

Detection of *Bacteraemia* in an Inadequate Volume of Blood

AISHA M. SIDDIQUI, MRCP(UK)* AHMAD T. ELTAHAWY, MBCh, MSC, PhD**, and
AHMAD A. BAHNASSY, MSC, MSPH***

Department of Medicine, **Department of Microbiology, and *Department
of Community Medicine, Faculty of Medicine & Allied Sciences,
King Abdulaziz University, Jeddah, Saudi Arabia*

ABSTRACT. It was recently discovered that 15% of adult blood culture specimens at King Abdulaziz University Hospital were inadequate in volume where only 2 ml were collected instead of the required 8 ml using the Signal oxoid medium. A comparison of 263 matched pairs of standard-volume (8 ml) and low-volume (2 ml) blood cultures from adult patients in the medical ward and intensive care unit at King Abdulaziz University Hospital showed that standard-volume cultures had a higher detection rate for bloodstream infection than did low-volume cultures (89% compared with 69%; difference: 20%, $P = 0.01$). Our data show that the yield of blood cultures in adults increases approximately 3.3% per millilitre of blood cultured, and that the sensitivity of the standard-volume cultures is statistically higher than the sensitivity of the low-volume cultures (84% vs. 65%, $P < 0.01$).

Keywords: Blood, Blood culture, *Bacteraemia*

Introduction

To guide management of *Septicaemia*, clinicians understandably expect blood-culturing practices to be sensitive for the detection of *Bacteraemia* and *Candidemia*. The volume of blood drawn in adult patients is the most important single factor governing the sensitivity of blood cultures^[1-9], and 10 to 20 ml of blood per draw has been recommended^[4,6,10-12].

Correspondence & reprint requests to: Dr. A. Siddiqui, P.O. Box 80215, Jeddah 21589, Saudi Arabia.

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This recommendation is based on studies showing that during bloodstream infections, especially those in adults, there may be relatively few microorganisms present in a given volume of blood often in the range of < 1-10 colony forming unit (CFU) per millilitre^[10,13,14]. Moreover, in numerous studies of adult patients, a direct relationship between the diagnostic yield of blood cultures and the volume of blood cultured has been documented^[10]. It was discovered that 15% of adult blood culture specimens at King Abdulaziz University Hospital were inadequate in volume where only 2 ml were collected instead of the required 8 ml necessary to have a 10% dilution of blood with the culture media used, according to the requirements^[15-17]. Concerned that the low volumes of cultured blood might be compromising the sensitivity of blood cultures for detection of *Bacteraemia* in our adult patients, we studied the yield of low volume of blood used in culture media (2 ml) in comparison with adequate volume of blood (8 ml) in our adult patients in the medical ward and intensive care unit.

Materials and Methods

Blood specimens were collected from adult inpatients who had a temperature > 38.5°C or showed signs of *Septicaemia*. A standard-volume of blood culture specimen was defined as 8 ml of blood, and a low-volume specimen was defined as 2 ml of blood. Blood specimens were collected from peripheral veins using a strict aseptic technique and sterile equipment. The specimens were inoculated into the blood culture bottles, mixed with the medium, and incubated at 37°C for 7 days.

The medium was signal blood culture system (Oxoid) which was formulated to encourage growth of *Aerobic*, *Anaerobic*, and *Microaerophilic* organisms. It contained 80 ml of brain heart infusion broth and thioglycollate broth. Blood was injected aseptically through the central ring of the rubber stopper (a volume of 8 ml of blood was recommended by the manufacturer). The medium was designed to create pressure in the sealed bottle when organism growth is present. The medium did not contain any antibiotic removal device. To avoid contamination, no attempt was made to add such device to the culture medium. The presence of a positive pressure causes a quantity of the blood/broth mixture to be moved into the growth indicator chamber which is connected to the bottle after the blood specimen was added. A positive result is indicated when the blood/broth mixture rises above the green locking sleeve of the growth indicator device. Smears of the blood/broth were stained with gram stain and culture was done on to blood and chocolate agar plates. The isolated organisms were identified using standard methods^[18]. Gram-negative rods were identified using API 20 (Analytab).

Results

A total of 263 matched pairs of standard-volume (8 ml) and low-volume (2 ml) blood cultures were done. One hundred and sixty-nine (169) cases were males (64%), while 94 cases were female (36%). The nationality of the patients were: 113 Saudi

(43%) and 150 non-Saudi (57%). The mean age was 46 years ± 20.

Of the 263 matched pairs blood cultures, 36 (13.6%) were positive and 227 (86.4%) were negative. As shown in Table 1, 89% of the 36 positive blood cultures were detected by standard-volume cultures, whereas 69% were detected by low-volume cultures, a difference in the yield of 20% (P = 0.01).

TABLE 1. Yield of standard and low volume blood cultures in 36 positive bloodstream infections.

Variable	Classification of bloodstream pathogens					
	Gram positive		Gram negative		Total	
	No.	%	No.	%	No.	%
Organisms detected by standard volume cultures	16/18	89	16/18	89	32/36	89*
Organisms detected by low volume cultures	13/18	72	12/18	67	25/36	69

8 ml (CI 89%, 0.79 to 0.99)

2 ml (CI 69%, 0.53 to 0.84)

*P = 0.01

The respective sensitivities and specificities of standard and low-volume blood cultures in the detection of *Bacteraemia* is presented in Table 2. The standard-volume method had a fairly good sensitivity as it detected 84% from the positive cases and a high specificity where it detected 95.4% of the normal cases. The sensitivity of the low-volume method is significantly lower than that of the standard volume--65.6% vs. 84% (P = < 0.01).

TABLE 2. Sensitivity and specificity of the standard- and low-volume blood cultures.

	Low volume blood culture (2 ml)		
	Positive	Negative	Total
Standard volume blood culture (8 ml)			
positive	21	11	32
negative	4	227	231
Total	25	238	263

Sensitivity of 8 ml = 21/25 = 84%

Specificity of 8 ml = 227/238 = 95.38%

On the other hand, the low-volume culture showed a higher specificity than that of the standard-volume (98.3% vs. 95.4%, respectively), but this difference is not statistically significant (P = > 0.05).

Table 3 shows the list of the organisms by the species isolated from the blood cultures by each method. *Anaerobes* and *yeasts* were not isolated during the study period. Only 49 patients (19%) had clinical evidence of *Septicaemia*; 97 (37%) of the patients were on concomitant antibiotics. More than 85% of the cases had abnormal CBC, renal and liver function tests. The number of isolates were nearly similar in both culture

methods, but the standard-volume detected more organisms in patients with malignancies, congestive cardiac failure, and urinary tract infections (Table 4). Approximately 25% of the blood cultures were from diabetics.

TABLE 3. The species of microorganisms isolated from the blood culture by each method

Species	2 ml method (n = 25)	8 ml method (n = 32)
<i>Coagulate-negative staphylococci</i>	5	6
<i>Staphylococcus aureus</i>	6	8
<i>Streptococcus pneumoniae</i>	1	1
<i>Streptococcus morbillorum</i>	1	1
<i>Escherichia coli</i>	2	3
<i>Klebsiella pneumoniae</i>	5	6
<i>Enterobacter cloacae</i>	1	1
<i>Pseudomonas aeruginosa</i>	1	1
<i>Salmonella typhi</i>	1	2
<i>Salmonella species</i>	1	2
<i>Vibrio cholerae</i> non 0 1	1	1

TABLE 4. Number of positive blood cultures detected by both methods according to underlying diseases.

Underlying diagnosis	Total no. of cultures	%	+ve no. of cultures by 2 ml	%	+ve no. of cultures by 8 ml	%
Malignancy	40	15.2	2	5.0	4	10.0
Diabetes mellitus	63	24.0	11	17.5	10	15.9
Ischemic heart disease	27	10.3	3	11.1	3	11.1
Congestive cardiac failure	8	3.0	1	12.5	8	100.0
Bronchial asthma	11	4.2	2	18.2	1	9.1
Chest infection	42	16.0	4	9.5	4	9.5
Urinary tract infection	21	8.0	1	4.8	2	9.5
Others*	51	19.3	1	2.0	0	0.0

*Examples:

- Skin infections
- Eye infections
- Hypertension
- Connective tissue diseases
- Thyroid diseases

It was noticed that many patients had multiple underlying diseases, sources of infection, and multiple blood cultures. Intravenous cannulas, the gastrointestinal tract, and the respiratory tract, in this order, were the main sources of positive blood cultures by the two methods (Table 5). The source of *Bacteraemia* in the majority of the patients was determined microbiologically.

TABLE 5. Number of positive blood cultures detected by both methods according to source of infection.

Source of infection	Total no. of cultures	%	+ve no. of cultures by 2 ml	%	+ve no. of cultures by 8 ml	%
Urinary tract	18	18.0	2	11.1	2	11.1
Gastrointestinal tract	4	1.5	4	100.0	4	100.0
Respiratory tract	25	25.0	3	12.1	2	8.0
Intravenous cannula	19	7.2	16	84.2	19	100.0
Others*	72	---	---	---	5	6.9

*Examples: Skin infections, Eye infections, Ear infections, Throat infections.

Discussion

The yield of blood cultures from adults is clearly volume-dependent^[1-9] and increases approximately 3% for each additional millilitre of blood obtained^[3-4]. We found an increased yield of approximately 3.3% per millilitre in our study. The percentage of positive blood culture in our study (13.6%) compares favorably with the 11% reported by Li *et al*^[19]. Because about 15% of adult blood cultures in our hospital contained inappropriately low volumes of blood, and as has been proven in our study, we believe that a substantial number of bloodstream infections were reported negative.

The result of this study emphasizes the role of the microbiology laboratory in clinician education where few clinicians or nurses are aware of the prime importance of the volume of blood cultured per set for the successful detection of *Bacteraemia* or *Fungemia* in adult patients.

We conclude that in our study, the blood culture yield is largely volume-dependent and that the difference in the sensitivity between standard-volume and low-volume cultures is statistically significant.

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وجود التجزئ بكميات قليلة في مقدار الدم

عائشة صديقي*، أحمد الطحاوي**، وأحمد بهنسي***
 *قسم الطب، **قسم الكائنات الدقيقة، و***قسم طب المجتمع،
 كلية الطب والعلوم الطبية، جامعة الملك عبدالعزيز،
 جدة - المملكة العربية السعودية

المستخلص. اكتشف مؤخراً أن ١٥٪ من عينات مزرعة الدم للبالغين في مستشفى جامعة الملك عبدالعزيز كانت غير كافية حيث أن ٢ مل فقط من الدم قد جمع عوضاً عن ٨ مل المطلوبة في سيغنال اكسويد ميديم. أجريت مقارنة بين مزرعة ٢٦٣ عينة دم مزدوجة الكمية المعتادة (٨ مل) وكمية أقل (٢ مل) من مرضى البالغين منومين في عنبر الأمراض الباطنة والعناية المركزة في مستشفى جامعة الملك عبدالعزيز وقد شوهد أن حاصل مزرعة الكمية المعتادة من الدم كان أعلى من مزرعة الكمية القليلة من حيث اكتشاف تجزئ الدم (٨٩٪ مقارنة ب٦٩٪، فرق ٢٠٪، ٠,٠١) (أ). نتائجن تبين أن محصول مزارع الدم في البالغين تزيد تقريباً بنسبة ٣,٣٪ لكل مليليتتر من الدم وأن حساسية الكمية المعتادة من الدم للمزرعة إحصائياً أعلى من حساسية الكمية القليلة (٨٤٪ مقابل ٦٥٪، ٠,٠١) (أ).