ORIGINAL ARTICLE

Study of Colistin Resistant Gram Negative Organism in Hospitalized Patients: A Retrospective Study

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Abstract

Background: Intensive care units have become hotspots for antimicrobial resistance, particularly concerning colistin resistance, posing a threat of untreatable infections.

Aim: This study aims to analyze the epidemiological and clinical aspects of patients carrying colistin-resistant organisms. It focuses on identifying risk factors, the microbiological profile, susceptibility patterns, and treatment outcomes.

Materials and methods: Isolates with colistin MIC >2 µg/mL, identified via BD PHOENIX, were subjected to colistin broth disc elution testing (as per CLSI guidelines) in our Microbiology Department between January and December 2022.

Results: Among the 30 patients, colistin-resistant gram-negative isolates were found predominantly in blood cultures (50%), followed by ET/TT cultures (23.3%), urine cultures (10%), and other sites (16.7%). *Klebsiella pneumoniae* was the most common organism (80%), showing the highest sensitivity to Ceftazidime-avibactam + Aztreonam (CAZ-AVI + ATM) (76.7%). Of these patients, 66.7% recovered and were discharged, while 33.3% succumbed during hospitalization despite treatment.

Conclusion: The study underscores a notable presence of colistin-resistant gram-negative isolates, predominantly in blood cultures, with *K. pneumoniae* being predominant. The combination of CAZ-AVI + ATM exhibited the highest sensitivity. However, the mortality rate of 33.3% despite sensitive antibiotic treatment highlights the urgency for ongoing vigilance and research to combat colistin-resistant infections and improve patient outcomes.

Keywords: Colistin-resistant infections, Extensive drug resistance, Intensive care units.

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Highlights

- The intensive care unit, a hub for antimicrobial resistance, faces challenges with colistin-resistant infections, posing threats of untreatable cases.
- Investigating colistin-resistant organisms, the study reveals Klebsiella pneumoniae as predominant, primarily from blood cultures.
- Ceftazidime-avibactam + Aztreonam (CAZ-AVI + ATM) combo exhibits the highest sensitivity (76.7%), yet 33.3% mortality despite sensitive antibiotics underscores the urgency for research and vigilance in combating colistin-resistant infections in ICU settings.

Introduction

Injudicious antibiotic usage is a global concern, particularly in developing countries. The significant rise in carbapenem resistance among gram-negative pathogens in the last decade has led to a resurgence in the utilization of colistin antibiotics. The intensive care unit (ICU) has emerged as a focal point for antimicrobial resistance. However, the emergence of colistin resistance is becoming apparent, introducing the possibility of untreatable gram-negative bacteria (GNB) infections and challenging antibiotic therapies.[1]

Our objective was to conduct an observational study involving patients hospitalized from January to December 2022, where colistin-resistant GNBs were isolated. We aimed to analyze the epidemiological and clinical profiles of patients harboring colistin-resistant organisms. Additionally, we planned to investigate the risk factors associated with the emergence of colistin-resistant organisms, delve into the microbiological profile, and ascertain sensitivity patterns. We recorded the administered treatments and the outcomes observed in these patients. The findings from our study will aid attending physicians in identifying risk factors and making informed decisions regarding treatment. Furthermore, our study will underscore the significance of preventing the emergence of resistant bacteria through the implementation of antibiotic stewardship strategies.

Materials and Methods

All isolates with colistin MIC >2 µg/mL, as determined by BD PHOENIX, were identified. The same isolates were tested for

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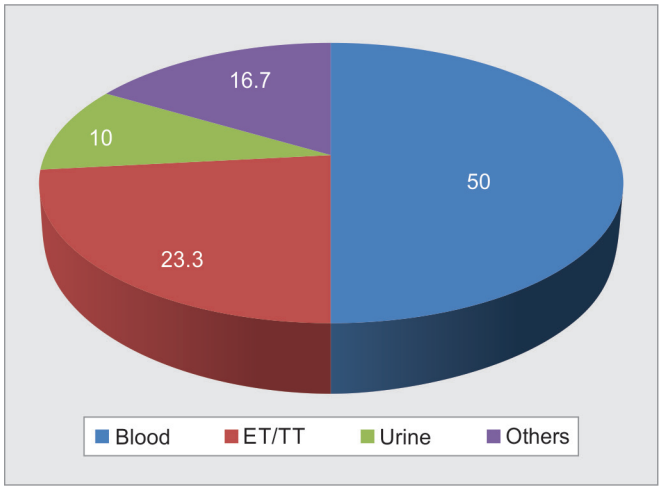

Fig. 1: Site of isolation for culture in admitted patients infected with colistin resistant gram-negative isolate

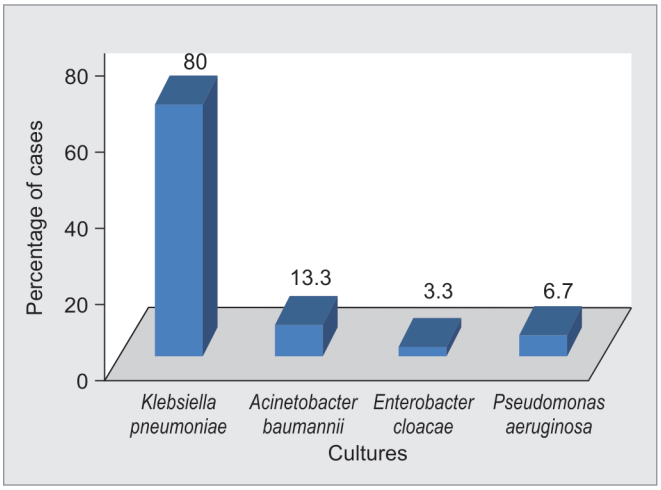

Fig. 2: Microbiological profile of positive cultures of colistin resistant gram-negative isolates

colistin MIC using the Colistin Broth Disc Elution test, following the Clinical and Laboratory Standards Institute (CLSI) guidelines, in our Microbiology Department between January 2022 and December 2022. Patient records were analyzed for variables such as age, sex, comorbidities, intensive care unit (ICU) stay, presence of indwelling devices, prior antibiotic exposure within 3 months, antibiotics used, clearance of infection, and outcome. Colonizers were excluded, and the site of isolation was noted. The outcomes of patients who were considered to have a true infection and were treated were analyzed. Organisms that are intrinsically resistant to colistin were excluded from the study. We documented the sensitivity pattern of these isolates, antibiotics that were administered, and treatment responses until patients were discharged or deceased. All patients infected with colistin-resistant GNB who were admitted to our hospital during the study duration were included in our analysis.

Results

We included 30 hospitalized patients with cultures showing colistin-resistant gram-negative organisms. We excluded colonizers from our study. The mean age of patients in our study was 59.1 ± 16.4 years. Out of the 30 patients, 19 (63.3%) were male, and 11 (36.7%) were female. Among the patients, 14 (46.7%) had hypertension, 12 (40.0%) were diabetic, and 4 (13.3%) had chronic kidney disease (CKD). Additionally, 9 (30.0%) patients were on immunosuppressant medications, 2 (6.7%) had carcinoma, and 1 (3.3%) patient was infected with HIV. Within the group of patients, 22 (73.3%) had a prior history of hospitalization, and 23 (76.7%) had used antibiotics within the last 3 months.

During the hospitalization period, Foley's catheter was inserted in 20 (66.7%) patients, CVP or HD catheter was inserted in 18 (60%) patients, and ET or TT was inserted in 9 (30%) patients.

Colistin-resistant gram-negative isolates were cultured from blood in 15 (50%) patients, from ET or TT cultures in 7 (23.3%) patients, from urine cultures in 3 (10%) patients, and from other sites (pus, bile, ascetic fluid) in 5 (16.7%) patients (Fig. 1).

The most common colistin-resistant gram-negative organisms isolated in our study were *K. pneumoniae* (80%), followed by *Acinetobacter baumannii* (13.3%), *Pseudomonas aeruginosa* (6.7%), and *Enterobacter cloacae* (3.3%) (Fig. 2). The highest sensitivity was

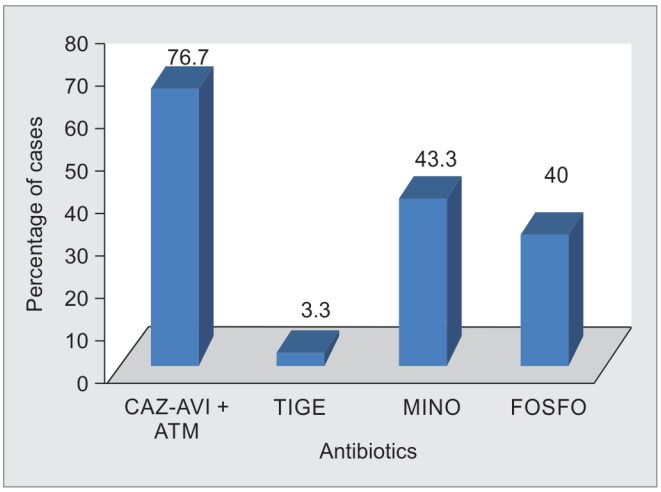

Fig. 3: Antibiotic susceptibility in colistin resistant isolate in admitted patients

observed with Ceftazidime-avibactam + Aztreonam (CAZ-AVI + ATM) (76.7% of cases), followed by Minocycline (43%), Fosfomycin (40%), and the lowest sensitivity was shown with Tigecycline (3.3%) (Fig. 3).

Regarding treatment during hospitalization, 46.6% of patients received CAZ-AVI + ATM, 3.3% received Tigecycline, 10% received Minocycline, 13.3% received Fosfomycin, 3.3% received a high dose of Polymyxin B, 20% received a combination therapy of CAZ-AVI + ATM and Minocycline, 23.3% received a combination therapy of CAZ-AVI + ATM, Minocycline, and Fosfomycin, and 3.3% received combination therapy of a high dose of Polymyxin B and Minocycline.

Out of the 30 patients, 20 (66.7%) recovered and were discharged, while 10 (33.3%) patients expired during the course of hospitalization.

Discussions

Our observational study was conducted at a tertiary care center. We included 30 hospitalized patients with cultures showing colistin-resistant gram-negative organisms. Colonizers were excluded from

our study. The mean age of patients considered in our study was 59.1 ± 16.4 years. Out of the 30 patients, 19 (63.3%) were male, and 11 (36.7%) were female. In a retrospective analysis of hospitalized patients infected with colistin-resistant gram-negative isolates, a total of 93 patients were included. The mean age of the patients was 61.8 years (28–84) with 58.1% being male and 41.9% being female. Another study from South India regarding infection with colistin-resistant GNB reported a mean patient age of 58.33 years and a higher infection rate in males compared to females.[2]

Various risk factors for the development of colistin resistance were considered in our study. According to our findings, out of the patients, 14 (46.7%) were hypertensive, 12 (40.0%) were diabetic, and 4 (13.3%) had CKD. Additionally, 9 (30.0%) patients were on immunosuppressant medications, 2 (6.7%) had carcinoma, and 1 (3.3%) patient was infected with HIV. Furthermore, 22 (73.3%) and 23 (76.7%) patients had a prior history of hospitalization and antibiotic use within the last 3 months, respectively.

In a similar study conducted by Syed et al., Diabetes mellitus was present in 39 (41.9%) patients, CKD in 22 (23.7%) patients, malignancy in 1 (1.1%), and long-standing immunosuppressive therapy in 4 (4.3%) patients with colistin-resistant isolates.[3] Richter et al. conducted a retrospective study involving positive cultures from any source over a 6-year period to assess the risk of infection with colistin-resistant gram-negative isolates, with a focus on *K. pneumoniae*. They found that a prior history of antibiotics uses within the last 3 months, mainly carbapenem uses, and a prolonged admission duration were significantly associated with colistin resistance. The use of steroids, chemotherapy, and immunosuppressant's was also linked to an increased risk of colistin-resistant infection.[4]

Regarding invasive procedures, out of the 30 patients studied during hospitalization, Foley's catheter was inserted in 20 (66.7%) patients, CVP or HD catheter was inserted in 18 (60%) patients, and ET or TT was inserted in 9 (30%) patients. According to Syed et al., indwelling catheters were considered a risk factor for colistin resistance. They reported that 41 (44.1%) patients were intubated and mechanically ventilated, 81 (87.1%) patients had urinary catheters, and central lines were inserted in 71 (76.3%) patients.[3] Yang et al. also found that indwelling urinary catheters, mechanical ventilation, recent β-lactam-β-lactamase inhibitors, fourth-generation cephalosporins, and/or carbapenem therapy were independent risk factors for colistin-resistant *K. pneumoniae* infection.[5]

In our study, colistin-resistant gram-negative isolates were primarily isolated from blood cultures in 15 (50%) patients, from ET or TT cultures in 7 (23.3%) patients, from urine cultures in 3 (10%) patients, and from other sites (bile, ascetic fluid) in 5 (16.7%) patients. A study by Panigrahi et al. found that colistin-resistant GNB isolates were mostly recovered from blood cultures (26.8%) followed by ulcer/surgical wound exudates (23.0%) and urine cultures (22.7%).[6] Richter et al. observed that respiratory secretions were the main source of colistin-resistant isolates (67.3%), followed by blood (10.9%) and wound/skin sources (10.9%). These findings align with our study, although there are some variations.[4]

The most common colistin-resistant gram-negative organism isolated in our study was *K. pneumoniae* (80%), followed by *A. baumannii* (13.3%), *P. aeruginosa* (6.7%), and *E. cloacae* (3.3%). In a study by Syed et al., *K. pneumoniae* was the most common organism isolated (91.4%), followed by E. coli (11%), *P. aeruginosa* (5.4%), and *A. baumannii* (4.3%).[3] Arjun et al. found that *K. pneumoniae* constituted the majority of isolates (87.5%), with smaller numbers of other organisms. The variations in these findings across studies highlight the regional differences in microbial prevalence.[2]

Regarding antibiotic sensitivity, the isolates in our study showed the highest sensitivity to CAZ-AVI + ATM (76.7% cases), followed by minocycline (43%), fosfomycin (40%), and the lowest sensitivity was observed with tigecycline (3.3%). In a study by Arjun et al., tigecycline was the most common antibiotic used for treatment (75% sensitivity), followed by other antibiotics with varying sensitivities. Unfortunately, CAZ-AVI + ATM was not tested for susceptibility or used for treatment in their study.[2]

In our study out of 30 patients, 20 (66.7%) patients recovered and were discharged, while 10 (33.3%) patients expired during the course of hospitalization. R Aggarwal et al. conducted a study in surgical ICU and found mortality up to 40% in colistin-resistant GNB. In there study out of the 5 patients, 3 patients survived and 2 had succumbed to death.[7]

Similar studies have reported varying survival rates, with mortality ranging from 25 to 29.9% in different studies. The presence of multiple comorbidities and prior hospitalization history were common factors among patients who died in our study.

The emergence of drug-resistant bacteria poses significant challenges to our ability to effectively treat infections. Gram-negative bacteria, in particular, present a major concern due to their inherent resistance to many antibiotics. Preventive measures to curb the misuse and overuse of antibiotics, especially colistin, and carbapenems, are essential to combat the high rate of colistin resistance observed in our study. Routine infection control and screening policies for antibiotic resistance should be established to address this issue.

Conclusion

Colistin resistance in Indian hospitals is increasing among GNB and is associated with 33.3% mortality in our study. Recent hospitalization, diabetes, hypertension, CKD, invasive device use, and prior antibiotic exposure are risk factors. Klebsiella pneumoniae is the predominant resistant organism, often found in elderly patients with co-morbidities and invasive procedures. CAZ-AVI + ATM and minocycline show high sensitivity in these patients underlying condition severity predicts mortality, but it's not easily changed.

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