Evaluation Of Antibiotic Usage Patterns, Patient Factors, And Economic Implications in ICU Settings: An Observational Study.

Abstract:

Background: One of today's most significant public health issues is antibiotic resistance, which is caused by the overuse or abuse of antibiotics. Effective antimicrobial therapy is essential for treating patients in the intensive care unit (ICU), including those with severe sepsis, septic shock, and infections linked to healthcare. This study assesses the economic burden of broad-spectrum antibiotic usage on the overall cost of ICU care.

Commented [u1]: This objective covers only the economic burden of the patients. This is better to write according to the title of the study.

Methods: An observational, cross-sectional study was conducted in the ICUs in a tertiary care center, over 1 month.

Results:

The gender distribution in the study shows a higher prevalence of male patients (60%) compared to female patients (40%), with a total sample size of 40 patients. Most of the patients were in the age group of 58–68 years (32.5%). The comorbidity scores indicate that a significant proportion of patients had a score of 4 (37.5%), which was also the most frequent score (mode). The most common length of stay was 2 days (mode), and the range extended from 1 to 9 days. Most patients had shorter stays, with 27.5% staying for 2 days and only a small fraction (2.5%) requiring a 9-day stay.

Commented [u2]: Result doesn't show any pattern of antibiotic usage.

Conclusion:

The study emphasizes the need for a careful balance between cost-effective antibiotic treatment and optimal patient care to improve health outcomes and reduce financial strain. It highlights

the crucial role of antimicrobial stewardship programs in promoting responsible antibiotic use, curbing resistance, and elevating patient care standards. Investing in diagnostics and educating healthcare providers about their advantages can further refine treatment approaches and long-term patient outcomes, particularly in resource-constrained environments.

Commented [u3]: Abstract should be written with 250 words. Conclusion might be curtailed.

Introduction

Antibiotic resistance is a major public health problem and a tough challenge of our time. The overuse or misuse of antibiotics is a contributing factor to antimicrobial resistance.[1] The treatment of patients in the intensive care unit (ICU), such as those with septic shock, severe sepsis, and those who develop healthcare-associated infections, depends on effective antimicrobial medication. Antibiotic therapy failure can be devastating and can result from a variety of reasons.[2] Multidrug-resistant organisms are becoming more prevalent and are associated with increased mortality rates, ICU admissions, and lengthier hospital stays. Because they increase the risk of morbidity and mortality and put patients in the intensive care unit (ICU) at high risk, microorganisms are of great clinical significance in hospitals.

Providers might take several actions to guarantee appropriate therapy and reduce adverse effects. Starting an efficient infection treatment depending on the patient's risk factors, gathering suitable cultures, daily assessment of clinical condition, lab results, such as antibiotic time outs, and shorter therapy sessions can help patients get better results. [2]

In intensive care units, antibiotic resistance is very high. Resistance is high for Gram-negative bacteria like Klebsiella spp. and other Enterobacteriaceae that have extended-spectrum b-lactamases, as well as Gram-positive cocci like methicillin-resistant Staphylococcus aureus (MRSA), glycopeptides-intermediate S. aureus (GISA), and vancomycin-resistant enterococci. [3] Clinically or microbiologically documented that bacterial pneumonia accounts for one-third of cases of ARF in immunocompromised patients. [4] While infections are associated with significant morbidity and mortality in immunocompromised critically ill patients, little specific data are available on the incidence, microbiology, management and outcomes of ICU-acquired infections in this population. [5] From a financial angle, all these factors are leading to the requirement of broad-spectrum antibiotics which are expensive and lead to an economic burden to the hospitals and the patients. The financial burden is so immense that it contributes up to 50%-70% of the hospital bills of critically ill patients creating a constant challenge to hospital clinical managers and business administrators.

The cost of antibiotics considerably impacts healthcare budgets and influences drug utilization patterns. To ensure rational use, patients should receive appropriate medications for their clinical needs, in the correct doses, for an adequate duration, and at the lowest possible cost to both them and their communities. High antibiotic usage constitutes a substantial part of overall healthcare expenses.[4]

Antimicrobials account for approximately 20% to 50% of a hospital's medication expenditures, with the majority being consumed in intensive care units (ICUs). ICUs, despite comprising less than 5% of hospital beds, can account for over a quarter of hospital budgets due to the high costs associated with antimicrobial use. The pharmacoeconomic analysis serves as a vital tool for monitoring the use of these drugs, focusing on their effectiveness, safety, and quality. [6,7]

ICUs are particularly focused on the challenge of bacterial resistance. Beyond the severe human costs of morbidity and mortality, treating multidrug-resistant infections leads to significant expenses, including prolonged hospital stays, side effects from additional treatments, increased clinical and laboratory tests, work absences, loss of income, and resources dedicated to monitoring and controlling bacterial resistance. Consequently, ICUs are a primary focus for tracking antibiotic usage and conducting pharmacoeconomic studies, especially given the pressing need to regulate healthcare expenditures.[7]

Specific challenges ICUs face include the diversity and severity of infections, immunocompromised states, and invasive procedures that predispose patients to infections. One of the most dangerous illnesses in the world, sepsis is characterised by an adverse host response to several acute diseases, which results in a high patient death rate. About 15% of sepsis-related deaths are acute, happening shortly after the illness starts, and 85% are late-phase, typically brought on by infections acquired in the intensive care unit. The length of stay (LOS), poor prognosis, and increased in-hospital mortality are all substantially correlated with ICU-acquired infections.[8] Multiple organ dysfunction syndrome (MODS) was also defined as the presence of altered organ function in acutely ill septic patients to the extent that homeostasis cannot be maintained without intervention, according to a consensus conference on sepsis definitions sponsored by the American College of Chest Physicians and the Society of Critical Care Medicine.[9]

Antibiotic resistance is an escalating global health issue, with ICUs being at the forefront due to their complex patient profiles and frequent exposure to multidrug-resistant organisms. In these settings, inappropriate or excessive antibiotic use not only undermines patient care by increasing the risk of resistance but also places a significant strain on healthcare resources. ICUs face challenges in this regard, as clinicians must balance the need for immediate, life-saving treatment against the risk of fostering resistant infections.[10]

Patient-specific factors further complicate antibiotic management in ICU settings. Variables such as age, underlying comorbidities, immune status, renal and hepatic function, and previous exposure to antibiotics can all influence both the selection and effectiveness of treatment. Understanding these factors is essential for tailoring antibiotic therapies that maximize patient outcomes while minimizing adverse effects.[11]

Aim and Objective

Primary Objective:

• To assess the economic burden of broad-spectrum antibiotic usage on the overall cost of ICU care.

Secondary Objectives:

• To identify the direct association with broad-spectrum antibiotics in ICU care.

• To evaluate the impact of antibiotic stewardship programs on reducing antibiotic costs in ICU settings.

• To explore the association between antibiotic overuse and patient outcomes.

Literature Review

Commented [u4]: Is the lit review needed separately where there is point of discussion?

A prospective cohort study conducted in Nepal tertiary care hospitals by **Nirmal Raj Marasine et al.** suggests that the utilization and cost of antibiotics are high in the medical intensive care unit of the hospital and E. coli was resistant to multiple antibiotics. Piperacillin/ tazobactam (45.2%) was the most prescribed antibiotic, and meropenem was the most expensive antibiotic (US$4440.70). Escherichia coli, Acinetobacter, and Pseudomonas sp. were the common organisms isolated and were found to be resistant to some of the commonly used antibiotics.[12]

In a multicentre observational study conducted by **Vu Quoc Dat et al**, interpreted that they observed d high-frequency use and a substantial variation in patterns of empirical antibiotic use in the Critical care units (CCUs) in Vietnam. It highlights the importance of continuous monitoring of antibiotic consumption in CCUs.[13]

A study conducted by **Ramya K et al** stated that their study showed that the average cost per patient who was not put on a ventilator was Rs 27,123 whereas for a ventilated patient per cost was Rs 44,812.The highest numbers of pneumonia were hospital-acquired/aspiration

Commented [u5]: This part is duplicate and needs to remove pneumonia. The cost of ventilator-supported pneumonia was two times more than non-ventilated pneumonia. Ventilator support was the most expensive intervention adding to the cost of care followed by the cost of antibiotics and investigations. [14]

In a study conducted by **Shiv Kumar et al. [e]** Penicillin was the most expensive class of antibiotics at 30% (9165rs) and in other words, carbapenem was the most expensive class of antibiotics at 40% (16448rs). Of 90 patients, In the emergency department, piperacillin/tazobactam was the most expensive antibiotic which was 29.94% (9075rs), and of 90 patients in other wards meropenem was the most expensive antibiotic with 40% (16448rs) and concluded that regular prescription audits and modifications of antibiotic policy are required to curtail the increased use of antibiotics and the economic burden on hospitals. [15]

Study conducted by **Rawshan Ara Perveen et al,** 25% of patients were treated with a single antibiotic and the remaining 75% of patients received one or more antibiotics during their ICU admission period. Multi-drug-resistant organisms made the situation more difficult both for patients and physicians. Three highly utilized antibiotics in this study were meropenem, levofloxacin, and ceftriaxone, on reviewing similar studies from India, it was observed that the five most utilized antibiotics are 3rd generation cephalosporins, meropenem, metronidazole, levofloxacin, and ceftriaxone and concluded that the high utilization rates and costs of antibiotics prescribed in the ICU are a matter of concern and need to be improved using local antibiogram guidelines, continuous surveillance and antibiotic restriction policies.[16]

A study conducted by **Tázia Lopes de Castro et al** their results showed that the total annual consumption (DDD/1000 patient-day) of antimicrobials in the ICUs was 14,368.85. β-Lactams had the highest total annual value, with a (Define Daily Dose) DDD/1000 patient-day of 7062.98, meropenem the antimicrobial that reached the highest consumption (3107.20), followed by vancomycin (2322.6). Total consumption was higher in COVID-19 ICUs than in

Commented [u6]: Not needed

General ICUs, and the annual direct cost of antimicrobials in ICUs was US$560,680.79 and concluded high consumption of broad-spectrum antimicrobials, highlighting the importance of structuring programs to manage the use of antimicrobials, both to reduce antimicrobial consumption and hospital costs, consolidating rational use even in pandemic scenarios.[17]

A study was conducted in the year 1995 by **P Blanc et al** in the study setting of an 11-bed intensive care unit (ICU) in a general hospital in the years 1994, 1995,1996. They decreased expenses for antibiotic drugs by 19% in 1995 and by 22% in 1996 and proved a positive economic impact of a rational policy in antibiotic therapy realized with a contract of agreed objectives. [18]

In a prospective observational study on antibiotic usage and cost pattern in an ICU conducted by **Suraj B et al** 68 patients (67.33%) received more than 1 antibiotic. Metronidazole was the most common antibiotic utilized at admission attributing to 29.70% and during the entire ICU stay accounting for 68.32%. Metronidazole followed by ceftriaxone and piperacillin/tazobactam were the maximally utilized antibiotics with 35.32, 31.22, and 23.82, DDD/100 bed-days, respectively. The average cost incurred for antibiotic therapy per patient was 1403 Indian rupees (INR) and concluded Metronidazole followed by ceftriaxone was the most prescribed antibiotic during ICU stay. A higher percentage of the total cost was attributed to meropenem. [19]

In a systematic review and meta-analysis done by **AK Narayan Poudel et al** Observed that studies conducted in tertiary care hospitals evidence indicates that the attributable cost of resistant infection ranges from -US$2,371.4 to +US$29,289.1 (adjusted for 2020 price) per patient episode; the mean excess length of stay (LoS) is 7.4 days (95% CI: 3.4–11.4), the odds ratios of mortality for resistant infection is 1.844 (95% CI: 1.187–2.865) and readmission is 1.492 (95% CI: 1.231–1.807) and concluded that There is still a lack of studies on the economic

Commented [u7]: Caps not reuired

burden of ABR from low-income economies, and lower-middle-income economies, from a societal perspective, and to primary care. The findings of this review may be of value to researchers, policymakers, clinicians, and those who are working in the field of ABR and health promotion.[20]

A study conducted in a monocentric, retrospective, and observational study in one year by **D Ismai**l finds that the global annual consumption of antibiotics accounted for 1410.21 defined daily doses (DDD) per 1000 bed-days from which β-lactams were the most consumed (768.95 DDD per 1000 bed-days). Community-acquired infections resulted in annual antibiotic consumption of 1340.82 vs 2483.69 g DDD for nosocomial infections. Multidrug-resistant infections resulted in annual consumption of 737.5 g DDD (52.2%). The global cost of prescribed antibiotics amounted to US$118,224.32. The consumption of β-lactams (38%) and fluoroquinolones (21%) combined cost ~60% of the total budget. The cost of antibiotics prescribed for the treatment of multidrug-resistant infections reached US$47,744.14. [21]

In a study conducted by **Devika D Misal et al** on the economic burden of antibiotic treatment of healthcare-associated infections (HCAIs) at a tertiary care hospital ICU in Goa, India results showed the incidence of HCAIs in the ICU was 16%. Ventilator-associated pneumonia (50%) was the most common HCAI, followed by urinary tract infection (35.6%). The total cost of antibiotic treatment for HCAIs in ICU over 1 year was approximately Rs. 2 million (US$32,000); the mean antibiotic cost per HCAI was calculated as Rs. 17,000 (US$255). HCAIs in the ICU thus put a significant economic burden on the patient and the healthcare network and should be prevented by implementing recommended infection control guidelines.

In a study conducted by **Sadatsharfi A et al** on the Economic Burden of Inappropriate Empiric Antibiotic Therapy: A Report from Southern Iran the study finds The most inappropriate prescribed antibiotics were carbapenems and aminoglycosides. frequency of antibiotic usage

Commented [u8]: The title of the study needs not to write here.

Commented [u9]: Please reconstruct the sentece incompatibility with the guidelines based on a dosing interval, duration of therapy and drug indication were 31.46%, 29.44% and 19.36%, respectively. General surgery and internal medicine wards had the least and the most inappropriate antibiotic administration, respectively. Antibiotic usage cost was 578,959.39 USD (24,316,294,800 Iranian Rials, IRR) for 6 months, and the excess costs of inappropriate antibiotic prescribing, was 471,319.69 USD (19,795,427,225 IRR). The estimated annual excess cost is 942,639.38 USD (39,590,854,450 IRR).

Research Methodology

Type of Study: Observational, cross-sectional study.

Study Setting: This study will be conducted in the ICUs in a tertiary care centre, over 1 month.

Commented [u10]: Is not the study conducted yet?

Study Population: Patients admitted to the ICU receiving broad-spectrum antibiotics during the study period.

Inclusion Criteria: Patients aged ≥18 years, ICU patients receiving at least one course of broad-spectrum antibiotics and Patients who have been in the ICU for at least 48 hours.

Sample Size: Based on hospital records from previous years, we anticipate a sample size of 40 ICU patients receiving broad-spectrum antibiotics to be sufficient to achieve statistical power.

Data Collection:

1. **Clinical Data:** Patient demographics, primary diagnosis, comorbidities, infection type, duration of ICU stay, and outcome (discharge, transfer, or mortality), SOFA Score, APACHE II Score and MODS.

Commented [u11]: Please abbreviate or use foot notes

2. **Antibiotic Data:** Type of broad-spectrum antibiotics used, duration, and reason for prescription (empiric or targeted therapy).

3. **Cost Data:** Direct costs (antibiotic cost, ICU stay costs, supportive care costs, diagnostics).

Statistical analysis:

The Formula for The Total Cost of Antibiotics

Total Cost=Total Occurrences×Cost per Dose×Number of Doses per Day×Length of Stay in Days

The formula for Total Cost per Day:

Total Cost=Total Occurrences×Cost per Dose×Number of Doses per Day

Total Occurrences = (number of patients receiving this drug)

Cost per Dose = (cost per dose of the drug)

Number of Doses per Day = (the drug is administered twice a day)

Length of Stay in Days = (average length of stay)

Data Analysis

Table 1: Gender Distribution:

Gender	N	%

Female	16	40
Male	24	60
Total	40	100

Table 2: Age distribution

Sno	**Age**	**N**	**%**
1.	18 - 28	0	0
2.	28 - 38	3	7.5
3.	38 - 48	4	10
4.	48 - 58	6	15
5.	58 - 68	13	32.5
6.	68 - 78	12	30
7.	78 - 88	1	2.5
8.	88 - 98	0	0
9.	98 - 108	1	2.5
Total		40	100%

Table 3: Comorbidity score

Commented [u12]: Please use a footnote here, wht is the score?

Sno	**Comorbidity Score**	**N**	**%**
1.	0	5	12.5
2.	1	1	2.5
3.	2	2	5
4.	3	6	15
5.	4	15	37.5

6.	5	5	12.5
7.	6	6	15
Total		40	100

Table 4: Number of Hospital stays of patients

Sno	**Number of days in Hospital**	**N**	**%**
1.	1	3	7.5
2.	2	11	27.5
3.	3	10	25
4.	4	6	15
5.	5	4	10
6.	6	1	2.5
7.	7	4	10
8.	9	1	2.5
Total		40	100

Table 5: SOFA Score

Commented [u13]: Use footnote here

Sno	**SOFA Score**	**N**	**%**
1.	0 - 2	7	17.5
2.	3 – 5	24	60
3.	6 – 8	6	15
4.	9 – 10	2	5
5.	11 - 13	1	2.5
Total		40	100

Table 6: Sepsis status:

	N	%
Sepsis	10	25
asepsis	30	75
Total	40	100

Table 7: Culture reports

Culture report	N	%
Sent	10	25
Not sent	30	75
Total	40	100

Table 8: APACHE II Score

Commented [u14]: Use footnote

Sno	APACHE II Score	N	%
1.	1 – 5	8	20
2.	6 – 10	15	37.5
3.	11 – 15	13	32.5
4.	16 – 20	1	2.5
5	21 – 25	3	7.5

Total		40	100

Table 9: Total Number of Antibiotics

Sno	Total Number of Antibiotics	N	%
1.	1	17	26.5
2.	2	32	50
3.	3	12	18.7
4.	4	1	1.5
5	5	1	1.5
6.	6	1	1.5
Total		64	100

Fig. 1

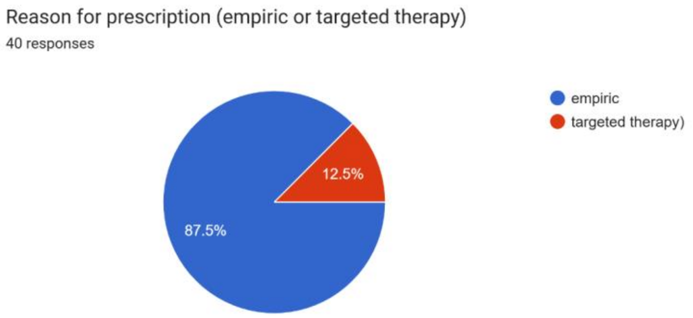

Table 10: De-escalation decision

	N	%
Procalcitonin	0	0
SOFA	13	32.5
Both	27	67.5
Total	40	100

Table 11: Multiplex PCR Usage

Commented [u15]: Abbreviation meaning? This table is not well clarified

	N	%
Financial	34	85
Unaware	6	15
Unavailability	0	0
Total	40	100

Table 12: Antibiotic usage and cost analysis

S. No	Drug name	N	%	Cost of the drug in INR	Total Cost/Per Day	Total Cost
1.	Cefoperazone Sulbactam	12	18.7	707	16,968	84,840
2.	Piperacillin Tazobactam	11	17.1	475	10,450	52,250

3.	Ceftriaxone	5	7.8	52	520	2,600
4.	Doxycycline	6	9.3	430	5,160	25,800
5.	Meropenem	5	7.8	639	6,390	31,950
6.	Clindamycin	5	7.8	380	3,800	19,000
7.	Metronidazole	6	9.3	23.562	282.72	1,413
8.	Ofloxacin	1	1.5	61.2	122.4	612
9.	Azithromycin	2	3.1	55.7	222.8	1,114
10.	Oseltamivir	2	3.1	1238	2,476	12,380
11.	Ceftazidime	1	1.5	185	370	1,850
12.	Amikacin	1	1.5	37.5	75	375
13.	Ceftazidime + Avibactam	1	1.5	5107	10,214	51,070
14.	Ofloxacin	2	3.1	61.2	244.8	1,224
15.	Levofloxacin	1	1.5	107	214	1,070
16.	Anti- Tuberculosis (Isoniazid, Rifampicin, Ethambutol, Pyrazinamide)	1	1.5	89.6	179.2	896
17.	Tigecycline	1	1.5	1296	2,592	12,960
18.	Acyclovir	1	1.5	76	152	760
Total		**64**	**100%**	**11020.76**	**60,433**	**3,02,164**

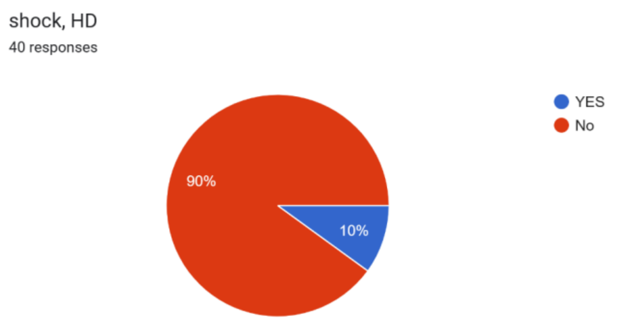

Figure 2: patient with Shock at the time of admission

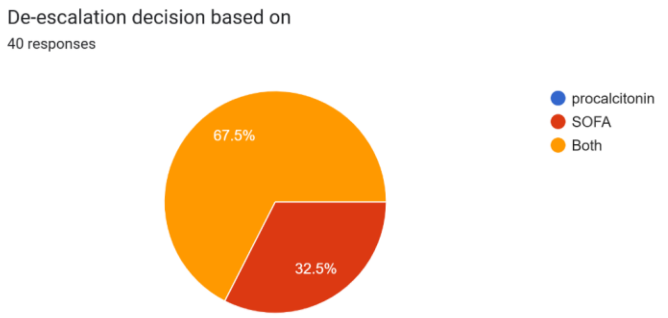

Figure 3: Antibiotic De-escalation was based on factor

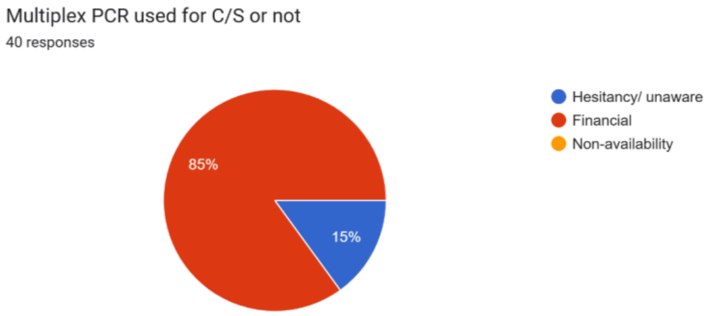

Figure 4: Multiplex PCR used for patients

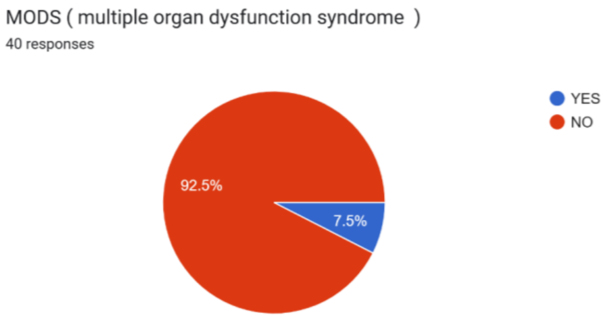

Figure 5: Does the patient in ICUs with MODS (Multiple Organ Dysfunction Syndrome)

Commented [u16]: Same data needs not to be shown in table as well as in pie chart

Discussion:

According to the World Health Organization global causes of death are categorized into three groups one is communicable diseases which include infections and parasitic diseases, as well as maternal, perinatal and nutritional conditions.

Severe acute respiratory infection (SARI) and sepsis are leading causes of mortality worldwide with more than 336 million episodes of SARI in 2106 and more than 19 million people with sepsis annually. Selection of empiric antibiotics depends on the patient's characteristics, suspected site of infections, differential diagnosis, local microbial susceptibility data and antibiotic stewardship. Other considerations of empirical therapy may include the cost of treatment, availability of antibiotics, potential drug intolerances and toxicity.

In a systematic analysis conducted by Authia Gray et al stated that in 2019, 13·7 million people worldwide died from infectious syndromes. Burden varies across age groups: adults aged 50–69 years face the highest burden from bloodstream infections, whereas children under the age of 5 years are most burdened by respiratory infections.In our study age groups with the majority in the 58–78 years range, reflect the vulnerability of older populations to severe diseases requiring hospitalization.

The severity of comorbid diseases was recorded and scored according to CCI. Patients were divided into three groups: mild, with CCI scores of 1–2; moderate, with CCI scores of 3–4; and severe, with CCI scores ≥5. CCI was calculated according to the scoring system established by Charlson et al. In our study comorbidity burden, as indicated by a mean score of 3.6 and a mode of 4, says that patients in ICU have a moderate risk of death which underscores the complexity of patient conditions.

Commented [u17]: Meaning of abbreviarion?

In a retrospective cohort study, the mean ICU length of stay was 3.4 (±4.5) days for intensive care patients who survived hospital discharge, with a median of 2 days (IQR 1–4). A third of patients (35.9%) spent only 1 day in the ICU and 88.9% of patients were in the ICU for 1–6 days, representing 58.6% of the ICU bed-days in the cohort. In our study Hospital stays exhibited variability, with most patients experiencing shorter stays average length of stay is 5 days.

A study conducted by Aditi Jain et al, found that the maximum score in survivors (3.92 ± 2.17) was significantly lower than in no survivors (8.9 ± 3.45). Moreno et al also demonstrated a strong correlation of maximum SOFA score with mortality outcome. In our study SOFA scores indicate that most of the patients (60%) were in a moderate severity range, correlating with the controlled use of antibiotics observed in this study. The relatively low prevalence of patients with SOFA scores above 8 (7.5%) suggests successful management of disease severity in most cases.

In our study, the sepsis status further reinforces the focus on effective clinical interventions, as only 25% of patients were diagnosed with sepsis. Culture reports were sent selectively (25%), emphasizing a targeted diagnostic approach, possibly influenced by resource constraints or clinical judgment.

A study conducted by Radhika T et al on mean SOFA score in comparison with APACHE II Score prediction concluded that APACHE II and SOFA scores are equally effective in assessing mortality in surgical patients with sepsis at the time of admission. In our study, we too observed that APACHE II scores align with the SOFA findings, with most patients exhibiting moderate disease severity. This reinforces the importance of accurate scoring systems in guiding treatment strategies and predicting outcomes.

In a study conducted on cost analysis of antibiotics usage results showed of 90 patients, In the emergency department, piperacillin/tazobactam was the most expensive antibiotic which was 29.94% (9075rs), and of 90 patients in other wards meropenem was the most expensive antibiotic with 40% (16448rs). In another study on cost and antibiotic utilization of pneumonia patients Carbapenems for 20%, anti-staphylococcal antibiotics for 51% of patients and macrolides and miscellaneous antibiotics were prescribed in 25.5% and 36.4% of patients respectively.

Beta-lactam antibiotic along with beta-lactamase inhibitor and clindamycin combination was the most prescribed antibiotic. The average cost per patient who was not put on a ventilator was Rs 27,123 whereas ventilated patients per cost was Rs44,812. The most frequently prescribed antibiotics were cefotaxime (22.3%), levofloxacin (19%) and ceftazidime (10.8%). Antibiotics were given in 31.5% of patients without diagnosis of infection.

In our study antibiotic usage trends indicate a controlled and targeted approach, with 50% of patients receiving two antibiotics and minimal usage of more than three antibiotics. The predominance of Cefoperazone Sulbactam and Piperacillin Tazobactam, coupled with the cost analysis, underscores the financial burden of antibiotic therapy. The overall cumulative antibiotic expenditure of ₹3,02,164 necessitates judicious use and cost-effective interventions to minimize economic strain on the healthcare system.

By preventing needless antibiotic use that might encourage the emergence of resistance, antibiotic de-escalation is a method that provides successful initial antibiotic treatment. It is a crucial component of serious sepsis treatment paradigms and antimicrobial stewardship initiatives. De-escalation is exemplified by the elimination, reduction, or narrowing of the range of the empirical antibiotic or antibiotics that were initiated based on microbiological results around the third day of therapy.

Using procalcitonin to guide antibiotic escalation when pathogen evidence is unavailable may result in a shorter length of stay for ICU patients with suspected bacterial infections, according to a study by Xu Wang et al. that involved 1109 patients and a study comparing the survival

Commented [u18]: Please make all the names of the antibiotics similar either start with caps or no small letter curves of patients who were de-escalated and those who were not on antibiotics revealed Charlson's comorbidity score (CCS) and the Sequential Organ Function Assessment (SOFA) score on the day of antimicrobial stewardship (AMS) intervention were variables linked to 30-day all-cause mortality. Both early and late antibiotics were not linked to a higher risk of death after confounders were considered.

The significance of evidence-based procedures in maximising antibiotic therapy and minimising antimicrobial resistance is demonstrated by the de-escalation decisions made in our study, which were predominantly informed by SOFA and Procalcitonin scores (67.5%).

Multiplex PCR is widely used in the field of antibiotics to detect multiple antibiotic-resistance genes and identify pathogens in a single reaction. This technique enables the simultaneous amplification of various DNA targets, making it highly efficient for diagnosing antimicrobial resistance.

It is commonly employed to detect resistance genes, such as mecA for methicillin resistance in Staphylococcus aureus, blaTEM and blaCTX-M for β-lactam resistance, and carbapenem resistance genes like KPC and NDM in Gram-negative bacteria. multiplex PCR assay for the detection of nine clinically relevant antibiotic resistance genes of *Staphylococcus aureus.*

Commented [u19]: Abbreviation meaning

Conditions were optimized to amplify fragments of *mecA* (encoding methicillin resistance), *aacA-aphD* (aminoglycoside resistance), *tetK*, *tetM* (tetracycline resistance), *erm*(A), *erm*(C) (macrolide-lincosamide-streptogramin B resistance), *vat*(A), *vat*(B), and *vat*(C) (streptogramin A resistance) simultaneously in one PCR amplification. An additional primer pair for the amplification of a fragment of the staphylococcal 16S rDNA was included as a positive control. The multiplex PCR assay was evaluated on 30 different *S. aureus* isolates, and the PCR results correlated with the phenotypic antibiotic resistance data obtained by the broth microdilution assay.

Multiplex PCR has an importance to detect multiple antibiotic resistance genes but the usage in our study was limited due to financial constraints, emphasizing the need to improve accessibility and awareness of advanced diagnostic tools in clinical practice. Addressing financial barriers could enhance early and accurate diagnosis, improving patient outcomes.

Table 1: Gender Distribution

The gender distribution in the study shows a higher prevalence of male patients (60%) compared to female patients (40%), with a total sample size of 40 patients.

Table 2: Age Distribution

Most of the patients were in the age group of 58–68 years (32.5%), followed closely by those aged 68–78 years (30%). A small percentage of patients were above 78 years, with the highest age category (98–108 years) accounting for 2.5%. There were no patients in the 18–28 and 88–98 age ranges. The age distribution indicates an older population predominantly affected in the study group.

Table 3: Comorbidity Score

The comorbidity scores indicate that a significant proportion of patients had a score of 4 (37.5%), which was also the most frequent score (mode). The mean comorbidity score was 3.6, with a median of 4.0, suggesting a relatively high comorbidity burden among the patients. The score range was from 0 to 6, illustrating variability in the patients' comorbid conditions.

Table 4: Number of Hospital Stays of Patients

Hospital stays varied widely, with a mean of 3.55 days and a median of 3 days. The most common length of stay was 2 days (mode), and the range extended from 1 to 9 days. Most patients had shorter stays, with 27.5% staying for 2 days and only a small fraction (2.5%) requiring a 9-day stay.

Table 5: SOFA Score

The Sequential Organ Failure Assessment (SOFA) scores were predominantly in the 3–5 range, accounting for 60% of the patients, followed by scores in the 0–2 range (17.5%). A small number of patients scored above 8, with only 5% scoring between 9–10 and 2.5% scoring between 11–13.

Table 6: Sepsis Status

Out of the 40 patients, 25% were diagnosed with sepsis, while the remaining 75% did not exhibit sepsis symptoms. This indicates a significant portion of patients in the study were non-septic.

Table 7: Culture Reports

In 25% of cases, culture reports were sent to assist in diagnosis and treatment planning, while in 75% of cases, culture reports were not sent, suggesting selective use of culture reporting in the study.

Table 8: APACHE II Score

The APACHE II scoring, used to assess disease severity, showed that most patients scored in the 6–10 range (37.5%), followed by those in the 11–15 range (32.5%). Only 2.5% of patients had a high score in the 16–20 range, and 7.5% scored in the 21–25 range, suggesting that most patients had moderate severity.

Table 9: Total Number of Antibiotics

The total antibiotic usage revealed that half of the patients (50%) received two antibiotics, while 26.5% were treated with a single antibiotic. Fewer patients required three or more antibiotics, with only 1.5% of cases needing four or more. This indicates a controlled and targeted antibiotic treatment approach in most cases.

Table 10: De-escalation Decision

De-escalation decisions were primarily based on both Procalcitonin and SOFA scores, guiding therapy in 67.5% of cases. SOFA alone accounted for 32.5% of the decisions, while Procalcitonin was not used in isolation for de-escalation decisions.

Table 11: Multiplex PCR Usage

The financial considerations influenced the use of Multiplex PCR, with 85% of patients not using PCR due to financial constraints. Lack of awareness was another factor, accounting for 15% of the cases, while unavailability was not cited as an issue.

Table 12: Antibiotic Usage and Cost Analysis

Antibiotic cost analysis revealed that **Cefoperazone Sulbactam** was the most prescribed drug, with a total expenditure of ₹84,840. **Piperacillin Tazobactam** and **Doxycycline** followed in both usage frequency and cost, contributing to total costs of ₹52,250 and ₹25,800, respectively. The highest-cost antibiotic per dose was **Ceftazidime + Avibactam** (₹51,070), while **Metronidazole** was the least expensive with a total cost of ₹1,413. The overall daily cost for antibiotics in the study was ₹60,433, with a cumulative expense of ₹3,02,164.

Conclusion

The study emphasises how complicated it is to care for patients in the intensive care unit who have serious infections and coexisting illnesses. Effective treatment of disease severity and reduction of antibiotic resistance was demonstrated by controlled antibiotic use, which was directed by scoring systems such as SOFA and APACHE II.

Financial limitations restricted the adoption of sophisticated diagnostic methods like multiplex PCR, even though focused approaches and de-escalation techniques improved results. To improve clinical outcomes and lessen the financial burden of antibiotic medication, the study emphasises the significance of striking a balance between cost-effective approaches and the best possible patient care.

While de-escalation strategies were implemented successfully in most cases, limited utilization of advanced diagnostic tools such as multiplex PCR due to financial constraints and lack of awareness highlights the need for improving accessibility to these technologies. Antibiotic cost analysis revealed significant economic implications, emphasizing the necessity for cost-effective prescribing practices without compromising patient outcomes.

The study underscores the importance of balancing cost-effective interventions with optimal patient care to enhance clinical outcomes and reduce the economic burden of antibiotic therapy.

Additionally, the study reinforces the importance of antimicrobial stewardship programs in promoting rational antibiotic use, reducing resistance rates, and enhancing patient care standards. Increased investment in diagnostics and education on their benefits could further optimize treatment strategies and long-term outcomes in resource-limited settings.

Commented [u20]: Make the conclusion specific, shorter and more focused

References

1. Silva ARO, Salgado DR, Lopes LPN, Castanheira D, Emmerick ICM, Lima EC. Increased Use of Antibiotics in the Intensive Care Unit During Coronavirus Disease (COVID-19) Pandemic in a Brazilian Hospital. Front Pharmacol. 2021 Dec 10;12:778386. doi: 10.3389/fphar.2021.778386. PMID: 34955847; PMCID: PMC8703131.
2. Campion M, Scully G. Antibiotic Use in the Intensive Care Unit: Optimization and De-Escalation. J Intensive Care Med. 2018 Dec;33(12):647-655. doi: 10.1177/0885066618762747. Epub 2018 Mar 13. PMID: 29534630.
3. Carlet, Jeana; Ben Ali, Adelb; Chalfine, Anniec. Epidemiology and control of antibiotic resistance in the intensive care unit. Current Opinion in Infectious

Diseases 17(4):p 309-316, August 2004. | DOI: 10.1097/01.qco.0000136927.29802.68.
4. Azoulay E, Russell L, Van de Louw A, Metaxa V, Bauer P, Povoa P, Montero JG, Loeches IM, Mehta S, Puxty K, Schellongowski P, Rello J, Mokart D, Lemiale V, Mirouse A; Nine-i Investigators. Diagnosis of severe respiratory infections in immunocompromised patients. Intensive Care Med. 2020 Feb;46(2):298-314. doi: 10.1007/s00134-019-05906-5. Epub 2020 Feb 7. PMID: 32034433; PMCID: PMC7080052.
5. Kreitmann L, Helms J, Martin-Loeches I, Salluh J, Poulakou G, Pène F, Nseir S. ICU-acquired infections in immunocompromised patients. Intensive Care Med. 2024 Mar;50(3):332-349. doi: 10.1007/s00134-023-07295-2. Epub 2024 Jan 10. PMID: 38197931.
6. Kumar, Shiv, Fransty Paul, and Alfi Mariya Davis. "Cost Analysis of Antibiotics Utilization in Emergency Department and Other Wards: A Comparative Study." *Indian Journal of Pharmacy Practice,* 16.3 (2023).
7. de Castro, Tázia Lopes, et al. "Characterization of consumption and costs of antimicrobials in intensive care units in a Brazilian tertiary hospital." *Exploratory Research in Clinical and Social Pharmacy* 11 (2023): 100289.
8. Chakraborty RK, Burns B. Systemic Inflammatory Response Syndrome. 2023 May 29. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 31613449.
9. Kumar S, Paul F, Davis AM. Cost Analysis of Antibiotics Utilization in Emergency Department and Other Wards: A Comparative Study. Indian J Pharmacy Practice. 2023;16(3):221-6
10. Ramya K, Adhikari P, Rajm S. Cost and Antibiotic Utilization of Pneumonia Patients in Intensive Care Unit. J App Pharm Sci, 2016; 6 (02): 087-090.
11. Dat, Vu Quoc, et al. "Antibiotic use for empirical therapy in the critical care units in primary and secondary hospitals in Vietnam: a multicenter cross-sectional study." *The Lancet Regional Health–Western Pacific* 18 (2022).
12. Marasine NR, Shrestha S, Sankhi S, Paudel N, Gautam A, Poudel A. Antibiotic utilization, sensitivity, and cost in the medical intensive care unit of a tertiary care teaching hospital in Nepal. SAGE Open Medicine. 2021;9. doi:10.1177/20503121211043710
13. Perveen, Rawshan Ara, et al. "Antibiotics in ICU: The challenges of use, cost and response in a tertiary care hospital." *Int J Med Res Health Sci* 7.6 (2018): 94-9.
14. de Castro, Tázia Lopes, et al. "Characterization of consumption and costs of antimicrobials in intensive care units in a Brazilian tertiary hospital." *Exploratory Research in Clinical and Social Pharmacy* 11 (2023): 100289.
15. Blanc P, Von Elm BE, Geissler A, Granier I, Boussuges A, Durand Gasselin J. Economic impact of a rational use of antibiotics in intensive care. Intensive Care Med. 1999 Dec;25(12):1407-12. doi: 10.1007/s001340051089. PMID: 10660849.
16. Suraj, B., et al. "A prospective study on antibiotic usage and cost pattern in an intensive care unit of a tertiary care hospital." *National Journal of Physiology, Pharmacy and Pharmacology* 11.3 (2021): 238-238.
17. Poudel, Ak Narayan, et al. "The economic burden of antibiotic resistance: A systematic review and meta-analysis." *Plos one* 18.5 (2023): e0285170.
18. Ismail D. Cost of antibiotics in medical intensive care. J Hosp Infect. 2022 Jun;124:47-55. doi: 10.1016/j.jhin.2022.03.003. Epub 2022 Mar 12. PMID: 35288254.

19. Misal, Devika D., Saleel V. Maulingkar, and Sushma Bhonsle. "Economic burden of antibiotic treatment of healthcare-associated infections at a tertiary care hospital ICU in Goa, India." *Tropical doctor* 47.3 (2017): 197-201.
20. Sadatsharifi A, Davarpanah MA, Namazi S, Mottaghi S, Mahmoudi L. Economic Burden Of Inappropriate Empiric Antibiotic Therapy: A Report From Southern Iran. *Risk Manag Healthc Policy*. 2019;12:339-348 https://doi.org/10.2147/RMHP.S222200

Commented [u21]: Please follow the same rules for writing the references