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Original Research Article

Optimizing the number of blood cultures for lower and middle income countries: a large scale study in a public sector tertiary care teaching hospital of Southern India

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ABSTRACT

Background: Blood culture is widely accepted as the gold standard investigation for the diagnosis of blood stream infections (BSI). The number of blood cultures collected has a considerable impact on the organism isolation. This study aims to optimize the number of blood cultures needed, for an optimal diagnostic yield in BacT/ALERT VIRTUO system mainly in a resource limited setting.
Methods: All the blood cultures (BCs) obtained in BacT/Alert bottles per patient during a 24-h period were included as 'one episode' and categorized as single bottle, 1-set (2 aerobic bottles), 2 sets and 3 sets. BC bottles were incubated in the BacT/ALERT VIRTUO (bioMérieux) for a period of five days. Bottles flagged positive were subjected to Gram staining and culture plating. Colonies grown were identified by MALDI-TOF MS, VITEK MS, bioMérieux.
Results: Cumulative positivity rate increased (21.7%, 41.4%, 56.1%, 60.6%) and pathogen isolation rate increased (10.3%, 21.8%, 30.4% and 33.8%) progressively when collected in single bottle, 1, 2 and 3 sets respectively. The pathogen detection rate for GNB and GPC were 45.1% and 42.6% respectively with one bottle and this got upsurged to 85.6% and 98.9% for GNB and 83.6% and 98.2% for GPC when collected in ≤1 set and ≤2 sets respectively.
Conclusions: Two BC sets over a 24-h period can detect approximately 98% of the pathogens with a cumulative positivity rate of 60% and hence it is a justifiable alternative approach to the standard practice of 3-sets of BCs.

Keywords: Blood culture, Bloodstream infections, BacT/ALERT VIRTUO

INTRODUCTION

Bloodstream infections (BSIs) and sepsis pose a significant impact on global health. Although the global burden of sepsis is difficult to ascertain, World Health Organization (WHO) estimated that about 49 million cases of sepsis and 11 million sepsis-related deaths occur worldwide annually, accounting for almost 20% of all global deaths. Low- and middle-income countries (LMICs) account for approximately 85% of global sepsis burden.[1] Early and accurate diagnosis of BSIs is the cornerstone for institution of appropriate pathogen-directed antimicrobial therapy.

Despite of advancement in molecular techniques and biomarkers, blood culture is widely accepted as the gold standard investigation and the first line tool for the diagnosis of BSIs.[2,3] With the advent of continuous-monitoring blood culture systems (CMBCS), there has been a sustained improvement in the pathogen isolation in blood cultures.[4] In spite, there are a number of preanalytical factors which influence the outcome of a BC investigation-number of BCs drawn, method of skin asepsis, amount of blood volume, source of collection, timing of sampling with respect to antibiotic administration etc.[5] Among the factors stated above, the number of BCs collected has a considerable impact on

the organism isolation. Most guidelines recommend to obtain three sets (six bottles, 8-10mL per bottle) of blood culture for optimal pathogen recovery. Several studies in the literature stated that the diagnostic yield of blood cultures significantly improves with the increase of the number of blood cultures drawn (67%, 80% and 96% with 1, 2 and 3 sets of BCs respectively).[3,6] However, implementing the practice of drawing multiple sets of BCs is extremely difficult, particularly in LMICs, which may be attributed to financial, manpower, ethical and infrastructure-related constraints. The situation is more difficult in public sector settings catering to poor people, where it is often observed that clinicians tend draw only one or two BC bottles, which results in a very poor organism isolation.[7]

While drawing extraordinarily suboptimal specimen (1 BC bottle) definitely has a poor diagnostic yield, at the same time obtaining 3 sets of BCs appears to be far from reality in public sector facilities of LMICs.[6,7] It is also believed that the newer CMBCS such as BacT/ALERT VIRTUO may detect bacteremia at lower levels than older systems like BacT/ALERT.[8,9]

Therefore, this study has been undertaken to revisit the BC collection guideline, and to optimize the number of blood cultures needed, for an optimal diagnostic yield in BacT/ALERT VIRTUO system.

METHODS

This was prospective observational study conducted from May 2019 to April 2021 at diagnostic blood culture division, Department of Microbiology, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry.

Inclusion criteria

All the blood culture bottles received in the microbiology laboratory were included in the study.

Exclusion criteria

Blood culture bottles without appropriate labelling or mismatch between patient details on bottle and request form was excluded from analysis.

As this was a prospective study, sample size was not defined as we were collecting data from the entire samples received in the laboratory for the period of study duration.

The study was conducted as a part of routine investigation. As no additional sample was collected as part of project, ethical approval was not obtained as there were no active interventions which were done on a patient. It is purely a lab-based study which included only samples received in the laboratory for analysis without representing demographic details of the patient during analysis.

Procedure

BCs were obtained in BacT/Alert FA plus aerobic bottles at the bedside by the clinical team as per the standard collection protocol.[10] All the blood cultures obtained per patient during a 24-h period were included as ‘one episode’; the specimens obtained beyond 24h was considered as ‘separate episode’. In this study, blood culture set is defined as the combination of two aerobic BC bottles.[11] The clinical significance (true infection versus contamination) of the positive blood culture was determined by bedside visit through pathogen-directed antimicrobial stewardship (AMSP) audit, conducted by the microbiology resident doctors. BCs received at the microbiology laboratory were incubated in the BacT/ALERT VIRTUO (bioMérieux) CMBCS for a period of five days. Bottles flagged positive were subjected to Gram staining, followed by plating on suitable culture media and the colonies grown were identified by matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS, VITEK MS, bioMérieux).

Data collection and statistical analysis

The relevant data collected were entered in Microsoft Excel and statistical analyses were performed with IBM SPSS Statistics V22.0 software.[12] The parameters used for the comparison of BC performance when collected in single bottle and multiple samples (1, 2 and 3 sets) have been defined in Table 1.

Table 1: Parameters used for the comparison of BC performance collected in single bottle and multiple samples.

Parameters	Definition
Cumulative positivity rate	Number of BSI episodes where at least one BC bottle is flagged positive (pathogen *plus* contaminant) X100/Total BSI episodes
Pathogen isolation rate	Number of BSI episodes (at least one BC bottle) flagged positive for pathogens X100/Total BSI episodes
Contamination rate	Number of BSI episodes (at least one BC bottle) flagged positive for contaminants X100/Total BSI episodes
Sterile rate	Number of BSI episodes flagged negative (i.e. reported sterile) X100/Total BSI episodes
Pathogen detection rate	Number of a specific pathogen isolated from a particular set X 100/Total number of same pathogen isolated from all BSI episodes

The comparison of cumulative positivity rate, pathogen isolation rate, and pathogen detection rate between the episodes collected in single and multiple sets was carried out by using Kruskal–Wallis test (nonparametric).[12] Values of p <0.05 were considered as statistically significant. The agreement between increase in pathogen isolation rate and increase in contamination rate has been analysed by using Cohen's kappa statistics.[13]

RESULTS

A total of 55,825 BC bottles were collected during the study period, from 38,901 BSI episodes from 24,128 patients. The blood cultures received in single set, two and three sets and their cumulative positivity rate are depicted in the Table 2.

Table 2: The blood cultures received in different sets, and their cumulative positivity rate.

Blood culture bottles received	No. of BSI episodes (N=38,901)	*Cumulative positivity rate
Single BC bottle obtained	66.5% (25,869)	21.7 % (5616/25,869)
1 set (two bottles) obtained	26.9% (10,458)	41.4% (4331/10,458)
2 sets (four bottles) obtained	6.0% (2,358)	56.1% (1323/2,358)
3 sets (six bottles) obtained	0.6% (216)	60.6% (131/216)

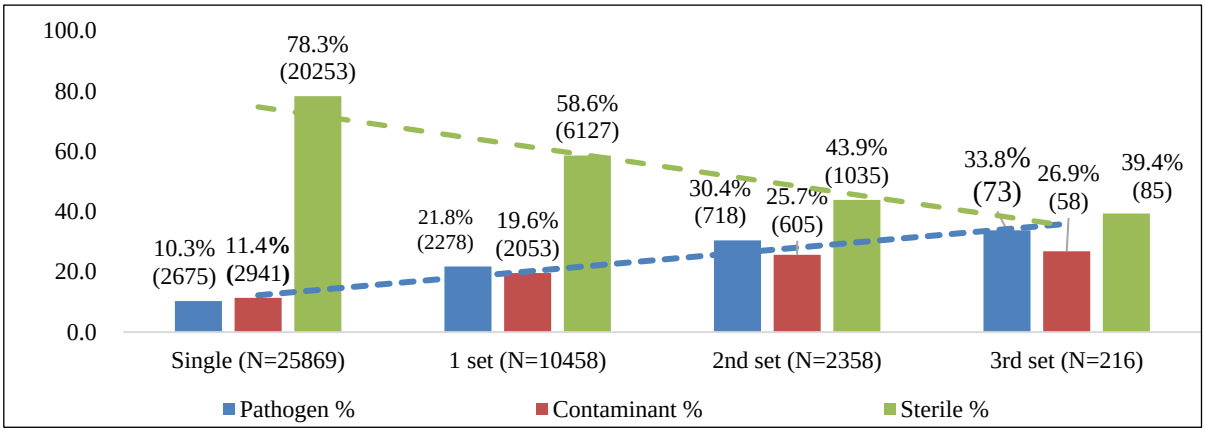

Figure 1: Comparison of outcome of blood culture investigation when collected in different sets.

Table 3: Comparison of pathogen isolation rates for the BSI episodes collected in multiple sets.

BSI episodes flagged positive for pathogens only	Isolation rate	Net gain
One set (two bottles) is obtained	10,458	
Total positive episodes	21.8% (2,278)	12.6%
Any one bottle flagged positive for pathogen	10.9%* (1,136)	
Both bottles flagged positive	10.9% (1,142)	
Yielded different organisms	1.7% *(178)	
Yielded same organism	9.2% (964)	
Two sets (four bottles) are obtained	2,358	
Total positive episodes (any one out of 4 bottles flagged positive)	30.4% (718)	8.3%
Only 1st set flagged positive	12.5% (294)	
Only 2nd set flagged positive	4.9%$ (115)	
Both sets flagged positive	13.1% (309)	
Yielded different organisms	3.4%$ (80)	
Yielded same organism	9.7% (229)	
Three sets (six bottles) are obtained	216	
Total positive episodes (any one out of 6 bottles flagged positive)	33.8% (73)	12.9%
Only 1st set flagged positive	5.1% (11)	
Only 2nd set flagged positive	3.2%# (7)	
Only 3rd set flagged positive	2.3% # (5)	
Any 2 sets flagged positive	8.3% (18)	
Yielded different organisms	0.9%# (2)	

Continued.

BSI episodes flagged positive for pathogens only	Isolation rate	Net gain
Yielded same organism	7.4% (16)	
All sets flagged positive	14.8% (32)	
Yielded different organisms	6.5%# (14)	
Yielded same organism	8.3% (18)	

Abbreviation: BSI, bloodstream infection; *sum of the values indicates net gain in the pathogen isolation rate when 1 set is supplemented; $sum of the values indicates net gain in the pathogen isolation rate when 2 sets are supplemented; #sum of the values indicates net gain in the pathogen isolation rate when 3 sets are supplemented

Table 4: Pathogen detection rate (i.e. frequency distribution of pathogens isolated) when collected in different sets.

Organisms recovered	Frequency distribution of pathogen isolated		
	Single bottle	**≤ 1 set received***	**≤ 2 sets received****
Gram-negative bacilli group (N=4269)	45.1% (1927)	85.6% (3653)	98.9% (4224)
Escherichia coli (N=925)	47.9% (443)	84.9% (785)	98.6% (912)
Klebsiella pneumoniae (N=840)	45.1% (379)	85.6% (719)	98.8% (830)
Enterobacter spp. (N=164)	39.0% (64)	87.2% (143)	98.8% (162)
Salmonella spp. (N=86)	64.0% (55)	89.5% (77)	100.0% (86)
Other Enterobacterales (N=126)	43.6% (55)	88.1% (111)	99.2% (125)
Acinetobacter baumannii (N=759)	41.0% (311)	84.6% (642)	98.7% (749)
Other *Acinetobacter* spp. (N=146)	45.2% (66)	82.9% (121)	100.0% (146)
Pseudomonas aeruginosa (N=341)	42.2% (144)	86.5% (295)	99.1% (338)
Other *Pseudomonas* spp. (N=247)	47.0% (116)	83% (206)	98.4% (243)
Burkholderia spp. (N=139)	23.7% (33)	82.7% (115)	99.3% (138)
Stenotrophomonas spp. (N=148)	41.2% (61)	87.8% (130)	100.0% (148)
Elizabethkingia spp. (N=176)	73.3% (129)	95.5% (168)	100.0% (176)
Other Non-enterobacterales (N=172)	41.3% (71)	82.0% (141)	99.4% (171)
Gram-positive cocci group (N=1465)	42.6% (624)	83.6% (1224)	98.2% (1438)
Staphylococcus aureus (N=589)	43.8% (258)	85.2% (502)	98.1% (578)
Enterococcus spp. (N=551)	39.4% (217)	82.9% (457)	98.9% (545)
Streptococcus pyogenes (N=69)	37.7% (26)	82.6% (57)	98.6% (68)
Streptococcus pneumoniae (N=67)	62.7% (42)	91.0% (61)	98.5% (66)
Streptococcus agalactiae (N=23)	52.2% (12)	78.3% (18)	100.0% (23)
Viridans Streptococci (N=166)	41.5% (69)	77.7% (129)	95.1% (158)
Yeast (N=447)	44.1% (197)	85.2% (381)	98.4% (440)
Total (N=6181)	44.5% (2748)	85.1% (5258)	98.7% (6102)

*≤1 set received includes the no. of episodes in which bottles received as single bottles + 1 set; **≤2 sets received includes the no. of episodes in which bottles received as single bottles + 1 set + 2 sets

Figure 1 depicts the comparison of outcome of blood culture investigation when collected in different sets. The pathogen isolation rate was increased when collected in multiple sets (21.8%, 30.4% and 33.8% for 1, 2 and 3 sets respectively) compared to when collected in single bottle (10.3%). At the same time, there was a steady decline in the false negative episodes-78.3% of single bottle collections were reported as sterile; as compared to 58.6%, 43.9% and 39.4% of episodes of 1, 2 and 3 sets collections respectively were reported as sterile.

Table 3 describes the comparison of pathogen isolation rates for the BSI episodes collected in multiple sets. Out of the episodes where BC were collected in one set, the net gain in the positivity rate was about 12.6% when the second bottle was implemented-10.9% of episodes flagged positive for any one bottle and 1.7% of episodes flagged positive for both bottles but yielded different organisms. Among the BSI episodes with two sets (four bottles) of BCs collected, the net gain in the positivity rate of 2nd set was found to be 8.3-4.9% of episodes flagged positive only for the 2nd set and 3.4% of episodes flagged positive for both the sets, but yielded different organisms. Amid the episodes with three sets (six bottles) of BCs collected, the net gain in the positivity rate was 12.9% when multiple sets were supplemented.

The impact of multiple samples on pathogen detection rate (i.e. frequency distribution of pathogens) has been depicted in Table 4. Out of all gram-negative bacilli isolated during the study period, 45.1% were isolated from the episodes received with one bottle, whereas 85.6% and 98.9% were isolated from the episodes

received with ≤1 set and ≤2 sets respectively. Likewise, the pathogen detection rate for gram-negative cocci group also upsurged from 42.6% (when collected in single bottle) to 83.6% and 98.2% when collected in ≤1 set and ≤2 sets respectively. Individual organism analysis also revealed a concordance finding of increase in the detection rate of most of the pathogens with the increase in the number of bottles sampled-highest yield was observed for *Burkholderia* spp. and *Streptococcus pyogenes*. Only a minor proportion of organisms (1.1% of gram-negative and 1.8% of gram-positive) were additionally detected when the 3rd set was supplemented.

DISCUSSION

Blood culture (BC) has been regarded as the lifesaving gold standard investigation for patients with bloodstream infection (BSI), who are often found to be critically ill with a higher risk of morbidity and mortality.[14,15] There are several pre-analytical factors which determine the performance of BCs; out of which the most critical parameter is optimal sampling.[5] Most guidelines recommend to obtain two to three BC sets over a 24-h period for the optimal detection of BSIs.[3,6,16] Although the isolation rate increases with multiple sampling; the financial and ethical restrictions make this strategy difficult to implement, especially in LMICs and public sector facilities catering to poor people.[7] With the advent of newer CMBCS such as BacT/ALERT VIRTUO, the isolation rate has been reported to be increased.[8,9] Therefore, this study has been commenced to determine the number of blood cultures optimally needed for a LMIC public sector setting, to achieve a reasonable diagnostic yield when BacT/ALERT VIRTUO system is used.

In the present study, a substantial proportion of the BSI episode (66.5%) were collected in single BC bottle; whereas multiple samples were obtained only from the remainder of episodes (26.9% in 1-set, 6.0% in 2-sets and 0.6% in 3-sets) (Table 2). This points towards an urgent need of intensified continuous educational intervention to persuade the clinical team to draw BCs in multiple sets. The cumulative positivity rate was significantly increased when collected in multiple sets: 21.7% vs 41.4%; between 1 bottle and 1-set (p value<0.0000001), 41.4% vs 56.1%; between 1-set and 2-sets (p value<0.0000001). However, the increase was not found to be significant between 2-sets and 3-sets (i.e. 56.1% vs 60.6%; p value =0.1979).

We also observed that the pathogen isolation rate was gradually increased when collected in multiple sets compared to single bottle [10.3% vs 21.8%; between 1 bottle and 1-set (p value<0.0000001), 21.8% vs 30.4%; between 1-set and 2-sets (p value<0.0000001)]; with a concordance steady decline in the false negative episodes [78.3% vs 58.6%; between 1 bottle and 1-set (p value<0.0000001), 58.6% vs 43.9%; between 1-set and 2-sets (p value<0.0000001)]. There was also decline in false negative episodes [43.9% vs 39.4%; (p value=0.1979)] and increase in pathogen isolation rate [30.4% vs 33.8%; (p value=0.3095)] between 2-sets and 3-sets, but not statistically significant. (Figure 1). The increase in the pathogen isolation rate was attributed to one of the following reasons: (i) obtaining multiple samples would increase the total volume of blood cultured, thereby improving the isolation.[3,17,18], (ii) obtaining multiple samples over 24 hours may improve the isolation for the episodes with intermittent bacteremia.[3,14,17], (iii) repeat isolation of same organism of uncertain pathogenicity in multiple samples may help in ascertaining its pathogenicity (discriminating the pathogens from contaminants); subsequently reporting of these organisms as 'pathogen' in the clinical report.[19,20] Several other studies in the literature reported a similar finding of increased pathogen isolation with a decrease in false negative reports when multiple samples were drawn.[3,7,17,18]

We also analysed the net gain in the pathogen positivity rates of the BSI episodes when multiple bottles were supplemented (Table 3). Out of the episodes collected in one set, the net gain in the positivity rate when the second bottle was implemented was about 12.6%. Similarly, among the episodes collected in two and three sets of BCs, the net gain in the positivity rate when the second bottle 8.3% and 12.9% respectively when multiple sets were supplemented. The gain in the positivity rate was partly attributed to more number of supplemented bottles flagged positive for the pathogens for the episodes in which the first set was flagged negative and also to some extent because of additional organisms recovered from the supplemented sets (i.e. polymicrobial infections) as compared to the first set for the episodes in which all the sets were flagged positive. This observation was seconded by several other studies in the literature.[6,7,12,21]

The frequency distribution of pathogens (detection rate) isolated when collected in multiple sets was evaluated (Table 4). Out of all organisms isolated during the study period, only minor proportion (42-45%) were isolated from the BC episodes received with one BC bottle, as compared to the BC episodes received with ≤1 set (83-85%) and ≤2 sets (~98%) with a net gain of pathogen detection of about ~40% and ~13% when one set is collected compared to single bottle and 2nd set is added to 1st set BC respectively. This observation was found to be true for most of the gram-negative, gram-positive organisms and yeast isolated. Several other authors published diverse results of positivity rate-85.6% (1 set), 96.5% (2 sets) and 100% (3 sets) by Elantamilan et al; 80.1% (1 set), 93.9% (2 sets) and 96.9% % (3 sets) by Lee et al.[12,21] Few studies showed that sampling BC in 1 set vs 2 sets vs 3 sets was associated with positivity rate of 65.0-75.7%, 80.4-89.2%, and 95.7-97.7%, respectively.[21-24] The difference in the positivity rate in our study could be attributed to use of an advanced automated blood culture system 'BacT/ALERT VIRTUO system' which claims to be superior in detection rate than

other systems.[8,9] These finding suggests that in a resource-constrained setting of LMICs, obtaining two sets of BCs within 24 hours is a reasonable alternative approach. Literature search revealed that numerous studies suggested different recommendations for optimal BC sampling-while some studies recommended at least two separate sets of BCs sampled during a 24-h period for the optimal diagnosis of BSIs; several other studies and guidelines recommended three to four BC sets.[21-23,25-27,16,28-29]

This study has few limitations. The impact of other pre-analytical factors such as blood volume, antibiotic administration with respect to collection, sample transport time and collection technique on pathogen isolation rate were not studied. However, the similar rates of growth observed in the two bottles of a set (1st vs 2nd, 3rd vs 4th and 5th vs 6th bottles) suggest that these parameters would not have differed significantly among individual bottles. Second, the sample size was too small for the BC episodes in which 3 sets were collected, compared to the BC episodes where one or two sets were collected.

CONCLUSION

The outcomes of the present study indicate that two BC sets over a 24-h period can detect approximately 98% of pathogens (detection rate) with a cumulative positivity rate of 60%. In LMICs, there is an existing practice of sending only single BC bottle despite frequent education and request. This practice is highly discouraged because of extremely poor isolation of pathogens. In a resource-limited setting (e.g. LMICs) with financial constraints, obtaining 2-sets of BCs within 24 hours may be a justifiable alternative approach to the standard practice of 3-sets of BCs; especially for the laboratories using the automated continuous-monitoring blood culture systems like BacT/ALERT VIRTUO system. However, other pre-analytical factors should be adjusted appropriately such as adequate blood volume (8-10mL per adult BC bottle), drawing sample prior to antibiotic administration, sample transport time of <2h etc.

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REFERENCES

1. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395(10219):200-11.
2. Peker N, Couto N, Sinha B, Rossen JW. Diagnosis of bloodstream infections from positive blood cultures and directly from blood samples: recent developments in molecular approaches. Clin Microbiol Infect. 2018;24(9):944-955.
3. Lamy B, Dargère S, Arendrup MC, Parienti JJ, Tattevin P. How to Optimize the Use of Blood Cultures for the Diagnosis of Bloodstream Infections? A State-of-the Art. Front Microbiol. 2016;7:697.
4. Gonzalez MD, Chao T, Pettengill MA. Modern blood culture: management decisions and method options. Clin Lab Med. 2020;40(4):379-392.
5. Willems E, Smismans A, Cartuyvels R, Coppens G, Van Vaerenbergh K, Van den Abeele AM, et al. The preanalytical optimization of blood cultures: a review and the clinical importance of benchmarking in 5 Belgian hospitals. Diagn Microbiol Infect Dis. 2012;73(1):1-8.
6. Rothe K, Spinner CD, Ott A, Querbach C, Dommasch M, Aldrich C, et al. Strategies for increasing diagnostic yield of community-onset bacteraemia within the emergency department: A retrospective study. PLoS One. 2019;14(9):e0222545.
7. Ombelet S, Barbé B, Affolabi D, Ronat JB, Lompo P, Lunguya O, et al. Best practices of blood cultures in low- and middle-income countries. Front Med (Lausanne). 2019;6:131.
8. Jacobs MR, Mazzulli T, Hazen KC, Good CE, Abdelhamed AM, Lo P, et al. Multicenter clinical evaluation of BacT/Alert virtuo blood culture system. J Clin Microbiol. 2017;55(8):2413-21.
9. Menchinelli G, Liotti FM, Fiori B, De Angelis G, D'Inzeo T, Giordano L, et al. In vitro Evaluation of BACT/ALERT® VIRTUO®, BACT/ALERT 3D®, and BACTEC™ FX automated blood culture systems for detection of microbial pathogens using simulated human blood samples. Front Microbiol. 2019;10:221.
10. WHO. Guidelines on drawing blood: best practices in phlebotomy, 2010. Available at: https://www.ncbi.nlm.nih.gov/books/NBK138650/pdf/Bookshelf_NBK138650.pdf.
11. Riley JA, Heiter BJ, Bourbeau PP. Comparison of recovery of blood culture isolates from two BacT/ALERT FAN aerobic blood culture bottles with recovery from one FAN aerobic bottle and one FAN anaerobic bottle. J Clin Microbiol. 2003;41(1):213-7.
12. Elantamilan D, Lyngdoh VW, Khyriem AB, Rajbongshi J, Bora I, Devi ST, et al. Comparative evaluation of the role of single and multiple blood specimens in the outcome of blood cultures using BacT/ALERT 3D (automated) blood culture system in a tertiary care hospital. Indian J Crit Care Med. 2016;20(9):530-3.
13. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb). 2012;22(3):276-82.
14. Seifert H. The clinical importance of microbiological findings in the diagnosis and

management of bloodstream infections. Clin Infect Dis. 2009;48 Suppl 4:S238-45.
15. Prowle JR, Echeverri JE, Ligabo EV, Sherry N, Taori GC, Crozier TM, et al. Acquired bloodstream infection in the intensive care unit: incidence and attributable mortality. Crit Care. 2011;15(2):R100.
16. Clinical and Laboratory Standards Institute (CLSI). Principles and Procedures for Blood Cultues; Approved Guideline. CLSI document M47-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2007.
17. Lamy B, Roy P, Carret G, Flandrois JP, Delignette-Muller ML. What is the relevance of obtaining multiple blood samples for culture? A comprehensive model to optimize the strategy for diagnosing bacteremia. Clin Infect Dis. 2002;35(7):842-50.
18. Lin HH, Liu YF, Tien N, Ho CM, Hsu LN, Lu JJ. Evaluation of the blood volume effect on the diagnosis of bacteremia in automated blood culture systems. J Microbiol Immunol Infect. 2013;46(1):48-52.
19. MacGregor RR, Beaty HN. Evaluation of positive blood cultures. Guidelines for early differentiation of contaminated from valid positive cultures. Arch Intern Med. 1972;130(1):84-7.
20. Weinstein MP, Towns ML, Quartey SM, Mirrett S, Reimer LG, Parmigiani G, et al. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. Clin Infect Dis. 1997;24(4):584-602.
21. Lee A, Mirrett S, Reller LB, Weinstein MP. Detection of bloodstream infections in adults: how many blood cultures are needed?. J Clin Microbiol. 2007;45(11):3546.
22. Cockerill FR, Wilson JW, Vetter EA, Goodman KM, Torgerson CA, Harmsen WS, et al. Optimal testing parameters for blood cultures. Clin Infect Dis. 2004;38(12):1724-30.
23. 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):2765-9.
24. Lee A, Mirrett S, Reller LB, Weinstein MP. Detection of bloodstream infections in adults: how many blood cultures are needed? J Clin Microbiol. 2007;45(11):3546-8.
25. Patel R, Vetter EA, Harmsen WS, Schleck CD, Fadel HJ, Cockerill FR. Optimized pathogen detection with 30- compared to 20-milliliter blood culture draws. J Clin Microbiol. 2011;49(12):4047-51.
26. Li J, Plorde JJ, Carlson LG. Effects of volume and periodicity on blood cultures. J Clin Microbiol. 1994;32(11):2829-31.
27. Mermel LA, Maki DG. Detection of bacteremia in adults: consequences of culturing an inadequate volume of blood. Ann Intern Med. 1993;119(4):270-2.
28. Weinstein MP. Current blood culture methods and systems: clinical concepts, technology, and interpretation of results. Clin Infect Dis. 1996;23(1):40-6.
29. O'Grady NP, Barie PS, Bartlett JG, Bleck T, Carroll K, Kalil AC, et al. American College of Critical Care Medicine; Infectious Diseases Society of America. Guidelines for evaluation of new fever in critically ill adult patients: 2008 update from the American College of Critical Care Medicine and the Infectious Diseases Society of America. Crit Care Med. 2008;36(4):1330-49.
30. Baron EJ, Miller JM, Weinstein MP, Richter SS, Gilligan PH, Thomson RB, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2013 recommendations by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM)(a). Clin Infect Dis. 2013;57(4):e22-e121.

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