RESEARCH ARTICLE

Analysis of Blood Culture Data influences Future Epidemiology of Bloodstream Infections: A 5-year Retrospective Study at a Tertiary Care Hospital in India

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Abstract

Background: Blood cultures are the most significant samples received in a microbiology laboratory. Good quality control of pre-analytic, analytic, and post-analytic stages can have a significant impact on patient outcomes. Here, we present the improvements brought about by reviewing blood culture data with clinicians at a tertiary care institute in India.

Methods: Four-year blood culture data (phase I—February 2014–February 2018) were shared with clinicians in the clinical grand round. Several take-home messages were discussed in a quiz format, and a number of holistic quality control measures were implemented at different levels. Based on observable changes in blood culture reports, another data set was analyzed and compared in phase II (April 2018–April 2019).

Results: In phase II, the blood culture contamination rate improved from 6 to 2% along with four times reduction in ICU isolates and three times increased isolation of salmonellae and pneumococci. The development of resistance in *Klebsiella pneumoniae* to carbapenems and piperacillin–tazobactam was reduced. Colistin resistance in ICU isolates hovered around 15%. Vaccine-preventable pneumococcal serotypes were predominant in the under-five age-group. Typhoidal salmonellae were more commonly isolated from adults with 50% showing sensitivity to pefloxacin and 97% to ampicillin, chloramphenicol, and cotrimoxazole. *Candida parapsilosis* was the leading non-*albicans Candida* (NAC). Fluconazole resistance was observed in 50% of NAC.

Conclusion: Reviewing blood culture data with clinicians mutually helped us to improve the overall quality of blood culture reports. It had a major impact on epidemiological trends and thus, found to be superior to just sharing an antibiogram with the clinicians.

Keywords: Blood culture, Bloodstream infections, *Candida parapsilosis*, Fluconazole resistance, Pneumococci, Salmonellae.

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Introduction

Blood cultures are crucial specimens for diagnosing bloodstream infections (BSIs) and directly influence the use of appropriate antimicrobial therapy (AMT).[1] The mortality in intensive care units (ICUs) due to BSIs can be very high (70%). "Surviving Sepsis Campaign" recommends the use of an appropriate antimicrobial agent within 1 hour of suspecting sepsis, and this empirical therapy may fail in one-fifth of the cases. Increasing fungemia makes this situation more grim.[2] In developing countries, a threat of "post-antibiotic era" in ICUs has forced stakeholders to implement diagnostic and therapeutic stewardship.[3,4] Here, we present the impact of reviewing blood culture data with clinicians on the future epidemiology of BSIs at a tertiary care hospital in India.

Methods

A hospital-based retrospective study was carried out on blood culture data between February 2014 and February 2018 at the Department of Microbiology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India. During the study period, a total of 2,549 blood cultures were received and the BACTEC FX system (Becton Dickinson, Sparks, Maryland) was used for incubation. Mostly one blood culture bottle was received from each patient (BD BACTEC Plus Aerobic/Peds Plus bottle). The identification of isolates was done using conventional microbiological techniques. Microscan Walkaway system was used for isolates that failed to be identified by the routine methods. Antimicrobial sensitivity testing was performed as per Clinical and Laboratory Standards Institute (CLSI) guidelines. Internal and external quality controls were established during the study period. These laboratory data were used to determine BSI pathogen profile and their antimicrobial susceptibility pattern. The study was approved by the Institutional Ethics Committee of AIIMS, Jodhpur (Ref. No. AIIMS/IEC/2018/1237) and adhered to the Declaration of Helsinki. These data were

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presented at ASM Microbe 2018 Conference, USA and subsequently in the clinical grand round of the institution. Several take-home messages were discussed in a quiz format. There were observable differences in subsequent blood culture reports. Therefore, to compare a reasonably similar number of blood culture isolates, data from April 2018 to April 2019 were evaluated for observing the impact on epidemiology and outcomes.

Data Collection and Analysis

The data collected were subjected to descriptive analysis. Microsoft Excel 2010 was used for preparing tables, bar charts, and line diagram.

Results

The bed strength of our institute gradually increased from 75 to 400 during February 2014 to February 2018 (phase I), while during April 2018 to April 2019 (phase II), it became a 500-bedded hospital. The ICU strength remained the same throughout during these 5 years. In phase I, the total number of isolates was 441 out of 2,549 blood culture samples (17.3%), whereas in phase II, it was 425 out of 3,912 samples (10.8%). Notable differences were observed after reviewing the data with clinicians. Figure 1 shows that the contamination rate decreased from 6 to 2%, paired samples increased from 2.4 to 4.7%, and isolates from ICUs decreased from 12 to 3%. During phase I, *Klebsiella pneumoniae* and *Candida* spp. were the predominant isolates (Figure 2) whereas subsequently, *Escherichia coli* became the most common isolate and Candida ranked seventh in the frequency of isolation. Another significant change was salmonellae becoming the third most common isolate. The isolation of pneumococci also increased three times in phase II.

For *E. coli* ($n = 32$ vs 69), the sensitivity rate was almost similar during both the phases for cephalosporins (13%), fluoroquinolones (13%), cefoperazone–sulbactam (62%), and colistin (100%); while for carbapenems, it improved from 69 to 75%, for aminoglycosides from 44 to 78%, and for piperacillin–tazobactam from 44 to 69%. The number of ICU isolates decreased from 43.7 to 13% ($n = 14$ vs 9).

For *K. pneumoniae* ($n = 48$ vs 56), there was not much change in the sensitivity for cefoperazone–sulbactam (19%), but it decreased for aminoglycosides from 34 to 21%, for cephalosporins from 22 to 7%, for fluoroquinolones from 25 to 19%, and for colistin from 100 to 86%. Figure 3 shows a constant rise in carbapenem and piperacillin–tazobactam resistance at a doubling rate over the initial 4 years, but after the review, there was a decreased pace for it. Overall, there is a constant worsening of resistance rates for this pathogen (66 and 72%, respectively, for these two drugs). ICU isolates decreased from 73 to 43% ($n = 35$ vs 24) in phase II.

A similar downward trend was seen for another important ICU pathogen, *Acinetobacter baumanii* ($n = 26$ vs 38). The sensitivity for carbapenems decreased from 27 to 13%, for amikacin from 23 to 18%, for fluoroquinolones from 27 to 13%, and for cefoperazone–sulbactam from 75 to 50%. Surprisingly, colistin resistance decreased from earlier 10 to 5%, though it is emerging in both these above isolates. Pan-resistant isolates were seen in both the phases. ICU isolates decreased from 69 to 47% ($n = 18$ in both the phases).

Among *Pseudomonas aeruginosa* ($n = 11$ vs 26), multidrug-resistant (MDR) isolates comprised 20% and carbapenem resistance rose to 57% from earlier 10% in phase II. Other organisms increasingly isolated were *Burkholderia cepacia* complex (BCC), *Stenotrophomonas maltophilia*, *Elizabethkingia meningosepticum*, *Brucella* spp., and *Serratia marsescens*, at times with small outbreaks.

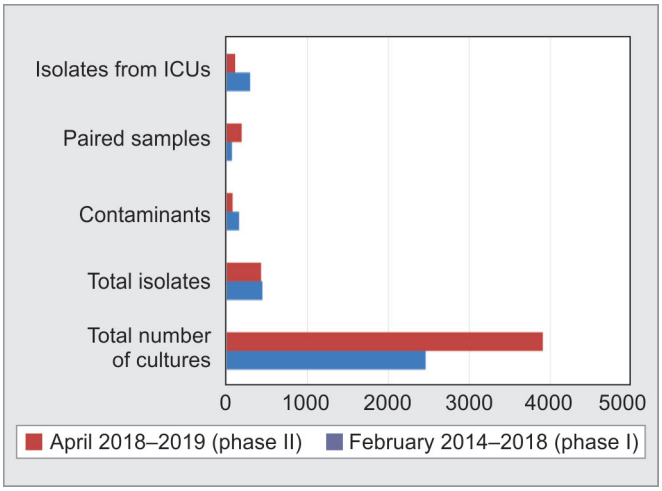

Fig. 1: Comparison of blood culture data following the review in March 2018

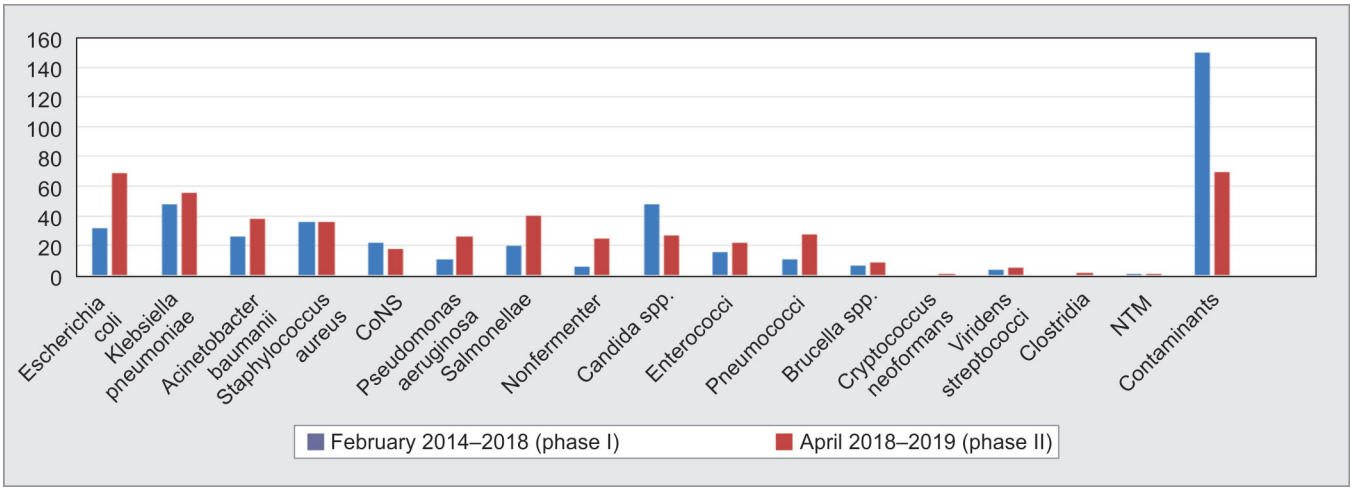

Fig. 2: Comparison between microbial isolates in both the phases

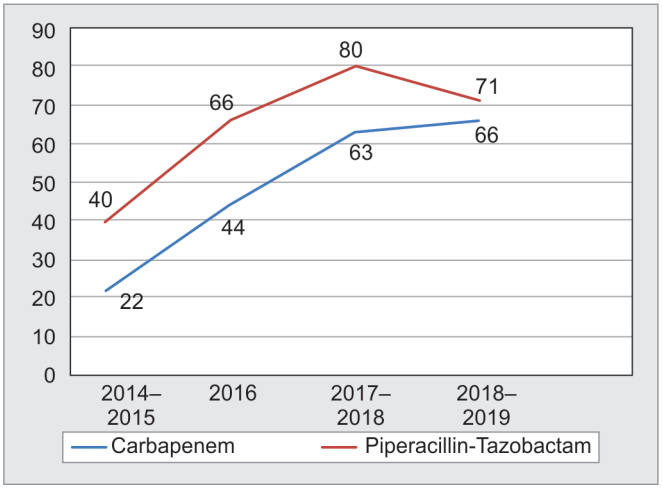

Fig. 3: Resistance to piperacillin–tazobactam and carbapenems in both the phases

The isolation of typhoidal salmonellae doubled during phase II (20 vs 40) with the isolation of *Salmonella enterica* serovar Typhi (12 vs 27) and *S. enterica* serovar Paratyphi A ($n = 8$ vs 13). Resistance to pefloxacin (HiMedia Laboratories Pvt. Ltd., Mumbai) was observed in the isolates of *S. Typhi* (9/12 and 11/27) and of *S. Paratyphi* A (5/8 and 4/13) during both the phases. All isolates were sensitive to ceftriaxone and azithromycin. Except for two isolates of *S. Paratyphi* A, all were sensitive to ampicillin, chloramphenicol, and cotrimoxazole. Interestingly, individuals above 20 years were most commonly affected ($n = 42$, 70%) followed by 6 to 15 years ($n = 9$, 15%), 0 to 5 years ($n = 6$, 10%), and 16 to 20 years ($n = 3$, 5%) age-groups.

Forty-four percent of *Staphylococcus aureus* isolates ($n = 36$ vs 36) were resistant to cefoxitin, i.e., methicillin-resistant *S. aureus* (MRSA) with most being suggestive of community-associated MRSA on the basis of drug sensitivity. All isolates were sensitive to vancomycin, teicoplanin, and linezolid. Eighty percent of the isolates were sensitive to gentamicin, while 60% were sensitive to each of cotrimoxazole and clindamycin. There was a sharp fall in the sensitivity to quinolones from 54 to 16%. The sensitivity to erythromycin remained near 33%.

Only 33% of enterococcal isolates ($n = 16$ vs 22) were sensitive to ampicillin and high-level gentamicin, while all were sensitive to linezolid in both the phases. Vancomycin resistance was seen in 18% isolates, mostly in *Enterococcus faecium*.

The isolation of *Streptococcus pneumoniae* increased in phase II ($n = 11$ vs 28). The sensitivity to cotrimoxazole was observed only in 25%, while all isolates were sensitive to vancomycin, linezolid, cefotaxime, and levofloxacin. Susceptibility to erythromycin was noted only in half of the isolates. One-fourth of the isolates showed resistance to oxacillin disc. However, molecular analysis conducted under a national multicentric project showed no evidence of penicillin resistance. Eight isolates were subjected to serotyping in 2018 under the said project, and the prevalent serotypes were 5, 6A, 6B, 9V, 14 ($n = 2$), 15C, and 19E. All these isolates were from the under-five age-group.

Candida spp. ($n = 48$ vs 48) was the biggest challenge during phase I of our study as 48% of total blood culture isolates were from ICUs. Overall, 37% of the candida isolates were from neonatal ICU, 18% from pediatric ICU, and 23% from medicine wards. Extremes of age (<2 and >65 years) were most commonly affected (65%). An overall male preponderance was observed in our study (63%). The most common risk factors identified were broad-spectrum antibiotics > prolonged ICU stay > immunosuppressive therapy > central venous catheter > prematurity > neutropenia > total parenteral nutrition > congenital anomalies > abdominal surgery. Non-*albicans Candida* (NAC) comprised 71% of the isolates, while 29% ($n = 28$) were *C. albicans*. Among NAC, *C. parapsilosis* was the leading isolate ($n = 19$, 20%) followed by *C. tropicalis* ($n = 17$, 19%), *C. glabrata* ($n = 11$, 11%), *C. krusei* ($n = 10$, 10%), and other uncommon species, like *C. dubliniensis*, *C. guilliermondii*, *C. famata*, and *C. kefyr* ($n = 11$, 11%). Antifungal susceptibility testing was performed by epsilometer test using Ezy-MIC strips (HiMedia Laboratories Pvt. Ltd., Mumbai). Overall, fluconazole resistance was observed in 50% of the isolates with *C. glabrata* and *C. krusei* showing complete resistance, while it was 63% for *C. parapsilosis*, 54% for *C. tropicalis*, and 18% for *C. albicans*. Voriconazole resistance was seen in 30% isolates. Resistance to echinocandins was observed in 5 to 6%, and all the isolates were sensitive to amphotericin B. Maximum antifungal resistance was observed in *C. parapsilosis*.

Discussion

Prompt therapeutic interventions are a cornerstone in the management of sepsis for a better outcome and infection prevention strategies. Currently, rapid advances in diagnostics have reduced the turnaround time from days to hours.[5] In developing countries, the majority of the microbiology laboratories still resort to conventional methods of blood culture. We used automated systems optimally in an establishing tertiary care institute. Emphasis was put on quality control of laboratory reporting.

Blood culture data were collected over 4 years and discussed with clinicians in the "clinical grand round." Pre-analytical factors were targeted for enhancing the quality of results. "One-hour sepsis bundle care" strongly recommends collection of blood culture samples before starting antimicrobial therapy.[6] Another strong parameter that can singularly influence results is the volume of blood. Each additional milliliter of blood increases the yield by 3 to 5% in adults as the bacterial load is less in adults (average 1 CFU/mL). This increased yield beyond 10 mL inoculum is more marked for *Enterobacterales* (especially for salmonellae) than for gram-positive bacteria, non-fermenters, and yeasts.[7] A blood culture is defined as a culture of blood obtained from a single venepuncture, and if inoculated in more than one bottle, it is called a "blood culture set."[8] In India, laboratories mostly use a single aerobic blood culture bottle to curtail the cost. "One set" of aerobic and anaerobic bottle is used to maximize the yield of diverse pathogens from challenging cases. Paired blood culture (PBC) samples are commonly obtained at our hospital to diagnose central line-associated BSI, whereas CLSI guidelines recommend it to diagnose BSIs as well. It increases the yield in adult patients.[9] Gram-positive and fastidious organisms are recovered more in automated blood culture systems.[10] Just as false-negative blood cultures can miss the diagnosis and increase the cost of further investigations, so can false-positive cultures jeopardize the antimicrobial stewardship and total cost besides affecting the patient microbiome. Therefore, it is vital to follow strict criteria for blood culture sample collection.[9,10]

Two blood cultures from two venepuncture sites inoculated in two types of media one aerobic and one anaerobic, collected with complete asepsis, and transported rapidly to the microbiology laboratory for incubation in automated culture system can make

significant improvements in reporting as per our experience. We discouraged paired samples from the femoral vein or arterial lines because of the contamination.

Paired blood cultures collected from existing intravenous catheters usually grow contaminants or colonizers.[9] Gonsalves et al. hypothesize that the contamination rate increases in the samples with a lower volume of blood collected, mainly due to compromise in asepsis because of poor venous access.[11] CLSI mentions that collecting 40 mL of blood from adults and 12 mL from children can detect 90 to 95% of bacteremia. Here, two blood culture sets are being recommended, each bottle inoculated with 10 mL in adults and 3 mL in children. Two venepunctures are important to rule out contaminants and to establish coagulase-negative staphylococci (CoNS) as pathogens.[12,13] No single blood culture medium can detect all the pathogens of BSI; the use of anaerobic media helps in a better recovery of streptococci and other facultative anaerobes.[13] Several studies have shown that only 10 to 26.4% of CoNS isolates, 38% of viridans streptococci, and 70% of enterococci are clinically significant. The acceptable contamination rate in blood cultures is 2 to 3%.[14] The present study showed three times reduction in contamination rate and two times increase in PBC in phase II. The isolation of salmonellae increased with an adequate volume of blood for culture. All these were achieved with rigorous training of our phlebotomists on blood culture collection techniques. There was a sharp fall in isolates from ICUs because of an increase in indoor patients in comparison to earlier imported cases, better infection prevention and control, and better antimicrobial stewardship practices. All pan-resistant isolates were isolated from imported cases. Emergency service in the microbiology laboratory is another important area of improvement. An increased isolation rate of pneumococci during phase II was mainly because they tend to autolyze on delay in subculture beyond 24 hours.

We compared our antibiograms with a national data through the Global Antimicrobial Resistance Surveillance System (GLASS). It was showing the same trend as ours except for salmonellae.[15] Salmonella isolates from our area were less resistant than the rest of India. There was no MDR strain. Increasing extended-spectrum beta-lactamase production is being reported from Asian isolates of *S. enterica* serovar Typhi, and we need to remain alert for such eventuality.[16,17]

Gray et al. highlighted how gram-negative BSIs (GNBSIs) are alarmingly rising worldwide and need to be addressed by promptly identifying urinary tract infections. The United Kingdom has formed a national target to halve the GNBSIs by 2021, in patients hospitalized during the past 28 days.[18] Wattal et al. reviewed blood culture data from pediatric patients, our isolates in comparison showed higher resistance to fluoroquinolones and cefoperazone–sulbactam.[12] Saksena et al. from India reported a high prevalence of fluoroquinolone resistance (60%) on day one of life in newborns. It is because of its misuse as the first-line drug for possibly all infectious etiologies. It is also proposed that heavy fluoroquinolone use can select ciprofloxacin resistance.[19] We stressed on "stepping down" of antimicrobial therapy after receiving the culture reports.

Candidemia has been reported to be 4 to 15 times higher in the developing world due to earlier colonization of newborns after birth, leading to higher prevalence in neonatal ICU. Our study showed a unique finding with *C. parapsilosis* as the leading cause of candidemia. It is known to form biofilms and therefore, causes device-associated infections. It is also transferred through the hands of healthcare workers. Kaur et al.[20] also reported increased isolation of *C. parapsilosis* in their study. However, there was a huge difference in their antifungal resistance profile as compared to our study. It is imperative to use standard methods of identification and antifungal susceptibility testing with a rapid turnaround time because of the emergence of multidrug-resistant superbug *C. auris*. It is important to publish local epidemiological data for future reference.

With new antimicrobial agents in the armamentarium, it becomes all the more important to detect the type of carbapenemase production rapidly, possibly directly from blood culture bottles.[21] Disruption in the homeostasis of normal flora can occur even with a single dose of antimicrobial agent, leading to metabolic, immunological, and developmental disorders in neonates.[22] Not to forget that mycobiome turns into opportunistic pathogens, which carries a high mortality rate.[23] Human microbiome restoration methods like fecal microbiota transplant and probiotics carry safety concerns, and they still need to get regulated.[24] Retrospective studies show earliest evidence of *C. auris* from Pakistan and India, which has turned into a major global public health threat.[25]

Conclusion

Reviewing blood culture data with clinicians improves the overall quality of blood culture reports and promotes the rational use of antimicrobial agents. It has a positive impact on epidemiological trends and drug susceptibility profile of microbial isolates, and thus, superior to just sharing antibiogram with clinicians. A holistic approach involving diagnostic microbiology and clinicians is needed to optimize laboratory services, antimicrobial prescription, and infection control practices for better patient management and outcomes.

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Author Contributions

An.S. and Ar.S. conceptualized the study. An.S., Ar.S., A.M., V.H., N.G., P.K., K.S., and V.L.N. contributed to the study design. An.S., Ar.S., H.N., T.S., and N.G. acquired the data. An.S and Ar.S analyzed the data. Ar.S, An.S, V.H., N.G., and K.S. interpreted the data. An.S. and Ar.S. drafted the manuscript. All authors critically reviewed the manuscript and approved it for publication.

Ethical Approval

The study has been approved by the ethical committee of AIIMS, Jodhpur (Ref. No. AIIMS/IEC/2018/1237), and it conforms to standards currently applied in India.

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References

1. Snyder JW. Blood cultures: the importance of meeting pre-analytical requirements in reducing contamination, optimizing sensitivity of detection, and clinical relevance. Clin Microbiol Rev 2015;37(7):53–57. DOI: 10.1016/j.clinmicnews.2015.03.001.
2. Brooks D, Polubothu P, Young D, Booth MG, Smith A. Sepsis caused by bloodstream infection in patients in the intensive care unit: the impact of inactive empiric antimicrobial therapy on outcome. J Hosp Infect 2018;98(4):369–374. DOI: 10.1016/j.jhin.2017.09.031.
3. Wattal C, Javeri Y, Goel N, Dhar D, Saxena S, Singh S, et al. Convergence of minds: for better patient outcome in intensive care unit infections. Indian J Crit Care Med 2017;21(3):46–51. DOI: 10.4103/ijccm.IJCCM_365_16.
4. Morgan DJ, Malani P, Diekema DJ. Diagnostic Stewardship-Leveraging the laboratory to improve antimicrobial use. JAMA 2017;318(7):607–608. DOI: 10.1001/jama.2017.8531.
5. Edmiston CE, Garcia R, Barnden M, DeBaun B, Johnson HB. Rapid diagnostics for bloodstream infections: a primer for infection preventionists. Am J Infect Control 2018;46(9):1060–1068. DOI: 10.1016/j.ajic.2018.02.022.
6. Kalantari A, Rezaie SR. Challenging the one-hour sepsis bundle. West J Emerg Med 2019;20(2):185–190. DOI: 10.5811/westjem.2018.11.39290.
7. Bouza E, Sousa D, Rodríguez-Créixems M, Lechuz JG, Muñoz P. Is the volume of blood cultured still a significant factor in the diagnosis of bloodstream infections? J Clin Microbiol 2007;45(9):2765–2769. DOI: 10.1128/JCM.00140-07.
8. Cockerill FR 3rd, Wilson JW, Vetter EA, Goodman KM, Torgerson CA, Harmsen WS, et al. Optimal testing parameters for blood cultures. Clin Infect Dis 2004;38(12):1724–1730. DOI: 10.1086/421087.
9. Tarai B, Das P, Kumar D, Budhiraja S. Comparative evaluation of paired blood culture (aerobic/aerobic) and single blood culture, along with clinical importance in catheter versus peripheral line at a tertiary care hospital. Indian J Med Microbiol 2012;30(2):187–192. DOI: 10.4103/0255-0857.96689.
10. Gautam V, Saigal K, Awasthy V, Ray P. Analysis of samples processed in automated blood culture system with blood culture samples processed by conventional manual method. Correspondence. Indian J Med Microbiol 2016;34(3):401–403. DOI: 10.4103/0255-0857.188379.
11. Gonsalves WI, Cornish N, Moore M, Chen A, Varman M. Effects of volume and site of blood draw on blood culture results. J Clin Microbiol 2009;47(11):3482–3485. DOI: 10.1128/JCM.02107-08.
12. Wattal C, Goel N. Correction to: pediatric blood cultures and antibiotic resistance: an overview. Indian J Pediatr 2020;87(2):486. DOI: 10.1007/s12098-019-03123-y.
13. Wilson ML, Mitchell M, Morris AJ, Murray PR, Reimer LG, Reller LB, et al. Principles and procedures for blood cultures; approved guidelines, CLSI document M47-A, vol. 27. Wayne, PA: Clinical and Laboratory Standard Institute; 2007. https://clsi.org/standards/products/microbiology/documents/m47/
14. Hall KK, Lyman JA. Updated review of blood culture contamination. Clin Microbiol Rev 2006;19(4):788–802. DOI: 10.1128/CMR.00062-05.
15. Veeraraghavan B, Walia K. Antimicrobial susceptibility profile & resistance mechanisms of Global Antimicrobial Resistance Surveillance System (GLASS) priority pathogens from India. Indian J Med Res 2019;149(2):87–96. DOI: 10.4103/ijmr.IJMR_214_18.
16. González-López JJ, Piedra-Carrasco N, Salvador F, et al. ESBL-producing Salmonella enterica serovar Typhi in traveler returning from Guatemala to Spain. Emerg Infect Dis 2014;20(11):1918–1920. DOI: 10.3201/eid2011.140525.
17. Pokharel BM, Koirala J, Dahal RK, Mishra SK, Khadga PK, Tuladhar NR. Multidrug-resistant and extended-spectrum beta-lactamase (ESBL)-producing Salmonella enterica (serotypes Typhi and Paratyphi A) from blood isolates in Nepal: surveillance of resistance and a search for newer alternatives. Int J Infect Dis 2006;10(6):434–438. DOI: 10.1016/j.ijid.2006.07.001.
18. Gray J, Oppenheim B, Mahida N. Preventing healthcare-associated Gram-negative bloodstream infections. J Hosp Infect 2018;98(3):225–227. DOI: 10.1016/j.jhin.2018.01.008.
19. Saksena R, Gaind R, Sinha A, Kothari C, Chellani H, Deb M. High prevalence of fluoroquinolone resistance amongst commensal flora of antibiotic naïve neonates: a study from India. J Med Microbiol 2018;67(4):481–488. DOI: 10.1099/jmm.0.000686.
20. Kaur H, Singh S, Rudramurthy S, Ghosh AK, Jayashree M, Narayana Y, et al. Candidaemia in a tertiary care centre of developing country: monitoring possible change in spectrum of agents and antifungal susceptibility. Indian J Med Microbiol 2020;38(1):110–116. DOI: 10.4103/ijmm.IJMM_20_112.
21. Cointe A, Walewski V, Hobson CA, et al. Rapid carbapenemase detection with Xpert Carba-R V2 directly on positive blood vials. Infect Drug Resist 2019;12:3311–3316. DOI: 10.2147/IDR.S204436.
22. Langdon A, Crook N, Dantas G. The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation. Genome Med 2016;8:39. DOI: 10.1186/s13073-016-0294-z.
23. Hall RA, Noverr MC. Fungal interactions with the human host: exploring the spectrum of symbiosis. Curr Opin Microbiol 2017;40:58–64. DOI: 10.1016/j.mib.2017.10.020.
24. Daliri EB, Tango CN, Lee BH, Oh DH. Human microbiome restoration and safety. Int J Med Microbiol 2018;308(5):487–497. DOI: 10.1016/j.ijmm.2018.05.002.
25. Meis JF, Chowdhary A. Candida auris: a global fungal public health threat. Lancet Infect Dis 2018;18(12):1298–1299. DOI: 10.1016/S1473-3099(18)30609-1.