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Original Research Article

The Impact of Microbiological Cultures on Antimicrobial Prescriptions in Septicemic Patients and Evaluation of Antimicrobial Usage by WHO AWaRe Index in a Tertiary Care Teaching Hospital

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Abstract

Background: Septicemia remains a critical cause of mortality, particularly in low- and middle-income countries like India. Rising antimicrobial resistance (AMR) necessitates evidence-based prescribing to improve clinical outcomes. This study aimed to assess the impact of microbiological culture results on antimicrobial prescribing patterns.

Methods: A prospective observational study was conducted in a tertiary care teaching hospital over 12 months. Blood culture–positive patients of all ages and both genders were included. Data regarding demographics, clinical diagnosis, organism isolates, culture sensitivity results, empirical and definitive antimicrobial therapy, and adverse drug reactions were collected using a pre-validated proforma and analyzed using descriptive statistics.

Results: Out of 120 patients, 53% were male and 47% female. Staphylococcus aureus (48%) was the most common isolate followed by Klebsiella pneumoniae (18%) and Enterococcus species (8%). A total of 248 antimicrobials were prescribed empirically with penicillins, aminoglycosides and cephalosporins groups being the most common. Only a small proportion belonged to the Access group. Therapy was modified in 42% of cases following culture sensitivity reports. Vancomycin, meropenem, and piperacillin–tazobactam were the most commonly used definitive agents. Resistance patterns showed high MRSA prevalence, while vancomycin and linezolid retained full sensitivity. Two mild and preventable adverse drug reactions were reported.

Conclusion: The Study highlights a predominance of Gram-positive pathogens and extensive use of Watch and Reserve antimicrobials. Culture-guided modification significantly optimized therapy in many cases. Strengthening antimicrobial stewardship and promoting Access-group antimicrobial use are crucial to curb rising AMR and improve septicemia outcomes.

Keywords: Antimicrobial Prescribing Pattern, Antimicrobial Resistance, AWaRe Classification, Culture Sensitivity, Septicemia.

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Introduction

Septicemia, defined as 'the presence of pathogenic microorganisms or their toxins in the bloodstream,' is a severe condition that triggers a systemic inflammatory response known as "sepsis". [1] It is one of the major causes of morbidity and mortality and the most common healthcare associated infection. [2]

A recent scientific publication estimated that in 2017 there were 48.9 million cases and 11 million sepsis-related deaths worldwide, which accounted for almost 20% of all global deaths. In 2017, nearly 50% of worldwide sepsis cases were in children, amounting to around 20 million cases. This condition led to approximately 2.9 million deaths among children under the age of 5. Regional disparities in sepsis incidence and mortality exist; approximately 85% of sepsis cases and sepsis-related deaths worldwide occurred in low- and middle-income countries. [3] India is burdened by a high incidence of sepsis, with an estimated 11 million individuals affected yearly and a mortality rate of nearly 3 million. As per study by an international research consortium, sepsis claims more lives in India than in other South Asian countries except Afghanistan. [4]

Treatment for septicemia requires antimicrobials and antimicrobial resistance (AMR) is a key contributor to the failure of treatment, leading to the rapid progression of sepsis and septic shock. Sepsis patients with resistant pathogens have been found to have a higher risk of hospital mortality. [5] In 2019 alone, worldwide 1.27 million deaths were directly caused by AMR, surpassing the total of HIV and Malaria combined. [6] Alarmingly, by 2050, Asia is predicted to experience 4.7 million deaths directly by AMR. India possesses one of the world's highest antimicrobial resistance rates. [7]

To combat antimicrobial resistance, the AWaRe classification of antimicrobials was developed in 2017 by the WHO Expert Committee on Selection and Use of Essential Medicines as a tool to support antimicrobial stewardship efforts at local, national and global levels. The AWaRe classification is intended as a tool for monitoring antimicrobial consumption, defining targets and monitoring the effects of stewardship policies that aim to optimize antimicrobial use and curb antimicrobial resistance. Antimicrobials are grouped into three categories called Access, Watch, and Reserve. These groups consider how different antimicrobials affect antimicrobial resistance. It's important to use antimicrobials correctly to make sure they keep working well. [8]

The WHO's plan from 2019 to 2023 aims for each country to use at least 60% of all antimicrobials from the Access group. These antimicrobials are considered safer and less likely to lead to resistance, so using more of them helps to protect their effectiveness. [9] The distribution of pathogens and their susceptibility pattern to antimicrobials vary regionally and even in the same region, they change over time. [10]

Therefore, the knowledge on the frequency of the causative microorganisms and their susceptibility to various antimicrobials, is needed to provide guidance toward an empirical therapy.

The present study was conducted to assess the sensitivity and resistance profiles of microorganisms isolated from septicemic patients and it will help to find the best treatment for a bacterial infection. An AWaRe index could be help to estimate the relative use of narrow spectrum and broad-spectrum antimicrobials in clinical practice.

Materials and Methods

Study Design: A prospective observational study.

Study Setting: Departments of Pediatrics, Medicine, Surgery, Orthopedics, and OBGY in a tertiary care teaching hospital.

Study Duration: 12 months

Sample Size: 120

Ethical Considerations: The study protocol, proforma and informed consent form in English and Gujarati were submitted and approved by Institutional Ethics Committee (Approval No: PDUMC/IEC/50/2023). Written informed consent was taken from all participants or guardians (for pediatric patients).

Inclusion Criteria

- Patients who were diagnosed with septicemia with positive microbiological culture sensitivity testing.
- Patients of either sex and of all ages.

Exclusion Criteria

- Patients having malaria, tuberculosis and HIV infection.
- Inadequate case record or data.
- Not willing to participate.

Data Collection: Data were collected using a pre-validated proforma:

- Demographics
- Clinical diagnosis
- Empirical antimicrobial therapy
- Blood culture organism
- Sensitivity report
- Definitive antimicrobial therapy

Data Analysis: Data analyzed using descriptive statistics. Results presented as numbers and percentages.

Results

Total 120 blood culture positive septicemic patients were enrolled in the study for total 12 months. Out of 120 patients analyzed, 64(53%) were male and 56(47%) were female. Most of patients 57 (48%) belong to Adult age group (19- 65 years) followed by 55 (46%) belong to Child age group (up to12 years).

Table 1: Age group wise Distribution

Serial No.	Age Groups	Total Number of Patients [N=120]
1	0 – 12 years (Child)	55 (46%)
2	13 - 18 years(Adolescence)	05 (4%)
3	19- 65 years (Adult)	57 (48%)
4	>65 years (old age)	03 (2%)

Staphylococcus Aureus, a gram positive bacteria, was highest in number 58 (48 %) followed by the Klebsiella pneumoniae, a gram negative bacteria were 21 (18%) out of 120 patients have been isolated from blood culture followed by Enterococcus species were 10 (8%) and gram negative bacteria like Escherichia coli, Acinetobacter baumannii, Salmonella Typhi, and Pseudomonas Aeruginosa were 10 (8%), 10 (8%), 7 (6%) and 4 (4%) respectively.

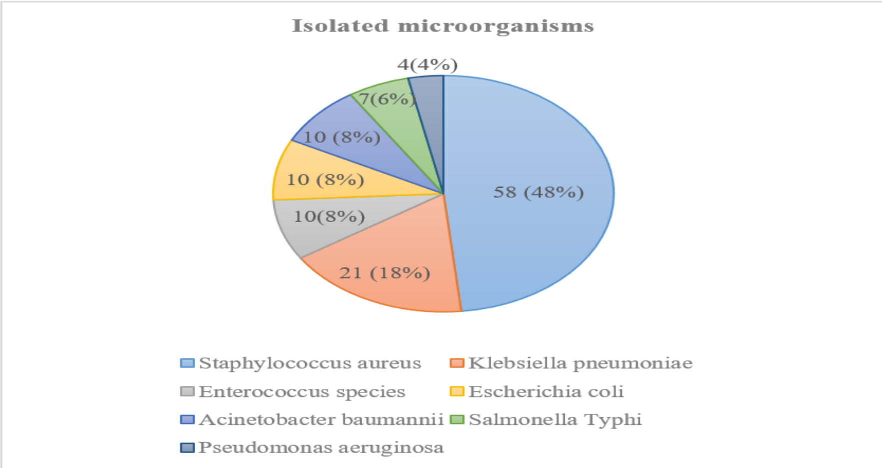

Figure 1: Bar chart showing distribution of isolated microorganisms

In total, 248 antimicrobials were prescribed among 120 patients as Empirical therapy. Among the 120 prescriptions analyzed, two antimicrobials per prescription were most common (n = 93), followed by three antimicrobials (n = 18), while a single antimicrobial was prescribed in nine cases (n = 9) only as shown in Table-2.

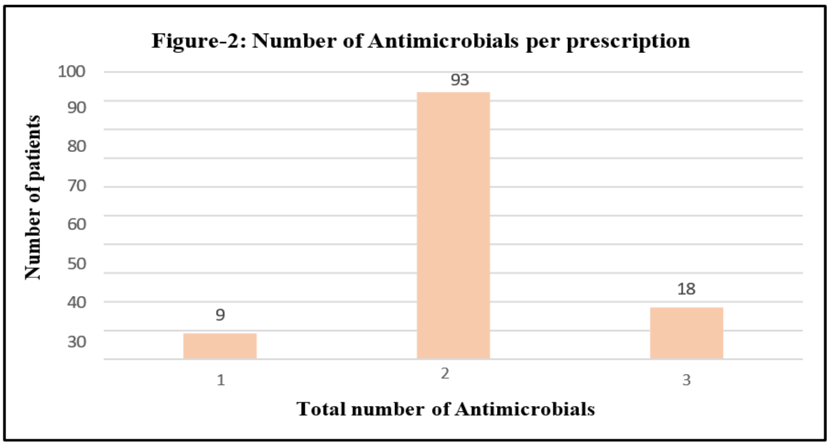

Figure 2: Number of antimicrobials per prescription

As shown in Table-2, Penicillin group of antimicrobials drugs like Ampicillin+ sulbactam, Piperacillin+ Tazobactam, Amoxicillin+ Clavulanic acid were prescribed most commonly. Second most common group was Aminoglycosides (Gentamycin and Amikacin) and third most common group was Cephalosporins (Ceftriaxone, Cefotaxime, Cefosulbactam, and Cefixime).

Table 2: Empirical antimicrobial drugs with their groups

Antimicrobial group	Name of drug	Number of patients receiving the drug [N-120]	Total no.of drug [N-248]
Penicillins	Ampicillin + sulbactam	36	56
	Piperacillin+ Tazobactam	16	
	Amoxicillin + Clavulanic acid	04	
Aminoglycosides	Gentamycin	36	50
	Amikacin	14	
Cephalosporins	Ceftriaxone	38	44
	Cefotaxime	03	
	Cefosulbactam	02	
	Cefixime	01	

Nitroimidazole	Metronidazole	41	41
Carbapenems	Meropenem	25	25
Glycopeptide	Vancomycin	22	22
Macrolides	Azithromycin	04	04
Fluoroquinolones	Levofloxacin	03	03
Lincosamide	Clindamycin	02	02
Polymyxin	Colistin	01	01

As shown in Table-2, total 16 Antimicrobial agents were prescribed as empirical treatments in which only 6 from Access group, 8 from Watch group and 2 from Reserve group of WHO AWaRe index. [8]

Out of 120 patients, empirical antimicrobial therapy had been changed to definitive antimicrobial therapy in 51(42%) patients after culture sensitivity testing. Total 71 antimicrobials were prescribed among 51 patients, in which antimicrobials therapy was changed after culture and sensitivity testing as Definitive therapy, 31 patients received 1 antimicrobial and 21 patients received 2 antimicrobials.

As shown in Table-3, Vancomycin was the most commonly used drug in definitive antimicrobial therapy. Second most common drug was Meropenem and third was Piperacillin + Tazobactam.

Table 3: Definitive antimicrobial drugs with their groups

Antimicrobial group	Name of drug	Number of patients receiving the drug [N-51]	Total number of drug [N-71]
Glycopeptide	Vancomycin	27	27
Carbapenems	Meropenem	17	17
Penicillin	Piperacillin+Tazobactam	09	09
Aminoglycosides	Amikacin	03	05
	Gentamycin	02	
Polymyxin	Colistin	05	05
Oxazolidinones	Linezolid	04	04
Lincosamide	Clindamycin	02	02
Cephalosporins	Ceftriaxone	01	02
	Cefotaxime	01	
Nitroimidazole	Metronidazole	01	01
Fluoroquinolones	Levofloxacin	01	01

As shown in Table-3, total 12 Antimicrobial agents were prescribed as definitive treatments in which only 4 from Access group, 6 from Watch group and 2 from Reserve group of WHO AWaRe index. [8]

Culture sensitivity and resistance testing of all microorganisms isolated from patients with septicemia was collected as part of the study. Gram positive microorganism, Staphylococcus Aureus was the most commonly isolated during the study.

Figure-3 shows the antibiogram of Staphylococcus Aureus.

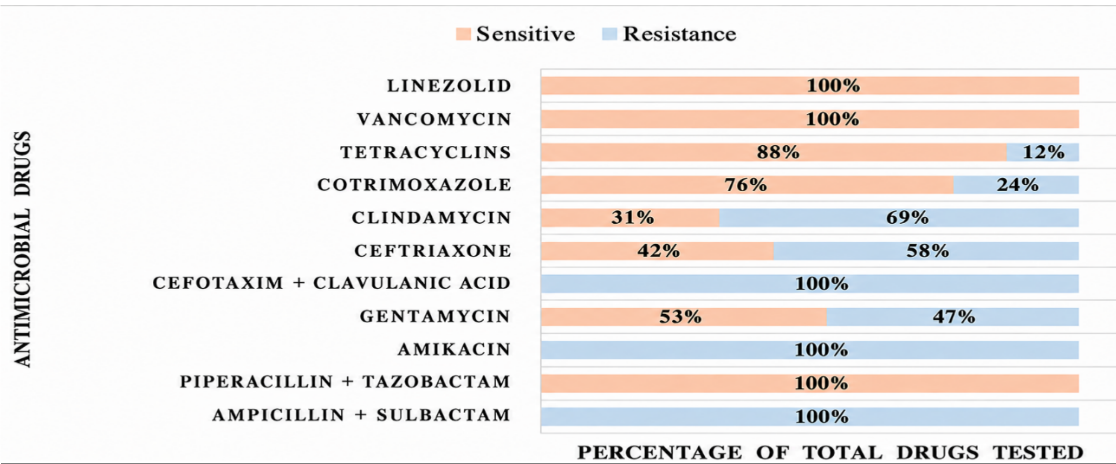

Figure 3: The antibiogram of Staphylococcus Aureus isolates showing Sensitivity

A Gram negative microorganism, Klebsiella pneumoniae was the second most common isolated during the study. Figure-4 shows the antibiogram of Klebsiella pneumoniae.

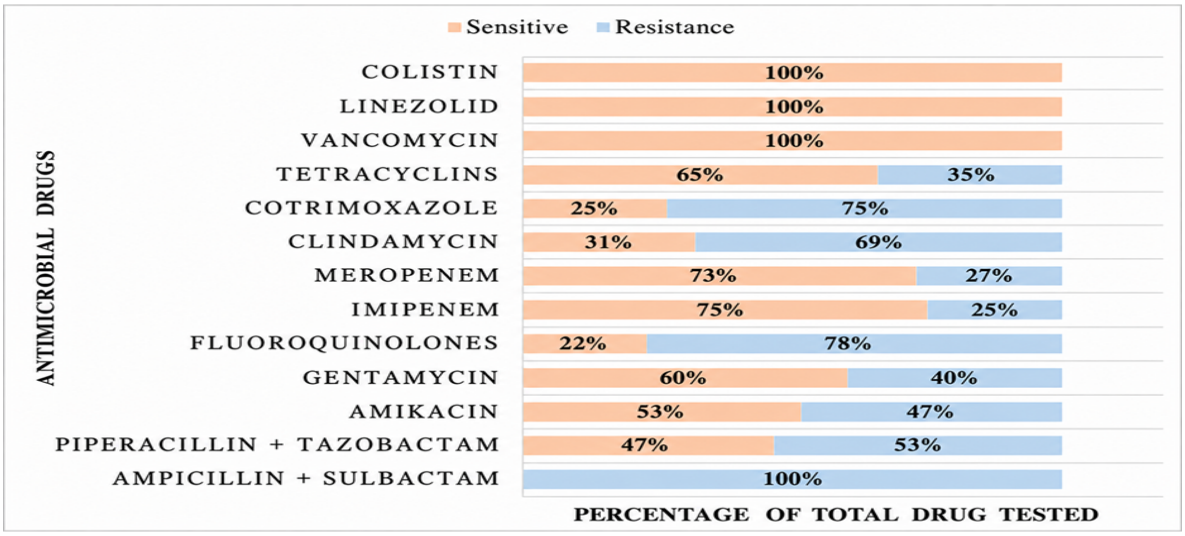

Figure 4: The antibiogram of Klebsiella pneumoniae isolates showing Sensitivity

Another Gram positive microorganism, Enterococcus species were the third most commonly isolated during the study. Figure-5 shows the antibiogram of Enterococcus species.

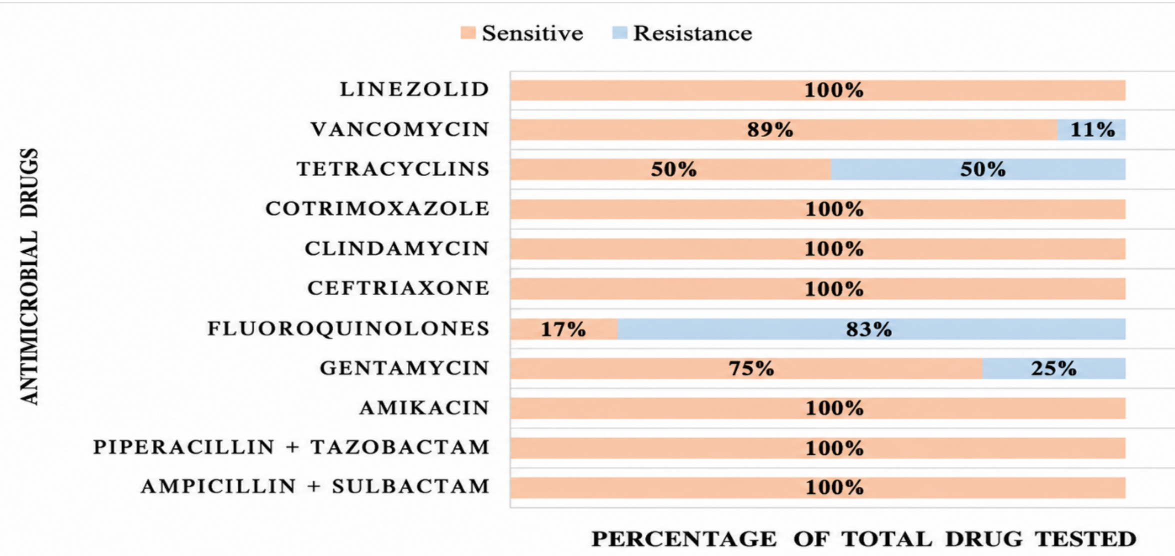

Figure 5: The antibiogram of Enterococcus species isolates showing Sensitivity

The comparison of antimicrobials used in the study with the Gujarat State Essential Drug List (2022–23), the National List of Essential Medicines (NLEM 2022), and the WHO Essential Medicines List (23rd edition, 2023) is shown in Table 4.

Most commonly used antimicrobials, including piperacillin–tazobactam, amoxicillin–clavulanic acid, gentamicin, amikacin, ceftriaxone, cefotaxime, cefixime, metronidazole, meropenem, vancomycin, azithromycin, levofloxacin, and clindamycin, were listed in all three essential medicine lists. Some antimicrobials such as ampicillin–sulbactam and cefosulbactam—were not included in any of the essential medicine lists. Colistin was included in the Gujarat state list and the WHO list, but was absent from NLEM 2022. Linezolid was listed only in the WHO Essential Medicines List.

This comparison highlights formulary differences and the essentiality assigned to various antimicrobials across state, national, and WHO guidelines.

Table 4: State essential drug list, NLEM and WHO essential medicine list

Sr No.	Name of antibiotics	State (Gujarat) Essential drug list (2022-23)	NLEM-2022	WHO Essential Medicine list (23rd) 2023
1	Inj. Ampicillin + sulbactam	No	No	No
2	Inj. Piperacillin+ Tazobactam	Yes	Yes	Yes
3	Inj. Amoxycillin + Clavulanic acid	Yes	Yes	Yes
4	Inj. Gentamycin	Yes	Yes	Yes
5	Inj. Amikacin	Yes	Yes	Yes
6	Inj. Ceftriaxone	Yes	Yes	Yes
7	Inj. Cefotaxime	Yes	Yes	Yes
8	Inj. Cefosulbactam	No	No	No
9	Inj. Cefixime	Yes	Yes	Yes
10	Inj. Metronidazole	Yes	Yes	Yes
11	Inj. Meropenem	Yes	Yes	Yes
12	Inj. Vancomycin	Yes	Yes	Yes
13	Inj. Azithromycin	Yes	Yes	Yes
14	Inj. Levofloxacin	Yes	Yes	Yes
15	Inj. Clindamycin	Yes	Yes	Yes
16	Inj. Colistin	Yes	No	Yes
17	Inj. Linezolid	No	No	Yes

Two cases of fixed drug eruption, each affecting one patient and suspected to be caused by nimesulide and ceftriaxone respectively. Both reactions were classified as probable on the WHO causality scale, assessed as mild on the Hartwig and Siegel severity scale, and judged preventable by the Modified Schumock & Thornton scale.

Discussion

This study assesses the impact of microbiological culture results on antimicrobial prescribing pattern in 120 blood culture proven septicemic patients. The usefulness of microbiological cultures has been questioned many times, but in the present era of increasing antimicrobial resistance it is more important than ever to avoid unnecessary broad-spectrum antimicrobial therapy. It has been demonstrated that adjusting antimicrobial therapy according to the results of microbiological culture findings leads to a narrowing of antimicrobial therapy. Thereby, the emergence of antimicrobial resistance can be avoided or delayed. [11]

In addition, it has been repeatedly demonstrated that 40-70% of use of these agents is inappropriate, with consequent waste of resources. Several hospitals have implemented different strategies to curb the overuse of specific antimicrobial agents, with varying outcomes. [12]

Our study observed a predominance of Gram-positive bacteria (56.66%), with Staphylococcus aureus being the most common isolate (48.33%). Similar findings have been reported in studies by Ajay L. Das et al. [2,13], whereas other reports document Gram-negative predominance. [10,14] Such variations likely reflect differences in regional epidemiology and local hospital infection patterns. A total of 248 antimicrobials were prescribed empirically, with most patients receiving two antimicrobials. Study performed by Tamma et al on combination therapy for treatment of infections with bacteria do not support the use of combination antimicrobial therapy. The potential benefits of combination therapy for patients with severe sepsis warrant further investigation through well-designed randomized trials. [15]

Penicillin group [total-56] of antimicrobials drugs like Ampicillin+ sulbactam, Piperacillin+ Tazobactam, Amoxicillin + Clavulanic acid and aminoglycosides [total-50] antimicrobial agent like Gentamycin and Amikacin were most commonly used drugs as an empirical antimicrobial therapy in our study. Similar results were shown in the study performed by Berlid et al. [11] Whereas study performed by Savita Choudhary et al showing Cephalosporins, Piperacillin + Tazobactam and Clindamycin were prescribed most commonly as empirical therapy. [13] The reason behind use of these drugs may be the most patients were from Pediatric and Medicine departments where these drugs are commonly prescribed.

In our study in 51[42%] patients, antimicrobial therapy was modified or changed according to the blood culture and sensitivity reports. Study conducted by Panaligan et al. has shown that modification of therapy was in 7.2% patients only and another study has shown modification in 27% patients. [14,16] This could be because physicians were more inclined to start on newer broad-spectrum antimicrobials and those were sensitive to organisms. Berild et al study has shown modification of therapy in 64.60% patients. [11] In our study, Total 71 antimicrobials were prescribed among 51 patients, in which antimicrobials therapy was changed after culture and sensitivity testing as

Definitive therapy. Vancomycin [27] was the most commonly used drug in definitive antimicrobial therapy. Second most common drug was Meropenem [17] and third was Piperacillin + Tazobactam [09]. Choudhary S et al study has shown that Meropenem, Teicoplanin, and Piperacillin + Tazobactam were the most commonly prescribed drugs. [13]

Resistance patterns observed in this study were concerning. Among S. aureus isolates, 43% were MRSA, and high resistance was noted to multiple agents including penicillin (96%) and ciprofloxacin (89%), while no resistance was observed to vancomycin or linezolid. These findings mirror those of Dharmapalan D. et al.[17] Enterococcus species showed high resistance to macrolides and fluoroquinolones but preserved susceptibility to vancomycin and linezolid, similar to prior data. [17]

Klebsiella pneumoniae isolates exhibited very high resistance to cephalosporins and moderate resistance to aminoglycosides and fluoroquinolones, while retaining susceptibility to colistin. Comparable resistance trends have been documented in regional studies. [17,18] Rising resistance to cephalosporins and aminoglycosides reflects global patterns, as highlighted by surveillance data from the European Union. [18]

Study performed by Eiland III et al showed that early treatment of infections with appropriate, definitive antimicrobial therapy has proven to reduce mortality, length of hospital stay, and healthcare costs. [19] Another study performed by Kollef showed that inappropriate inadequate initial empirical therapy is associated with increased mortality, morbidity, and length of hospital stay. [20] To ensure the rational use of antimicrobials and prevent the development of resistance, it's crucial to implement antimicrobial stewardship programs and establish a local antibiogram specific to the hospital's microorganisms. This involves adopting control measures such as restricting the use of certain antimicrobials, implementing therapeutic guidelines, and continuously monitoring the resistance patterns of common pathogens in the hospital. These actions are recommended to enhance the appropriate and effective utilization of antimicrobials.[21] Effective stewardship programme can decrease antimicrobial use by 20-40%, incidence of health care associated infections, lengths of stay, and prevalence of bacterial resistance. [22]

The future of antimicrobial and survival of every human being that acquires a bacterial infection will depend on the serious commitment of many stakeholders including government authorities, policy makers, health-care workers, pharmaceutical companies and consumers. Addressing antimicrobial resistance is challenging; paradoxically, raising antimicrobial prices could control their overuse, yet we must maintain a delicate balance to ensure access. Innovative approaches in quality assurance, healthcare financing, and social marketing offer promising avenues for tackling this complex issue. [23]

Conclusion and Limitations

Our study shows that microbiological culture results affect antimicrobial prescribing in only 42% of cases. However, this finding should not undermine the essential role of microbiological investigations in diagnosing suspected infections. Integrating the review of microbiological results into medical practice for patients receiving antimicrobials can significantly improve antimicrobial prescribing practices.

Standard treatment guidelines are issued at national and state levels but routine survey and updating of sensitivity profile of microbial organisms at every hospital /setup is necessary to keep pace with the development of resistance. Therefore, Each and every hospital must have its own local antibiogram mentioning empirical therapy options and circulated among clinical branches to disseminate the sensitivity profile at regular interval.

The study also has important limitations, including its single-center design with a small sample size, inclusion of only culture-positive cases and being a one-time study, continuous surveillance of antimicrobial sensitivity patterns was not assessed.

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