antimicrobial prophylaxis (SAP) for more than 72 hours, followed by 35.4% who received it for 48 hours. This aligns with findings from Switzerland (52), where inappropriately extended postoperative SAP occurred in 42% of patients. Additionally, the hospital mortality rate for patients with HAIs in this study was 0.7%, which is markedly lower than the 17.7% reported in Jimma (28). This difference may be explained by the broader patient inclusion in the study, which covered three wards, compared to only two wards in the current study. To minimize prolonged and unnecessary SAP use, hospitals should enforce evidence-based perioperative antimicrobial guidelines specifying optimal timing and duration. Surgeons and perioperative teams should receive targeted training on SAP protocols, with pharmacist-led audits to ensure adherence. For HAI outcomes, continuous infection prevention and control measures and early, appropriate management of infections should be prioritized to sustain low mortality rates and further improve patient outcomes.

This study's multivariate logistic regression analysis indicated that ceftriaxone and metronidazole use in patients with HAIs reduced the risk of inappropriate antibiotics use therapy by 98.0%, a finding consistent with results from the Netherlands, where the RR (95% CI) for ceftriaxone was 0.66 (0.42–1.04) and for metronidazole was 0.59 (0.37–0.93) (38). Similar results were reported from Jimma, with COR (95% CI) values of 0.44 (0.21–0.94) for ceftriaxone and 0.27 (0.14–0.48) for metronidazole (28). This association could be due to the effectiveness of these antibiotics in reducing the occurrence or severity of hospital-acquired infections, thereby minimizing treatment complications. Hospitals should ensure that ceftriaxone and metronidazole are used appropriately and in line with local antimicrobial resistance patterns. Their use should be guided by evidence-based protocols and microbiological data to prevent overuse and resistance development. Continuous surveillance of antibiotic effectiveness and periodic review of prescribing patterns will help maintain their efficacy while ensuring rational antimicrobial use.

This study also found that patients taking ≤ 2 antibiotics were less likely to experience inappropriate antibiotics use compared to those with ≥ 3 antibiotic exposures, which aligns with findings from Jimma (AOR = 4.838, p = 0.006) (28). This association may be explained by the fact that using multiple antibiotics increases the risk of drug–drug interactions, adverse effects, and non-adherence to treatment. Clinicians should aim to minimize the number of antibiotics prescribed by selecting the most effective regimen with the narrowest spectrum necessary to treat the infection. Regular medication reviews by antimicrobial stewardship teams can help identify opportunities to streamline therapy, thereby reducing unnecessary antibiotic exposure, improving adherence, and minimizing the risk of adverse outcomes.

The current findings indicate that patients treated with Ceftazidime and Vancomycin had a significantly reduced risk of inappropriate antibiotics use therapy (AOR = 0.004; 95% CI: 0.00–0.207). This aligns with evidence from the Netherlands, where reduced risks were also observed for Ceftazidime (RR = 0.66; 95% CI: 0.42–1.04) and Vancomycin (RR = 0.91; 95% CI: 0.41–2.0) (38). However, these results contrast with studies from Pakistan and Switzerland, where cephalosporin, penicillin with β-lactamase inhibitors, and cephalosporin use were linked to higher rates of inappropriate antibiotic use (22, 52). Such discrepancies may be attributable to variations in antimicrobial utilization practices, prescribing guidelines, and resistance patterns between countries. Therefore, local antibiotic stewardship programs should consider national prescribing patterns and resistance profiles when formulating recommendations.

The present study found that 60.5% of patients had a history of self-medication and were seven times more likely to experience inappropriate antibiotics use. The main reasons cited were cost-cutting (37.1%) and long waiting times in health facilities (27.5%). This finding contrasts with a study from Sidama, where 37.9% reported self-medication, and the predominant reason for inappropriate use was prolonged delays in health facilities (46.1%) (53). The discrepancy may be attributed to differences in economic status and the extent to which patients can tolerate waiting times in hospitals. Furthermore, the current study revealed that patients receiving anti-emetics were also seven times more likely to experience inappropriate antibiotics use therapy. Strengthening public awareness on the risks of self-medication, coupled with targeted interventions to improve access to timely healthcare services, may help reduce inappropriate antibiotics use.

Multivariate logistic regression analysis showed that patients taking 4–6 drugs were five times more likely to have inappropriate antibiotics use therapy compared to those taking ≤ 3 drugs. This finding is consistent with reports from Dilla (AOR = 13.51; 95% CI: 4.67–39.05) (50) and Ilu Ababor (AOR = 3.23; 95% CI: 1.43–7.27) (54) (59). This could be explained by the fact that a higher number of medications increases the probability of drug–drug interactions, which may contribute to inappropriate antibiotics use therapy. To reduce the risk of inappropriate antibiotics, use among patients on multiple medications, healthcare providers should conduct regular medication reviews, avoid unnecessary polypharmacy, and ensure close monitoring for potential drug–drug interactions. Integrating clinical pharmacists into the care team can further enhance antimicrobial stewardship efforts.

The present study also revealed that patients with a hospital stay of ≤ 20 days were less likely to develop **inappropriate antibiotics use** compared to those staying ≥ 21 days. This aligns with findings from Jimma (AOR = 3.53; p = 0.007) (28). Prolonged hospitalization increases the risk of acquiring healthcare-associated infections (HAIs) and subsequently raises the likelihood of **inappropriate antibiotics use** occurrence. Healthcare facilities should implement strategies to minimize unnecessary prolonged hospital stays, including early discharge planning, efficient patient management, and enhanced infection prevention measures. Reducing the length of hospitalization can help lower the risk of **inappropriate antibiotics use** and HAIs.

Conclusion

Inappropriate antibiotics use therapy are public health problems in today's world. HAP and SSI were the most commonly encountered HAIs. Inappropriate choice was the most frequent class of inappropriate antibiotics use problems, followed by being too late to change IV to PO. The antibiotics used for treatment of HAIs were Vancomycin, Ceftazidime, and Metronidazole, respectively. Nearly three-fourths of the patients had a history of antibiotic exposure within the past 3 months before admission, and the majority of the antibiotics were prescribed by the Watch Group. In this study, for the majority of patients, preoperative and postoperative antibiotics prophylaxes were administered inappropriately. A decrease in the likelihood of inappropriate antibiotics use was identified in patients taking ceftriaxone and metronidazole, ceftazidime and vancomycin, anti-seizure medications, taking ≤ 2 antibiotics, for patients IV to PO conversion made, and those who stayed ≤ 20 days in hospital. However, patients who had a self-medication history, patients who were taking anti-emetics, and patients who were taking 4-6 drugs increased the likelihood of inappropriate antibiotics use therapy.

Strength of the study

The current study was to ascertain the proportion of inappropriateness of antibiotics use among patients who developed hospital-acquired infection. Furthermore, this finding might be strengthened by the fact that the study design was a prospective follow-up that generated accurate data directly from the patient and the prescribers.

Limitations of the study

Although it was a prospective study, the current study had several limitations. First, the Respondent recall bias could make it difficult for participants to recollect details when answering questions about which complaints were involved while the use of antibiotics. Additionally, the treating physicians did not document all the necessary information about the initiation of antibiotics therapy, and the antibiotics administered were not appropriately documented on the medication administration sheet. Furthermore, the findings of this study cannot be generalized because it was conducted on a small sample size and in a single hospital setting.

Declarations

Data Availability Statement

All data generated or analyzed during this study are included in this article and its Supplementary Material. Further inquiries can be directed to the corresponding author.

Ethical consideration and consent to participate

Before starting the study, ethical approval was obtained from the Ethical Review Committee (RERC Minutes number: 1034/2023), Institute of Health Science, Wollega University. Additionally, permission was secured from the Department of Pharmacy and the hospital's medical director to carry out the research. **Written informed consent was obtained from all study participants and/or their legal guardians** after providing detailed information about the purpose of the study and potential risks, including the time required for the interview. For participants who could not read or write, verbal informed consent was obtained. Confidentiality was maintained by using code numbers instead of personal names. Patients were informed of the reasons for their selection and assured that refusing to participate would not affect their access to treatment. They were also told they could withdraw from the study at any time.

Author Contributions

RS: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Writing – Original Draft, Writing – Review & Editing.

HB and FS: Conceptualization, Data Curation, Project Administration, Resources, Software, Validation, Visualization, Writing – Review & Editing.

DD and GK: Conceptualization, Resources, Software, Validation, Writing – Review & Editing. **ML:** Conceptualization, Data Curation, Formal Analysis, Methodology, Validation, Writing

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Conflict of Interest

The authors declare no commercial or financial relationships that could be perceived as a potential conflict of interest.

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Figures

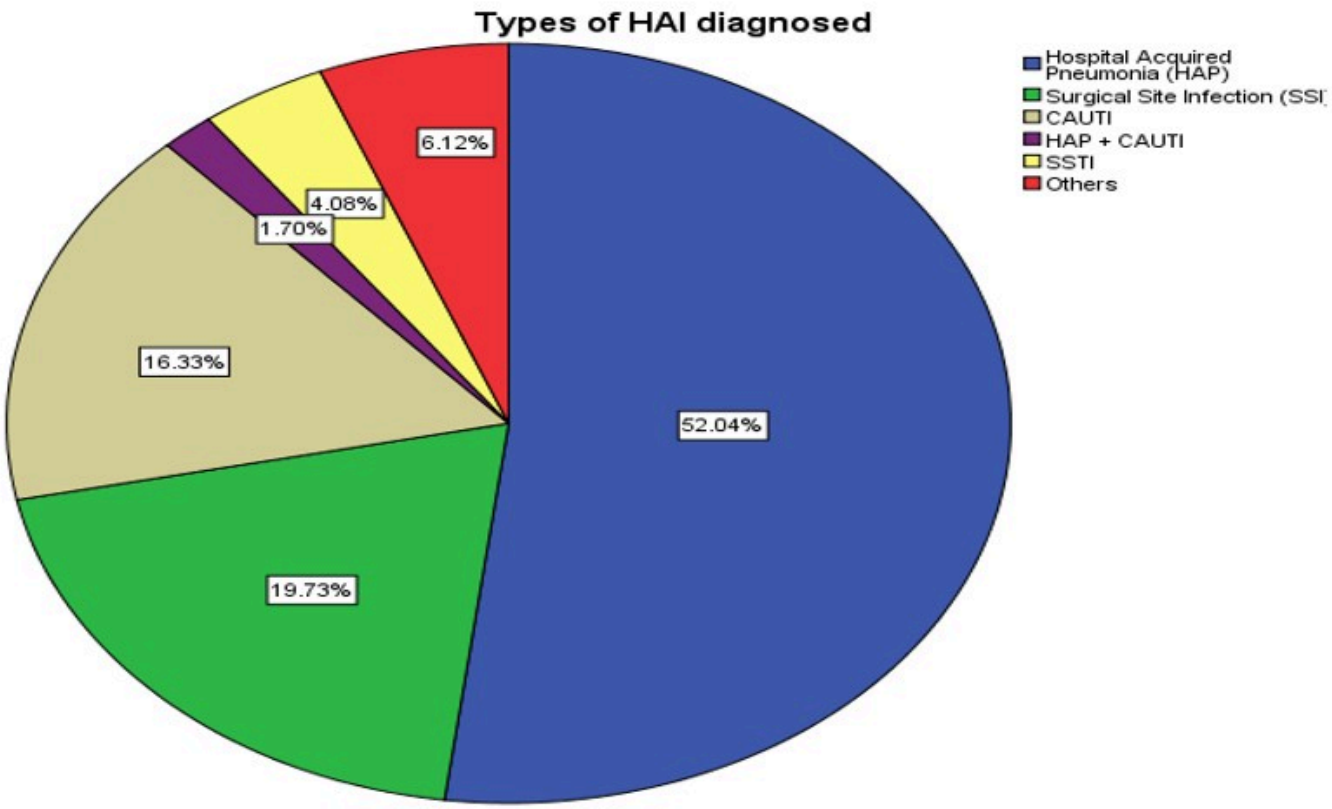


Figure 1

Types of HAI identified during the study period at the medical and surgical ward of Wallaga University Referral Hospital, Nekemte, Ethiopia,2023