Journal of Cardiothoracic Surgery

RESEARCH

Open Access

Appropriate use of vancomycin in a cardiac surgical unit

Sanaa Mekdad[1,2*], Leenah Alsayed[1] and Suzan Alkhalaif[1]

Abstract

Background Antibiotic resistance is a rapidly growing problem. Methicillin-resistant *staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) are major worries, particularly in developing nations where cost-effectiveness is essential. Use of vancomycin must be restricted to prevent resistant to it. Examining the appropriateness rate of vancomycin use in light of the recommendations of the Infectious Disease Society of America (IDSA) in the cardiac surgery ward was the aim of this study.

Methodology This study was a retrospective analysis of the medical records of patients who received vancomycin over the previous year, from January 2023 to December 2023. The collected patient data included demographics, indications for vancomycin use, culture and sensitivity test results, concurrent antibiotic medications, vancomycin serum levels, and diagnoses. The appropriateness of vancomycin use was classified according to the recommendations of the Infectious Diseases Society of America (IDSA).

Results A total of 294 patients received vancomycin. The appropriate use of vancomycin was significantly higher than its inappropriate use ($p=0.001$). Approximately 41% ($n=120$) of patients were administered vancomycin for treatment purposes, while the remainder received it empirically, but not as surgical prophylaxis. Appropriate use of vancomycin was observed in 89.1% ($n=262$) of patients. However, there remained a notable rate of inappropriate vancomycin use ($n=32$, 10.9%). The most common reason for inappropriate use was the continuation of vancomycin beyond 72 h without further evidence of a Gram-positive infection ($n=21$, accounting for 65.6% of all inappropriate use).

Conclusions The current study demonstrated that 89.1% of vancomycin use was appropriate, while approximately 10% was inappropriate, potentially contributing to vancomycin resistance. The majority of inappropriate use stems from frequent empirical prescribing, which requires further review and monitoring.

Keywords Antibiotic, Antimicrobial, β-lactam, Gram-positive, MRSA, Resistance, VRE

*Correspondence:
Sanaa Mekdad
smekdad@kfmc.med.sa
[1]King Fahad Medical City, Riyad, Saudi Arabia
[2]Clinical Pharmacy Department, King Fahad Medical City, Riyadh, Saudi Arabia

Introduction

Vancomycin is a glycopeptide antibiotic that is clinically utilized to treat severe infections caused by bacteria resistant to other antibiotics. It is particularly effective against Gram-positive bacteria. However, over the past decade, there has been a notable increase in vancomycin resistance [1]. Factors contributing to this rise include the overuse of vancomycin and prolonged therapy. Decreased susceptibility to vancomycin may lead to clinical treatment failures. Consequently, various strategies have been implemented to mitigate the risk of vancomycin resistance [2]. Numerous studies have examined the use of vancomycin in critically ill adult and pediatric patients from developed countries [3]. The majority of patients in these studies exhibited inappropriate vancomycin use, prompting researchers to recommend measures to reduce unnecessary vancomycin prescriptions [4].

The inappropriate use of vancomycin associated with vancomycin-resistant enterococcus (VRE) is a result of the rapid growth of VRE. In response to this, the IDSA committee published recommendations to stop and manage the spread of VRE [5].

Objectives

The objectives of this study were to evaluate vancomycin usage at a tertiary care hospital's cardiac center, calculate the percentage of vancomycin prescriptions that align with IDSA guidelines based on objective data obtained from chart reviews, and identify clinical correlates or patterns of inappropriate vancomycin use that could inform future interventions.

Methods

This study was a retrospective study done on the medical records of patients who received vancomycin over the previous year from the beginning of January 2023 to the end of December 2023. Data from the pharmacy information system was used to identify the patients. Patient data gathered, including demographics, vancomycin indications, culture and sensitivity tests, concurrent antibiotic medications, vancomycin serum levels, and diagnosis. Patients whose medical records were incomplete were not included in the study. The medical research and ethics committee gave its approval for the study.

- **Ethics approval and consent to participate** The research had been approved; IRB registration number with King Abdulaziz for Science and Technology, King Saudi Arabia (KACST, KSA): H-01-R-012. IRB registration Number with Office of Human Research Protection (OHRP/NIH), USA :IRB 00010471, Approve Number Federal Wide Assurance NIH, USA: FWA 00018774, IRB Log No: 21-395.
- All methods were performed in accordance with the **Declaration of Helsinki** guidelines and regulations.

IDSA guidelines for Vancomycin usage was utilized to categorize the appropriateness of vancomycin use.

Data Analyses was done with the appropriate inferential and descriptive statistics using the Statistical Package for Social Sciences (SPSS) version 22 for Windows. The association between variables and outcome was assessed using a suitable contingency table test (X 2 test or Fisher's exact test) at a confidence interval of 95%. Statistical significance was defined as a probability value less than 0.05 (p 0.05).

Appropriate use criteria

If the clinical indication meets the IDSA criteria, treatment should be administered to patients with risk factors as empirical therapy for methicillin-resistant *Staphylococcus aureus* (MRSA) when justified by hospital epidemiology or :

a. Treatment of serious infections caused by β-lactam-resistant, gram-positive organisms.
b. Treatment of infections caused by gram-positive microorganisms in patients with allergies to β-lactam antibiotic.
c. Prophylaxis, in patients with high risk for endocarditis, as recommended by the American Heart Association.
d. Prophylaxis for major surgical procedures involving implantation of prosthetic materials or devices at hospitals that have a high rate of infections caused by MRSA or methicillin-resistant *Staphylococcus epidermidis.*

Inappropriate use was subdivided into

a. Empiric therapy without risk factors.
b. Continued empirical treatment of patients whose samples did not reveal the presence of beta-lactam-resistant Gram-positive bacteria.
c. Therapy for infections brought on by Gram-positive bacteria that are responsive to beta-lactam antibiotics and have no history of allergic reactions to them.
d. If other blood cultures obtained over the same period turn out to be negative, treatment in response to a single positive blood culture for coagulase-negative staphylococcus.
e. Preventing infection or colonization of indwelling central or peripheral intravascular catheters through systemic or local measures [5].

Table 1 Variables and value of the study

Number of patients		
Age, mean +/- SD	52.5+/-14.9	
Comorbidities :		
Diabetes		218 74.14%
Ischemic heart disease		198 67.4%
Congestive heart failure		11 3.7%
Valvular disease		11 3.7%
ID Consultation	Yes ; 220 74.8% No: 74 25.2%	
Culture	Done : Not done : MRSA	292 99.3% 2 2.7% 18 6.1%
B-Lactam allergy		8 0.7%
Renal function	Crcl more than 90 ml/min	140 47.6%
	Crcl 60–90 ml/min	50 17%
	Crcl less than 60 ml/min	104 35.4%
	Crcl 30–60 ml/min	30 10.2%
	Crcl less than 30 ml/min	34 11.6%
	Patient on CRRT	14 4.8%
	Patient on intermittent dialysis	26 8.8%

SD : Standard deviation

Crcl : Creatinine clearance

CRRT : Continuous renal replacement therapy

Results

Patient demographics

Patient demographics: The study included 294 patients in total; (67.3%, $n=198$) of them were men, and (32.7%, $n=96$) were women. The mean age of patients was 52.5 +/- 14.9, the mean duration of Vancomycin therapy was 11.6 +/- 2.5 days. About (52.4%, $n=154$) of our population had renal impairment identified as creatinine clearance less than 60 ml/min. Other co-morbidities identified in the study were diabetes mellitus ($n=218$, 74.14%), Ischemic heart disease ($n=11$, 67.4%), congestive heart disease ($n=11$, 3.7%) and vulvar heart disease were other co-morbidities found in the study, allergies to beta-lactams were observed in 8 (2.7%) patients (Table 1).

Appropriateness of vancomycin

Overall, 294 patients were treated with vancomycin. The appropriate use of vancomycin was higher than inappropriate use ($p=0.001$). Appropriate use of vancomycin was observed in 89.1% ($n=262$) of patients, and the rate of inappropriate use was 10.9% ($n=32$) ($p=001$). Culture was done in 292 (99.3%) of patients treated with vancomycin. Empirical vancomycin therapy was given to 174 (59%) patients, and 153 (87.9%) of them were stopped after 72 h because of negative culture. A total of 52 (17.7%) patients were given vancomycin as monotherapy antibiotic, while 242 (82.3%) patients were given combination treatment with other antibiotics (Table 2). Culture was positive in 90 patients. 18 patients had MRSA positive, and 55 patients had culture positive for methicillin-susceptible Staphylococcus aureus bacteremia (MSSA). (Fig. 1).

Vancomycin serum level

Therapeutic drug monitoring of vancomycin was performed in 286 patients (97.3%). Out of the 286 patients who were monitored, 256 (87.1%) were found to be within the therapeutic range. Only 20 (6.8%) patients were found to have sub-therapeutic levels, which mean low trough level less than 10 umol/l, about ten patients achieving potentially toxic levels, more than 20 umol/l 10 (3.4%) (Table 3).

Combination therapy

78.9% of our patients use vancomycin with B-Lactam antibiotics, 3.4% use Aminoglycosides with vancomycin, which increases the risk of nephrotoxicity (Table 3).

Discussion

Vancomycin is one of the few medications used to treat certain potentially fatal and life-threatening infections caused by methicillin-resistant Staphylococcus aureus (MRSA) and other Gram-positive, beta-lactam–resistant bacteria as a first-line agent of choice [6]. It is widely utilized, particularly in developing nations, where it is more affordable and readily available than other antibiotics. Emergence of secondary resistance to Vancomycin in a major clinical concern [7].

In the past twenty years, nosocomial infections in Western Europe and the United States are increasingly caused by vancomycin-resistant enterococci (VRE9), [9] In the last decade, the number of infections reported to the Centers for Disease Control and Prevention (CDC) has increased more than twentyfold [11]. The co-colonization prevalence of MRSA and VRE in patients in intensive care units (ICUs) rose from 0.4–14% [12, 13]. Vancomycin-resistant bacteria (VRE) pose a threat of

Table 2 Results of Vancomycin audit

Use	N(%)
Appropriate	262 (89.1%)
Inappropriate	32 (10.1%)
a. Continue to use beyond 72 hours without further evidence of Gram-positive infection	21
b.Treatment of beta-lactam-sensitive microorganisms	9
c.Systemic prophylaxis for non-penicillin allergy patient	2

Chi-squared test; *p-value < 0.05 considered significant

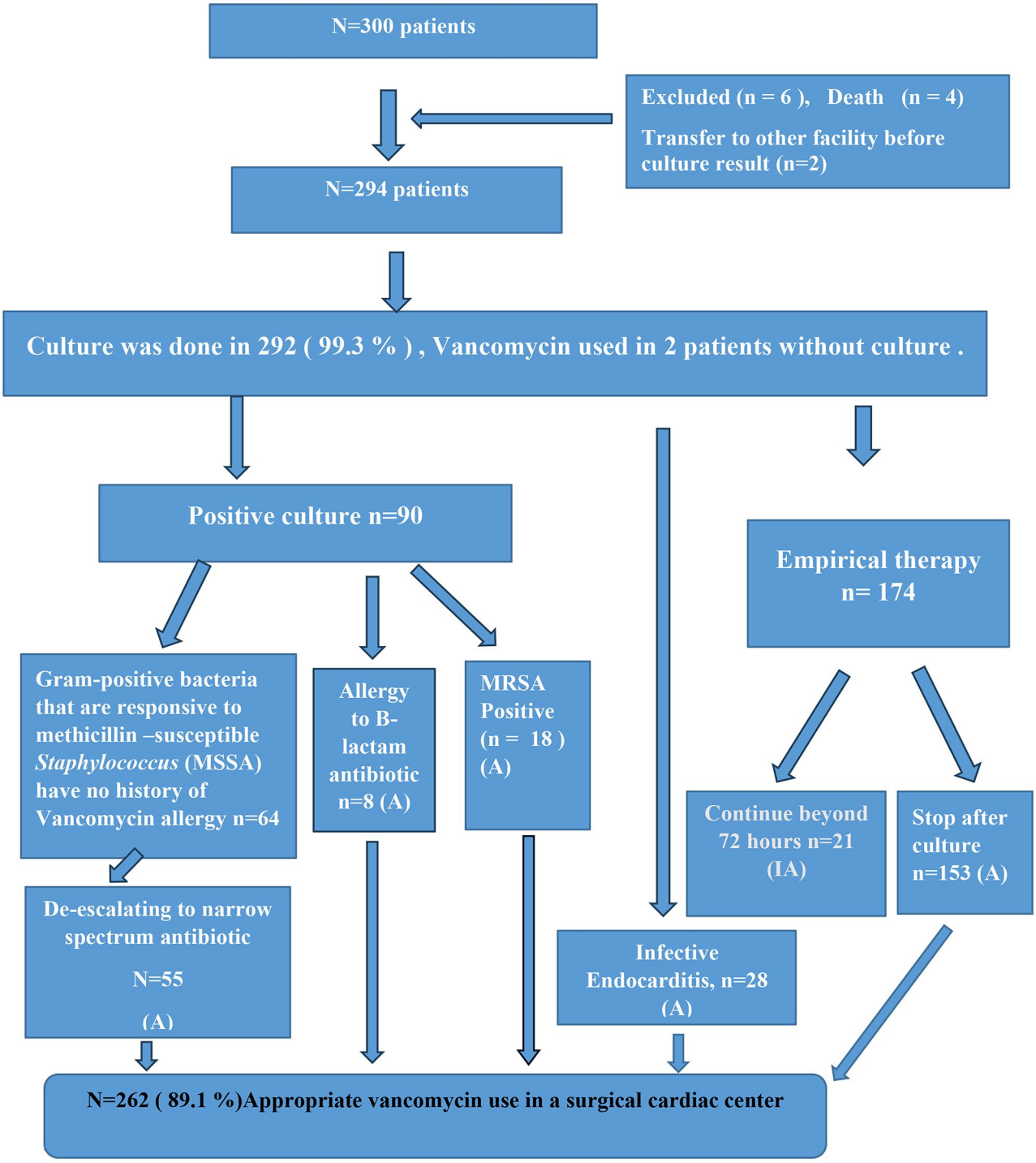

Fig. 1 CONSORT diagram: The overall flow of patients

resistance to multiple antibiotic strains and the potential transfer of resistance to other Gram-positive bacteria, including S. aureus [14].

Since vancomycin exposure has been identified as a significant risk factor for VRE colonization and infection, several American studies have evaluated the appropriateness of vancomycin use in the absence of restriction policies, with findings ranging from 20–50% [14]. Research conducted at universities and teaching hospitals has demonstrated a significant increase in the frequency of vancomycin use [15]. Furthermore, these studies indicate that the combination of vancomycin with other antibiotics heightens the risk of toxicity [16]. In contrast patients with MRSA bacteremia who received

Table 3 Vancomycin therapeutic drug monitoring in the study population ($n=294$)

Characteristics *n*(%)
Monitoring provided
Yes ($n=286$, 97.3%)
No ($n=8$, 2.7%)
Vancomycin levels ($n=286$, 97.3%)
Sub-therapeutic, less than 10 mg/L ($n=20$, 6.8%)
Therapeutic, 10–20 mg/L (256, 87.1)
Potential toxic, more than 20 mg /L ($n=10$, 3.4%)

Chi-squared test; *p-value < 0.05 considered significant

Table 4 Drug-drug interaction with Vancomycin may lead to increase in nephrotoxicity risk, ($n=294$)

Drug-drug interaction	Percentage of total cases
Vancomycin + B-Lactam antibiotics	232 78.9%
Vancomycin + Aminoglycosides	10 3.4%

delayed vancomycin therapy often experienced poor outcomes. Therefore, appropriate use of Vancomycin is of pivotal importance [17]. The Infectious Diseases Society of America strongly recommends use of baseline cultures and sensitivities and discontinuing empirical vancomycin treatment when culture and sensitivity results do not indicate the presence of β-lactam-resistant Gram-positive bacterial infections.

In our cardiac center, improper indications accounted for 11% of vancomycin orders,, even in cases where a Gram-positive bacterial infection was not identified within 72 h

Vancomycin was continued empirically despite negative cultures, and its administration was maintained due to the patient's critical condition.)

However, it is well-documented that a significant percentage of patients continue to receive empirical vancomycin treatment inappropriately. [19–21].

In various other studies, researchers found that, compared to specific institutional criteria and/or IDSA recommendations, up to 65% of vancomycin use was inappropriate [21].

These differing results may be attributed to several factors, including the prevalence of infectious disease consultations, the introduction of a policy restricting prescriptions, implementation of guidelines and mandatory order forms [24].

Similar to our study a research conducted at an Iranian hospital, revealed that 89.4% of the patients received appropriate treatment, while 10.6% received inappropriate treatment, according to the HICPAC recommendations. However, it is well-documented that a significant percentage of patients continue to receive empirical vancomycin treatment inappropriately. (19,20,21) In various studies, researchers found that, compared to specific institutional criteria and/or IDSA recommendations, up to 65% of vancomycin use was inappropriate [21].

Other possible reason for this behavior could be that doctors continue to use vancomycin empirically, despite the absence of MRSA in the cultures and the convenience of its use, as it effectively targets many Gram-positive bacteria, particularly in developing countries [22]. The broad spectrum of action against various Gram-positive bacteria further incentivizes its continued use, especially in developing nations [23, 24].

One of the most common reasons for administering vancomycin was septicemia, accounting for 15.5% of cases [25]. In our study, vancomycin was prescribed to 294 patients, of whom 174 (59.2%) received it empirically. Additionally, vancomycin was administered as a monotherapy to 52 patients (17.7%), while the remaining 242 patients (82.3%) did not receive it (Table 4).

Due to the drug's limited therapeutic range, monitoring serum concentrations of vancomycin is essential during its administration to minimize the risk of toxicity or sub-therapeutic levels in a clinical setting. Nephrotoxicity and ototoxicity are two of the primary side effects associated with vancomycin [26, 27]. In our study, vancomycin levels were monitored in 96.6% of the patients. The combination of vancomycin with other nephrotoxic medications increases the risk of nephrotoxicity. In our study, more than 72% of the patients received vancomycin in conjunction with other renally excreted antibiotics, such as aminoglycosides and β-lactam antibiotics [28].

Even so, there is ongoing debate regarding the monitoring of vancomycin, particularly in patients with normal renal function and uncomplicated infections. However, current guidelines indicate that monitoring serum vancomycin levels is essential for all patients receiving treatment for more than three to five days. This practice aims to reduce the risk of toxicity and achieve the target therapeutic trough level [29, 30].

In our study, approximately 52.4% of the patients exhibited renal impairment, indicated by a creatinine clearance of less than 60 ml/min. Of all the patients, 97.3% had their vancomycin levels monitored. Among those who were assessed, 82.5% had values within the therapeutic range. Only 12 patients (4.2%) presented with sub-therapeutic levels, while 8 patients (2.7%) reached potentially toxic levels (Table 3). For patients treated with vancomycin over an extended length of time, a multimodal intervention to establish a vancomycin dosage and monitoring guideline greatly improved prescribing, monitoring, pharmacokinetic, and safety outcomes [32].

Controlling the inappropriate use of vancomycin requires a collaborative, multidisciplinary, institution-wide effort to ensure that physicians are aware of the Infectious Diseases Society of America (IDSA) standards. Educational lectures for physicians that explain the IDSA guidelines, and stewardship strategies may contribute to reducing the inappropriate use of vancomycin.

Additionally, a labor-intensive approach used in some institutions involves obtaining verbal consent from an infectious diseases specialist before administering vancomycin [33].

Study limitations

Study limitations. This study has several limitations. Firstly, the small sample size may reduce the significance of the results. Another limitation is the data sampling from only one hospital, which limits the generalizability. In addition, the retrospective design was also a limitation

Conclusion

The current study showed that there was inappropriate use in about one-tenth of all vancomycin use, which could potentially contribute to vancomycin resistance. Most of the inappropriate use is due to frequent empirical use, with lack of follow up and modifications according to cultures and sensitivities. Findings from this study provide a basis for improving and strengthening the use of vancomycin in order to conform to the guidelines. In addition, the implementation of IDSA guidelines and monitoring protocol at each hospital would be extremely important. More research in this specific area may lead to firmer guidelines that can be used to optimize the use of vancomycin in patients undergoing heart surgery

Abbreviations

CRCL	Creatinine Clearance
CRRT	Continuous Renal Replacement Therapy
IDSA	Infectious Disease Society of America
MRSA	Methicillin-Resistant Staphylococcus Aureus
MSSA	Methicillin –Susceptible Staphylococcus
SD	Standard Deviation
VRE	Vancomycin– resistant enterococci

Acknowledgements

I acknowledged the clinical pharmacy department and cardiac center team who supported me in this research.

Author contributions

S.M. : Idea , design, writing the proposal, approval of IRB , recruiting the subjects, conducting the Interviews, writing the manuscript. L.A. : Revising design, Analysis of Data, revising the manuscript and preparation for publication. S.A. : Revising design, Analysis of Data, and collecting data .

Funding

The research had not been funded.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Consent for publication

King Fahad Medical center (KFMC) and all authors agree for publication.

Consent to participate

Not applicable' as the research was retrospective and all patient's name and identification had been removed under the supervision of KFM research center .

Competing interests

The authors declare no competing interests.

Received: 6 May 2024 / Accepted: 26 November 2024
Published online: 20 December 2024

References

1. Sivaradjy M, Gunalan A, Priyadarshi K, Madigubba H, Rajshekar D, Sastry AS. (2021). Increasing trend of vancomycin-resistant enterococci bacteremia in a tertiary care hospital of South India: a three-year prospective study. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine, 25(8), 881.
2. Boneca IG, Chiosis G. (2003). Vancomycinresistance: occurrence, mechanisms and strategies to combat it. Expert opinion on therapeutic targets, 7(3), 311–28.
3. Abbas Q, Haq AU, Kumar R, Ali SA, Hussain K, Shakoor S. Evaluation of antibiotic use in pediatric intensive care unit of a developing country. Indian J Crit care Medicine: peer-reviewed Official Publication Indian Soc Crit Care Med. 2016;20(5):291.
4. Acta Anaesthesiologica Scandinavica, 64(9), 1295–1304.
5. IDSA Home (idsociety.org).
6. Ayobami O, Willrich N, Reuss A, Eckmanns T, Markwart R. The ongoing challenge of Vancomycin-resistant Enterococcus faecium and Enterococcus faecalis in Europe: an epidemiological analysis of bloodstream infections. Emerg Microbes Infections. 2020;9(1):1180–93.
7. Mandal S, Kundu A, Borah D, Ray MS, Mondal C. Methicillin Resistant Staphylococcus aureus (MRSA) an underestimate threat. Airborne biocontaminants and their impact on Human Health. Aug. 2024;20:214–57.
8. Selim S. Mechanisms of grampositive Vancomycin resistance. Biomedical Rep. 2022;16(1):1–6.
9. Joshi S, Shallal A, Zervos M. Vancomycin-resistant enterococci: epidemiology, infection prevention, and control. Infect Disease Clin. 2021;35(4):953–68.
10. Schrank GM, Snyder GM, Davis RB, Branch-Elliman W, Wright SB. The discontinuation of contact precautions for methicillin-resistant Staphylococcus aureus and Vancomycin-resistant Enterococcus: impact upon patient adverse events and hospital operations. BMJ Qual Saf. 2020;29(10):1–2.
11. Li G, Walker MJ, De Oliveira DM. Vancomycin resistance in Enterococcus and Staphylococcus aureus. Microorganisms. 2022;11(1):24.
12. Rybak MJ, Le J, Lodise TP, Levine DP, Bradley JS, Liu C, Mueller BA, Pai MP, Wong-Beringer A, Rotschafer JC, Rodvold KA. Therapeutic monitoring of Vancomycin for serious methicillin-resistant Staphylococcus aureus infections: a revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious diseases pharmacists. Am J Health-System Pharm. 2020;77(11):835–64.
13. Van Der Heggen T, Buyle FM, Claus B, Somers A, Schelstraete P, De Paepe P, Vanhaesebrouck S, De Cock PA. Vancomycin dosing and therapeutic drug monitoring practices: guidelines versus real-life. Int J Clin Pharm. 2021;43(5):1394–403.
14. Amberpet R, Sistla S, Parija SC, Rameshkumar R. Risk factors for intestinal colonization with Vancomycin resistant enterococci'A prospective study in a level III pediatric intensive care unit. J Lab Physicians. 2018;10(01):089–94.
15. Sivaradjy M, Gunalan A, Priyadarshi K, Madigubba H, Rajshekar D, Sastry AS. Increasing trend of Vancomycin-resistant enterococci bacteremia in a tertiary care hospital of South India: a three-year prospective study. Indian J Crit Care Medicine: Peer-reviewed Official Publication Indian Soc Crit Care Med. 2021;25(8):881.
16. Özger HS, Fakıoğlu DM, Erbay K, Albayrak A, Hızel K. Inapropriate use of antibiotics effective against gram positive microorganisms despite restrictive antibiotic policies in ICUs: a prospective observational study. BMC Infect Dis. 2020;20(1):289.
17. Scaglione V, Reale M, Davoli C, Mazzitelli M, Serapide F, Lionello R, La Gamba V, Fusco P, Bruni A, Procopio D, Garofalo E. Prevalence of antibiotic resistance over time in a third-level university hospital. Microb Drug Resist. 2022;28(4):425–35.
18. Burnham JP, Burnham CA, Warren DK, Kollef MH. Impact of time to appropriate therapy on mortality in patients with Vancomycin-intermediate Staphylococcus aureus infection. Antimicrob Agents Chemother. 2016;60(9):5546–53.
19. Kim NakHyun KN, Koo HeiLim KH, Choe PyeongGyun CP, Cheon ShinHye CS, Kim MoonSuk KM, Lee MyungJin LM. Jung YoungHee JY, Park WanBeom PW,

Song KyoungHo SK, Kim EuSuk KE, Bang JiHwan BJ. Inappropriate continued empirical Vancomycin use in a hospital with a high prevalence of methicillin-resistant Staphylococcus aureus.
20. Zuccaro V, Columpsi P, Sacchi P, Lucà MG, Fagiuoli S, Bruno R. Antibiotic stewardship and empirical antibiotic treatment: how can they get along? Dig Liver Disease. 2017;49(6):579–84.
21. Tabah A, Bassetti M, Kollef MH, Zahar JR, Paiva JA, Timsit JF, Roberts JA, Schouten J, Giamarellou H, Rello J, De Waele J. Antimicrobial de-escalation in critically ill patients: a position statement from a task force of the European Society of Intensive Care Medicine (ESICM) and European Society of Clinical Microbiology and Infectious diseases (ESCMID) critically Ill patients Study Group (ESGCIP). Intensive Care Med. 2020;46:245–65.
22. Bottalico L, Charitos IA, Potenza MA, Montagnani M, Santacroce L. The war against bacteria, from the past to present and beyond. Expert Rev Anti-infective Therapy. 2022;20(5):681–706.
23. Verma MK, Gayathri S, Ashokkumar B, Varalakshmi P. Trends in Antimicrobial Therapy: Current Approaches and Future Prospects. Biomolecular Engineering Solutions for Renewable Specialty Chemicals: Microorganisms, Products, and Processes. 2021 Oct 25:111 – 40.
24. Gomez J, Garcia-Vazquez E, Banos R, Canteras M, Ruiz J, Baños V, Herrero JA, Valdes M. Predictors of mortality in patients with methicillin-resistant Staphylococcus aureus (MRSA) bacteraemia: the role of empiric antibiotic therapy. Eur J Clin Microbiol Infect Dis. 2007;26:239–45.
25. YaddolahiFar M, Sheybani F, Eslami S, Taherzadeh Z, Naderi H, Mohseni M, Zakeri E, Khosravi N. Why Vancomycin is overly prescribed despite the lack of supporting Microbiological data: to design a Concept Map. Infect Dis Clin Pract. 2021;29(2):e101–4.
26. Ghollar MA, Rangchian M, Etminaniesfahani M. Retrospective drug utilization evaluation of Vancomycin usage in infectious wards and intensive care units in Hamedan teaching hospitals, April to September 2020. Avicenna J Pharm Res. 2021;2(2):55–9.
27. Rhee C, Kadri SS, Dekker JP, Danner RL, Chen HC, Fram D, Zhang F, Wang R, Klompas M, CDC Prevention Epicenters Program. Prevalence of antibiotic-resistant pathogens in culture-proven sepsis and outcomes associated with inadequate and broad-spectrum empiric antibiotic use. JAMA Netw open. 2020;3(4):e202899.
28. Mahi-Birjand M, Ziaee M, Bijari B, Khalvati R, Abedini MR, Golboei Mousavi H, Ziaee A. Evaluation of Vancomycin use in university-affiliated hospitals in Southern Khorasan Province (East Iran) based on HICPAC guidelines. Drug, Healthcare and Patient Safety. Apr. 2019;8:29–35.
29. Yuliandra Y. Targeting Bacterial Resistance: Rational Design and Evaluation of Antibiotic Combinations with Adjuvants (Doctoral dissertation).
30. Lim AS, Foo SH, Seng JJ, Ng TT, Chng HT, Han Z. Area-under-curve–guided Versus Trough-guided monitoring of Vancomycin and its impact on nephrotoxicity: a systematic review and Meta-analysis. Ther Drug Monit. 2023;45(4):519–32.
31. Phillips CJ, McKinnon RA, Woodman RJ, Gordon DL. Sustained improvement in Vancomycin dosing and monitoring post-implementation of guidelines: results of a three-year follow-up after a multifaceted intervention in an Australian teaching hospital. J Infect Chemother. 2018;24(2):103–9.
32. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, Srinivasan A, Dellit TH, Falck-Ytter YT, Fishman NO, Hamilton CW. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis. 2016;62(10):e51–77.
33. Alavi-Moghadam M, Shahim F, Sistanizad M, Pourheidar E, Hassanpour R. Vancomycin prescription pattern in a teaching hospital: the promising role of antimicrobial control programs. J Pharm Care. 2020 Jun;26:53–6.

Publisher's note