International Journal of Basic & Clinical Pharmacology
Velusamy S et al. Int J Basic Clin Pharmacol. 2025 Nov;14(6):1002-1008
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20253376

Original Research Article

Factors influencing the clinical ineffectiveness of antibiotics in non-responders

Sivakumar Velusamy[1]*, Saravanan Thangavelu[2], Monica Sherin Thomas[1], Monisha Harinathan[1]

[1]Department of Pharmacy Practice, PSG College of Pharmacy, Coimbatore, India
[2]Department of General Medicine, PSG Super Speciality Hospitals, Coimbatore, India

Received: 17 September 2025
Accepted: 10 October 2025

***Correspondence:**
Dr. Sivakumar Velusamy,
Email: sivakumar7868@psgpharma.ac.in

ABSTRACT

Background: Antibiotic ineffectiveness and clinical non-responsiveness remain significant challenges in healthcare. Non-responders-patients who fail to improve despite appropriate antibiotic therapy-pose a substantial clinical burden. Identifying factors influencing such outcomes is essential for improving treatment success. To investigate patient, hospital-related factors contributing to antibiotic ineffectiveness despite culture sensitivity.
Method: A six-month ambispective observational study was conducted at PSG Hospitals, Coimbatore, India. A total of 480 inpatients were included into the study. Highly prescribed antibiotics-Cefoperazone+Sulbactam, Meropenem, Piperacillin Tazobactam, and Ceftriaxone-were analyzed. Factors such as age, gender, type of bacteria, prior antibiotic exposure, prior hospitalization, invasive procedures, and length of hospital stay were examined. Statistical analysis was performed using SPSS, with p values < 0.05 considered significant.
Results: Among 480 patients equally divided across four antibiotic groups, age was significant in the Meropenem group ($p=0.044$) in contrast to the rest of the groups. Prior antibiotic exposure (OR range: 1.091–1.889; $p<0.05$) and longer hospital stay (OR range: 1.271–1.710; $p<0.001$) were significantly associated with non-response across all the four antibiotic groups. *Klebsiella pneumoniae* was significantly linked to non-response across all groups (OR range: 1.025–1.801; all $p<0.01$). Invasive procedures were significant for Cefoperazone–Sulbactam (OR=2.148, $p=0.030$) and Piperacillin–Tazobactam (OR=1.643, $p=0.012$).
Conclusion: Prior antibiotic exposure, prolonged hospital stays, and the presence of *Klebsiella pneumoniae* were significantly associated with antibiotic non-responsiveness. This suggests a multifaceted approach addressing patient, microbial, and institutional factors might lessen disruptions to optimal clinical effectiveness.

Keywords: Ineffectiveness, Antibiotics, Non-response, Factors, Culture sensitivity

INTRODUCTION

One of the most concerning clinical challenges is the increasing number of non-responders that do not show clinical improvement despite receiving appropriate antibiotic therapy, as confirmed by microbial sensitivity tests. Non-responders or those who do not show clinical improvement despite receiving antimicrobial therapy suggested based on susceptibility results, might experience worsening symptoms, prolonged recovery times, and elevated risks of complications, including sepsis, organ failure, and mortality.[2] The growing prevalence of non-responders is particularly alarming in intensive care units (ICUs) accounting for 20-40% of non-responders, especially in patients with diabetes and sepsis.[3] However, despite the early successes of antibiotics, their clinical effectiveness has been increasingly compromised due to various factors.[1] Comprehension of the factors that do contribute to the clinical ineffectiveness of antibiotics in non-responders is critical for the purpose of developing

much better treatment strategies. Many factors concerning the pathogen, the patient, and the hospital fully represent thorough categories. Antibiotic ineffectiveness is most assuredly contributed to by pathogen-related factors, to a great extent. Bacteria are able to develop a number of mechanisms for resistance, such as by producing enzymes like beta-lactamases that inactivate antibiotics through modifying drug targets, and through using efflux pumps so as to expel antibiotics from the cell that protect bacteria from therapy.[4] Biofilm formation shields bacterial colonies from antibiotic treatments in addition to the host's immune system because biofilms are protective matrices that encase them.[5,14] Eradicating biofilm-associated infections is notoriously difficult, frequently leading to chronic and recurrent infections.[6] Patient-related factors are of equal importance in determining the success of antibiotic therapy. Patients are more likely than not to experience a certain degree of treatment failure in the event that they have fairly compromised immune systems, such as those living with HIV or undergoing chemotherapy. These patients rely greatly on antibiotic therapy to control infections. However, their weakened immune systems may be unable to clear infections even by when the appropriate antibiotic is used. Comorbidities each can alter drug pharmacokinetics, such as diabetes and chronic kidney disease. This alteration can result in suboptimal drug concentrations especially in critically ill patients.[7,15] Treatment is further complicated in that patients that have these conditions are also more likely to harbour multidrug-resistant organisms (MDROs).[8] Non-adherence to antibiotic regimens is another patient-related factor that contributes to the clinical ineffectiveness of antibiotics. Studies have shown that patients who do not complete the full course of antibiotics or who take them incorrectly are more likely to develop antibiotic-resistant infections.[9] This non-adherence can lead to sub-therapeutic drug levels in the body, giving bacteria an opportunity to mutate and become resistant.[10] Hospital-related factors also play a significant role in the ineffectiveness of antibiotics. Hospital-acquired infections (HAIs), particularly in ICUs, are often caused by drug-resistant bacteria.[11] The usage of increased number or prolonged duration of broad-spectrum antibiotics in hospital settings can lead to the disruption of the patient's normal microbiota, increasing the risk of secondary infections such as Clostridioides difficile.[12] Additionally, the length of hospital stays and the performance of invasive procedures, such as catheterization or mechanical ventilation, have been associated with higher rates of non-response to antibiotic therapy.[13]

Several studies have investigated the factors contributing to antibiotic ineffectiveness. For example, Chaturvedi et al found that bloodstream infections caused by multidrug-resistant gram-negative bacteria were significantly associated with longer hospital stays and higher mortality rates.[13] Given the growing threat of the increasing incidence of non-responders (30%), it is crucial to identify the factors that contribute to clinical ineffectiveness. Understanding these factors is essential for developing targeted interventions to improve patient outcomes and reduce the burden on healthcare systems. This study aims to investigate patient, hospital-related factors that influence the ineffectiveness of antibiotics.

METHODS

This research was conducted as an ambispective observational study with an aim to identify the factors leading to clinical ineffectiveness of antibiotics despite culture sensitivity. The study was conducted at PSG Hospitals, Coimbatore, India. The study was conducted over a period of six months, starting in April 2024 to September 2024. Commonly used antibiotics cefoperazone+ sulbactam, meropenem, piperacillin+ tazobactam and ceftriaxone were taken into analysis. Sample size was calculated by using Rao software, which is a sample size calculator that helps determine optimal survey sample sizes based on population, confidence level, and margin of error.

A sample size of 480 was calculated with 5% margin of error, 95% confidence interval, 50% response distribution which was determined based on the number of eligible patients identified from the hospital's medical records and ongoing treatment cases during the study duration. The data collection form was designed to capture relevant demographic, clinical, and treatment-related information. The form included fields for patient demographic such as age, gender, medical history, diagnosis, type of bacteria, previous antibiotic exposure (14 days prior admission were included, beyond 14 days were not included and exposure of all kinds of antibiotics were included), previous hospitalization (3 months prior admission), clinical factors such as length of hospital stay, invasive procedures and admission settings. The prospective data was taken from patient electronic medical records.

Retrospective data was collected from the hospital's medical database, covering patient records from prior to the study period (2022-2024 March). Independent T Test (Mann Whittney U Test - age and length of hospital stay) and Chi – Square Test (gender, type of bacteria, previous antibiotic exposure, previous hospitalization, invasive procedures and admission settings) were performed using SPSS software for statistical analysis.

Inclusion criteria

Patients above 18 years, inpatients received either antibiotic monotherapy or combination therapy. Patient with bacterial infectious disease

Exclusion criteria

Patients whose antibiotic therapy was abruptly stopped or discontinued. Patients without culture report. Patients who are not willing to participate in the study.

RESULTS

Demographic characteristics

A total of 480 patients were included in the study, comprising 240 responders and 240 non-responders. The majority of patients in both groups were over 60 years of age, accounting for 51.24% of responders and 59.71% of non-responders. Adults aged 18–60 years made up 43.11% of responders and 40.29% of non-responders, with no individuals below 18 years. Gender distribution was comparable across groups, with males comprising 51.06% of responders and 51.08% of non-responders. Among comorbidities, diabetes mellitus was most common (50.0% in responders, 53.23% in non-responders), followed by hypertension (37.17% and 34.46%, respectively). A higher percentage of non-responders had a recorded medical history (41.73%) compared to responders (29.43%). The most common diagnosis in responders was urinary tract infection (64.05%), whereas non-responders more frequently presented with sepsis (39.30%).

Type of bacteria

A diverse range of bacterial pathogens was identified among the isolates included in this study, with Escherichia coli emerging as the most frequently encountered organism, representing the majority of isolates across both responder and non-responder groups. *Klebsiella pneumoniae* also constituted a notable proportion of isolates, particularly among non-responders, suggesting a potentially greater significance. Additionally, Pseudomonas aeruginosa and several less frequently encountered organisms-including *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Acinetobacter baumannii*-were detected, collectively comprising a smaller subset.

Factors influencing antibiotic non response

Factors including age, gender, previous hospitalization, previous antibiotic exposure, length of hospital stay, invasive procedures and admission settings were taken into analysis. Here age, gender, prior hospitalization and admission settings did not show any significance over the antibiotic groups suggesting there is no influence on the effectiveness of the antibiotics. Previous antibiotic exposure and length of hospital stay were highly significant, showing increased influence on the effectiveness of the antibiotics. Detailed analysis of the factors is discussed according to the antibiotic group included into the study.

Cefoperazone–Sulbactam, n=120 (responder=60, non-responder=60)

Among patients treated with Cefoperazone–Sulbactam, age did not significantly differ between responders and non-responders (p=0.594), and neither did gender (male OR=0.961, p=0.197; female OR=0.846, p=0.098). Previous hospitalization was not statistically associated with treatment outcome (p=0.075). However, previous antibiotic exposure was significantly associated with non-response (OR = 1.889, p < 0.001), indicating that patients with prior antibiotic use had nearly 1.9 times higher odds of not responding to Cefoperazone–Sulbactam. Length of hospital stay was also a significant factor, with non-responders having longer durations (mean 7.3 vs. 4.9 days), and an OR of 1.710 (p<0.001) suggesting that longer stays were associated with higher odds of non-response. Regarding microorganisms, Klebsiella pneumoniae was significantly associated with non-response (OR=1.801, p<0.001), suggesting nearly 1.8 times increased odds of non-response when this organism was isolated. Invasive procedures also demonstrated a significant association with non-response (OR=2.148, p=0.030), indicating more than double the odds compared to those who did not undergo invasive procedures. Admission setting showed no significant association (p=1.011).

Meropenem, n=120 (responder=60, non-responder=60)

In the Meropenem group, age was significantly associated with non-response (p = 0.044), with non-responders being older on average (62.8 vs. 57.9 years), indicating that advanced age may contribute to poorer outcomes. Gender did not show a significant association (male OR=0.281, p=0.265; female OR=0.269, p=0.409). Previous hospitalization was not significant (p=0.683). Previous antibiotic exposure was significantly associated with non-response (OR=1.091, p=0.001), suggesting an increased likelihood of non-response in patients with prior antibiotic treatment.

Similarly, length of hospital stay was significantly longer among non-responders (mean 8.8 vs. 5.7 days), with an OR of 1.341 (p<0.001), implying a 34% increase in odds of non-response for each category increase in stay duration. Among pathogens, Klebsiella pneumoniae was significantly associated with non-response (OR=1.025, p=0.005), indicating a slight but statistically relevant increase in odds of treatment failure in its presence. Other variables, including invasive procedures (p=0.838) and admission settings (p=0.915), were not significantly associated.

Piperacillin–Tazobactam, n=120 (responder=60, non-responder=60)

In the Piperacillin–Tazobactam group, age and gender were not significantly associated with non-response (p=0.962; male OR=0.214, p=0.271; female OR=0.143, p=0.539). Previous hospitalization also showed no statistical association (p=0.758). However, prior antibiotic exposure was significantly associated with non-response (OR=1.609, p=0.012), meaning patients were over 1.6 times more likely to fail therapy if previously exposed to antibiotics. Length of hospital stay was significantly longer among non-responders (mean 8.6 vs. 6.0 days), with an OR of 1.271 (p<0.001), reinforcing that longer hospital stays are associated with treatment failure. The presence of

Klebsiella pneumoniae was also significantly associated with non-response (OR=1.275, p=0.017), suggesting 27.5% increased odds of non-response. Additionally, invasive procedures were significantly related to non-response (OR=1.643, p=0.012), indicating a higher risk in those undergoing such interventions. Admission setting was not a statistically significant factor (p=0.091).

Ceftriaxone, n=120 (responder=60, non-responder=60)

For Ceftriaxone, age and gender were not significantly associated with non-response (p=0.848; male OR=0.391, p=0.661; female OR=0.144, p=0.537). Prior hospitalization was also non-significant (p=0.379). Previous antibiotic exposure was significantly associated with non-response (OR=1.297, p<0.001), suggesting approximately 30% increased odds of treatment failure in patients with prior antibiotic use. Length of hospital stay was also significantly longer in non-responders (mean 6.4 vs. 5.2 days), with an OR of 1.487 (p < 0.001), indicating a strong relationship between extended hospitalization and poor treatment response. *Klebsiella pneumoniae* was again a significant factor (OR=1.619, p<0.001), reflecting a more than 60% increased likelihood of non-response in its presence. In contrast, invasive procedures (p=0.232) and admission setting (p=0.067) were not significantly associated with outcomes.

Therefore, among the 8 factors taken into the analysis, prior antibiotic exposure and prolonged hospital stay were strongly associated with antibiotic non-responsiveness across all treatment groups (p<0.001). *Klebsiella pneumoniae* was consistently linked to non-response, highlighting its significance. Invasive procedures significantly contributed to non-responsiveness in patients receiving Cefoperazone–Sulbactam and Piperacillin–Tazobactam. Conversely, admission setting and prior hospitalization showed no significant impact on treatment outcomes.

Table 1: Demographic details.

Demography	Responders, n=240	Non-responders, n=240	% Responders	% Non-responders
Age (in years)				
<18	0	0	0	0
18-60	122	112	43.11	40.29
> 60	145	166	51.24	59.71
Gender				
Male	144	142	51.06	51.08
Female	138	136	48.94	48.92
Co-morbid conditions				
Diabetes mellitus	152	173	50	53.23
Hypertension	113	112	37.17	34.46
Hypothyroidism	23	26	7.57	8
Chronic kidney disease	16	14	5.26	4.31
Medical history				
Present	83	116	29.43	41.73
Absent	199	162	70.57	58.27
Diagnosis				
UTI	212	166	64.05	44.39
Pneumonia	38	61	11.48	16.31
Sepsis	81	147	24.47	39.3

Table 2: Factors.

Factors	Cefoperazone–sulbactam, n=120		Meropenem, n=120		Piperacillin–tazobactam, n=120		Ceftriaxone, n=120	
Age (in years)								
< 18	R: 0	NR: 0	R: 0	NR: 0	R: 0	NR: 0	R: 0	NR: 0
18-60	R: 28	NR: 26	R: 28	NR: 23	R: 18	NR: 23	R: 34	NR: 26
>60	R: 32	NR: 34	R: 32	NR: 37	R: 42	NR: 37	R: 26	NR: 34
Mean	59.1	60	57.9	62.8	60.1	62.8	54.7	55
Statistical interpretation	p=0.594		p=0.044		p=0.962		p=0.848	
Gender								
Male	R: 39	NR: 29	R: 29	NR: 24	R: 30	NR: 30	R: 25	NR: 33
Statistical interpretation	OR=0.961	p =0.197	OR=0.281	p =0.265	OR=0.214	p =0.271	OR=0.391	p =0.661

Continued.

Factors	Cefoperazone–sulbactam, n=120		Meropenem, n=120		Piperacillin–tazobactam, n=120		Ceftriaxone, n=120	
Female	R: 21	NR: 31	R: 31	NR: 36	R: 30	NR: 30	R: 35	NR: 27
Statistical interpretation	OR=0.846	p = 0.098	OR=0.269	p = 0.409	OR=0.143	p = 0.539	OR=0.144	p = 0.537
Previous hospitalization								
Yes	R: 25	NR: 37	R: 39	NR: 35	R: 34	NR: 20	R: 22	NR: 29
No	R: 35	NR: 23	R: 21	NR: 25	R: 26	NR: 40	R: 38	NR: 31
Statistical interpretation	p=0.075		p=0.683		p=0.758		p=0.379	
Previous antibiotic exposure								
Yes	R: 14	NR: 22	R: 14	NR: 16	R: 11	NR: 15	R: 10	NR: 17
No	R: 46	NR: 38	R: 46	NR: 44	R: 49	NR: 45	R: 50	NR: 43
Statistical interpretation	OR=1.889	p < 0.001	OR=1.091	p = 0.001	OR=1.609	p = 0.012	OR=1.297	p < 0.001
Length of hospital stay (in days)								
3–5	R: 43	NR: 20	R: 27	NR: 15	R: 35	NR: 15	R: 38	NR: 22
6–10	R: 17	NR: 37	R: 32	NR: 30	R: 24	NR: 35	R: 21	NR: 37
>10	R: 0	NR: 5	R: 1	NR: 15	R: 1	NR: 10	R: 1	NR: 1
Mean	4.9	7.3	5.7	8.8	6.0	8.6	5.2	6.4
Statistical interpretation	OR=1.710	p < 0.001	OR=1.341	p < 0.001	OR=1.271	p < 0.001	OR=1.487	p < 0.001
Type of bacteria								
Escherichia coli	R: 51	NR: 29	R: 35	NR: 32	R: 37	NR: 30	R: 41	NR: 28
Statistical interpretation	OR=0.378	p = 0.453	OR=0.840	p = 0.055	OR=0.981	p = 0.127	OR=0.619	p = 0.461
Klebsiella pneumoniae	R: 8	NR: 11	R: 10	NR: 19	R: 12	NR: 24	R: 7	NR: 24
Statistical interpretation	OR=1.801	p <0.001	OR=1.025	p = 0.005	OR=1.275	p = 0.017	OR=1.619	p <0.001
Pseudomonas aeruginosa	R: 3	NR: 8	R: 7	NR: 12	R: 6	NR: 4	R: 2	NR: 3
Statistical interpretation	OR=0.073	p =0.114	OR=0.638	p =0.211	OR=0.442	p =0.509	OR=0.423	p =0.648
Others	R: 0	NR: 12	R: 8	NR: 2	R: 5	NR: 5	R: 10	NR: 5
Statistical interpretation	OR=0.831	p =0.061	OR=0.495	p =0.084	OR=0.000	p =1.000	OR=0.788	p =0.168
Invasive procedures								
Yes	R: 6	NR: 5	R: 19	NR: 16	R: 6	NR: 8	R: 4	NR: 8
No	R: 54	NR: 55	R: 41	NR: 44	R: 54	NR: 42	R: 56	NR: 52
Statistical Interpretation	OR=2.148	p = 0.030	OR=0.620	p = 0.838	OR=1.643	p=0.012	OR=2.004	p=0.232
Admission settings								
General ward	R: 34	NR: 45	R: 40	NR: 35	R: 38	NR: 45	R: 42	NR: 50
Private ward	R: 26	NR: 15	R: 20	NR: 25	R: 22	NR: 15	R: 18	NR: 10
Statistical interpretation	OR=1.050	p=1.011	OR=0.938	p=0.915	OR=1.024	p=0.091	OR=1.004	p=0.067

R: Responders, NR: Non- Responders, OR: Odds Ratio, Others: *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Pseudomonas putida*, *Enterococcus faecalis*, *Enterococcus faecium*, *Pseudomonas vulgaris*, *Pseudomonas mirabilis*, *Pantoea dispersa*, *Hemophilus influenzae*, *Acinetobacter baumannii*.

DISCUSSION

This study presents insights of the factors influencing the clinical ineffectiveness among non-responders in highly prescribed antibiotics-Cefoperazone-Sulbactam, Meropenem, Piperacillin–Tazobactam, and Ceftriaxone-in hospitalized patients, despite culture sensitivity. The findings suggest that factors, especially prior antibiotic exposure and prolonged hospital stay, play a more significant role in determining clinical ineffectiveness. Among all groups studied, prior antibiotic exposure was significantly associated with non-response. Patients previously treated with antibiotics had up to 1.8 times greater odds of non-responsiveness. This highlights a critical challenge in inpatient care-antibiotic history potentially alters the patient's microbial data, selecting for resistant or persistent strains even before culture-directed therapy begins. Previous literatures confirm that repeated antibiotic use can promote the development of less susceptible organisms which may not be detected in routine sensitivity testing.[1] Length of hospital stay was another major predictor of poor treatment response. Non-

responders consistently had longer hospitalizations than responders across all antibiotic groups, with significant odds ratios. Extended hospital stays may increase the risk of secondary infections or exposure to nosocomial pathogens, many of which possess resistance traits. Moreover, prolonged stays often reflect greater illness severity, leading to more complex infection profiles that are harder to resolve with standard antibiotic regimens. These findings are consistent with national surveillance studies showing a direct relationship between hospitalization duration and the prevalence of healthcare-associated infections.[2]

The presence of *Klebsiella pneumoniae* was also significantly associated with antibiotic ineffectiveness in all four groups. Patients infected with this organism had a higher likelihood of non-response. Klebsiella pneumoniae is a known opportunistic and nosocomial pathogen associated with resistance to multiple antibiotic classes, particularly in settings where prior treatment use is common. Its pathogenicity, combined with its ability to acquire extended-spectrum beta-lactamase (ESBL) and carbapenemase traits, makes it a significant threat to empirical and even targeted antibiotic strategies.[14]

Additionally, invasive procedures were significant predictors of non-response in patients treated with Cefoperazone–Sulbactam and Piperacillin–Tazobactam. These findings may be attributed to increased exposure to infection sources not captured in initial cultures. While our study did not investigate biofilm formation, the correlation between invasive techniques and poor outcomes underlines the importance of strict procedural protocols and infection prevention measures in patients receiving advanced interventions. In contrast, age, gender, previous hospitalization, and admission setting did not show consistent associations with treatment outcomes. Although age was significant in the Meropenem group, this was not observed in the other antibiotic groups. Prior hospitalization and admission setting were also not statistically significant, indicating that clinical responsiveness is more likely driven by acute patient factors and microbial behaviour than structural or demographic variables. This supports earlier findings that demographic characteristics influence pharmacokinetics but may not independently determine antibiotic success.[15]

An important implication of our findings is the disconnect between in vitro sensitivity and in vivo clinical effectiveness. Despite relying on culture sensitivity reports, a substantial proportion of patients still did not respond to therapy. This gap suggests that laboratory testing alone may be insufficient to guide effective treatment, particularly when prior exposures, hospital factors, or resistant organisms are in play. A more holistic treatment approach-considering antibiotic history, hospital stay duration, and microbial patterns-is essential.

Overall, the findings strongly support the implementation of hospital-based antimicrobial stewardship programs. Limiting unnecessary antibiotic use, shortening hospital stays where feasible, and implementing stricter infection control protocols could significantly reduce non-response rates.

This study is limited by its single-center setting and ambispective design, which may influence the generalizability and completeness of the data. Multi-center studies with molecular diagnostics and extended outcome monitoring are recommended to validate these findings.

CONCLUSION

This study identifies key factors-notably prior antibiotic exposure, prolonged hospital stays, and invasive procedures-as significant contributors to the clinical ineffectiveness of antibiotics, even when treatment is guided by culture sensitivity reports. While patient-related factors such as age, gender, medical history, and prior hospitalization did not show consistent statistical significance, their potential clinical relevance-particularly prior hospitalization-cannot be entirely ruled out and may warrant further subgroup analysis. The multifaceted nature of this study highlights that clinical ineffectiveness is not driven by a single factor, but rather by an interplay of patient, microbial, and hospital-related factors-underscoring the need for comprehensive, system-level interventions.

Further research is necessary to investigate the ineffectiveness of other commonly prescribed antibiotics and to explore pathogen-specific mechanisms such as biofilm formation, which may better inform clinical strategies and support more effective, individualized patient care.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. Pharm Ther. 2015;40(4):277–83.
2. Kollef MH. Inadequate antimicrobial treatment: an important determinant of outcome for hospitalized patients. Clin Infect Dis. 2000;31(4):131–40.
3. Bagshaw SM, Bellomo R, Jacka MJ, Egi M, Hart GK, George C; ANZICS CORE Management Committee. The impact of early hypoglycemia and blood glucose variability on outcome in critical illness. Crit Care. 2009;13(3):91.
4. Donlan RM. Biofilms and device-associated infections. Emerg Infect Dis. 2001;7(2):277–81.
5. Costerton JW, Stewart PS, Greenberg EP. Bacterial biofilms: a common cause of persistent infections. Science. 1999;284(5418):1318–22.
6. Høiby N. A short history of microbial biofilms and biofilm infections. APMIS. 2017;125(4):272–5.

7. Pea F, Viale P, Pavan F, Furlanut M. Pharmacokinetic considerations for antimicrobial therapy in patients receiving renal replacement therapy. Clin Pharmacokinet. 2007;46(12):997–1038.
8. Huttner A, Harbarth S, Carlet J, Cosgrove S, Goossens H, Holmes A, et al. Antimicrobial resistance: a global view from the 2013 World Healthcare-Associated Infections Forum. Antimicrob Resist Infect Control. 2013;2:31.
9. Fischer MA, Stedman MR, Lii J, Vogeli C, Shrank WH, Brookhart MA, et al. Primary medication non-adherence: analysis of 195,930 electronic prescriptions. J Gen Intern Med. 2010;25(4):284–90.
10. Ali M, Garba KA, Abdallah MS. Antibiotic susceptibility profile of bacteria responsible for urinary tract infection (UTI). South Asian J Biol Res. 2018;1(1):12–27.
11. Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, et al. Multistate point-prevalence survey of health care-associated infections. N Engl J Med. 2014;370(13):1198–208.
12. Wongsurakiat P, Chitwarakorn N. Severe community-acquired pneumonia in general medical wards: outcomes and impact of initial antibiotic selection. BMC Pulm Med. 2019;19:94.
13. Chaturvedi P, Lamba M, Sharma D, Mamoria VP. Bloodstream infections and antibiotic sensitivity pattern in intensive care unit. Trop Doct. 2020;50(4):290–4.
14. Podschun R, Ullmann U. Klebsiella spp. as nosocomial pathogens: epidemiology, taxonomy, typing methods, and pathogenicity factors. Clin Microbiol Rev. 1998;11(4):589–603.
15. Roberts JA, Abdul-Aziz MH, Lipman J, Mouton JW, Vinks AA, Felton TW, et al. Individualised antibiotic dosing for patients who are critically ill: challenges and potential solutions. Lancet Infect Dis. 2014;14(6):498–509.

Cite this article as: Velusamy S, Thangavelu S, Thomas MS, Harinathan M. Factors influencing the clinical ineffectiveness of antibiotics in non-responders. Int J Basic Clin Pharmacol 2025;14:1002-8.