ARSI UNIVERSITY COLLEGE OF HEALTH SCIENCE DEPARTMENT OF PEDIATRICS AND CHILD HEALTH

Isolated Pathogens, Antimicrobial Resistance Patterns and Associated Risk Factors Among Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital

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Title of the Research Project	Isolated Pathogens, Antimicrobial Resistance Patterns and Associated Risk Factors Among Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025
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ABSTRACT

Background: Antimicrobial resistance (AMR) is a global public health crisis. Pediatric intensive care units (PICUs) provide care for critically ill children who are at high risk for infections caused by multidrug-resistant (MDR) pathogens. Patients with infections caused by drug-resistant bacteria are at increased risk of worse clinical outcomes including death and increased health care cost.

Objectives: To assess the isolated microbial pathogens, antimicrobial resistance patterns, and associated risk factors among PICU patients beyond the neonatal age group at Asella Teaching and Referral Hospital (ATRH).

Method: A hospital-based cross-sectional study was conducted using medical records of children aged 29 days to 14 years admitted to the PICU of ATRH. Medical records of 217 patients meeting inclusion criteria were included. Data wase coded and entered in to EPI-INFO version 7.2.7.0 and analyzed by Statistical Package for Social Science (SPSS) version 27. In the binary logistic regression analysis odds ratios (OR), 95 % confidence intervals (CI) and P-values was used to determine factors associated with AMR. Variables with P <0.25 in the bivariate analysis was analyzed for multivariate logistic regression. A P-value of less than 0.05 will be considered statistically significant.

Results: Among 217 pediatric ICU admissions, 114 (52.5%) had positive cultures, and 66 isolates underwent antimicrobial susceptibility testing. Coagulase-negative staphylococci were the most frequent isolated organisms, followed by Klebsiella and Enterobacter species. High-risk Antimicrobial resistance (AMR) was identified in 45 (68.2%) isolates. Prolonged PICU stay (>7 days) was independently associated with high-risk AMR (AOR = 7.59; 95% CI: 1.10–52.60). Mortality during PICU admission was also significantly associated with high-risk AMR (AOR = 8.22; 95% CI: 1.39–48.63).

Conclusion: A high prevalence of high-risk antimicrobial resistance was observed among pediatric patients admitted to the PICU. The findings are consistent with Ethiopian hospital-based studies and WHO global surveillance reports. Prolonged length of stay in the PICU and death during PICU admission were significantly associated with high-risk antimicrobial resistance. These findings highlight the close relationship between hospitalization duration, disease severity, and high-risk antimicrobial resistance, and emphasize the need for targeted interventions in pediatric intensive care settings.

Key words: Antimicrobial resistance, Pediatric ICU, Hospital-acquired infections, Asella, Ethiopia

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ABBREVIATION AND ACRONYMS

AMR- Antimicrobial Resistance

ATRH- Asella Teaching and Referral Hospital

BSI-Blood Stream Infections

CAI- Community Acquired Infection

CI- Confidence Interval

CRE- Carbapenem- Resistant Enterobacteriaceae

ESBL-Extended- Spectrum β- lactamase

HAI- Hospital Acquired Infection

KPCs- Klebsiella Pneumoniae–associated Carbapenemases

MDR- Multidrug-Resistant

MRSA- Methicillin- Resistant Staphylococcus Aureus

OR- Odds Ratio

PICU- Pediatric Intensive Care Unit

SPSS- Statistical Package for the Social Sciences

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1. INTRODUCTION

1.1 Background

Antimicrobial resistance (AMR) is a global public health crisis, particularly in low-resource settings where empirical antibiotic use is widespread (1). In 2021, estimated 1.14 million deaths were attributable to AMR and it was forecasted that an estimated will increase to 1.91 million deaths in 2025 (2).

Culture isolates were positive in 19.35% of PICU patients from study at tertiary care hospital in Assam North India from December 2018 to August 2020. Gram negative bacteria were the predominant pathogens mostly Klebsiella species while Enterococcus species were the most common among Gram positive bacteria. Isolates showed multiple drug resistance to commonly used antimicrobials (3).

Africa has the highest global mortality rate from AMR infections. In 2019 it was associated with an estimated 1.05 million deaths in the WHO African region. The most common pathogen-drug combinations contributing to these deaths were Methicillin Resistant Staphylococcus Aureus (MRSA) and third-generation cephalosporin-resistant Klebsiella pneumoniae(4). In Minia University Hospital, Egypt from retrospective cross-sectional study conducted from December 2021 to July 2022, frequency of MDR Organisms among the PICU Patients in was 34.7%. Klebsiella species and Staphylococcus aureus species were the most prevalent MDR Organisms(5).

In Sub-Saharan Africa data indicated that the AMR rates were increasing. In 2019 it had the highest mortality rate (23.5 deaths per 100,000) attributable to AMR compared to other regions. The region was most affected by AMR, in part due to high levels of poverty, high burden of infectious diseases, poor regulation of antimicrobial use, and a lack of alternatives to ineffective antimicrobials(6). Sub-Saharan Africa region had faced a rise in AMR with a prevalence of MRSA and Extended- Spectrum β- lactamase (ESBL) producing Enterobacterales of around 40% and high prevalence of fluconazole-resistant candidiasis and cryptococcosis. Antimicrobial resistance leads to increased mortality, prolonged hospital stays, and higher healthcare costs, with Sub-Saharan Africa projected to face 4.1 million AMR related deaths annually by 2050 without action(4).

In Ethiopia from two cross-sectional studies done in 2018 and 2020 to November 2021 at University of Gondar comprehensive specialized hospital 17.7% of the bacterial isolates were isolated from blood samples PICU patient(7), and MDR antimicrobial susceptibility pattern was observed in 76% of the

bacterial isolates(8). From a hospital-based cross-sectional study conducted at Nekemte Comprehensive Specialized Hospital, Oromia, Ethiopia from June to September 2024 on midstream urine samples the MDR rate was 44/78(56.4%). Of the isolates, the predominant MDR bacterial species were E. coli, Klebsiella spp. and S. aureus(9).

Despite the growing public health concern, there is limited data on the microbiological profile and resistance patterns in the PICU population at Asella Teaching and Referral Hospital.

1.2 Statement of Problem

Infectious diseases remain a leading cause of morbidity and mortality among pediatric populations globally, particularly in low-resource setting(10). (11). Pediatric intensive care units (PICUs) provide care for critically ill children who are at high risk for infections caused by MDR pathogens. Multidrug resistant organisms are common in PICU due to critically ill patients are admitted, and the risk of nosocomial infections is high due to invasive procedures and compromised immunity(12).(13)

There are several health and economic impacts of AMR for individuals, households, health systems and society. Individuals who contract AMR infections are at risk of mortality, long-term disability, catastrophic health expenditure, lost income, delay of effective treatment with suffering and socioeconomic impacts for families and communities. In health systems AMR is responsible for increased hospitalization rates, greater length of stay, increased treatment costs and reduced ability to safely provide treatments such as chemotherapy and surgical care(14).

The estimated impacts of AMR on global economy corresponds to a GDP decline of 3.8% or 6.1 trillion in 2050 compared to the baseline 2017 case in the high-AMR scenario. Health care expenditures would increase with the rising AMR burdens. Globally, estimated annual additional health expenditures due to AMR would be 8% higher than the base case in 2050 with estimated additional expenditures of $0.33-1.2 trillion annually. Developing countries will be hurt the most by AMR making eliminating extreme poverty harder to reach and could result in additional 24.1 million extremely poor people by 2030, of whom 18.7 would be in low-income countries(15).

The impact of infectious diseases on African countries is beyond health issues affecting education, social status, productivity and economic growth(16). In developing countries there is limited evidence on the microbiological spectrum and resistance patterns among PICU patients. This limited data interferes with effective empirical treatment, infection control practices, and antimicrobial stewardship efforts.

Consequently, PICU patients may be exposed to inappropriate antibiotics, prolonged hospital stays, increased costs, and higher morbidity and mortality(17).

In Ethiopia the retrospective cross-sectional study done on the bacterial culture and antibiotic susceptibility reports of different clinical specimens referred to the Bacteriology Laboratory of Ethiopian Public Health Institute from September 2015 to August 2019 showed that multidrug resistance rates were alarming. Antibiotic sensitivity patterns were tested on 840 culture isolates from which Escherichia coli and Klebsiella pneumoniae revealed more than 57% and 70% resistance to seventeen antibiotics respectively. The overall detected MDR was 64.29%. The highest MDR was reported in Acinetobacter strains (84%) followed by K. pneumoniae (80%)(18).

Despite the increasing burden of MDR infections, there is limited data on the microbiological profile and resistance patterns in the PICU population in ATRH. This gap affects effective antimicrobial stewardship and clinical decision making.

1.3. Significance of the Study

Antimicrobial resistance is a major global health threat, and its impact on PICU patients is concerning due to the high risk of severe infections and mortality in this population. Global data show increasing resistance to antibiotics in PICU populations but there was no prior study has characterized the microbial profiles, AMR pattern, or risk factors for infections in Asella Teaching and Referral Hospital PICU necessitating local investigation. This study will fill this critical gap in local AMR and contribute to a better understanding of AMR patterns in PICU and guiding empirical treatment.

The finding of this study will be primarily important for critically ill PICU patients, who will benefit from evidence based empirical antibiotics therapy that reduce mortality and morbidity. The healthcare professionals at ATRH will also benefit through improved data for optimizing antimicrobial use. It will inform Oromia Health Bureau and Ministry of Health about AMR, and can be used for antimicrobial stewardship programs and AMR surveillance input. Additionally, this study can serve as a reference for future researchers on AMR in Ethiopia.

2. LITERATURE REVIEW

2.1 Overview of Antimicrobial Resistance

Antimicrobial resistance is one of the top global public health threats in the 21st century that occurs when microorganisms no longer respond to antimicrobial medicines. Antimicrobial resistance (AMR) occurs when microorganisms (bacteria, viruses, fungi, parasites) evolve mechanisms that reduce or eliminate the effectiveness of antimicrobial drugs that previously controlled them. This leads to treatment of infections caused by bacteria, parasites, viruses and fungi to be ineffective. It also complicates modern medical care (surgery, chemotherapy, neonatal and intensive care) where effective antimicrobials are essential. Patients with infections caused by drug-resistant bacteria are at increased risk of worse clinical outcomes including death and increased health care cost(19).

The excessive and improper utilization of antibiotics in healthcare facilities, agricultural practices, and veterinary medicine, has resulted in the emergence of drug-resistant strains of microorganisms that affects both human and animal health. By the year 2050, it is projected that approximately 10 million deaths and $100 trillion USD economic loss by 2050 annually associated with AMR(20).

Specific antibiotic therapy is optimally based on a microbiologic diagnosis from antimicrobial susceptibility testing. However, given the high risk of mortality and disability associated with serious bacterial infections in young infants and children, it is based on clinical diagnoses and empirical use of antibacterial medicines. In hospital settings, especially in PICU, selection pressure from frequent empirical use of broad-spectrum antibiotics and invasive procedures favors the emergence and transmission of multidrug-resistant organisms (MDROs) such as extended-spectrum β-lactamase (ESBL)–producing Enterobacterales, carbapenem-resistant Enterobacterales (CRE), methicillin-resistant Staphylococcus aureus (MRSA), Pseudomonas aeruginosa, and Acinetobacter spp. These organisms are of particular concern because they limit therapeutic options and are associated with increased morbidity, length of stay, and mortality(21).

Critically ill children in PICUs are vulnerable to AMR for multiple reasons. Immature or compromised immunity, frequent healthcare contacts, high exposure to empirical antibiotics, and use of invasive devices such as endotracheal tubes, central lines, urinary catheters. AMR in pediatric populations has direct implications for clinical outcomes in PICUs including treatment failure and increased complications. This AMR has reached crisis proportions by the emergence of new resistance mechanism of carbapenemases, including Klebsiella pneumoniae–associated carbapenemases (KPCs)(21).

2.2 Magnitude of Antimicrobial Resistance

In 2019 there were an estimated 4.95 million deaths associated with bacterial AMR from which 1.27 million deaths were directly attributable to bacterial AMR. Western sub-Saharan Africa region had highest level of death rate attributable to resistance at 27.3 deaths per 100,000. The six leading pathogens for deaths associated with resistance included Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa.(22).

From study which was conducted at Dr.Soetomo Hospital, Surabaya, Indonesia from 2011 to 2016, positive microbial culture result was seen in 1138 PICU patients. Most of these positive results came from blood in 44.46% and urine in 19.15% of patients. Others samples including sputum, stool, cerebrospinal fluid, endotracheal tube, and pleural fluid contributed to 11.59%, 8.96%, 7.50%, 4.04%, 2.89%, and 1.41% repetitively. Both gram-negative bacteria and gram-positive bacteria isolates had multiple drug resistance to commonly used antibiotic(23).

From study done at İstanbul University, Turkey PICU patients who were found to had Gram-negative infections, the most common causative agents included Pseudomonas aeruginosa (38.5%), Kleibsiella pneumonia (24.6%) and Acinetobacter baumannii (21.5%). Acinetobacter baumannii isolates were resistance against piperacillin-tazobactam and meropenem at rate of 96.4% and 89.3% respectively (24).

Study done at India tertiary hospital PICU revealed among the114 culture positive isolates 50% were gram negative and 22.8% were gram positive organisms. The remaining 14% had fungal growth and 12.2% were contaminants. The most common isolate from gram negative organisms was Acinetobacter baumannii and Enterococcus from gram positive organisms. From the isolates all gram-negative organisms were resistant to carbepenems except Pseudomonas which was100% sensitive(25).

Other study in India showed that Blood stream infections (BSI) due to MDR organisms in PICU were increasing. Klebseilla pneumoniae and S. aureus were the major pathogens observed in BSI from PICU. There was an emergence of candidemia due to non-albicans candida. High prevalence of AMR was seen to commonly used antibiotics like ampicillin (94.9%–90.7%), cefotaxime (92.4%–71.4%), piperacillin-tazobactum (31.2%–27.5%) and levofloxacin (42.4%–39.8%)(26).

Study from Helwan university, Egypt revealed that out of 318 bacterial samples, 290 (91%) were found to be MDR strains from which MDR percentage was 92% for Gram-positive isolates and 90% for Gram-negative isolates(27).

According to Study in East Africa Gram-negative infections showed high levels of AMR to commonly used antibiotics, including 50% to100% resistance to ampicillin and cotrimoxazole infections, 20% to 47% to gentamycin and 46% to 69% to ceftriaxone. Among Gram-positive infections, extensive resistance was reported to ampicillin (100%), gentamicin and ceftriaxone (50% to100%) with MRSA prevalence was ranging from 2.6% to 4.0%(28).

Antimicrobial resistance is a significant concern in Ethiopian healthcare facilities. A systematic review from 131 studies revealed high resistance rates among both Gram-positive and Gram-negative bacteria to the commonly used antimicrobial agents. Reported resistance of S. aureus to anti-Staphylococcal penicillins ranged from 35% to 47%. Over half of K. pneumoniae, E. coli, Proteus, Enterobacter species, Citrobacter, Acinetobacter and Pseudomonas isolates were resistant to amoxicillin/clavulanic acid. Resistance to ceftriaxone of Gram-negative bacteria ranged between 38% to 74%(29).

Study done in Addis Ababa 25.43% of cultures had growth. Gram-negative was contributed to 68.63% of identified isolates. Acinetobacter species account for 28.57%, followed by Klebsiella pneumoniae and E. coli 13.725%. Higher antimicrobial resistance was reported to cephalosporin and penicillin. The mortality rate was 32.1% (30).

From study conducted at University of Gondar Comprehensive Specialized Hospital ICU (intensive care unit) 25% of samples were culture positive. K.pneumoniae was the predominant isolate in PICU. The prevalence of MRSA and ESBL enzyme producers was 57.1% and 78.8%, respectively. Age and sex were significantly associates factors with BSI(8).

2.3 Factors Related to Antimicrobial Resistance

The drivers of AMR in humans are complex and include the mix of factors such as gender, living situations, educational level, healthcare access, poor governance, human mobility, conflict, climate change, agriculture and pollution. Social, cultural and biological factors make women are more likely than men to experience occupational exposure to AMR and to be prescribed antimicrobials. The risk of AMR is high for populations living in urban, overcrowded environments and with limited access to clean water, sanitation and hygiene infrastructure(14).

From retrospective observational study conducted in a tertiary care PICU at Mazumdar Shaw Medical Centre, Narayana Health City, Bengaluru India from July 2016 to June 2019, positive culture was reported in 10.8% from 3157 cultured specimen. Tracheal secretions had the highest yield with 35.6%

being positive. The number of drug-resistant strains of MDR Acinetobacter, E. coli, and Klebsiella were significantly higher in culture specimens collected after 48 hours of Intensive care unit (ICU) admission isolates when compared to those specimens collected within 48 hours of admission(31).

A systematic review of the prevalence of Gram-negative bacteria in PICUs of Saudi Arabia a mean prevalence was 38.5%. Common pathogens included Klebsiella pneumoniae, Escherichia coli, and Acinetobacter baumannii. The rate of MDR Gram-negative pathogens ranged from 18.2% to 63.7%, with a mean of 47%. Identified risk factors include previous PICU stays, invasive procedures, and prior antibiotic use(32).

From India, retrospective study included 288 children admitted to the PICU of a tertiary care hospital in New Delhi from December 2020 to January 2022 the overall mortality was 22.2%, with the AMR group had higher mortality as compared to the non-AMR group (45.2% vs. 15.9%). The incidence of AMR was 21.5% with 44% of them being Hospital Acquired Infection (HAI). The AMR cohort had higher median procalcitonin value at admission, received longer duration of ventilation and vasoactive medications. Predominant isolates for community acquired infection (CAI) were Escherichia coli (30%) and Klebsiella pneumonia (30%); for HAI were Acinetobacter baumannii (29%) and Pseudomonas aeruginosa (21%). Gram-positive isolates reported in 17.2% of CAI and 10% of HAI(33).

A cases and controls study conducted from July 1st 2018 to June 30th 2019 in Italy showed that Length of PICU stay, the duration of mechanical ventilation > 5 days, parenteral nutrition, coma, urinary catheter indwelling, invasive operation, 2 or more antibiotics use were associated with MDR infections. Coma, parenteral nutrition, 2 or more antibiotics use and the duration of mechanical ventilation > 5 days were independent risk factors associated with MDR infections(34).

In single center study of PICU of Children's Hospital of Zhejiang University School of Medicine, China from January 2022 to March 2024 immunocompromised patients and patients with underlying diseases were more likely to develop resistance to antibiotics. Children with AMR showed significantly increased C-reaction protein, score of pediatric sequential organ failure assessment and pediatric risk of mortality of children and longer hospital stay and ICU stay(35).

Study from Helwan university, Egypt on MDR bacteria isolated from PICU showed toddlers are among the most vulnerable age groups to the MDR infections with the percentage of 95.5% (27). In Sub–Saharan Africa dysfunctional healthcare system, environmental factors contributed for development of AMR.

These factors included overuse of antibiotics, poverty, expansion of intensive farming and livestock production, conflicts, global warming, and climate disasters(4).

A cross-sectional study conducted at Tikur Anbessa Specialized Hospital between September 2018 and March 2019 showed that children were highly affected by drug resistant BSI. The gram-negative isolates showed a 95.3% rate of MDR or above MDR. This included 55.8%, 32.2%, and 7.3% of MDR, extensive drug resistant and pan drug resistant isolates respectively(36).

From prospective multicenter study conducted from June 2021 to December 2023 in three tertiary hospitals in Ethiopia among 2483 children under-5 who were suspected of having sepsis, 530 (21.3%) were infected with K. pneumoniae. About 92.1% and 47.4% of the isolates were confirmed to produce ESBLs and -carbapenemases, respectively. Factors contribute to an increased risk of sepsis caused by multidrug-resistant K. pneumoniae include history of ICU admission (OR: 13.3; 95%CI: 4.2 − 22.1, $P < 0.001$), pneumonia (OR = 6.1; 95%CI: 2.4 − 14.1, $P < 0.001$), meningitis (OR = 22.3; 95%CI: 11.9–34.1, $P < 0.001$),co-morbidity (OR = 18.2; 95%CI: 5.1–33.2, $P < 0.001$), UTI (OR = 3.2; 95%CI: 1.8–9.3, $P = 0.01$), and invasive medical procedures or catheter or mechanical ventilation(OR = 10.4; 95%CI: 8.1–22.4, $P < 0.001$). This showed that children who underwent indwelling catheterization or invasive medical procedures were five times more likely to acquire infections from MDR K. pneumoniae than were those who did not (AOR = 4.8; 95%CI: 1.4–15.5; $P < 0.001$)(37).

Study done on risk factors of Nosocomial Infection in Ayder PICU, Tigray region from 2019 to 2020 showed that invasive procedures such as urinary catheter and mechanical ventilation were done in 13.9% and 17.9% of PICU admitted children respectively(38).

In addition to the well-established risk factors, antimicrobial resistance itself is a determinant of adverse outcomes in pediatric intensive care. Infections caused by multidrug-resistant organisms (MDROs) are consistently associated with higher morbidity and mortality compared with infections caused by susceptible strains. Approximately 2.2 million deaths were reported among school-age children and young people in 2019, and infectious diseases was the leading cause of mortality. Countries with lower and low-middle sociodemographic index accounted for over 80% of deaths in this age group(39).

Similarly, multicenter data from Argentina demonstrated that infections due to multidrug-resistant organisms (MDROs) were associated with a significantly increased duration of PICU admission,

reflecting the complexity of management, delayed effective therapy, and limited treatment options in these patients(40).

In PICU of the Abuzar pediatric hospital Ahvaz, Iran among the 688 patients enrolled in the study, the most common causes of admission were pneumonia (22.9%), bronchiolitis (8.6%), and septicemia (7.9%). The mean duration of hospitalization was 3.3 days and the mortality rate was 16.5% with a mean age of 2.2 years. The mortality was more common in patients admitted with septicemia (36.6%), liver failure (31.6%), chronic renal failure (28.6%), and meningitis (27.3%). Patients who had undergone intubation before admission, decreased level of consciousness, and prolonged duration of hospitalization were significantly correlated with the mortality(41). Other PICU in Qazvin, Iran, A total of 106 children died during the study, with 41 (38.7%) cases being male. In these patients, sepsis (15.85%) and pneumonia (12.19%) were the main causes of death(42).

In a PICU-based study, Foglia et al. reported that children with nosocomial infections caused by antibiotic-resistant organisms had significantly longer PICU stays compared with those infected by susceptible organisms, even after adjustment for underlying disease severity and comorbid conditions. It showed higher mortality among patients infected with resistant organisms, with antibiotic resistance remaining an independent predictor of death after multivariable adjustment(43).

From study conducted in PICU of Ain Shams University Hospitals, Egypt, Africa, from June 2019 to January 2020 higher mortality was detected in patients colonized with MDR Organisms (34.6%) than non-MDR Organisms colonized patients (12.5%). Additionally, patients infected with MDR Organisms did have significantly greater PICU stay and longer ventilation days than those non- infected(44). Additional study done in Egypt focusing on extensively drug-resistant (XDR) Klebsiella pneumoniae infections in a pediatric intensive care unit found significantly increased association between death and highly resistant organisms including extensively drug-resistant Klebsiella pneumoniae. Mortality increased by 139 folds among children infected with XDR strains compared with non-XDR infections(45).

In Sub-Saharan Africa the clinical effects of AMR were include severe infections, increased morbidity, treatment failure, and mortality. High-risk populations were newborns, patients admitted to ICUs, and those with underlying comorbidities(6).

In Ethiopia a cross-sectional study was conducted at Wolaita Sodo and Hawassa University teaching hospitals a total of 396 PICU patients were included in study, and 165 (41.7%) deaths were recorded. Patients from rural areas, with co morbidities, those admitted with acute respiratory distress syndrome and patients on mechanical ventilation are more likely to die than patients with no these factors. Co-morbid disease, residency, the use of inotropes, and the length of ICU stay were all statistically significant predictors of death(46).

From other study in PICUs Jimma Medical Center and St. Paul's Hospital Millenium Medical College of 206 study participants 28.6% patients died. Respiratory failure was the commonest cause of death followed by septic shock. In-ICU complications, sepsis diagnosis, GCS < 8 and use of sedative drugs were associated with increased risk of in-ICU mortality(47).

2.4 Conceptual Framework

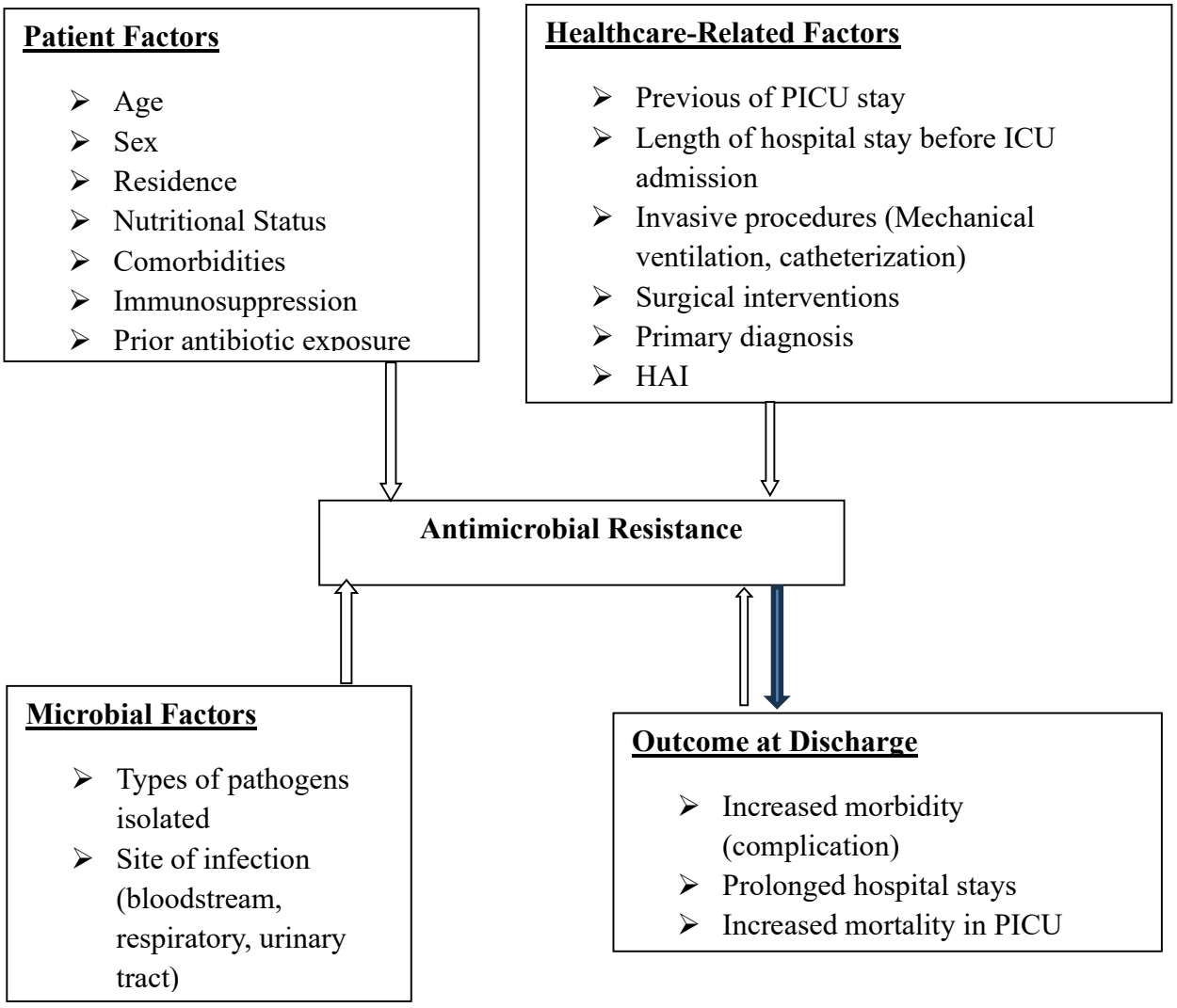

Figure 1: Conceptual frame work about Isolated Pathogens, Antimicrobial Resistance Patterns and Associated Risk Factors Among Pediatric ICU Patients Beyond the Neonatal Age Group

This conceptual frame work was developed by researcher based on literature review(4),(6),(14),(35).

3. OBJECTIVES

3.1 General Objective

To assess the isolated microbial pathogens, antimicrobial resistance patterns, and associated risk factors among pediatric ICU patients beyond the neonatal age group at Asella Teaching and Referral Hospital from July 2020 to June 2025.

3.2. Specific Objectives

- To assess the microbial pathogens isolated from pediatric ICU patients beyond the neonatal age group at Asella Teaching and Referral Hospital from July 2020 to June 2025.
- To examine the antimicrobial resistance patterns of pathogens isolated from PICU patients beyond the neonatal age group at ATRH from July 2020 to June 2025.
- To identify risk factors associated with AMR among PICU patients beyond the neonatal age group at ATRH from July 2020 to June 2025.

4. METHODS AND MATERIALS

4.1 Study Area and Period

This study was conducted at Asella Teaching and Referral Hospital which is located in Asella town about 165 KM to southeast of Addis Ababa in Arsi zone, Oromia Regional State, Ethiopia. The hospital gives service as referral Hospital for approximately 3.5 million catchment area populations. It has 284 admission beds and major departments including Pediatrics and Child Health, Gynecology and Obstetrics, Internal Medicine, Surgery, Ophthalmology, Dermatology and Oncology. The hospital is also serving for teaching of both undergraduate and postgraduate specialties in 4 departments (Pediatrics and Child Health, Gynecology and Obstetrics, Internal Medicine, and General Surgery). The hospital has a total of 1420 staffs from which 445 are health workers, 407 are academic staff and 568 are administrative staff.

The department of Pediatric and Child health has106 beds in unit of pediatric emergency OPD, pediatric OPD, NICU, Pediatric ward and PICU. The department has 14 pediatrician, 23 pediatric and child health residents, 4 General Practitioners. There are 15 nurses who are assigned to PICU. The PICU unit is in the same room with adult ICU. It has 6 beds at which both adult and pediatric critical patients are admitted.

The study was conducted from September to November, 2025.

4.2. Study Design

A hospital based cross-sectional study design was used.

4. 3. Population

4.3.1 Source Population: All pediatric patients aged 29 days to 14 years old admitted to the PICU at ATRH from July 1, 2020 to June 30, 2025.

4.3.2 Study Population: Pediatric ICU patients beyond the neonatal age group with culture test records during the study period who met inclusion criteria.

4.4 Inclusion and Exclusion criteria

4.4.1 Inclusion Criteria

Medical records of PICU patients aged from 29 days to 14 years old admitted at ATRH during the study period with complete microbiological records.

4.4.2 Exclusion Criteria

Patients with incomplete medical records, whom culture specimen was not sent or missing laboratory culture result.

4.5 Sample Size and Sampling Technique

A census of all eligible pediatric ICU patients admitted to PICU in ATRH from July 1, 2020 to June 30, 2025 was performed. All patients who meet the inclusion criteria was included without sampling because the total number of eligible patients during the period is manageable. This approach followed standard methodological guidance for participant selection and minimizes sampling error and selection bias for small target populations. It also addresses limited number patient with culture result. There were 403 children admitted to PICU July 1, 2020 to June 30, 2025 from hospital register from which 217 fulfilled inclusion criteria and included in study.

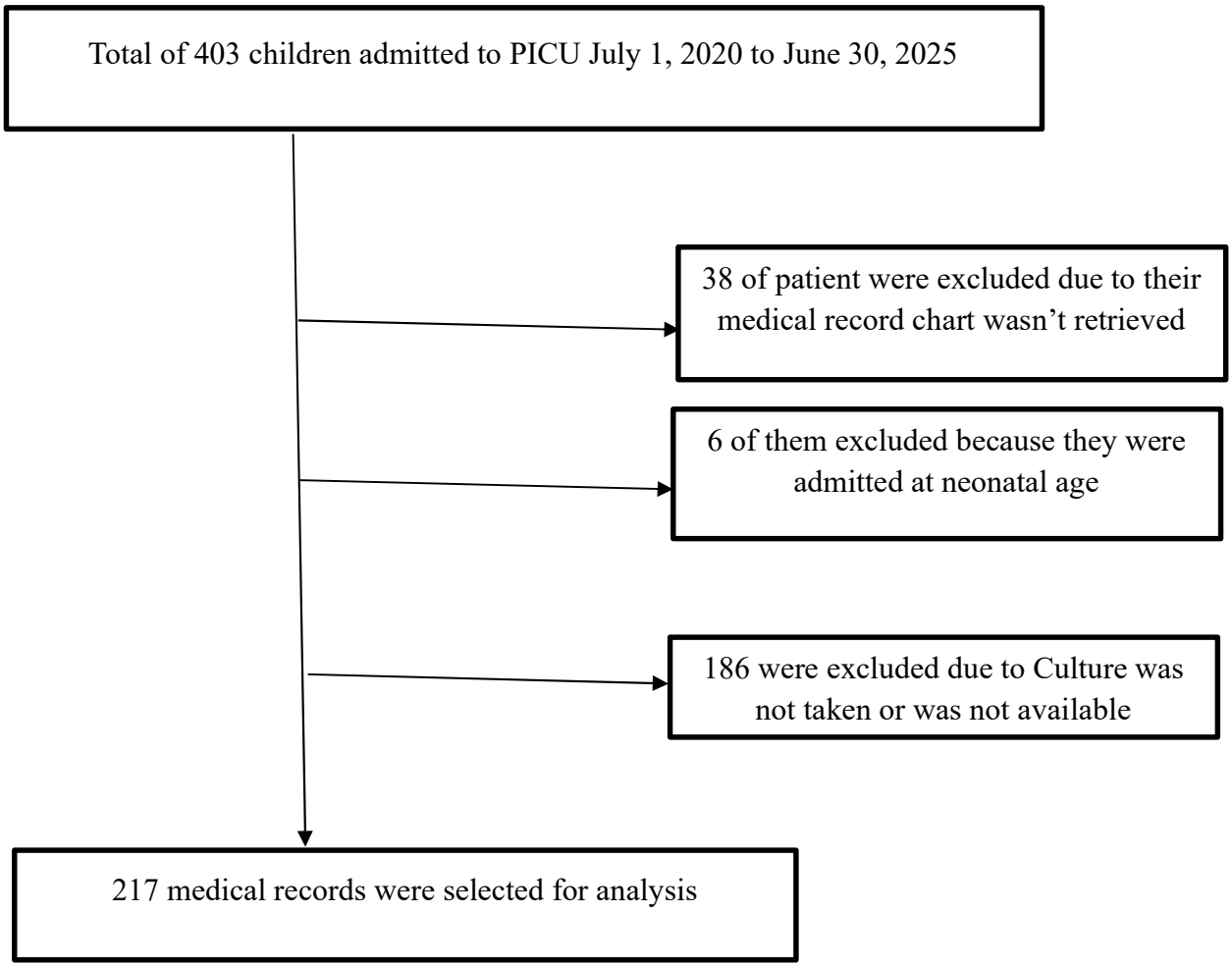

Figure 2: Case selection flow diagram of Isolated Pathogens, Antimicrobial Resistance Patterns and Associated Risk Factors Among Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

4.6. Variables of the Study

4.6.1 Dependent Variables

Antimicrobial resistance

4.6.2 Independent Variables

- Sociodemographic variables: Age (months/years), Sex, Residence.
- Clinical variables: Primary diagnosis on admission, Comorbidities (e.g. malnutrition, congenital anomalies, chronic illnesses), Prior antibiotic use, Use of invasive procedures (mechanical ventilation, catheterization, central line), Presence of hospital-acquired infection, Immunization status.
- Microbiological variables: Type of pathogen isolated, Source of specimen (blood, CSF, urine).
- Health service variables: Duration of hospitalization before PICU admission, use of empirical antibiotics.

4.7. Operational Definition

- **Antimicrobial Resistance (AMR)**: Resistance of a bacterial isolate to one or more antibiotics tested using standard antimicrobial susceptibility testing.
- **Antimicrobial Resistance Pattern**: The proportion of bacterial isolates resistant or sensitive to specific antimicrobial agents tested.
- **Extended-spectrum beta-lactamase (ESBL) producing organism**: An isolate that produces enzymes conferring resistance to penicillin's, cephalosporins, and aztreonam
- **Invasive Procedures**: Medical procedures that require entry into the body through skin or mucosal surfaces (e.g., insertion of a central venous catheter, urinary catheterization, mechanical ventilation).
- **Microbiological Profile:** The distribution and types of microorganisms isolated from clinical specimens of PICU patients during their admission.
- **Multidrug-resistant (MDR):** Resistance to at least one agent in three or more antimicrobial classes.
- **Pediatric Intensive Care Unit**: Intensive care unit for admission of patients aged 29 days to 14 years old for intensive monitoring or management of critical illness.

- **Hospital Acquired Infection**: Infection that develops in hospitalized patient after 48 hours of admission that was neither present nor incubating at time of admission.
- **High-risk antimicrobial resistance**: resistance which need special emphasis and has limited or no treatment option including multidrug-resistant (MDR), extensively drug-resistant (XDR), pan drug-resistant (PDR), carbapenem-resistant Enterobacterales (CRE), and extended-spectrum beta-lactamase (ESBL)–producing organisms(48), (49).
- **High antimicrobial resistance (AMR) prevalence**: Resistance to at least one first-line antimicrobial agent in ≥50% of isolates of a bacterial species or the presence of multidrug-resistant (MDR), extensively drug-resistant (XDR), or carbapenem-resistant organisms (CRO) regardless of prevalence(50)(51).

4.8. Data collection procedure

Data was collected using check list from medical record. Four general practitioners from ATRH were selected for data collection since they understand the subject matter on the research topic. One day of training was given to all data collectors on the study objectives, ethical considerations and confidentiality. Pre-test was done on 5% of samples 20 children admitted to Adama Comprehensive Specialized Hospital PICU. Quality of data collection and data collectors was ensured through training for data collectors, conducting pretest, daily supervision by principal investigator, and handling confidentiality by using unique study codes instead of personal identifiers. The principal investigator ensured the collected data was stored after verifying its completeness and consistency to minimize the risk of data loss.

4.9. Data Collection Tools

Data was extracted using a structured checklist from laboratory registers and patient medical records. It was adapted from Global antimicrobial resistance and use surveillance system (GLASS) report 2022 and Antimicrobial Resistance Surveillance Guidance for the African Region checklist(51),(52).

4.10. Data processing and Analysis

After data collection it was coded and entered in to EPI-INFO version 7.2.7.0 then exported to Statistical Package for Social Science (SPSS) version 27. Analysis was done using SPSS version 27. Descriptive analysis was carried out to and summarized as frequencies, proportions, median, and Interquartile range. In the binary logistic regression analysis odds ratios (OR), 95 % confidence intervals (CI) and p-values were used to determine association between independent variables with AMR. Variables with $P < 0.25$ in the bivariate analysis were included in the multiple variable models for Multi variable logistic regression to see independent effect of each variable. After adjusting the confounders p value of < 0.05 and 95% CI was considered statistically significant. Results were summarized and presented in graphs and tables.

4.11. Ethical Considerations

Ethical clearance was obtained from Arsi University, Asella Referral and Teaching Hospital Institutional Ethical Review Committee to conduct the research. Data confidentiality was strictly maintained, and patient and health care profession who had treated patient identifier information was be recorded on the data extraction format.

4.12. Result dissemination

The result of the study will be submitted and presented to Arsi University, College of Health Science, the School of Post Graduate, and the Department of Pediatrics and Child Health in partial fulfillment of the requirement for the Specialty Certificate in Pediatrics and Child Health. The final result of this thesis will be accessed from Arsi University, Health Science College library, as the source for future learning. It will be submitted as a hard copy for ATRH and the Arsi Zone Health Bureau, which will be used as an input for health care professional training and development. Finally, efforts will be made to publish in reputable peer-reviewed national or international journals.

5. RESULTS

5.1. Socio-demographic characteristics

In this study a total of 217 children were involved, of which 106 (48.8%) were aged less than one year, 74 (34.1%) from one year to five years and 37(17.1%) from five years to fourteen years. Median age was 12 months (IQR: 6–36 months). Their sex distribution showed 114 (52.5%) of them were males and 103 (47.5%) of them were females. The majority of them were from rural area 184 (84.8%), 33 (15.2%) were from urban area.

Table 1: Socio-demographic and baseline of Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Variables	**Category**	**Frequency**	**Percent (%)**
Sex	Male	114	52.5
	Female	103	47.5
Age	<1 year	106	48.8
	1-5 years	74	34.1
	5-14 years	37	17.1
Residence	Urban	33	15.2
	Rural	184	84.8

5.2 Clinical Information of the patients

5.2.1 Nutritional and Vaccination Status

Out of 217 children 171 (78.8%) had normal nutrition while 14 (6.5%) and 32(14.7%) had moderate acute Malnutrition and severe acute Malnutrition respectively. One hundred seventy-five (80.6%) of total children were fully vaccinated. Twenty-one (9.7%) were partially vaccinated and 19(8.8%) not vaccinated. The vaccination status of 2 children (0.9%) was not known as it was not reported.

Table 2: Nutritional and Vaccination Status of Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025 N=217

Clinical Information		**Frequency**	**Percent (%)**
Nutritional Status	Normal	171	78.8
	Moderate acute Malnutrition	14	6.5
	Severe acute malnutrition	32	14.7
Immunization status	Fully Vaccinated	175	80.6
	Partially Vaccinated	21	9.7
	Unvaccinated	19	8.8
	Unknown	2	.9

5.2.2: Primary diagnosis/reason for PICU admission of Pediatric ICU Patients

Among participants, Pneumonia was accounted Pneumonia 88 (40.6%), meningitis 39(18%) and septic shock 23(10.6%) were the top 3 major causes of PICU admission. Others cause of admission summarized in table below. In addition to primary diagnosis for admission 28 (12.9%) patient had other comorbidities including Cardiac disease 7(3.2%), Down syndrome 10(4.6%), Cerebral palsy 4(1.8%), Bronchial asthma 2(0.9%) and other disease such as Posterior Urethral Valve, Interstitial Lung Disease, Global Developmental Delay, Spinal Muscular Atrophy and Hypothyroidism totally accounts 5 (2.3%).

Table 3: Primary diagnosis/reason for PICU admission of Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Primary diagnosis	**Frequency**	**Percent (%)**
Pneumonia	88	40.6
Meningitis	39	18.0
Bronchiolitis	13	6.0
PARDS	18	8.3
Upper airway obstruction	2	.9
Sepsis	19	8.8
Septic shock	23	10.6
Severe asthma	5	2.3
Traumatic brain injury	4	1.8
Other diagnosis	6	2.8
Total	217	100.0

N.B Other primary diagnosis includes Guillain Barre Syndrome 3 (1.4%) Status epilepticus 2 (0.9%) and congenital Diaphragmatic hernia 1 (0.5%).

5.3 Risk Factor Assessment

5.3.1 Prior hospitalization or antibiotics exposure within last 3 months

From total 217 admission 35 (16.1%) had hospital-acquired infection at admission. Thirty-six (16.6%) had history Prior Hospitalization within last 3 months whereas 63 (29.0%) had history of antibiotic use within last 3 months prior to presentation to hospital.

5.3.2 Invasive device use

Invasive device was used to manage the cases in 202 (93.1%) of them during PICU admission. Out of this mechanical ventilator was used in 190 (87.6%), mechanical ventilator and urinary catheter in 10 (4.6%) and urinary catheter only in 2 (0.9%). Duration of invasive devices in days showed that in 20 (9.2%) of them was less than 2 days, three to seven days in 99 (45.6%), eight to fourteen days in 70 (32.3%) and greater than fourteen days in 11 (5.1%) of them. Duration of use was not documented in 2 patients.

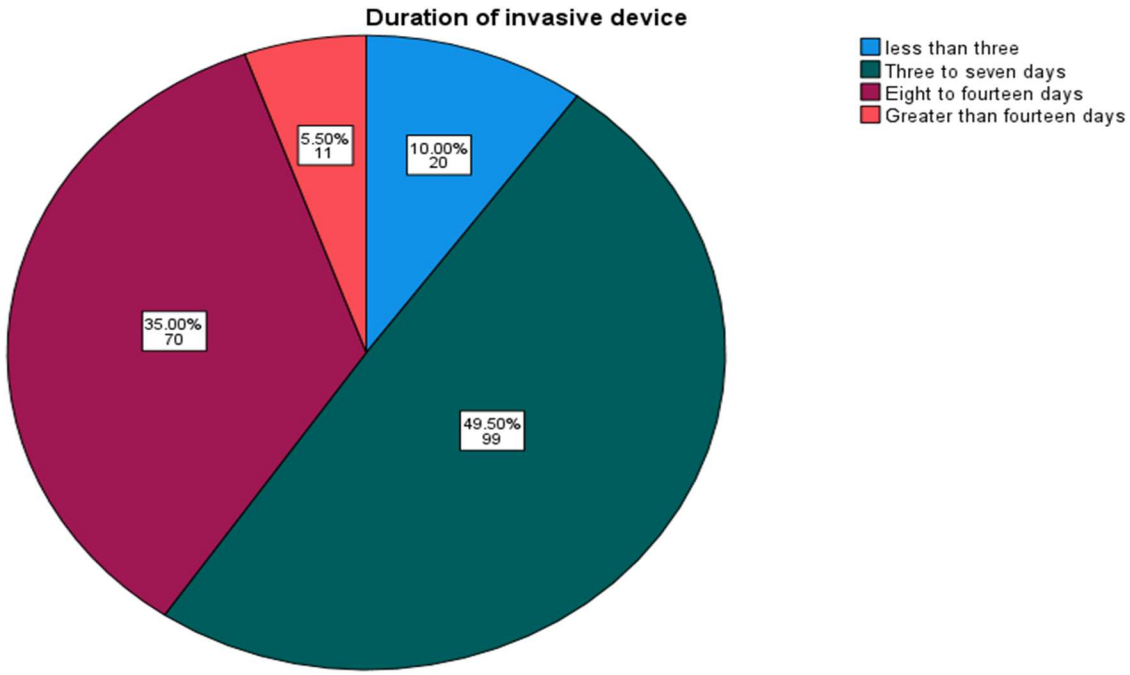

Figure 3: Pie chart showing duration of invasives device use in Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

5.3.3 Number of Antibiotics Prescribed during hospitalization for Pediatric ICU Patients

During PICU admission 210 (96.8%) had used empirical antibiotic regimen before culture results. Total number of antibiotics prescribed during PICU stay was range from 1 to 6 antibiotics. Four (1.8%) of them were taken only single antibiotic and one of child was given six types of antibiotics whereas 100 (46.1%), 72 (33.2%), 36 (16.6%), and 4 (1.8%) were taken two, three, four, and five types of antibiotics respectively. Out of total admission 39 (18.8%) had been prescribed corticosteroids drug during admission. Twenty-eight (12.9%) of them had surgical procedure.

Table 4: Number of Antibiotics Prescribed during hospitalization for Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Number of Prescribed antibiotics	**Frequency**	**Percent (%)**
One type	4	1.8
Two types	100	46.1
Three types	72	33.2
Four types	36	16.6
Five types	4	1.8
Six types	1	.5
Total	217	100.0

5.3.4 Primary admission places and length of hospital stay before PICU admission

Most of patients 153 (70.5%) were admitted from Pediatric emergency OPD while 62 (28.6) were transferred from pediatric ward. Each 1 patient was admitted from Referral from other health facility and from Operation Room directly to PICU. Length of stay (LOS) in hospital before admission to PICU showed that less than three days in 156 (71.9%), three to seven days in 47(21.7%) and greater than seven days in 14 (6.5%) of all admission.

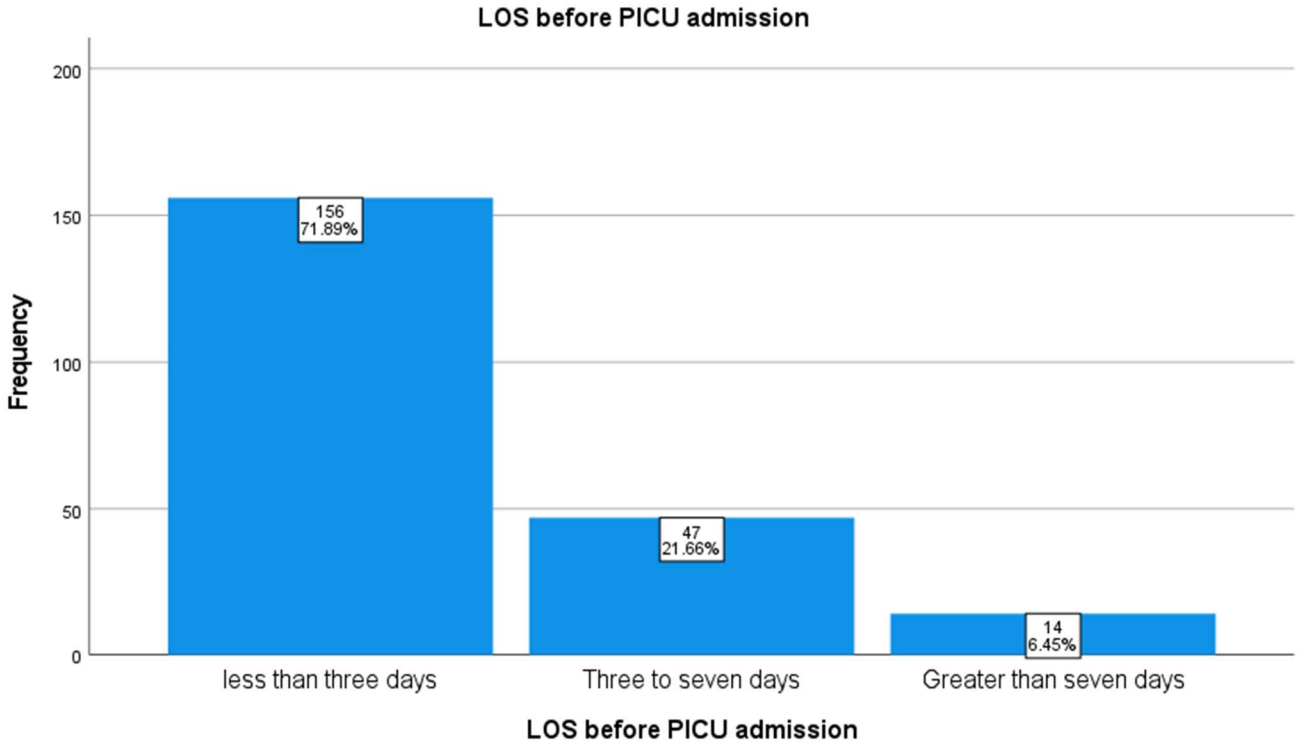

Figure 4: Bar graph showing length of hospital stay before PICU admission of Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

5.4 Microbiological Data

5.4.1 Specimen Information

Specimen for culture was collected from blood in 174 (80.2%), Cerebrospinal fluid in 20 (9.2%), Urine 16 (7.4%), Wound abscess in 3 (1.4%) and Stool and tracheal aspirate each 2 (0.9%). The source of infections was respiratory tract 116 (53.5%), Central nervous system in 40 (18.4), Blood stream in 29 (13.4%), Urinary tract in 17 (7.8%), Gastrointestinal in 11 (5.1%), Wound abscess in 3 (1.4%) and Surgical Wound or Abscess in 4 (1.8%) of cases. Culture specimens were obtained before antibiotic initiation in 10 (4.6%). At the time of sampling 97 (44.7%) were hospitalized for more than 2 calendar days and 120 (55.3%) were hospitalized for less than 2 calendar days.

Table 5: Specimen Type of Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Specimen Type	**Frequency**	**Percent (%)**
Blood	174	80.2
Urine	16	7.4
Cerebrospinal fluid	20	9.2
Wound abscess	3	1.4
Stool	2	.9
Tracheal aspirate	2	.9
Total	217	100.0

5.4.2 Results of Culture growth and gram reaction

From a total of 217 culture sent to laboratory 114 (52.5%) had microbial growth whereas 103 (47.5%) had no growth. Gram reaction of bacterial isolates was Gram-positive in 51 (45.5%) and Gram-negative in 61 (54.5%).

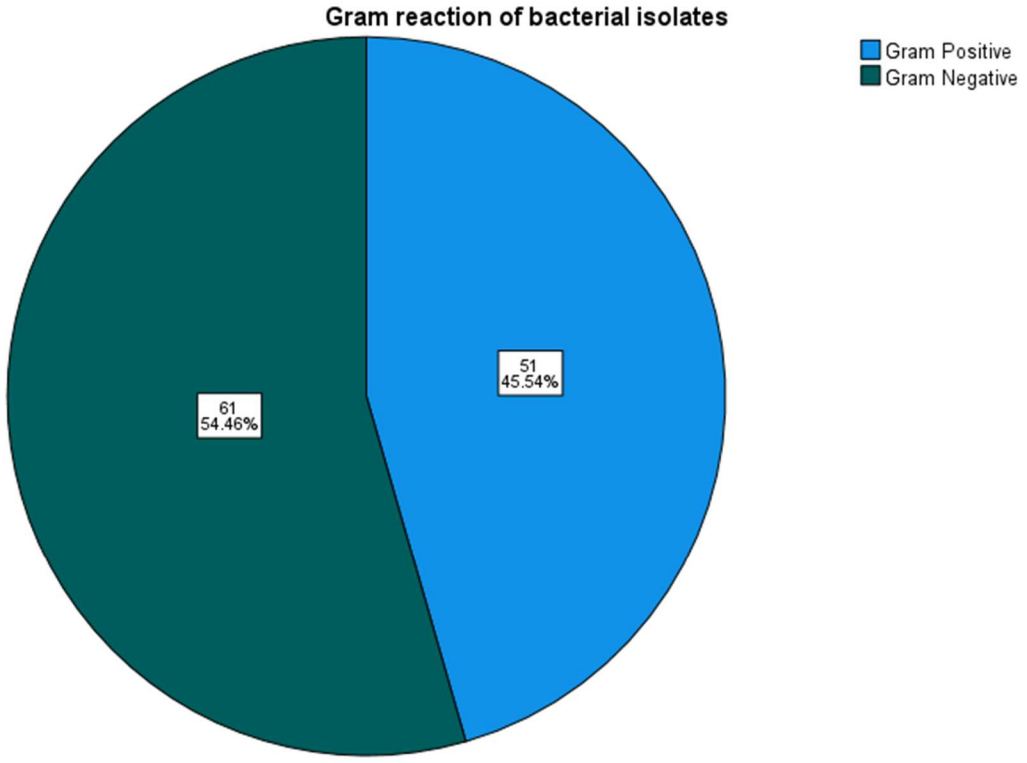

Figure 5: Pie chart showing gram reaction distribution of bacterial isolates in Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

5.4.3 Types of detected Microorganisms by culture

The identified microorganisms on culture growth include Coagulase negative staphylococcus (CONS) 46 (40.4%), Klebsiella species 25 (21.9%), Enterobacter 10 (8.8%), Acinetobacter, E. Coli and Pseudomonas each 5 (4.4%), Serratia species 4 (3.5%), S. pneumoniae and Citrobacter each 3 (2.6%), S. aureus, Shigella species and Haemophilus Influenzae each 2 (1.8%). Fungal yeast was identified in 2 (1.8%) of samples.

Table 6: Name of identified pathogen from Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Name of identified pathogen	Frequency	Percent (%)
E. Coli	5	4.4
Klebsiella species	25	21.9
Acinetobacter	5	4.4
S. aureus	2	1.8
S. pneumoniae	3	2.6
Shigella species	2	1.8
CONS	46	40.4
Serratia	4	3.5
Enterobacter	10	8.8
Citrobacter	3	2.6
Haemophilus Influenzae	2	1.8
Pseudomonas	5	4.4
Fungal yeast	2	1.8
Total	114	100.0

5.4.4 Antibiotic Susceptibility Test Result

Out of total 114 microbial isolates antibiotic susceptibility testing was done for 66 (57.9%). It was not done for all CONS and fungal yeast isolates. From these 61 (92.4%) were resistance to at least one antibiotic and 5 (7.6%) were susceptible to all antibiotics for which AST was done. Resistance categories (per CDC/WHO criteria) for bacterial isolates showed that they were susceptible to all done antibiotics in 5 (7.6%), Extended-Spectrum Beta-Lactamases producing (ESBL) 13 (19.7%), Carbapenem-Resistant Enterobacterales (CRE) 4 (6.1%), (13.6%), Multi-Drug Resistant (MDR) 9 (13.6%), Extensively drug resistant 10 (15.2%) and Pan drug resistant 9 (13.6%). Sixteen (24.2%) of bacterial isolates are unclassified to these classes as they didn't fit to any group as they were resistant to at least one antibiotic from antimicrobial group but in less than three groups of antibiotics.

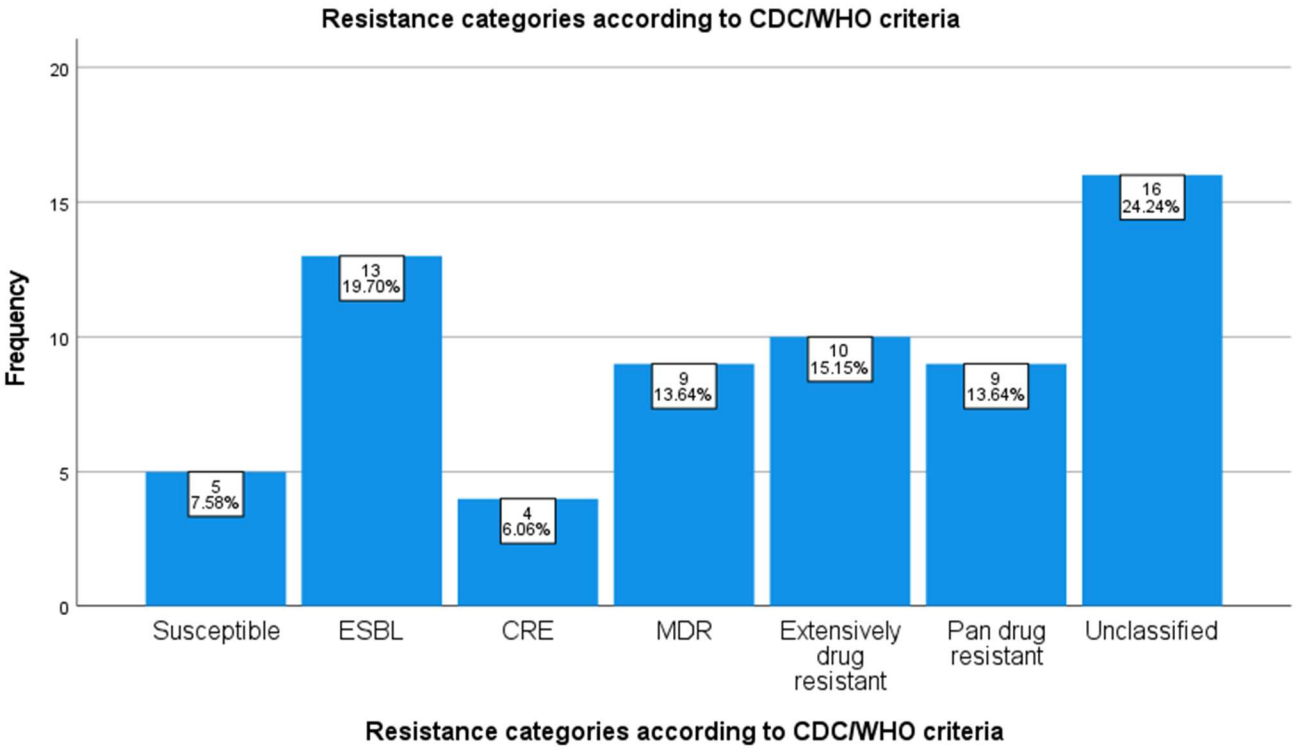

Figure 6: Bar graph showing Resistance categories of microbial isolates of Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Among Gram-negative isolates, Klebsiella species showed multiple resistance phenotypes, including ESBL production (20.0%), CRE (12.0%), MDR (16.0%), XDR (20.0%), and PDR (16.0%). E. coli isolates were mainly ESBL producers (40.0%), with other proportions classified as MDR and XDR (each 20.0%). Most Gram-positive isolates were either susceptible or unclassified, with no MDR, XDR, or PDR isolate was observed.

Table 7: Resistance categories of microbial isolates by types of pathogens of Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Types of pathogens		**Resistance Categories**							
		Susceptible	**ESBL**	**CRE**	**MDR**	**XDR**	**PDR**	**Unclassified**	**Total**
E. coli	Frequency	1	2	0	1	1	0	0	5
	Percent (%)	20.0	40.0	0.0	20.0	20.0	0.0	0.0	100
Klebsiella species	Frequency	0	5	3	4	5	4	4	25
	Percent (%)	0.0	20.0	12.0	16.0	20.0	16.0	16.0	100
Acinetobacter	Frequency	0	4	0	0	0	1	0	5
	Percent (%)	0.0	80.0	0.0	0.0	0.0	20.0	0.0	100
S. aureus	Frequency	1	0	0	0	0	0	1	2
	Percent (%)	50.0	0.0	0.0	0.0	0.0	0.0%	50.0	100
S. pneumoniae	Frequency	1	0	0	0	0	0	2	3
	Percent (%)	33.3	0.0	0.0	0.0	0.0	0.0	66.7	100
Shigella	Frequency	1	0	0	0	0	0	1	2
	Percent (%)	50.0	0.0	0.0	0.0	0.0	0.0	50.0	100
Serriatia	Frequency	0	1	1	0	0	1	1	4
	Percent (%)	0.0	25.0	25.0	0.0	0.0	25.0	25.0	100
Enterobacter	Frequency	0	1	0	3	0	3	3	10
	Percent (%)	0.0	10.0	0.0	30.0	0.0	30.0	30.0	100
Citrobacter	Frequency	0	0	0	0	1	0	2	3
	Percent (%)	0.0	0.0	0.0	0.0%	33.3	0.0	66.7	100
Haemophilus influenzae	Frequency	0	0	0	0	1	0	1	2
	Percent (%)	0.0	0.0	0.0	0.0	50.0	0.0	50.0	100
Pseudomonas	Frequency	1	0	0	1	2	0	1	5
	Percent (%)	20.0	0.0	0.0	20.0	40.0	0.0	20.0	100
Total	Frequency	5	13	4	9	10	9	16	66
	Percent (%)	7.6	19.7	6.1	13.6	15.2	13.6	24.2	100

5.4.5 Risk categories of antibiotic resistance strains

When antimicrobial resistance is classified as low-risk AMR including Susceptible to all done antibiotics and unclassified categories and high-risk AMR including all others categories Low risk resistance contributed to 21 (31.8%) whereas High risk AMR contributed to 45 (68.2%).

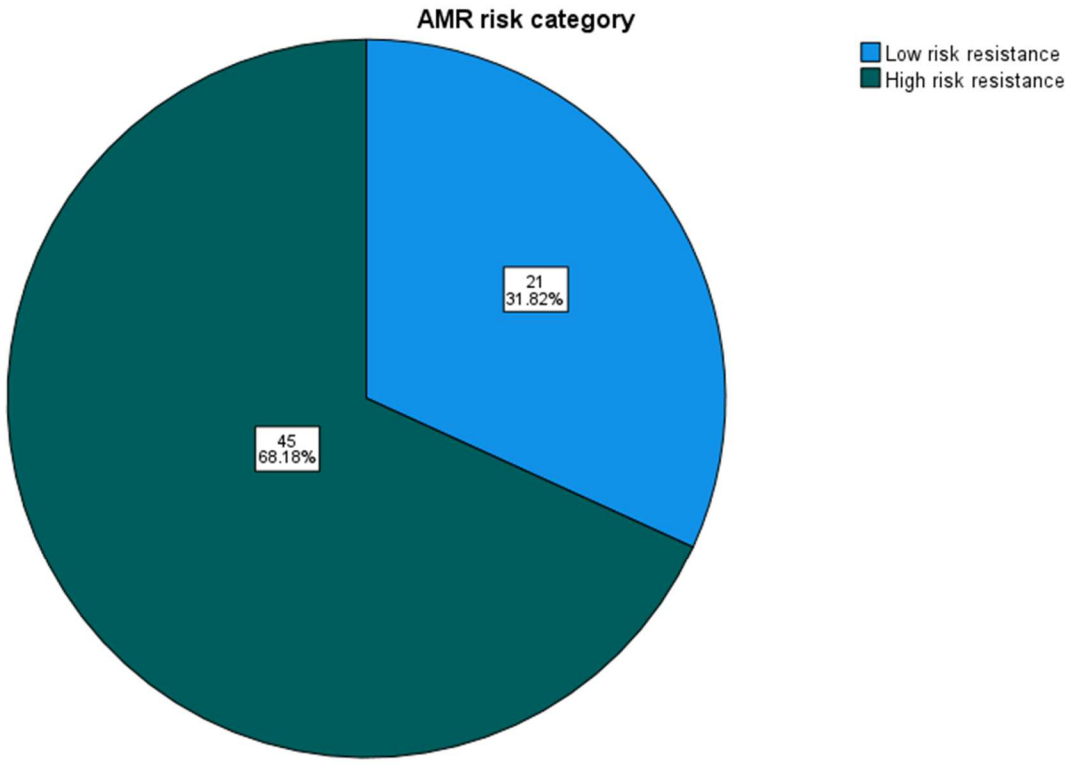

Figure 7: Pie chart showing AMR risk categories of bacterial isolates in Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

5.4.6 Antimicrobial Resistance Patterns of Bacterial Isolates

High resistance was observed to most commonly used β-lactam antibiotics, including ampicillin (91.3%), ceftriaxone (81.0%), ceftazidime (92.3%), cefuroxime (85.7%), and piperacillin-tazobactam (75.8%). Other agents also demonstrated substantial resistance, including ciprofloxacin (74.1%), cotrimoxazole (77.6%), and gentamicin (76.9%). Relatively better susceptibility was noted for amikacin (83.0% susceptible), while carbapenems also showed high resistance, with meropenem resistance of 59.6% and

imipenem resistance of 66.7%. No susceptibility to doxycycline was detected for 2 isolates in which AST was done.

Table 8: Antimicrobial Resistance Patterns of Bacterial Isolates Among Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Antibiotics	**AST Status**			
	Susceptible (%)	**Resistant (%)**	**Intermediate (%)**	**Total (%)**
Amikacin	44 (83)	9 (17)	0 (0.0)	53 (100)
Ampicillin	2 (8.7)	21 (91.3)	0 (0.0)	23 (100)
Augmentin	5 (16.1)	25 (80.6)	1 (3.2)	31 (100)
Cefazolin	4 (33.3)	8 (66.7)	0 (0.0)	12 (100)
Ceftriaxone	8 (19)	34 (81)	0 (0.0)	42 (100)
Ceftazidime	2 (7.7)	24 (92.3)	0 (0.0)	26 (100)
Cefotaxime	3 (30)	7 (70)	0 (0.0)	10 (100)
Cefepime	4 (13.8)	23 (79.3)	2 (6.9)	29 (100)
Cefuroxime	6 (14.3)	36 (85.7)	0 (0.0)	42 (100)
Chloramphenicol	4 (66.7)	1 (16.7)	1 (16.7)	6 (100)
Ciprofloxacin	12 (22.2)	40 (74.1)	2 (3.7)	54 (100)
Cotrimoxazole	10 (20.4)	38 (77.6)	1 (2.0)	49 (100)
Doxycycline	0 (0.0)	2(100)	0 (0.0)	2(100)
Gentamycin	12 (23.1)	40 (76.9)	0 (0.0)	52 (100)
Imipenem	3 (33.3)	6 (66.7)	0 (0.0)	9 (100)
Meropenem	15 (31.9)	28 (59.6)	4 (8.5)	47 (100)
Nitrofurantoin	3 (33.3)	5 (55.6)	1 (11.1)	9 (100)
Piperacillin-tazobactam	8 (24.2)	25 (75.8)	0 (0.0)	33 (100)
Tobramycin	1 (33.3)	2 (66.7)	0 (0.0)	3 (100)

5.5 Clinical Outcome during PICU stay

5.5.1 Length of PICU stay

Tota length of stay in days in PICU was less than three days in 13 (6.0%), three to seven days in 96 (44.2%), eight to fourteen days in 84 (38.7%) and greater than fourteen days in 24 (11.1%) patients. The minimum observed length of stay was 1 day while the maximum was 57 days. The Median length of stay was 7 days (IQR: 4–11 days).

Table 9: Tota length of stay in days in PICU of Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

LOS in PICU	**Frequency**	**Percent (%)**	**Cumulative Percent (%)**
Less than three days	13	6.0	6.0
Three to seven days	96	44.2	50.2
Eight to fourteen days	84	38.7	88.9
Greater than fourteen days	24	11.1	100.0
Total	217	100.0	

5.5.2 Complication developed in PICU

Thirty-eight (17.5% of all admission) cases developed complications while they are in PICU. Hospital acquired infection was the most common complication occurred in 16 contributed to 42.11% of all complications. Ventilator associated pneumonia 9 (23.68%), Septic shock 6 (15.79%), Air leak Syndrome 4 (13.16%) and Sepsis 2 (5.26%).

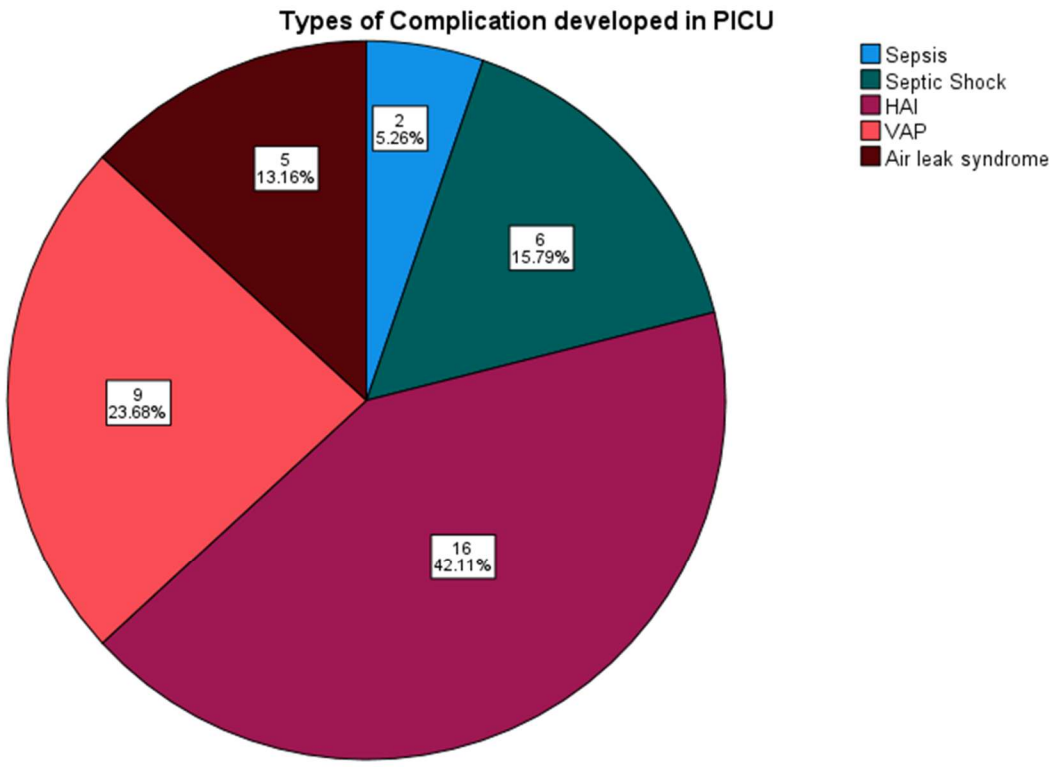

Figure 8: Pie chart showing complication developed in PICU in Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

5.5.3 Outcome at discharge from PICU

The outcome at discharge showed that 155 (71.4) of admitted patients were improved and transferred to ward, 52 (24.0%) died in PICU, 9 (4.1%) discharged against medical advice while 1 (0.5%) referred to other hospital.

5.6 Binary logistic regression

5.6.1 Bivariate binary logistic regression

On binary logistic regression Age, duration invasive Devices used (days), antibiotic Use Prior to admission within last 3 months, Source of infection and Culture obtained after antibiotic initiation are associated with resistance to at least one antibiotic. When entered to multivariate binary logistic regression none of them showed significant association.

Table 10: Bivariate analysis of resistance to at least one antibiotic in Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Independent variable	**Sig.**	**Exp(B)**	**95% C.I. for lower**	**95% C.I. for upper**
Age in months	.030	.979	.960	.998
Duration invasive Devices used (days)	.184	1.232	.906	1.676
Antibiotic Use Prior to Admission within last 3 months	.165	.288	.050	1.667
Source of infection	.016	.456	.241	.865
Culture obtained before antibiotic initiation	.147	.145	.011	1.971

In the bivariate analysis for high-risk AMR the duration of invasive device use, length of stay in PICU, gram reaction of bacterial isolates, and outcome at discharge showed statistically significant associations with the high-risk AMR. Duration of invasive device use (days) was significantly associated with the high-risk AMR. For each additional day of invasive device use, the odds of the high-risk antimicrobial resistance increased by 1.28% (COR = 1.28; 95% CI: 1.05–1.55; p = 0.012). Length of stay in PICU (days) was also significantly associated with the high-risk antimicrobial resistance. Each additional day of PICU stay increased the odds of the high-risk antimicrobial resistance by 1.16% (COR = 1.16; 95% CI: 1.01–1.34; p = 0.033).

Gram reaction of bacterial isolates was significantly associated with the high-risk antimicrobial resistance. Patients infected with gram-negative isolates had 10.35 times higher odds of the outcome compared to those with gram-positive isolates (COR = 10.35; 95% CI: 1.07–99.37; p = 0.043). Outcome at discharge was significantly associated with the high-risk antimicrobial resistance. Patients died in PICU had 4.8 times higher odds of the high-risk antimicrobial resistance compared to those improved and transferred to ward (COR = 4.80; 95% CI: 1.23–18.63; p = 0.023).

Complication developed in PICU also showed association with the outcome. Patients who developed complications had 3.6 times higher odds of the high-risk antimicrobial resistance compared to those without complications; however, this association did not reach statistical significance (COR = 3.64; 95% CI: 0.93–14.23; p = 0.063).

5.6.2 Multivariable Binary Logistic Regression Analysis

Variables with p-value <0.25 in the bivariate analysis were entered into the multivariable binary logistic regression model. After adjusting for potential confounders, length of stay in PICU and outcome at discharge remained independently associated with the outcome.

Length of stay in PICU remained a statistically significant predictor. Patients with PICU stays greater than seven days had 7.6 times higher odds of the high-risk AMR compared to those stayed less than seven days (AOR = 7.59; 95% CI: 1.10–52.60; p = 0.040). Outcome at discharge also remained independently associated with the high-risk antimicrobial resistance. Patients who died in PICU had 8.2 times higher odds of the outcome compared to patients who improved and transferred to ward (AOR = 8.22; 95% CI: 1.39–48.63; p = 0.020).

Duration of invasive device use (AOR = 0.53; 95% CI: 0.09–3.33; p = 0.500), complication developed in PICU (AOR = 5.27; 95% CI: 0.82–34.11; p = 0.081) and Gram reaction of bacterial isolates (AOR = 22.37; 95% CI: 0.64–781.30; p = 0.086) did not retain statistical significance after adjustment.

Table 11: Bivariate and Multivariable binary logistic regression of high-risk resistance of Pediatric ICU Patients Beyond the Neonatal Age Group at Asella Teaching and Referral Hospital from July 2020 to June 2025

Variables	**Bivariate binary logistic regression**		**Multivariate binary logistic regression**	
	P-value	COR (95%CI)	P-value	AOR (95%CI)
Duration invasive Devices used (days)	.012	1.28 (1.05-1.55)	.500	.532 (.085-3.325)
Length of stay in PICU (days)	.033	1.16 (1.01-1.34)	.040	7.589 (1.095-52.604)
Complication developed in PICU	.063	3.64 (.93-14.23)	.081	5.274 (.815-34.113)
Gram reaction of bacterial isolates	.043	10.35 (1.07-99.37)	.086	22.372 (.641-781.299)
Outcome at discharge	.023	4.80 (1.23-18.63)	.020	8.216 (1.388-48.627)

6. DISCUSSION

This hospital-based cross-sectional study assessed isolated microbial pathogens, antimicrobial resistance patterns, and associated risk factors among pediatric ICU patients. Among 217 patients, 52.5% had microbial growth, of which 57.9% underwent antimicrobial susceptibility testing (AST). Gram-negative organisms were more common, contributing to 54.5% of isolates. Klebsiella species were predominant (21.9%), followed by Enterobacter species (8.8%), while Escherichia coli, Acinetobacter, and Pseudomonas each accounted for 4.4%. Among Gram-positive isolates, coagulase-negative staphylococci (CONS) were most frequent (40.4%), with Staphylococcus aureus (1.8%) and Streptococcus pneumoniae (2.6%) less common. These findings are comparable to reports from the University of Gondar Comprehensive Specialized Hospital, Ethiopia, where Gram-negative bacteria predominated, particularly Klebsiella pneumoniae and E. coli, while CONS accounted for approximately 20% of isolates(8). Similarly, WHO GLASS 2025 surveillance identifies E. coli and K. pneumoniae as leading invasive bacterial pathogens globally(50).

Of the isolates tested, 68.2% exhibited high-risk antimicrobial resistance (AMR), defined as multidrug-resistant (MDR), extensively drug-resistant (XDR), pan drug-resistant (PDR), carbapenem-resistant Enterobacterales (CRE), or ESBL-producing organisms. This proportion is comparable to findings from the Ethiopian Public Health Institute (64.29%)(18) and University of Gondar (76%)(8). This is also consistent with WHO report of approximately one in six laboratory-confirmed bacterial infections worldwide were caused by bacteria resistant to antibiotics and resistance extent in the African Region is exceeding 70% for E. coli and K. pneumoniae pathogens(50). It is higher than study from Sub-Saharan Africa region reports (40%) and lower than Study from Helwan university, Egypt (91%) (4),(27).

Multivariable analysis demonstrated that prolonged PICU stay and discharge outcome were showed a significantly associated with high-risk AMR. Patients with PICU stays greater than seven days had 7.6 times higher odds of the high-risk AMR compared to those stayed less than seven days (AOR = 7.59; 95% CI: 1.10–52.60; p = 0.040). This finding is consistent with reports from both Ethiopian and international pediatric intensive care settings. A study from northern Ethiopia Ayder Hospital demonstrated that PICU stays longer than two weeks were associated with increased odds of nosocomial infection (AOR = 4.10; 95% CI: 2.00–8.60)(38). Similarly, finding from study at large pediatric teaching hospital in United States reported that infections caused by antimicrobial-resistant organisms were independently associated with prolonged PICU stay, although with a lower magnitude of effect (OR = 2.40; 95% CI: 1.03–5.61)(43). Differences in effect size may reflect variations in patient severity,

antimicrobial exposure, and infection prevention practices across settings. Prolonged PICU stay reflects disease severity, repeated antibiotic exposure, invasive procedures, increased exposure to the hospital environment and cross-transmission of resistant organisms, all of which facilitate the emergence of resistant pathogens.

The study also demonstrated that outcome at discharge was independently associated with high-risk antimicrobial resistance. Patients who died in PICU had 8.2 times higher odds of the high-risk AMR compared to patients who improved and transferred to ward (AOR = 8.22; 95% CI: 1.39–48.63; p = 0.020). This finding is also in line with studies reporting significantly increased association between death and highly resistant organisms including extensively drug-resistant Klebsiella pneumoniae increased odds 139 folds although the magnitude of effect in that study exceeded our finding(45).

This association may reflect the bidirectional relationship between severe illness and antimicrobial resistance. On one hand, high-risk AMR infections are associated with delayed appropriate therapy, limited treatment options, prolonged illness, and increased mortality. On the other hand, critically ill patients often require prolonged hospitalization, multiple antibiotic courses, and invasive device support, which predispose them to infection with resistant organisms. This finding underscore clinical impact of high-risk antimicrobial resistance in pediatric critical care settings and highlights the contribution of antimicrobial resistance to adverse patient outcomes.

Other factors, such as duration of invasive device use, Gram reaction of bacterial isolates, and development of complications, were associated with high-risk AMR in bivariate analysis but lost significance in multivariable modeling. This suggests these factors may be confounded by length of stay and disease severity, and the wide confidence intervals indicate limited sample size and sparse data, potentially reducing statistical power. In contrast, resistance to at least one antibiotic did not show significant associations with clinical or microbiological characteristics, suggesting that low-level resistance is widespread and influenced by multiple background factors, whereas high-risk AMR is more strongly associated with clinical severity, prolonged hospitalization, and adverse outcomes.

7. STRENGTH AND LIMITATIONS OF THE STUDY

7.1 Strengths

The study was conducted in setting where evidence on antimicrobial resistance remained scarce and needed to inform clinical practice and stewardship interventions. Data were obtained from a tertiary referral hospital PICU, enhancing the relevance of findings for critically ill pediatric populations. Additionally, the study focused on high-risk antimicrobial resistance, which has greater clinical and public health significance.

7.2 Limitations

The study was conducted in a single center, which may limit generalizability to other hospitals or regions. The sample size may have been insufficient to detect some associations, as suggested by wide confidence intervals in the multivariable analysis.

8. CONCLUSION AND RECOMMENDATION

8.1. Conclusion

This study found that high-risk antimicrobial resistance including multidrug resistant (MDR), extensive drug resistant (XDR) pan-drug resistant (PDR), Carbapenem- Resistant Enterobacteriaceae (CRE), and Extended-spectrum beta-lactamase (ESBL) producing organism is a significant problem among pediatric patients admitted to the PICU. Prolonged length of stay in the PICU and death in PICU were demonstrated strong association with high AMR.

The higher level of high-risk antimicrobial resistance observed in this study is comparable Ethiopian hospital-based studies and WHO global surveillance reports reinforcing clinical challenge in pediatric intensive care settings. The findings highlight the critical role of hospitalization duration and disease severity in the emergence of high-risk AMR and emphasize the need for targeted interventions in pediatric intensive care settings.

8.2 Recommendations

We recommend the hospital to implement strategies to reduce unnecessary prolonged PICU stays, including early step-down care when clinically appropriate.

Implementing enhanced infection prevention and control measures are important to decrease emerging AMR.

Further studies using multicenter study area are recommended to improve representativeness of the study.

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ANNEX

Checklist

Data collection checklist for study on Isolated Pathogens, Antimicrobial Resistance Patterns and Associated Risk Factors Among Pediatric ICU Patients Beyond the Neonatal Age Group at ATRH from July 1, 2020 to June 30

S. No	Variable	Response
I.	Socio-demographic Information	
1.	Unique Patient ID_____	
2.	Age (in months or years)	_____
3.	Sex	1. Male 2. Female
4.	Address	Region: _____ Zone: _____ Woreda: _____
5.	Residence	1. Urban 2. Rural
6.	Date of admission	____/____/_____
7.	Date of Discharge/Death	____/____/_____
II.	Clinical Information	
8.	Nutritional Status	1. Normal 2. Moderate acute malnutrition 3. Severe acute malnutrition
9.	Immunization status	1. Up to date /Fully Vaccinated 2. Partially Vaccinated 3. Unvaccinated 4. Unknown
10	Primary diagnosis/reason for PICU admission	1. Sepsis 2. Septic shock 3. Pneumonia 4. PARDS

		5. Meningitis 6. Severe asthma 7. Bronchiolitis 8. upper airway obstruction 9. Traumatic brain injury 10. Other _____
11.	Presence of hospital-acquired infection	1.Yes 0.No
12.	Comorbidities	1. HIV/AIDS 2. Diabetes Mellitus 3. Cardiac disease 4. Genetic disorder 5. Cerebral palsy 6. Bronchial asthma 7. Chronic Renal disease 8. Malignancy 9. Others_____
III.	Risk Factor Assessment	
13.	Invasive Devices used (MV, Urinary catheter, Central venous catheter)	1.Yes 0.No
14.	Duration of Invasive Device if used (in days)	1. Mechanical Ventilator___ 2. Urinary catheter____ 3. Central venous catheter ____
15.	Prior Hospitalizations (within last 3 months)	1. Yes 2. No 3. Unknown
16.	Antibiotic Use Prior to Admission (within last 3 months)	1. Yes 2. No 3. Unknown
17.	Empirical Antibiotic Regimen (drugs used before culture results)	_____

18	Number of Antibiotics Prescribed during hospitalization	_____
19	Use of corticosteroids or immunosuppressants:	1.Yes 0.No
20	Source unit of patient admitted from	1. Pediatric Emergency OPD 2. Pediatric Ward 3. Referral from other health facility 4. Operation Room
21	Length of Hospital stay before PICU admission (days)	_____
22	Surgical Procedure during admission	1.Yes 0.No
IV.	Microbiological Data	
23	Specimen Type	1. Blood 2. Urine 3. Cerebrospinal fluid 4. Sputum 5. Abscess 6. Stool 7. Other (specify)_____
24	Source of infection	1. Bloodstream 2. Respiratory tract 3. Urinary tract 4. Central Nervous System 5. Cardiovascular System 6. Gastrointestinal 7. Surgical/Wound/Abscess 8. Skin 9. Other (specify)_____

25	Had the patient been hospitalized for more than 2 calendar days at the time for sampling?		1.Yes 0.No		
26	Culture obtained before antibiotic initiation		1.Yes 0.No		
27	Culture Result (if no growth go to Q35)		1. Has growth 2. No growth		
28	If it has microbial growth, is it polymicrobial infection		1.Yes 0.No		
29	Identified Pathogen (if bacterial growth)		1. Gram Positive 2. Gram Negative		
30	Identified Pathogen list		1. E. coli 2. K. pneumoniae 3. A. baumannii 4. S. aureus 5. S. pneumoniae 6. Salmonella spp. 7. Shigella spp. 8. N. gonorrhoeae 9. CONS 10. Other (specify) _____		
31	Antibiotic Susceptibility Testing (AST) Results done		1.Yes 0.No		
32	If antibiotic susceptibility test done, is the result positive for antibiotic resistance (resistance to at least one antibiotic)		1.Yes 0.No		
33	If yes for Question 32 which kind of	Antibiotics	S: Susceptible	I: Intermediate	R: Resistant
		A. Cefoxitin			
		B. Cefotaxime			

	antibiotic AST patterns	C. Ceftazidime			
		D. Ceftriaxone			
		E. Cefixime			
		F. Cefepime			
		G. Ampicillin			
		H. Gentamycin			
		I. Amikacin			
		J. Ciprofloxacin			
		K. Levofloxacin			
		L. Meropenem			
		M. Imipenem			
		N. Vancomycin			
		O. Azithromycin			
		P. Ampicillin			
		Q. Oxacillin			
		R. Penicillin G			
		S. Colistin			
		T. Co-trimoxazole			
		U. Minocycline			
		V. Tigecycline			
		Other			
34	Resistance categories (per CDC/WHO criteria)	1. Susceptible 2. MRSA 3. ESBL 4. CRE 5. MDR 6. Extensively drug resistant 7. Pan drug resistant 8. Other (specify): _____			

V.	Outcome	
35	Length of stay in PICU (days)	_____
36	New Complication developed in PICU	1. Sepsis 2. Septic shock 3. HAI 4. Ventilator associated pneumonia 5. Deep venous thrombosis 6. Air leak Syndrome 7. Other (specify) _____
37	Outcome at discharge	1. Improved and transferred to ward 2. Referred to another facility 3. Died in PICU 4. Discharge against medical advice

Declaration

Declaration of investigator

I, the undersigned Pediatrics and Child Health Resident, declare that this Thesis is my original work in partial fulfillment of the requirement for the Specialty certificate in Pediatrics and Child Health to my best knowledge.

Name of investigator: Abdi Hayato

Signature: _____ Date_____

Declaration of Advisors

We, the undersigned Advisors, declare that this Thesis is the investigator original work in partial fulfillment of the requirement for the Specialty certificate in Pediatrics and Child Health. We confirmed that this Thesis is ready for defense with our approval as the university Advisors.

Date of Submission: _____

Name of Advisor:	Signature	Date
1. _____	_____	_____
Name of Advisor:	Signature	Date
2. _____	_____	_____