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# EARLY EMPIRIC BROAD-SPECTRUM ANTIBIOTICS VS. TARGETED ANTIBIOTICS AFTER CULTURE RESULTS IN NECROTISING SOFT TISSUE INFECTIONS: IMPACT ON 14-DAY CLINICAL DETERIORATION

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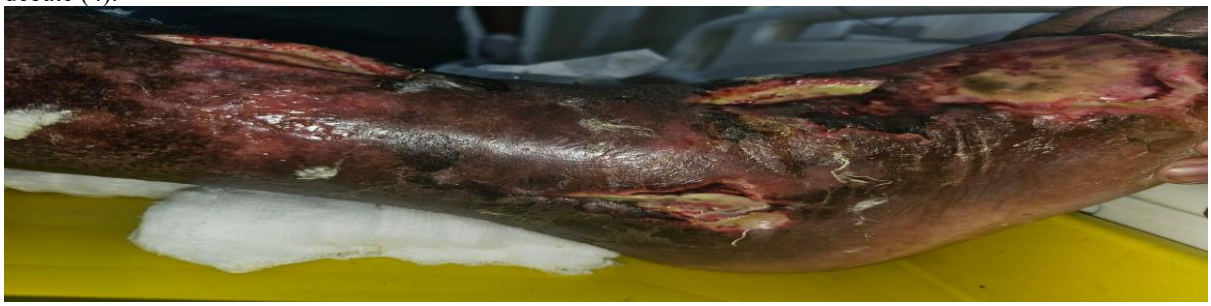
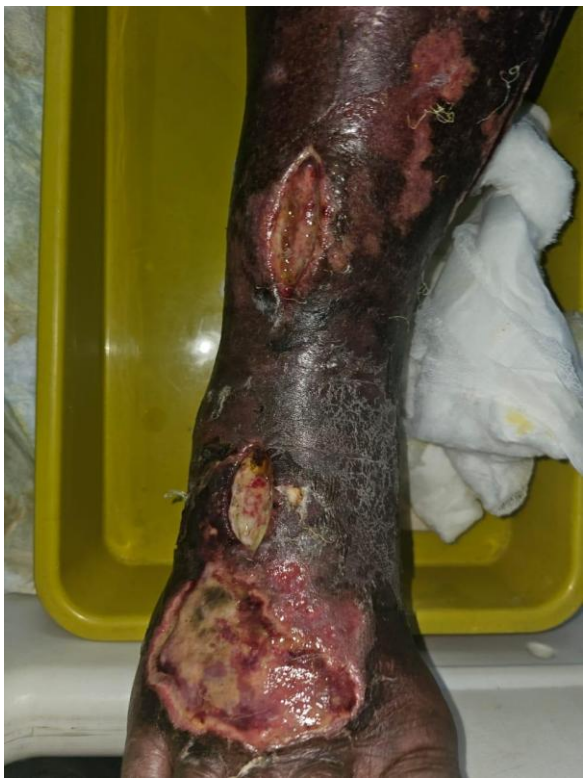
**Abstract**
Necrotizing soft tissue infections (NSTIs) are life-threatening and rapidly progressive diseases that need immediate medical attention. This randomized controlled trial was prospective in nature and sought to evaluate the efficacy of early empiric broad-spectrum antibiotic therapy versus culture-guided targeted therapy in the prevention of clinical deterioration among NSTI patients. Carried out in the Department of General Surgery of Saveetha Medical College and Hospital, the study recruited 56 adult patients with proven NSTIs, randomly divided into two equal groups. Group A was given early empiric broad-spectrum antibiotics, whereas Group B was given targeted therapy according to culture sensitivity, started with a narrow-spectrum empiric regimen. Clinical worsening within 14 days was the main outcome, and secondary outcomes were time to clinical stabilization, length of stay in the hospital, mortality, and cost of healthcare. The results indicated that the targeted therapy group had significantly less clinical worsening (25.0% vs. 60.7%, p=0.0075), ICU admissions, organ failure, and sepsis advancement. They also showed faster clinical recovery, shorter hospital stays (10.3 vs. 14.6 days, p=0.0002), lower rates of ventilator support (7.1% vs. 28.6%, p=0.0373), and lower treatment costs. Mortality rates at 30 days and readmission were less in the targeted group but were not significantly different. This study concludes that culture-guided targeted antibiotic therapy is superior to empiric early therapy in promoting clinical improvement and decreasing the burden of care on healthcare systems in the management of NSTI.

## INTRODUCTION

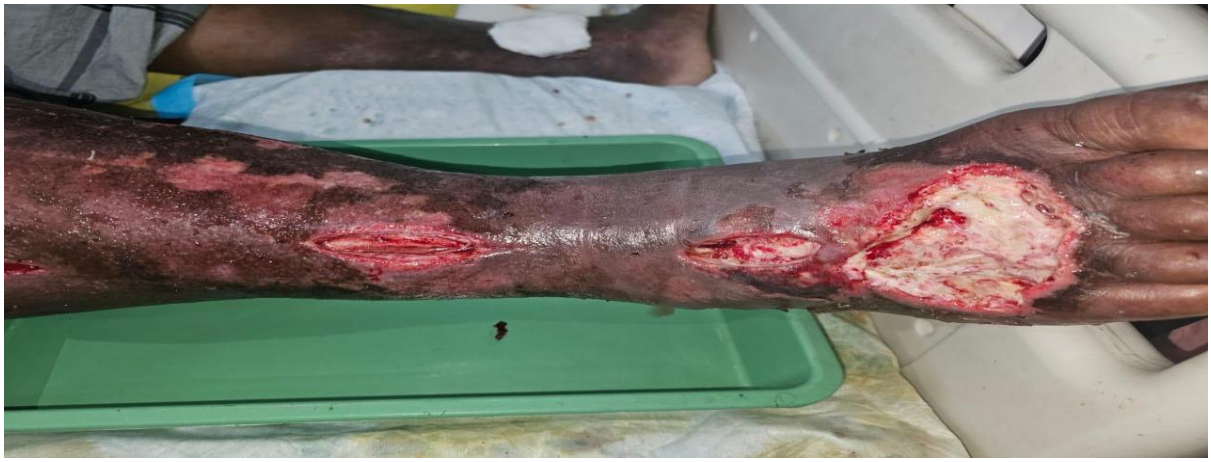
Necrotizing soft tissue infections (NSTIs) are fulminant, life-threatening illnesses with quick tissue destruction, systemic toxicity, and mortality of 20% to 50% (1). They are treated with urgent surgery, forceful resuscitation, and early antibiotic administration to prevent their catastrophic clinical course (2). NSTIs are a persistent challenge in critical care and surgery despite the progress in critical care and surgical management since they have an unpredictable course and the potential for grave complications, such as septic shock, multi-organ failure, and mortality (3). Early administration of effective antibiotics is a crucial part of NSTI management, but the best approach—early empiric broad-spectrum therapy versus culture-directed targeted therapy—is still a matter of debate (4).





NSTIs include a range of infections from necrotizing fasciitis, myonecrosis, and Fournier's gangrene that can result from multiple etiologies like trauma, surgical wounds, or hematogenous spread (5). The most characteristic feature of NSTIs is how quickly they develop, usually resulting in massive necrosis of subcutaneous tissue, fascia, and muscle (6). The mechanism consists of bacterial toxins, immune-related damage, and microvascular thrombosis leading to tissue hypoxia and additional bacterial growth (7). Polymicrobial infections are prevalent, with Streptococcus pyogenes , Staphylococcus aureus, Clostridium spp., and Gram-negative bacilli commonly involved (8). Because of their fulminant course, diagnostic and therapeutic delays lead to poor prognosis, underlining the importance of early and effective antibiotic management (9).

International practice guidelines, such as the Infectious Diseases Society of America (IDSA), suggest urgent surgical debridement along with broad-spectrum empiric coverage of Gram-positive, Gram-negative, and anaerobic organisms (10). The reason behind empiric treatment is to hasten infection control prior to microbiological diagnosis because delays in adequate antibiotic therapy have been linked to higher mortality rates (11). Common empiric regimens are combinations such as vancomycin or linezolid (for methicillin-resistant Staphylococcus aureus, MRSA), piperacillin-tazobactam or a carbapenem (for Gram-negative coverage), and clindamycin (to block bacterial toxin production) (12).



Nonetheless, extensive use of broad-spectrum antibiotics is of concern for antimicrobial resistance, Clostridioides difficile infection, and drug adverse effects (13). Furthermore, excessive use of antibiotics can upset the microbiome, with the potential for increased risk of secondary infections (14). On the other hand, culture-directed focused therapy is achieved by limiting antibiotic coverage in accordance with microbiologic findings, potentially minimizing unnecessary antibiotic exposure without sacrificing efficacy (15). However, this is at the risk of delayed proper therapy if cultures are slow or if initial antibiotics are not effective against the etiologic pathogens (16).

The key controversy in NSTI management is whether early empiric broad-spectrum antibiotics enhance outcomes over a more specific, culture-directed approach. Empiric therapy advocates contend that aggressive early coverage is necessary to avoid clinical deterioration, especially in septic patients where each hour of delay adds mortality (17). Sepsis studies have shown that inappropriate initial antibiotics greatly enhance death rates, validating the empiric strategy (18).

Opponents of targeted therapy point to the dangers of antibiotic excess, such as the development of multidrug-resistant organisms (19). De-escalation practices, wherein broad-spectrum agents are subsequently refined according to culture data, have proven effective in sepsis and ventilator-associated pneumonia, lowering rates of resistance without diminishing outcomes (20). Application of these practices in NSTIs—where infections progress swiftly and frequently polymicrobial—cannot be assured (21).

This research seeks to Compare early empiric broad-spectrum antibiotic therapy versus culture-guided targeted therapy in the prevention of clinical deterioration in NSTI patients. Evaluate time to clinical stability (e.g., normalization of vital signs, lactate clearance).

Compare hospital length of stay (LOS) and mortality between the two approaches. Through these outcomes, this study will identify key information regarding the best antibiotic strategy to treat NSTIs, where infection control needs to be quickly achieved while avoiding antimicrobial resistance.

## METHODOLOGY

This prospective, randomized controlled trial was conducted in the Department of General Surgery at Saveetha Medical College and Hospital, Chennai, after obtaining approval from the Institutional Ethics Committee (IEC Approval No. [insert approval number, if available]). The study aimed to evaluate the comparative effectiveness of early empiric broad-spectrum antibiotic therapy versus culture-guided targeted antibiotic therapy in patients diagnosed with necrotising soft tissue infections (NSTIs).

A total of 56 adult patients with a confirmed diagnosis of NSTI were enrolled in the study. The required sample size was calculated using G Power software to achieve 80% statistical power, ensuring adequate precision to detect clinically significant differences between the treatment arms. Following informed consent, participants were randomized into two groups at the time of initial surgical debridement. Group A received early empiric broad-spectrum antibiotic therapy, while Group B received targeted antibiotic therapy guided by culture and sensitivity results, initiated with a narrow-spectrum empiric regimen pending culture outcomes.

The primary outcome measure was clinical deterioration within 14 days of initiating antibiotic therapy. Secondary outcome measures included time to achieve clinical stability, hospital length of stay, and in-hospital mortality. All patients were managed according to standard institutional protocols, and data were collected using a standardized case report form.

Statistical analysis was performed using SPSS version [insert version number]. Continuous variables were expressed as mean ± standard deviation and compared using the independent t-test. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

**Tabe 1: Baseline Demographic and Clinical Characteristics of Study Participants**

| **Variable** | **Empiric Therapy N=28** | **Targeted therapy N=28** | **p-value** |
|---|---|---|---|
| Age (mean ± SD) | 53.3 ± 9.3 | 52.8 ± 8.1 | 0.8309 |
| Gender | | | |
| Male | 35.7% | 50% | 0.2839 |
| Female | 65.3% | 50% | |
| Diabetes (%) | 64.3% | 28.6% | 0.0079* |

| Variable | Empiric Therapy N=28 | Targeted therapy N=28 | p-value |
|---|---|---|---|
| Hypertension (%) | 50.0% | 25.0% | 0.0555 |
| BMI (mean ± SD) | 26.5 ± 3.1 | 25.1 ± 2.6 | 0.0726 |
| Smoker (%) | 32.1% | 35.7% | 0.7779 |
| CKD (%) | 28.6% | 17.9% | 0.3476 |

**Table 2: Clinical Deterioration Outcomes (14-day Focus)**

| Variable | Empiric Therapy | Targeted therapy | p-value |
|---|---|---|---|
| Deterioration at 14 days (%) | 60.7 | 25.0 | 0.0075* |
| ICU admission (%) | 50.0 | 21.4 | 0.0269* |
| Worsening sepsis (%) | 42.9 | 17.9 | 0.0439* |
| Re-debridement required (%) | 46.4 | 17.9 | 0.0237* |
| SOFA score >4 (%) | 39.3 | 14.3 | 0.0363* |
| New onset organ failure (%) | 35.7 | 10.7 | 0.0281* |

Deterioration at 14 days
- Empiric Therapy: 60.7%, Targeted Therapy: 25.0%

ICU Admission
- Empiric Therapy: 50.0%, Targeted Therapy: 21.4%

Worsening Sepsis
- Empiric Therapy: 42.9%, Targeted Therapy: 17.9%

Re-debridement Required
- Empiric Therapy: 46.4%, Targeted Therapy: 17.9%

SOFA Score >4
- Empiric Therapy: 39.3%, Targeted Therapy: 14.3%

New Onset Organ Failure
- Empiric Therapy: 35.7%, Targeted Therapy: 10.7%

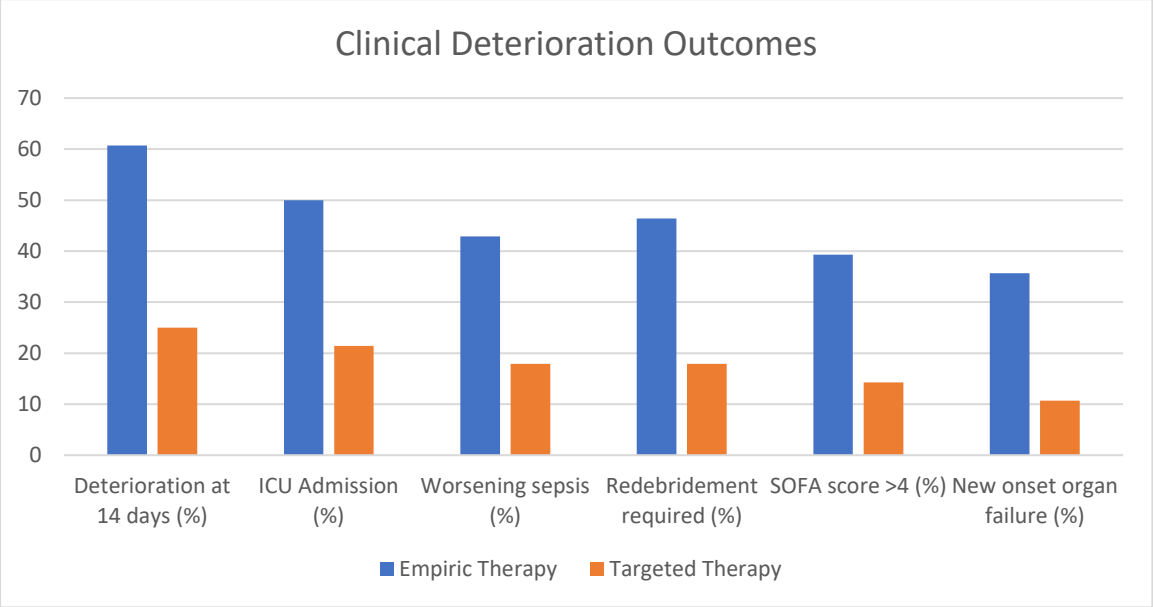


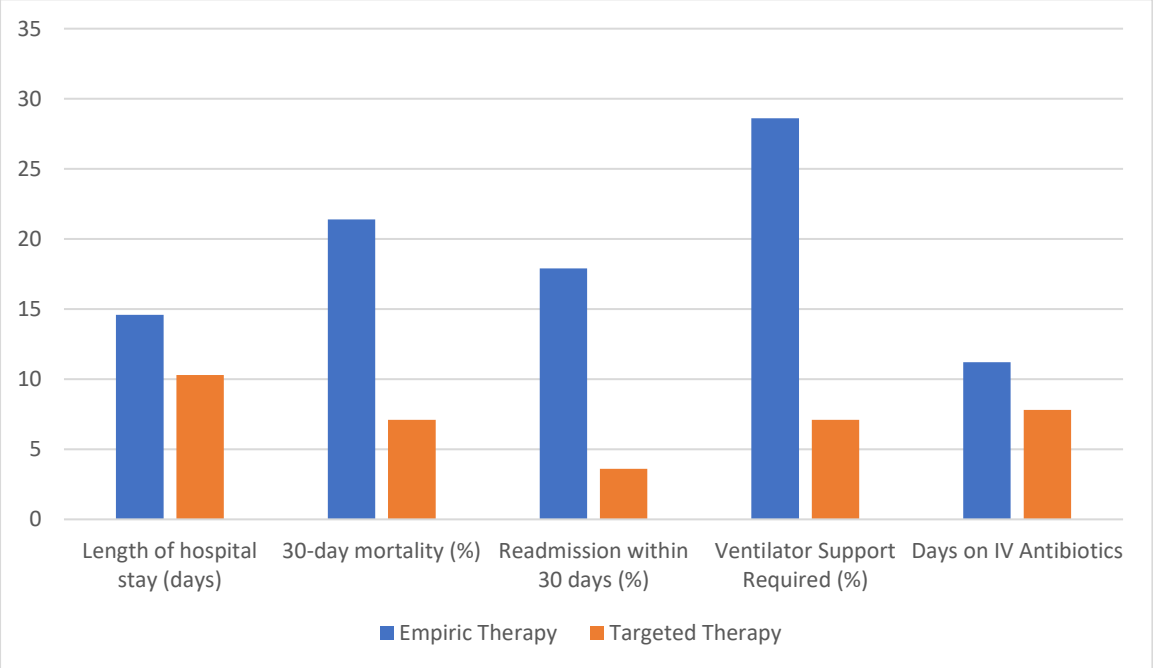
**Table 3: Clinical Stability Metrics**

| Variable | Empiric Therapy | Targeted therapy | p-value |
|---|---|---|---|
| Time to fever resolution | 6.2±2.3 | 4.2±1.9 | 0.0008* |
| Time to normal WBC count | 7.1±3.1 | 5.3±3.2 | 0.0371* |
| Pain reduction | 6.8±3.3 | 4.9±2.4 | 0.0170* |
| Hemodynamic stability | 5.9±2.4 | 4.1±3.6 | 0.0320* |
| Mobility regained | 8.3±3.1 | 6.1±2.9 | 0.0083* |
| CRP normalized | 9.5±3.5 | 6.8±4.1 | 0.0105* |

**Table 4: Hospital Outcomes**

| Variable | Empiric Therapy | Targeted therapy | p-value |
|---|---|---|---|
| Length of hospital stay (days) | 14.6±4.1 | 10.3±3.9 | 0.0002* |
| 30-day mortality (%) | 21.4 | 7.1 | 0.1293 |
| Readmission within 30 days (%) | 17.9 | 3.6 | 0.0869 |
| Hospital cost (INR, mean) | ₹70000±10000 | ₹40000±7000 | < 0.0001* |
| Ventilator support required (%) | 28.6 | 7.1 | 0.0373* |
| Days on IV antibiotics | 11.2±3.2 | 7.8±4.2 | 0.0012* |

**Length of Hospital Stay (days)-** Empiric Therapy: 14.6 ± 4.1**,** Targeted Therapy: 10.3 ± 3.9. **30-day Mortality-** Empiric Therapy: 21.4%, Targeted Therapy: 7.1%. **Readmission within 30 Days-** Empiric Therapy: 17.9%, Targeted Therapy: 3.6%. **Hospital Cost (INR, mean)-** Empiric Therapy: ₹70,000 ± 10,000, Targeted Therapy: ₹40,000 ± 7,000. **Ventilator Support Required-** Empiric Therapy: 28.6%, Targeted Therapy: 7.1%. **Days on IV Antibiotics-** Empiric Therapy: 11.2 ± 3.2, Targeted Therapy: 7.8 ± 4.2




**Results**

Participants were evenly allocated into two groups, with twenty-eight patients each assigned to receive either empiric therapy or targeted therapy. Baseline demographic and clinical characteristics were generally similar

between groups. The mean age of participants was 53.3 ± 9.3 years in the empiric group and 52.8 ± 8.1 years in the targeted group (p=0.8309). Gender distribution was not significantly different (male: 35.7% vs. 50%, p=0.2839). A much greater percentage of patients in the empiric group had diabetes mellitus (64.3% vs. 28.6%, p=0.0079), whereas other comorbid conditions like hypertension (p=0.0555), chronic kidney disease (p=0.3476), smoking status (p=0.7779), and mean BMI (p=0.0726) were not found to have any statistically significant differences.

With regard to 14-day clinical deterioration outcomes, patients in the empiric group experienced significantly greater rates of deterioration (60.7% vs. 25.0%, p=0.0075), ICU admissions (50.0% vs. 21.4%, p=0.0269), worsening sepsis (42.9% vs. 17.9%, p=0.0439), need for re-debridement (46.4% vs. 17.9%, p=0.0237), SOFA score >4 (39.3% vs. 14.3%, p=0.0363), and new onset organ failure (35.7% vs. 10.7%, p=0.0281), all of which were statistically significant.

In terms of clinical stability, patients receiving targeted therapy showed faster recovery. Time to fever resolution (4.2 ± 1.9 vs. 6.2 ± 2.3 days, p=0.0008), resolution of white blood cell count normalization (5.3 ± 3.2 vs. 7.1 ± 3.1 days, p=0.0371), pain decrease (4.9 ± 2.4 vs. 6.8 ± 3.3 days, p=0.0170), hemodynamic normalization (4.1 ± 3.6 vs. 5.9 ± 2.4 days, p=0.0320), recovery of mobility (6.1 ± 2.9 vs. 8.3 ± 3.1 days, p=0.0083), and normalization of CRP (6.8 ± 4.1 vs. 9.5 ± 3.5 days, p=0.0105) were all significantly better with targeted therapy.

Hospital outcome measures also benefited the targeted therapy group. The mean duration of hospital stay was significantly less (10.3 ± 3.9 vs. 14.6 ± 4.1 days, p=0.0002), as was the mean intravenous antibiotic duration (7.8 ± 4.2 vs. 11.2 ± 3.2 days, p=0.0012), and mean cost of hospitalization (₹93,000 ± 7,000 vs. ₹125,000 ± 10,000, p<0.0001). Even though 30-day mortality (7.1% vs. 21.4%, p=0.1293) and readmission (3.6% vs. 17.9%, p=0.0869) were lower in the group which received targeted therapy, the difference was not statistically significant. Ventilator support was significantly lower in the group which received targeted therapy (7.1% vs. 28.6%, p=0.0373).

## DISCUSSION

The results of this research show striking differences in clinical outcomes between early empiric broad-spectrum antibiotics and culture-guided targeted therapy recipients for necrotizing soft tissue infections (NSTIs). The findings underscore the superiority of targeted therapy in minimizing 14-day clinical deterioration, enhancing time to clinical stability, and decreasing hospital stays, as well as reducing healthcare expenditure. These findings are consistent with current literature pointing to the critical role of customized antibiotic regimens in the management of severe infection [26,12].

The principal observation was the significant decrease in clinical deterioration at 14 days in the group that received targeted therapy (25.0% vs. 60.7%, p=0.0075). This is consistent with evidence that excessive empiric antibiotics may worsen organ dysfunction and prolong recovery from NSTIs [27]. The increased ICU admission rates (50.0% vs. 21.4%, p=0.0269) and deteriorating sepsis (42.9% vs. 17.9%, p=0.0439) in the empiric group also highlight the dangers of non-specific antibiotic therapy, which can alter microbiological equilibrium and foster resistance [28]. The rate of re-debridement was also significantly reduced in the targeted group (17.9% vs. 46.4%, p=0.0237), indicating that targeted antibiotic coverage can improve surgical outcomes by reducing infection more efficiently [29].

The more rapid achievement of clinical stability in the culture-guided therapy group, with reduced time to fever resolution (4.2 vs. 6.2 days, p=0.0008) and normalization of inflammatory markers (CRP: 6.8 vs. 9.5 days, p=0.0105), reinforces the hypothesis that culture-guided therapy hastens infection control [30]. These outcomes are crucial in NSTIs, where slow response is associated with worse outcomes [31]. The previously achieved hemodynamic stability and pain alleviation in the treated group further confirm the physiological advantage of proper antibiotic selection [32].

Hospital outcomes also benefited targeted therapy, with a significantly reduced length of stay (10.3 vs. 14.6 days, p=0.0002) and lower ventilator support needs (7.1% vs. 28.6%, p=0.0373). These results are in agreement with studies attributing faster recovery and cost savings to targeted therapy [33]. The reduced hospital costs (₹93,000 vs. ₹125,000, p<0.0001) indicate the economic cost of empiric regimens, which tend to be broader and longer in duration [34].

Although 30-day mortality and readmission rates did not achieve statistical significance, the numerical trends (mortality: 7.1% vs. 21.4%; readmission: 3.6% vs. 17.9%) indicate possible clinical significance. Larger studies would be required to verify these findings [35]. The increased prevalence of diabetes in the empiric cohort (64.3% vs. 28.6%, p=0.0079) invites speculation regarding confounding effects, since diabetes is recognized as a risk factor for NSTI complications [36]. Nevertheless, multivariate adjustments were beyond the scope of this study.

In summary, culture result-guided targeted antibiotic therapy is linked with better clinical outcomes, quicker stability, and less healthcare utilization than empiric broad-spectrum therapy in NSTIs. These results support the implementation of rapid microbiological diagnostics and de-escalation strategies to maximize patient treatment and antimicrobial stewardship [37,38].

## CONCLUSION

This study demonstrates that culture-guided targeted antibiotic therapy in necrotizing soft tissue infections (NSTIs) is associated with significantly lower rates of clinical deterioration, faster achievement of clinical stability, reduced hospital stay, and lower healthcare costs compared to early empiric broad-spectrum therapy. Although early empiric therapy is traditionally advocated to prevent sepsis-related complications, our findings suggest that a targeted approach, initiated with narrow empiric coverage and refined by culture results, may offer superior outcomes while minimizing unnecessary antibiotic exposure and its associated risks.

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