

BLOODSTREAM INFECTIONS IN ICU PATIENTS FROM TERTIARY CARE HOSPITAL ON AUTOMATED BLOOD CULTURE BD BACTEC AND VITEK 2 COMPACT SYSTEM

Sangeeta Kumari¹, Jagriti Bansal² Ashish³ Sandhiya⁴

^{1,2,3}PhD Scholar, ⁴Post Graduate Student ^{1,2}Department of Microbiology, Santosh Medical College and Hospital Ghaziabad, Uttar Pradesh, India. Email: sangeeta.chaudhary2012@gmail.com

^{3,4}Department of Microbiology, Shree Guru Gobind Singh Tricentenary University Main Author Sangeeta Kumari

***Corresponding Author:** Jagriti Bansal

Email: jagritibansal16@gmail.com

Abstract

Background: Bloodstream infections are a leading cause of morbidity and mortality, especially in ICU patients. This prospective observational study analyzed 750 ICU cases from May 1, 2022, to May 31, 2023, using automated BACTEC™ blood culture methods. These methods showed higher sensitivity, specificity, and faster results compared to traditional cooked meat enrichment broth methods.

Aim: The study employed the VITEK 2 system, an advanced iteration of the original 1970s VITEK system, to identify organisms and conduct antimicrobial susceptibility testing (AST).

Methods: A standardized method was employed using the 750 samples subjected to the BD BACTEC™ blood culture system. Extended microbiological culture for two weeks is unnecessary with BACTEC™ methods, as most clinically significant organisms are detected within three days. The VITEK2 system, an automated platform for organism identification and antimicrobial susceptibility testing (AST) monitors reactions in every 15 minutes during incubation.

Results: This prospective observational study included 750 samples, admitted to the ICU. Samples were cultured and assessed for antimicrobial susceptibility patterns: out of 132 positive samples, 84 (63.63%) blood cultures showed microbial growth with mono-microbial presence. Gram-negative bacilli were identified in 45 cases (53.57%), with *E. coli* being the most common, while Gram-positive organisms accounted for 39 cases (47.42%), predominantly *S. haemolyticus*.

Conclusions: Gram-negative isolates exhibited sensitivity to only a limited number of drugs. Blood culture isolates from critically ill patients in the intensive care unit were multidrug-resistant, including MRSA, highlighting a significant concern regarding the rise of severe antibiotic resistance.

Keywords: BD BACTEC™, VITEK 2 COMPACT, ICU, GNB

Introduction:

Bloodstream infection (BSI) continues to be a major contributor to morbidity and mortality worldwide¹. BSI is defined by the presence of a positive blood culture in a patient exhibiting systemic signs of infection, and it can either be secondary to a known source or primary with no identifiable origin.²

A wide range of organisms has been identified as causes of BSI, with variations influenced by geographical differences.³ BSI remains one of the most challenging issues for clinicians treating ICU patients. The inappropriate use of antibiotics in managing BSI not only raises patient mortality but also heightens the risk of drug-resistant strains emerging. These infections lead to prolonged hospital stays, increased healthcare costs, and higher morbidity and mortality rates.⁴ In India, where the burden of infectious diseases is among the highest in the world, the misuse and overuse of antimicrobials have contributed to the growing problem of antimicrobial resistance (AMR). Additionally, poor financial conditions, inadequate infrastructure, a high disease burden, and unregulated over-the-counter sales of inexpensive antibiotics have exacerbated the AMR crisis in India.^{5,6} Routine laboratories are now utilizing instrumented blood culture systems like BD BACTECTTM for incubating various sterile site specimens. This continuous detection system eliminates the need for daily inspections and terminal subculturing.⁷ The automated system for identification and antimicrobial susceptibility testing (AST) has evolved into the VITEK 2 system, which automatically completes all necessary steps for organism identification.⁸

Technological advancements enabling rapid bacterial identification and antimicrobial susceptibility testing (AST) are now acknowledged for their clinical and financial advantages.⁹ This system performs kinetic analysis by reading each test every 15 minutes. It uses an optical system that integrates multichannel fluorimeter and photometer readings to capture fluorescence, turbidity, and colorimetric signals. Given the rising incidence of infections caused by these microorganisms and the growing resistance to various antimicrobial agents, these innovations have become increasingly important¹⁰⁻¹⁴

The rising prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) bacterial pathogens is a significant public health issue, placing a substantial economic strain on healthcare systems due to extended hospital stays and increased morbidity and mortality.¹⁵ Tigecycline, a tetracycline-class antibacterial agent, has been developed to treat polymicrobial MDR infections.¹⁶

Further studies have demonstrated that tigecycline is effective against severe infections caused by resistant pathogens.^{17,18} However, there is limited data available specifically for ICU patients with bacteraemia.¹⁹ These analyses have concentrated on approved indications,^{20,21} global microbiological results²² and safety concerns.²³

Therefore, this study aims to identify gram-negative organisms causing BSI in our hospital, especially in the ICU section using the original 1970s VITEK system and conduct its antimicrobial susceptibility testing (AST) of the isolated strains.

Materials and methods

This prospective observational study was carried out over a one-year period, from May 2022 to May 2023, at a tertiary care teaching hospital. It focused on consecutive cases of ICU patients who were treated with antibiotics. During the study, the Department of Clinical Microbiology processed a total of 750 clinical specimens.

Exclusion/inclusion criteria:

- The inclusion criterion was the effectiveness of tigecycline in treating bloodstream infections. The study was independently designed and involved a thorough review of all data related to bacterial infections. Only blood samples were included.
- Excluded other samples such as pus, sputum and endotracheal aspirates were excluded.

Out of 150 clinical specimens, 150 yielded microbial growth, with 132 consisting of Gram-negative bacilli and Gram-positive cocci. Among these, 84 samples (63.63%) were positive for mono-microbial growth. Gram-negative bacilli made up 53.57% of the cases, with *E. coli* being the most common, while Gram-positive cocci constituted 46.42%, with *Staphylococcus haemolyticus* being predominant. The BD BACTECTTM instrumented blood culture system and the VITEK 2 COMPACT system were used for identification and antimicrobial susceptibility testing (AST). All clinical specimens were plated on CLED, MacConkey, and Blood agar, and incubated at 37°C for 48 hours before being reported as sterile if no growth was observed.²⁴ Isolates that showed non-lactose fermenting colonies on MacConkey agar were further identified using a standard protocol, with gram staining morphology being one of the assessed characteristics.

Results

During the study period, out of 132 samples, 84 blood cultures tested positive, with the majority of isolates being Gram-negative bacilli (GNB) from bloodstream infections

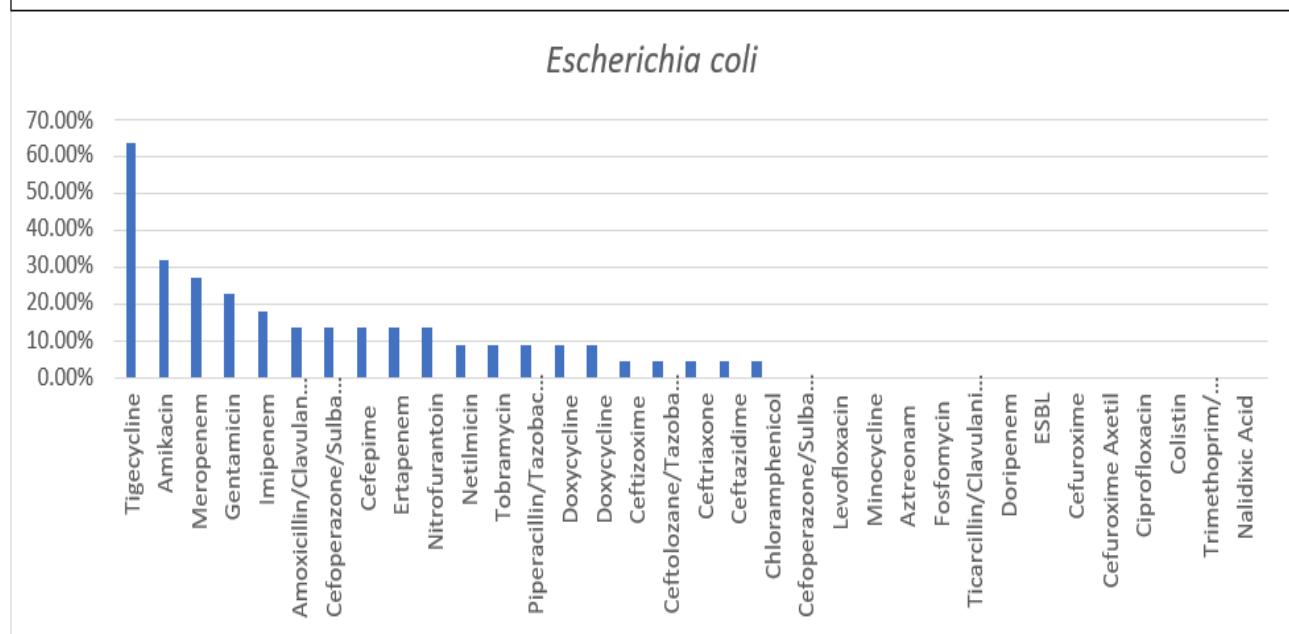
STRAIN	TOTAL	BLOOD SAMPLE
GNB	90 (68.18%)	45 (53.57%)
GPC	42 (31.81%)	39 (46.42%)
TOTAL	132 (100%)	84 (63.63%)

In this study, tigecycline demonstrated greater sensitivity compared to other drugs, particularly against Gram- negative bacilli (GNB), with success rates similar to those observed in clinical studies of severe infections.

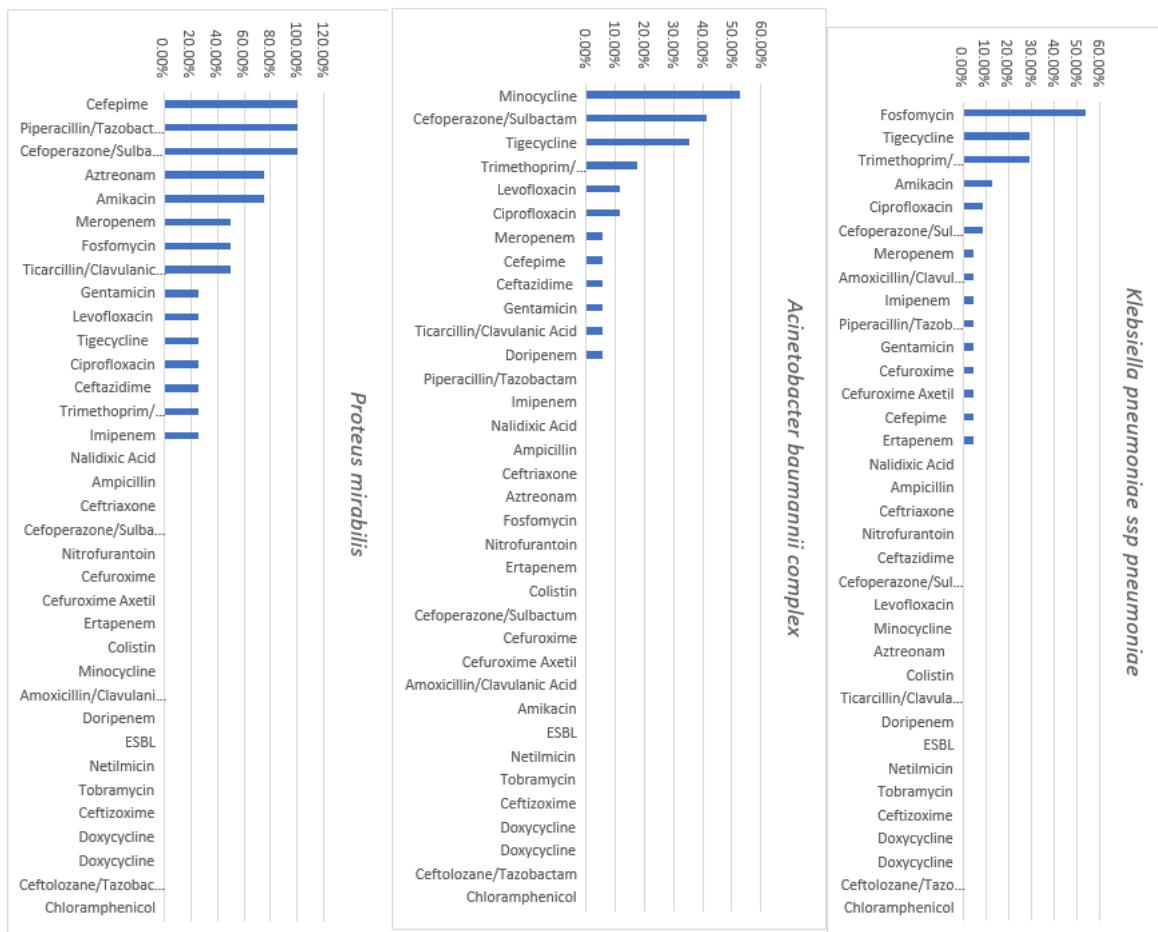
Unlike its use in other countries, tigecycline here is primarily utilized in combination with agents specifically targeting Gram-negative microorganisms.

ISOLATED STRAINS OF GNB	PERCENT AGE	T. ISOLATES
<i>Escherichia coli</i>	24.44	22
<i>Klebsiella pneumoniae ssp pneumoniae</i>	26.67	24
<i>Acinetobacter baumannii complex</i>	18.89	17
<i>Proteus mirabilis</i>	4.44	4
<i>Pseudomonas aeruginosa</i>	3.33	3
<i>Enterobacter cloacae complex</i>	2.22	2
<i>Achromobacter denitrificans</i>	1.11	1
<i>Achromobacter xylosoxidan</i>	2.22	2
<i>Acinetobacter lwoffii</i>	1.11	1
<i>Brevundimonas diminuta/vesicularis</i>	1.11	1
<i>Citrobacter amalonaticus</i>	1.11	1
<i>Morganella morganii ssp morganii</i>	1.11	1
<i>Ochrobactrum anthropic</i>	2.22	2
<i>Pandoraea spp</i>	2.22	2
<i>Salmonella enterica ssp diarizonae</i>	1.11	1
<i>Sphingomonas paucimobilis</i>	2.22	2
<i>Stenotrophomonas maltophilia</i>	4.44	4

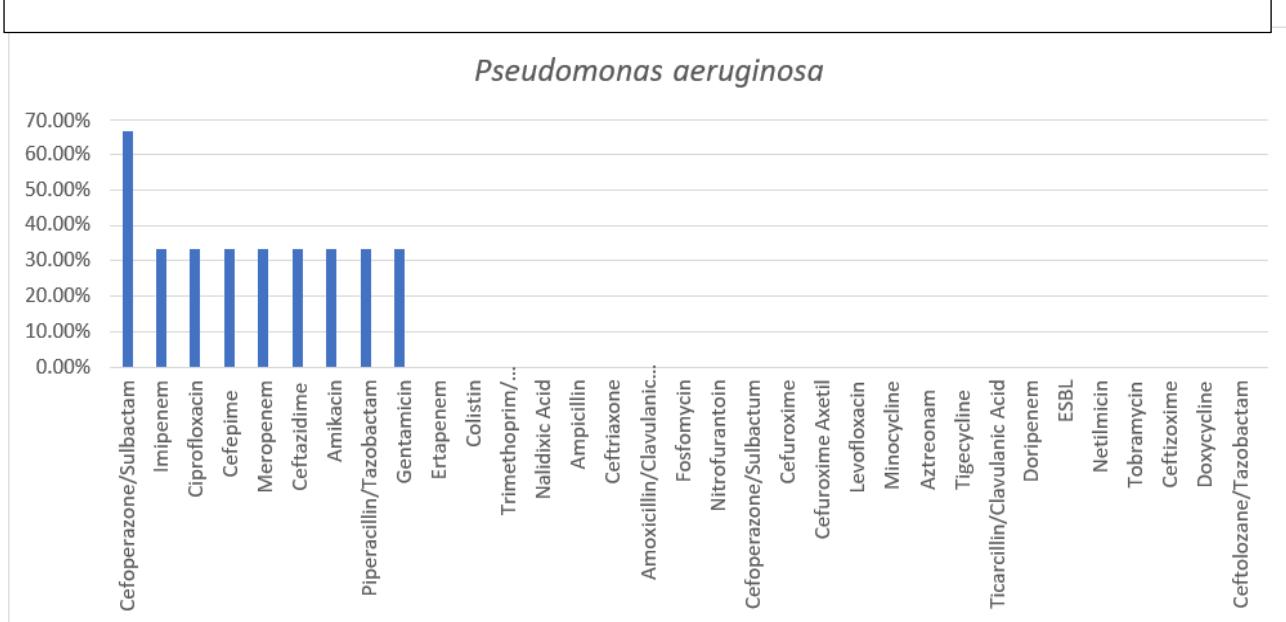
Graph1: Distribution of *Escherichia coli* strains based on the Antimicrobial Susceptibility Testing



Graph 2: Distribution of *Proteus mirabilis*, *Acinetobacter baumannii* complex and *Klebsiella pneumoniae* spp *pneumoniae* based on Antimicrobial Susceptibility Testing



Graph 2: Distribution of *Pseudomonas aeruginosa* based on Antimicrobial Susceptibility Testing



Discussion

We used the BD BACTECT™ instrumented blood culture system as a convenient, easy-to-use, and rapid diagnostic method. Our results demonstrated that it reliably detects slow-growing organisms, such as *Propionibacterium* species, without the need for prolonged culture periods. These findings can support earlier decisions on final antimicrobial prescribing.²⁵

Using the VITEK 2 COMPACT system, 35 different antibiotics were tested for susceptibility against all Gram-negative Volume 10 Issue 01-March, 2024

bacilli (GNB) strains. The most prevalent organisms identified in ICU patients with GNB infections were *E. coli*, *Klebsiella pneumoniae* spp., *Acinetobacter baumannii* complex, *Proteus mirabilis*, and *Pseudomonas aeruginosa*.⁶ The most frequently isolated Gram-negative bacilli were *E. coli* (24.44%) and *Klebsiella* spp. (26.67%), followed by *Acinetobacter* spp. (18.89%) and *P. aeruginosa* (3.33%). *E. coli* was the most common organism isolated from the bloodstream (17.6%). In contrast, *A. baumannii* and *K. pneumoniae* were the predominant organisms isolated from bloodstream infections in other studies.²⁶ *E. coli* is primarily associated with urinary tract infections, bloodstream infections, intra-abdominal infections, and wound infections, with fewer cases of respiratory tract infections, consistent with its distribution in the Asia-Pacific region, Latin America, and Southern Africa. Notably, while *E. coli* had the highest isolation rate, this rate has shown a fluctuating downward trend over the past 10 years. In contrast, the isolation rates of *K. pneumoniae* and *A. baumannii* have generally increased, except for a decline in 2021, likely due to the more severe antimicrobial resistance of *A. baumannii* and *K. pneumoniae* compared to *E. coli*.²⁷

E. coli emerged as the leading pathogen responsible for septicemia, with tigecycline being the most effective drug against Gram-negative bacteria. Regular, unit-based microbiological surveillance, along with timely and repeated investigations of bloodstream infections (BSI) bacterial flora, is crucial. Fortunately, *E. coli* exhibited the lowest resistance rates to imipenem and meropenem, which have remained stable over the past 10 years, aligning with similar findings in Europe, Asia, and Latin America. Notably, despite both being third-generation cephalosporins, ceftazidime showed greater activity against *E. coli* and *K. pneumoniae* compared to ceftriaxone, likely due to ceftriaxone's higher susceptibility to hydrolysis.²⁸

ICU patients are particularly vulnerable due to severe underlying conditions, impaired host defenses, and weakened immunity.²⁹ Additionally, multiple surgeries and the use of invasive devices—such as mechanical ventilation, tracheal tubes, arterial catheters, and central venous catheters—increase the risk of infection and colonization by multidrug-resistant (MDR) organisms.³⁰ Infections caused by MDR pathogens have become more prevalent in ICUs, making the selection of effective antimicrobial agents challenging. This contributes directly to higher morbidity, mortality, and increased hospitalization costs.³¹

Conclusion

750 samples from ICU patients were taken for our study. 132 positive isolates, Blood C/S had the highest frequency of isolated ICU samples. *E. coli*, *Klebsiella* spp., *Acinetobacter* spp., and *P. aeruginosa* were the most frequently isolated gram-negative bacilli. *Klebsiella* spp was the top one organism isolated from bloodstream, Tigecycline show the highest sensitivity rates. The antimicrobial susceptibility results were interpreted by CLSI. Rates of MDR and XDR in *Klebsiellapneumoniae*, *Acinetobacterbaumannii*, and *Pseudomonas aeruginosa* were investigated.

Reference

1. Wasihun A, Wlekidan L, Gebremariam S, et al. Bacteriological profile and antimicrobial susceptibility patterns of blood culture isolates among febrile patients in Mekelle Hospital, Northern Ethiopia. Springerplus 2015; 4: 314.
2. Timsit J, Ruppe' E, Barbier F, et al. Bloodstream infections in critically ill patients: an expert statement. Intens Care Med 2020;
3. Gohel K, Jojera A, Soni S, Gang S, Sabnis R, Desai M. Bacteriological profile and drug resistance patterns of blood culture isolates in a tertiary care nephrourology teaching institute. Biomed Res Int 2014; doi: 10.1155/2014/153747. Epub ahead of print 2014 Apr 7.
5. Savanur S and Gururaj H. Study of antibiotic sensitivity and resistance pattern of bacterial isolates in intensive care unit setup of a Tertiary Care Hospital. Ind J Crit Care Med 2019; 23: 547–555
6. Simkhada P, Raj KCS, Lamichhane S, et al. Bacteriological profile and antibiotic susceptibility pattern of blood culture isolates from patients visiting Tertiary Care Hospital in Kathmandu, Nepal. Global J Med Res Part C: Microbiol Pathol 2016; 16: 25–31.
7. Hughes HC, Newnham R, Athanasou N, Atkins BL, Bejon P, Bowler IC: Microbiological diagnosis of prosthetic joint infections: a prospective evaluation of four bacterial culture media in the routine laboratory. Clin Microbiol Infect 2011, 17:1528–1530
8. Funke, G., Monnet, C. deBernardis, A. von Graevenitz, and J. Freney. 1998. Evaluation of the VITEK 2 system for rapid identification of medically relevant gram-negative rods. J. Clin. Microbiol.
9. Barenfanger, J., C. Drake, and G. Kacich. 1999. Clinical and financial benefits of rapid bacterial identification and antimicrobial susceptibility testing. J. Clin. Microbiol.
10. Cornaglia, G., G. Lo Cascio, L. Masala, The Italian Surveillance Group for Antimicrobial Resistance, and R. Fontana. 2000. Macrolide resistance among *S. pneumoniae* isolates in Italy, p. 250–254. In S. H. Zinner, L. S. Young, J. F. Acar, and C. Ortiz-Neu (ed.), New considerations for macrolides, azalides, streptogramins, and ketolides. M. Dekker, Inc., New York, N.Y.
11. Fontana, R., M. Ligozzi, A. Mazzariol, G. Veneri, The Italian Surveillance Group for Antimicrobial Resistance, and G. Cornaglia. 1998. Resistance of enterococci to ampicillin and glycopeptide antibiotics in Italy. Clin. Infect.
12. Murray, B. E. 1990. The life and times of the enterococcus. Clin. Microbiol.
13. Pfaller, M. A., and L. A. Herwaldt. 1988. Laboratory, clinical, and epidemiological aspects of coagulase-negative staphylococci. Clin. Microbiol. Rev
14. Woodford, N., A. P. Johnson, D. Morrison, and D. C. E. Speller. 1995. Current perspective on glycopeptide resistance. Clin. Microbiol. Rev.
15. Ventola CL (2015) The antibiotic resistance crisis: part 1: causes and threats. Pharmacy and therapeutics 40(4):277

16. Tasina E, Haidich A-B, Kokkali S, Arvanitidou M (2011) Efficacy and safety of tigecycline for the treatment of infectious diseases: a meta-analysis. *Lancet Infect Dis* 11(11):834–844
17. Florescu I, Beuran M, Dimov R, Razbadauskas A, Bochan M, Fichev G, Dukart G, Babinchak T, Cooper CA, Ellis-Grosse EJ, Dartois N, Gandjini H et al (2008) Efficacy and safety of tigecycline compared with vancomycin or linezolid for treatment of serious infections with methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant enterococci: a phase 3, multicentre, double- blind, randomized study. *J Antimicrob Chemother* 62(Suppl 1):i17–i28. doi:10.1093/jac/dkn249
18. Vasilev K, Reshedko G, Orasan R, Sanchez M, Teras J, Babinchak T, Dukart G, Cooper A, Dartois N, Gandjini H, Orrico R, Ellis-Grosse E et al (2008) A phase 3, open-label, noncomparative study of tigecycline in the treatment of patients with selected serious infections due to resistant Gram-negative organisms including *Enterobacter* species, *Acinetobacter baumannii* and *Klebsiella pneumoniae*. *J Antimicrob Chemother* 62(Suppl 1):i29–i40. doi:10.1093/jac/dkn249
19. Gardiner D, Dukart G, Cooper A, Babinchak T (2010) Safety and efficacy of intravenous tigecycline in subjects with secondary bacteremia: pooled results from 8 phase III clinical trials. *Clin Infect Dis* 50:229–238. doi: 10.1086/648720
20. Bassetti M, Eckmann C, Bodmann KF, Dupont H, Heizmann WR, Montravers P, Guirao X, Capparella MR, Simoneau D, Sanchez Garcia M (2013) Prescription behaviours for tigecycline in real-life clinical practice from five European observational studies. *J Antimicrob Chemother* 68(Suppl 2):ii5–ii14. doi:10.1093/jac/dkt140
21. Montravers P, Bassetti M, Dupont H, Eckmann C, Heizmann WR, Guirao X, Garcia MS, Capparella MR, Simoneau D, Bodmann KF (2013) Efficacy of tigecycline for the treatment of complicated skin and soft-tissue infections in real-life clinical practice from five European observational studies. *J Antimicrob Chemother* 68(Suppl 2):ii15–ii24. doi: 10.1093/jac/dkt141
22. Heizmann WR, Dupont H, Montravers P, Guirao X, Eckmann C, Bassetti M, Garcia MS, Capparella MR, Simoneau D, Bodmann KF (2013) Resistance mechanisms and epidemiology of multiresistant pathogens in Europe and efficacy of tigecycline in observational studies. *J Antimicrob Chemother* 68(Suppl 2):ii45–ii55. doi: 10.1093/jac/dkt144
23. Guirao X, Sanchez Garcia M, Bassetti M, Bodmann KF, Dupont H, Montravers P, Heizmann WR, Capparella MR, Simoneau D, Eckmann C (2013) Safety and tolerability of tigecycline for the treatment of complicated skin and soft-tissue and intra-abdominal infections: an analysis based on five European observational studies. *J Antimicrob Chemother* 68(Suppl 2):ii37– ii44. doi: 10.1093/jac/dkt143
24. Mishra B, Bhujwala RA, Shriniwas. Non-fermenters in human infections. *Indian J Med Res* 1986;83:561–6.
- 25 Schafer P, Fink B, Sandow D, Margull A, Berger I, Frommelt L. Prolonged bacterial culture to identify late periprosthetic joint infection: a promising strategy. *Clin Infect Dis.* 2008;14:1403–1409. doi: 10.1086/592973. [PubMed] [CrossRef] [Google Scholar]
- 26 Barbier F., Andremont A., Wolff M., Bouadma L. (2013). Hospital-acquired pneumonia and ventilator-associated pneumonia: recent advances in epidemiology and management. *Curr. Opin. Pulm. Med.* 19,216–228. doi: 10.1097/MCP.0b013e32835f27be [PubMed] [CrossRef] [Google Scholar]
- 27 Morrissey I., Hackel M., Badal R., Bouchillon S., Hawser S., Biedenbach D. (2013). A review of ten years of the study for monitoring antimicrobial resistance trends (SMART) from 2002 to 2011. *Pharmaceuticals (Basel)* 6, 1335–1346. doi: 10.3390/ph6111335, PMID: [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- 28 Pitout J. D., Laupland K. B. (2008). Extended-spectrum beta-lactamase-producing Enterobacteriaceae: an emerging public-health concern. *Lancet Infect. Dis.* 8, 159–166. doi: 10.1016/S1473-3099(08)70041-0 [PubMed] [CrossRef] [Google Scholar] [Ref list]
- 29 Ramirez M. S., Tolmasky M. E. (2017). Amikacin: uses, resistance, and prospects for inhibition. *Molecules* 22:2267. doi: 10.3390/molecules2212267, PMID: [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]
- 30 Brusselaers N., Vogelaers D., Blot S. (2011). The rising problem of antimicrobial resistance in the intensive care unit. *Ann. Intensive Care* 23, 1:47. doi: 10.1186/2110-5820-1-47 [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]
- 31 Martin S. J., Yost R. J. (2011). Infectious diseases in the critically ill patients. *J. Pharm. Pract.* 24, 35–43. doi: 10.1177/0897190010388906 [PubMed][CrossRef] [Google Scholar] [Ref list]