International Journal of Research in Medical Sciences
Wani K et al. Int J Res Med Sci. 2015 Aug;3(8):1863-1867
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20150292

Research Article

Role of blood culture in critically sick paediatric patients and its clinical impact: a tertiary care hospital based study

Khurshid Wani[1], Imran Gattoo[2]*, Kaiser Ahmed[3], Wasim Qadir[4]

[1]Associate Professor, Post Graduate department of Paediatrics, [2]Registrar, Post graduate department of Paediatrics, [3]Department of Microbiology, [4]Resident, Post Graduate Department of Pediatrics, Government Medical College Srinagar J&K, India

Received: 23 May 2015
Accepted: 26 June 2015

***Correspondence:**
Dr. Imran Gattoo,
E-mail: immz24@gmail.com

ABSTRACT

Background: Blood cultures form a critical part of evaluation of patients with suspected sepsis. The present study was undertaken to study the risk factors, duration of incubation for obtaining positive cultures, and the clinical impact of the culture report.
Methods: A total of 224 samples from 110 critically sick pediatric patients presenting with suspected bacteraemia were processed aerobically.
Results: Cultures were positive in 25.45% of the Patients. Most of the positive cultures were obtained after 24 hours of incubation of the broth and no isolates were obtained beyond day 4 of incubation. Therapy was modified in 52.73% of the patients after receipt of culture report.
Conclusions: Incubation beyond four days (unless with specific indication like enteric fever) may be unnecessary for issuing a negative culture report. Repeated isolation of doubtful pathogens confirms true bacteraemia. Early culture report increases therapeutic compliance.

Keywords: Blood culture, Clinical impact, Septicaemia, Bacteraemia

INTRODUCTION

The detection of microorganisms in a patient's blood has great diagnostic and prognostic significance. Blood cultures provide essential information for the evaluation of a variety of diseases like endocarditis, pneumonia, pyrexia of unknown origin and particularly, in patients with suspected sepsis.[1] Many infections in neonatal and pediatric age group can only be established on the basis of etiological agent recovered from blood. A positive blood culture does not necessarily confirm infection, since contamination of blood can occur. The recovery of organisms traditionally considered as pathogens pose no problems in interpretation. However, recovery of organisms such as coagulase negative staphylococci (CoNS), *Corynebacterium* or *Candida* spp. is often difficult to interpret.[2] Additional information like the density of bacteraemia, number of positive cultures, duration of incubation of the broth to obtain a positive culture, presence of risk factors or an underlying disease, is required in order to determine whether infection is truly present.

One key determinant in the ultimate outcome of patients with sepsis is institution of early and appropriate antimicrobial therapy. It is a common practice to institute early empirical therapy with broad spectrum antibiotics in patients presenting with clinical features suggestive of septicaemia or bacteraemia. Given the severity of septicaemia, such empirical therapy may be justified, but the specific therapy based on the antibiogram of the isolate will definitely improve the therapeutic outcome. Sometimes even after receiving antibiotic susceptibility

report, physicians may prefer to maintain the original regimen in the setting of clinical improvement.[3] There is conflicting information on how much attention the physician should pay to the cultures and antibiotic susceptibility reports.

The present study was undertaken to identify the bacteriological profile of bacteraemia in critically sick pediatric patients including neonates. An attempt has been made to identify the possible risk factors involved, to evaluate the importance of repeat isolation of bacteria of doubtful significance, and to determine the maximum duration of incubation of culture broth with periodic subcultures to isolate the significant pathogens. All the patients were followed up for the impact of culture report.

METHODS

The present study was carried out at a tertiary care paediatric referral hospital. A total of 110 paediatric in-patients (less than 18 years of age) including 22 neonates with suspected septicaemia or bacteremia were included in the study. Detailed history was taken to identify the possible risk factors. History of antibiotic usage empirically either before or after admission was also obtained.

Blood samples for culture were collected following strict aseptic precautions. If empirical antibiotics were already started, the collection was timed before the next dose of antibiotic was due or about half an hour before the predicted peak of temperature. A second set was also collected in all patients about an hour later from a different venipuncture site. Three sets were collected in cases of suspected or sonographically diagnosed congenital heart disease. About 1 mL of blood in case of neonates and about 5 mL in case of children was collected in each set. Immediately after collection, the blood was inoculated into brain heart infusion (BHI) broth without switching needles. The bottles containing 10 mL of BHI broth were used in case of neonates and 50 mL were used for other children to allow 1:10 dilution.[4-7]

The culture bottles were incubated at 37°C aerobically. After overnight incubation, the samples were subcultured onto blood agar, MacConkey's agar, and chocolate agar. If there was no growth observed on the plates by the next day, subcultures were again repeated from the broth on day 3, day 4 and finally on day 7.[4,6] If there was any growth, it was identified and antibiotic susceptibility tests were performed according to the standard methods. The culture reports were issued and the patients were followed up for clinical impact and modification of the therapy. Modification of antibiotic therapy was defined as addition or discontinuation of an antimicrobial agent within 48 hours after *in vitro* sensitivities were available and, as indicated in records, a change in therapy based on the blood culture report.[3]

RESULTS

A total of 224 samples from 110 children were processed. Cultures were positive in 28 (25.45%).

Table 1: Various isolates in order of frequency from blood cultures.

Bacteria isolated	No of patients
Klebseilla spp	8
Citrobactor spp	4
Staph. aureus	4
CONS	4
Acinitobactor	4
E.coli	1
Viridans Streptococci	1
Candida Albicans	1
Alkaligens fecalis	1
Total (110pts)	28 (25.45%)

The culture positivity rate was observed to be highest in neonates (52.63%). Risk factors were identified in 38 (42.72%) of the cases.

Table 2: Relation between risk factor identified and organism isolated.

Risk factor	No of pts	No of isolates	Microorganisms
Valvular heart disease	4	4	Staph.aureus (3),Viridans streptococci (1)
Long standing IV cannula	2	1	CONS(1)
Peritonites	1	1	CONS(1)
Meningites	6	0	-
Pneumonia	6	2	-
UTI	12	3	Klebseilla(2)
Post operative	2	3	Citrobactor (1), CONS(1)
Neonates	8	3	Klebseilla (2Citrobactor (1)
PEM	4	1	Acinitobactor(1)
Vaginal candidiasis in mother	1	1	Candida (1)

Administration of empirical antibiotics was already initiated by the time of collection of sample for culture in 73 (66.36%) of the cases. Of these, only 10 (9%) had positive cultures with delayed culture growth. The duration of incubation of the broth (24, 48 and 72 hours and 7 days) after which positive cultures were obtained on plating, was also noted.

None of the cultures were positive beyond 72 hours of incubation of the broth. Almost all the isolates were

sensitive to cephalosporins and amikacin, while one isolate of *Staphylococcus aureus* was resistant to β-lactams. All the culture reports were followed up and the clinical impact was studied in terms of change in antibiotic therapy and clinical outcome of the patients.

Table 3: Various isolates in relation to duration of incubation before plating.

Organism	24 hrs	48 hrs	72 hrs	7 days	Total
Klebseilla spp	5	1	-	-	6
Citrobactor spp	4	1	-	-	5
Staph. aureus	3	1	-	-	4
CONS	3	1	-	-	4
Acinitobactor	3	0	-	-	3
E.coli	-	1	-	-	1
Viridans Streptococci	-	1	-	-	1
Candida Albicans	1	-	1	-	1
Alkaligens fecalis	1	-	1	-	1
Total (107) pts	20	6	2	nil	28

Table 4: The clinical impact of clinical report.

Impact	Positive culture	Negative culture	Total
Initated treatment	4	2	6
Changed treatment	8	10	18
Stoped treatment	0	33	33
No change	14	30	44
LAMA	2	7	9
	28	82	110

DISCUSSION

Septicaemia is a clinical syndrome associated with considerable morbidity and mortality. The timely detection of bacteraemia can have a profound influence on the final clinical outcome. One blood culture set is rarely sufficient to establish or rule out bacteraemia, and multiple cultures could maximize sensitivity.[8] A numerical scoring system has also been proposed to evaluate positive cultures in multiple sets to identify true bacteraemia.[9] We have processed 224 samples from 110patients including 22 neonates. In our study, the total number of positive cultures was in 28 patients (25.45%) Neonates are particularly vulnerable to infections because of their weak immunological barrier. A high rate of positive cultures (52.63%) was observed in neonates, *Klebsiella* spp. being the most common (28.57%) isolate. A study by Jain et al, also showed similar findings.[10]

Although any localized infection can disseminate to the blood stream, the most common primary foci are intravascular devices, the respiratory tract, the urinary tract and various intra-abdominal sites. The source of bacteraemia and fungaemia cannot be determined in about one-third of the patients.[10] In the present study, risk factors were identified in only 46 cases, of which 16 (34.78%) had positive cultures ($P < 0.05$). The CoNS, previously considered as a contaminant, has been recognized increasingly as a cause of bacteraemia. The ascendance of this group of staphylococci has created increased interpretative difficulties for the clinician, since the great majority of CoNS isolates continue to represent contamination rather than true bacteraemia.[11] In the present study, CoNS was initially isolated in four cases, but repeat isolation confirmed only one. This isolate was from a patient with postoperative wound infection and longstanding central venous catheter. The positive predictive value for the isolation of CoNS in the present study is 25%.

Isolation of *S. aureus* from blood usually signifies infection, but persistent bacteraemia has been observed only in two of three cases in the present study, who were having underlying cardiac pathology (Table 2). According to one study, up to 57% of cases where *S. aureus* was repeatedly isolated will have a cardiac pathology and all such patients with *S. aureus* bacteraemia should be thoroughly evaluated for the presence of any cardiac pathology as the cardiac vegetations serve as an important source of persistant *S. aureus* bacteraemia.[12] In contrast, *Acinetobacter* spp. is considered as a contaminant but it can cause septicaemia as well. We isolated *Acinetobacter* spp. from a case who presented with protein energy malnutrition and gastroenteritits. This isolate was also confirmed by repeat isolation from the second set from a different venipuncture site.

Maternal factors should also be considered as contributory risk factors for neonatal septicaemias. We isolated *Candida albicans* from a case of neonatal septicaemia, where the mother of the baby was having vaginal candidiasis contributing to colonization of the baby. The baby was on empirical broad spectrum antibacterials, which would have contributed to invasive candidiasis. In recent years, an increased incidence of systemic fungal infections has been reported in hospitalized intensive care unit patients. Systemic candidiasis is commonest among them. An increased use of broad spectrum antibacterials, invasive lines, endotracheal tubes etc. in these patients helps *Candida* to bypass the natural barriers of infection and contributes to deep-seated infections with *Candida* spp. Systemic fungal infections, previously considered to be a rare complication, occur in as many as 5% of low birth-weight babies. They are even more frequently diagnosed in very low-birth-weight babies (VLBW) receiving intensive care. The sources of candidiasis in neonatal intensive care units are often endogenous following colonization of the babies with fungi. Candidaemia is defined as presence of positive blood culture for *Candida* spp, which was confirmed by another blood culture obtained from a peripheral venipuncture at a different site.[13-15] The

presence of candidaemia in the present case has been confirmed by the repeat isolation in the second set of blood cultures also.

Prior empirical antibiotic therapy before collection of the samples for culture may result in negative blood cultures. In the present study, empirical antibiotics were already started by the time of collection of samples for culture in 73 (66.36%) of the cases. Of these, only 6 (5.45%) had positive cultures as compared to 14 (12.72%) positive cultures from 36 patients who did not receive any antibiotics before collection of samples for blood culture ($P < 0.005$). The duration of incubation of the broth to obtain a positive culture was observed to be more among the samples from the patients who were already on antibiotics by the time of collection. This was observed for one isolate each of *Acinetobacter* spp. and *E. coli* (Table 3). Though this was an interesting finding, the number was too small for a statistical evaluation for its significance. Among the positive cultures, we have observed that 71.4% of cultures were positive by first subculture itself (after 24 hours of incubation of the BHI broth), 21.42% and 7.1% of the cultures were positive by second subculture (after 48 hours) and third subculture (after 72 hours), respectively, while virtually no isolates were obtained later (subculture on day 7). Reller *et al* ., suggested that incubation beyond 7 days is generally unnecessary with relatively few clinically significant isolates detected.[16] But, in a recent study, it has been shown that 99.5% of the isolates were detected by day 4 (after 72 hours of incubation of the BHI broth). The predictive value of blood cultures that were negative at day 4 was similar to that of waiting for seven days of processing before discontinuing therapy.[17]

The information provided by the culture report with antibiogram can help the clinician to initiate an effective regimen or change to a cost effective regimen. In one study, 16.36% of the patients were changed to a cost-effective therapy while no change was indicated in 40% of the patients.[3,18] We observed that the treatment had been modified in 52.72% of the cases (Table 4) after receipt of culture report. Though statistically not significant ($P > 0.05$), this is an interesting finding. The clinicians did not modify the treatment regimens in eleven cases with positive cultures and 31 cases with negative cultures as the patients were progressing well with their "empirical" therapy and they have almost reached the end of a particular course of antibiotics by the time the culture report was received. All the patients with negative cultures recovered normally, while four neonates with positive cultures died of septicaemia. Ten patients left the hospital against medical advice in which blood culture came positive in two cases and negative in eight cases. The modification of antibiotic therapy to a less aggressive and less expensive regimen (n = 10) or stopping the antibiotics completely (n = 34) after a negative culture report in these cases had no significant influence on the clinical outcome but saved them from the burden of the cost and side effects of "empirical" antibiotics.

Blood cultures provide a valuable guide to the clinician in identifying the etiological agent and selecting an appropriate antibiotic. The isolates of doubtful pathogenicity have to be confirmed by repeated isolation for better clinical correlation. Repeated isolation of *S. aureus* in blood cultures should prompt a thorough evaluation for any underlying cardiac pathology.

In a high burden and resource limited settings like several Government healthcare institutions in our country, four day processing of blood cultures would be sufficient as the number of isolates obtained after four days would be virtually nil and processing beyond four days (unless there is a clear indication like enteric fever) does not justify the time and cost involved in processing the samples. In addition, this approach will save the patient from the cost and risks of prolonged hospital stay or cost and toxicity of "empirical" drugs. In fact, if the microbiology laboratory gives an early blood culture report, it would definitely increase the physician's compliance for which a constant coordination and rapport between the microbiologist and the clinician are extremely essential.

ACKNOWLEDGEMENTS

The authors would like to thank the parents and the guardians who consented for the participation of their children in the study.

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

REFERENCES

1. Yagupsky P, Nolte FS. Quantitative aspects of septicaemia. Clin Microbiol Rev. 1990;3:269-79.
2. Philips SE, Bradley JS. Bactaeraemia detected by lysis direct plating in a neonatal intensive care unit. J Clin Microbiol. 1990;28:1-4.
3. Arbo MD, Snydman DR. Influence of blood culture results on antibiotic choice in the treatment of bacteraemia. Arch Intern Med. 1994;154:2641-5.
4. Doern GV, Brueggemann AB, Dunne WM, Jenkins SG, Halstead DC, McLaughlin JC. Four-day incubation period for blood culture bottles processed with the Difco ESP blood culture system. J Clin Microbiol. 1997;35:1290-2.
5. Leisure MK, More DM, Schwartzman JD, Hayden GF, Donowitz LG. Changing the needle when inoculating blood cultures: A no-benefit and high-risk procedure. JAMA. 1990;264:2111-2.
6. Washington JA 2 nd. Blood cultures: Principles and techniques. Mayo Clin Proc. 1975;50:91-8.

7. Reimer LG, Wilson ML, Weinstein MP. Update on detection of bacteraemia and fungaemia. Clin Microbiol Rev. 1997;10:445-65.
8. Aranson MD, Bor DH. Diagnostic decision: Blood cultures. Ann Intern Med. 1987;106:246-53.
9. Bates DW, Goldman L, Lee TH. Contaminant blood cultures and resource utilization: The true consequences of false-positive results. JAMA. 1991;265:365-9.
10. Roy I, Jain A, Kumar M, Agarwal SK. Bacteriology of neonatal septicaemia in a tertiary care hospital of Northern India. Indian J Med Microbiol. 2002;20:156-9.
11. Roberts FJ, Geere IW, Coldman A. A Three-year study of positive blood cultures with emphasis on prognosis. Reviews Infect Dis. 1991;13:34-46.
12. Weems J Jr. The many faces of Staphylococcus aureus infection. Postgrad Med. 2002;3:33-41.
13. Chakrabarti A, Singh K, Das S. Changing face of nosocomial candidaemia. Indian J Med Microbiol. 1999;17:160-6.
14. Rao S, Ali U. Systemic fungal infections in neonates. J Postgrad Med. 2005;51:527-9.
15. Singhi SC, Reddy TC, Chakrabarty A. Oral Itraconazole in the treatment of candidaemia in a pediatric intensive care unit. Indian J Pediatr. 2004;71:973-7.
16. Reller LB, Murray PR, MacLowry JD. Cumitech IA. Blood cultures II. Coordinating ed, J A Washington II. American Society of Microbiology, Washington DC; 1982.
17. Vinod Kumar CS, NeelaGaud YF. Incubation period for culture positivity to detect septicaemia in neonates: Correspondence. Indian J Med Microbiol. 2005;23:270-1.
18. Trenholme GM, Raymond LK, Karakusis PH, Stine T, Fuhrer J, Landau W, et al. Clinical impact of rapid identification and susceptibility testing of bacterial blood culture isolates. J Clin Microbiol. 1989;27:1342-5.

Cite this article as: Wani K, Gattoo I, Ahmed K, Qadir W. Role of blood culture in critically sick paediatric patients and its clinical impact: a tertiary care hospital based study. Int J Res Med Sci 2015;3(8):1863-7.