Blood Culture Contaminants in a Paediatric Population

Retrospective study from a tertiary hospital in Oman

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Objective: Most children presenting with febrile illness require a blood culture to determine the causative organism as well as its sensitivity to antibiotics. However, false-positive results lead to unnecessary hospitalisations, prescriptions and tests. This study aimed to evaluate the impact of false-positive blood cultures among a paediatric population at a tertiary hospital in Oman.

Methods: This retrospective study included all 225 children <13 years old with positive blood cultures who presented to the Sultan Qaboos University Hospital, Muscat, Oman, between July 2011 and December 2013. Blood cultures were reviewed to determine whether they were true-positive or contaminated.

Results: A total of 344 positive blood cultures were recorded during the study period, of which 185 (53.8%) were true-positive and 159 (46.2%) were contaminated. Most true-positive isolates (26.5%) were coagulase-negative Staphylococcus spp. (CONS) followed by Escherichia coli (9.7%), while the majority of contaminated isolates were CONS (67.9%) followed by Streptococcus spp. (6.9%). Children with contaminated cultures were significantly younger (P < 0.001) while those with true-positive cultures required significantly more frequent hospital adsmissions, longer hospital stays and more frequent antibiotic prescriptions (P < 0.001 each).

Chronic illness and mortality was significantly more frequent among those with true-positive cultures (P < 0.001) while those with true-positive cultures required significantly more frequent hospital admissions, longer hospital stays and more frequent antibiotic prescriptions (P < 0.001 each).

Conclusion: In this population, CRP level was not an adequate marker to differentiate between true- and false-positive cultures.

Keywords: Blood Cultures; False Positive Reactions; Fever; Pediatrics; Length of Stay; C-Reactive Protein; Oman.

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Blood cultures are one of the most common investigations carried out among febrile children and are performed to identify the causative organism and determine its antibiotic sensitivity.\textsuperscript{1,2} However, differentiating between false-positive results and true pathogens is clinically challenging. Blood culture contamination is the predominant cause of false-positive blood cultures (FPBCs).\textsuperscript{2} Skin flora are the main source of blood culture contaminants, usually as a result of improper preparation of the collection site or sample handling.\textsuperscript{2,3}

In positive blood cultures, the prevalence of blood culture contamination is higher among paediatric patients, with the ratio of contaminants to true pathogens being equal.\textsuperscript{4} False-positive or contaminated blood cultures have significant clinical and financial consequences, including clinical misdiagnoses, the unnecessary administration of antibiotics, increased laboratory investigations, needless hospital admissions and extended hospital stays.\textsuperscript{2,5–8} As such, preventative measures—for example, special disinfectants, educational materials and phlebotomy training courses—are essential to minimise contamination rates.\textsuperscript{5,6}

The Sultan Qaboos University Hospital (SQUH) is one of two tertiary teaching hospitals located in Muscat, the capital of Oman. At SQUH, there are three paediatric wards with 24 beds each, a five-bed paediatric intensive care unit (ICU) and a 24-bed neonatal ICU. This study aimed to evaluate the impact of false-positive blood culture results on a paediatric population at SQUH, including rate of hospitalisation, length of hospital stay, use of antibiotics and indicators of morbidity and mortality.

**Methods**

This retrospective study included all 225 children >13 years old with documented positive blood cultures who presented to SQUH between July 2011 and December 2013. The blood cultures were taken as follows. A total of 2–5 mL of blood was collected from each patient through peripheral skin punctures after a standardised disinfection procedure. The blood samples inoculated in a BACTEC\textsuperscript{TM}/F line blood culture system (Becton, Dickinson and Company, Franklin Lakes, New Jersey, USA), which is a fully-automated walk-away testing system that uses a continuous monitoring instrument to agitate and incubate blood cultures bottles. Subsequently, microbial identification and susceptibility tests were performed using standard methods.\textsuperscript{9}

During the retrospective analysis, data on positive blood cultures were collected from the hospital information system and patient records. The blood culture results were then re-examined to determine whether they were true- or false-positives. Several organisms were immediately identified as significant or true-positive cultures because they are known to cause diseases in children.\textsuperscript{5,6,11} On the other hand, other organisms were presumed to be contaminants if they were rare or unusual causes of disease, particularly in the absence of any underlying disease in the patient, or identified among patients with intravascular catheters or indwelling vascular devices.\textsuperscript{6} Some organisms were considered equivocal and required a judgement decision by a clinical microbiologist to be classified as either pathogenic or a contaminant. In order to determine if a culture was true-positive, the following information was needed: the identity of the organism; the number of positive culture sets; the number of positive bottles within a set; the time needed for the organism to grow in the blood culture; the rate of growth in the blood culture; associated clinical and laboratory data; and the automated classification generated by the blood culture system.\textsuperscript{5,6,11} Table 1 shows the classification of various organisms as true-positive, false-positive or equivocal.

The demographic and clinical data of the patients was also collected, including age, gender, the date of the blood culture collection, the presence of any underlying chronic illnesses, the degree of fever (if present), hospital admissions, length of hospital stay, focus of infection, antibiotic prescriptions and mortality. A focus of infection was defined as a clear associated source of the infection detected during history-taking or a clinical examination, without the need for blood cultures. A change in antibiotic therapy was defined as any modification or interruption of an antibiotic prescription after a blood culture result was
reported. In addition, laboratory data at the time of blood collection were recorded, including white blood cell count (WBC), absolute neutrophil count (ANC) and C-reactive protein (CRP) levels.

Data were analysed using the Statistical Package for the Social Sciences (SPSS), Version 20, (IBM Corp., Armonk, New York, USA). Percentages of true- and false-positive blood cultures were determined. A Chi-squared test was used to compare categorical variables and an unpaired Student’s t-test or Mann-Whitney U test was used to compare numerical variables according to their normal distribution. The level of significance was set at an a priori two-tailed level of $P < 0.050$.

Ethical approval for this study was obtained from the Research & Ethics Committee of the College of Medicine & Health Sciences, Sultan Qaboos University (MREC #932).

### Results

A total of 344 positive blood cultures were identified among 225 patients. The median age of the patients was 1.8 years (interquartile range: 0.6–5.2 years old) and there were 112 males (49.8%) and 113 females (50.2%). The majority of the patients ($n = 109; 48.4%$) had no history of chronic illness [Table 2]. In total, 185 blood cultures (53.8%) were classified as significant/true-positive cultures and 159 (46.2%) were classified as contaminated/false-positive cultures. Among the true-positive cultures, most of the isolates were coagulase-negative $Staphylococcus$ spp. ([n = 49; 26.5%](#)) followed by $Escherichia coli$ ([n = 18; 9.7%](#)). For the contaminated cultures, the main isolates identified were coagulase-negative $Staphylococcus$ spp. ([n = 108; 67.9%](#)) and $Streptococcus$ spp. ([n = 11; 6.9%](#)) [Table 3].

Children with contaminated blood cultures were significantly younger than those with true-positive blood cultures (mean: 1.4 years versus 2.6 years, respectively; $P < 0.001$). Patients with true-positive blood cultures more frequently had chronic illnesses in comparison to those with false-positive cultures; this difference was statistically significant (82.7% versus 37.1%; $P < 0.001$). In addition, fever was significantly more common among true-positive cases than false-positive cases (77.8% versus 62.3%; $P = 0.002$). A focus of infection was more frequently observed among those with contaminated blood culture results (67.9% versus 29.2%; $P < 0.001$). Children with true-positive blood cultures were significantly more frequently hospitalised (67.6% versus 47.2%; $P < 0.001$), had longer hospital stays (median: 14 days versus 4 days, respectively; $P < 0.001$) and were more frequently

### Table 1: Classification of organisms isolated from positive blood cultures as true-positive, equivocal* or false-positive according to standard criteria6,10,11

| True-positive | Equivocal* | False-positive |
|--------------|-----------|---------------|
| $Acinetobacter baumannii$ | $Acinetobacter lwoffi$ | $Aerococcus viridans$ |
| $Candida krusei$ | $Acinetobacter haemolyticus$ | $Bacillus subtilis$ |
| $Candida tropicalis$ | $Alcaligenes faecalis$ | $Other Bacillus spp.$ |
| $Non-albicans Candida spp.$ | $CDC group Vb-3$ | $Brevundimonas domiina$ |
| $Citrobacter koseri$ | $Chryseobacterium indologenes$ | $Dermabacter hominis$ |
| $Enterobacter cloacae$ | $Chryseobacterium meningosepticum$ | $Dermacoccus nishinomiyaensis$ |
| $Enterococcus durans$ | $Citrobacter amalonaticus$ | $Kocuria kristinae$ |
| $Enterococcus raffinosus$ | $Delftia acidovorans$ | $Leifsonia aquatica$ |
| $Escherichia coli$ | $Diphtheroids$ | $Micrococcus luteus$ |
| $Haemophilus influenzae type B$ | $Emmepodobacter brevis$ | $Other Micrococcus spp.$ |
| $Klebsiella oxytoca$ | $Enterococcus faecium$ | $Propionibacterium acnes$ |
| $Klebsiella pneumoniae$ | $Moraxella spp.$ | $Staphylococcus caprae$ |
| $Morganella morgani$ | $Pantoea agglomerans$ | $Staphylococcus intermedia$ |
| $Neisseria meningitidis$ | $Pseudomonas spp. (including P. putida and P. stutzeri)$ | $Staphylococcus lugdunensis$ |
| $Proteus mirabilis$ | $Sphingomonas paucimobilis$ | $Staphylococcus pasteurii$ |
| $Pseudomonas aeruginosa$ | $Staphylococcus capitis$ | $Staphylococcus saprophyticus$ |
| $Salmonella enterica subsp. enterica$ | $Staphylococcus capitis subsp. urealyticus$ | $Staphylococcus warneri$ |
| $Other Salmonella spp.$ | $Staphylococcus epidermidis$ | $Streptococcus acidominimus$ |
| $Serratia marcescens$ | $Staphylococcus haemolyticus$ | $Streptococcus mitis$ |
| $Staphylococcus aureus$ | $Staphylococcus hominis$ | $Streptococcus salivarius$ |
| $MRSA$ | $Other coagulase-negative Staphylococcus spp.$ | $Streptococcus sobrinus$ |
| $Streptococcus bovis type II$ | $Stenotrophomonas maltophilia$ | $Other Streptococcus spp.$ |
| $Streptococcus pneumoniae$ | | |
| $Streptococcus pyogenes$ | | |

CDC = Centers for Disease Control and Prevention; MRSA = methicillin-resistant $Staphylococcus aureus$.

*A judgement decision as to whether these organisms are true pathogens or false-positive by a clinical microbiologist is needed.
In addition, the mortality rate was significantly higher among children with true-positive blood cultures (4.9% versus 0.0%; \( P = 0.004 \)). Children with true-positive blood cultures had significantly higher WBC (median: 10.9 x 10^9/L versus 4.9 x 10^9/L; \( P < 0.001 \)) and ANC (median: 4.9 x 10^9/L versus 1.9 x 10^9/L; \( P < 0.001 \)) values. However, there was no statistically significant difference in CRP levels between the two groups (\( P = 0.791 \)) [Table 4].

Discussion

Blood cultures are currently the gold standard method for the detection of bacteraemia; as such, the accurate interpretation of culture results—by differentiating contaminants from true pathogens—is critical for effective patient care.\(^{6,10,11}\) Often the identity of the organism that grows in a culture is a helpful clue as to whether it has been contaminated. The number of culture sets that grow organisms can also help to differentiate contamination from true infection; if only one of at least two sets grows an organism, this generally represents a contaminant.\(^{6,10,11}\) For true-positive bacteraemias, multiple sets will usually grow the same organism. Another method to detect contamination is to count the number of culture bottles that exhibit growth within a given set; theoretically, if only one bottle exhibits growth, the likelihood of contamination is greater, with an

### Table 2: Demographic and clinical data of children with positive blood cultures presenting to the Sultan Qaboos University Hospital, Muscat, Oman (N = 225)

| Characteristic                         | n (%)       |
|----------------------------------------|-------------|
| **Gender**                             |             |
| Male                                   | 112 (49.8)  |
| Female                                 | 113 (50.2)  |
| **Age at time of blood culture in years** |             |
| Range                                  | 0–13        |
| Median (IQR)                           | 1.8 (0.6–5.2)|
| **Chronic illness**                    |             |
| None                                   | 109 (48.4)  |
| Acute lymphoblastic leukaemia          | 32 (14.2)   |
| Chronic lung disease                   | 12 (5.3)    |
| Neurological disabilities              | 12 (5.3)    |
| Sickle cell disease                    | 11 (4.9)    |
| Aplastic anaemia                       | 4 (1.8)     |
| Inborn errors of metabolism            | 4 (1.8)     |
| Immune deficiencies                    | 4 (1.8)     |
| Other*                                 | 37 (16.4)   |

* IQR = interquartile range.
* Including perinatal asphyxia, graft-versus-host disease and renal diseases.

prescribed antibiotics (89.7% versus 59.7%; \( P < 0.001 \)). In addition, the mortality rate was significantly higher among children with true-positive blood cultures (4.9% versus 0.0%; \( P = 0.004 \)). Children with true-positive blood cultures had significantly higher WBC (median: 10.9 x 10^9/L versus 4.9 x 10^9/L; \( P < 0.001 \)) and ANC (median: 4.9 x 10^9/L versus 1.9 x 10^9/L; \( P < 0.001 \)) values. However, there was no statistically significant difference in CRP levels between the two groups (\( P = 0.791 \)) [Table 4].

### Table 3: Organisms isolated from positive blood cultures identified at the Sultan Qaboos University Hospital, Muscat, Oman (N = 344)

| Organism                     | True-positive cultures (n = 185) | False-positive cultures (n = 159) |
|------------------------------|---------------------------------|----------------------------------|
| **Organism**                 | n (%)                           | n (%)                            |
| Coagulase-negative Staphylococcus spp.* | 49 (26.5)                    | 108 (67.9)                     |
| Escherichia coli             | 18 (9.7)                        | 11 (6.9)                         |
| Staphylococcus aureus        | 15† (8.1)                       | 9 (5.7)                          |
| Klebsiella pneumoniae        | 13 (7.0)                        | Diphtheroids (n = 6 (3.8))       |
| Salmonella spp.              | 12‡ (6.5)                       | Viridans streptococci (n = 6 (3.8)) |
| Pseudomonas aeruginosa       | 9 (4.9)                         | Pseudomonas spp.* (n = 3 (1.9))  |
| Candida spp.                 | 8 (4.3)                         | Bacillus spp. (n = 2 (1.3))      |
| Enterobacter cloacae         | 8 (4.3)                         | Other§ (n = 14 § (8.8))          |
| Strepotococcus pneumoniae    | 8 (4.3)                         |                                 |
| Chryseobacterium spp.*       | 5 (2.7)                         |                                 |
| Streptococcus pyogenes       | 5 (2.7)                         |                                 |
| Other Pseudomonas spp.*      | 5 (2.7)                         |                                 |
| Serratia marcescens          | 4 (2.2)                         |                                 |
| Stenotrophomonas maltophilia*| 4 (2.2)                         |                                 |
| Acinetobacter spp.*          | 3 (1.6)                         |                                 |
| Enterococcus spp.*           | 3 (1.6)                         |                                 |
| Alcaligenes faecalis*        | 2 (1.1)                         |                                 |
| Citrobacter spp.*            | 2 (1.1)                         |                                 |
| Other Klebsiella spp.        | 2 (1.1)                         |                                 |
| Morganella morganii          | 2 (1.1)                         |                                 |
| Other¶                        | 8 (4.3)                         |                                 |

* Classified based on criteria proposed by Hall et al., MacGregor et al. and Weinstein et al.\(^{6,10,11}\) Including two cases of methicillin-resistant Staphylococcus aureus. Including five cases of Salmonella typhi. Including one case each of the following: Aerococcus viridians, Brevundimonas diminuta, Centers for Disease Control and Prevention group Vb-3, Delftia acidovorans*, Dermabacter hominis, Dermacoccus nishinomiyaensis, Gram-negative bacilli, Kocuria kristinae, Leifsonia aquatica, Moraxella spp.*, Neisseria spp.*, Pantoea agglomerans*, Propionibacterium acnes and a case of mixed growth of three organisms.

† Including one case each of the following: Diphtheroids*, Encephalobacter brevis*, Haemophiilus influenzae type b, Moraxella spp.*, Neisseria meningitidis, Proteus mirabilis, Sphingomonas paucimobilis* and Viridans streptococci*.
Blood Culture Contaminants in a Paediatric Population
Retrospective study from a tertiary hospital in Oman

Increase in the number of positive bottles increasing the predictive value for a true-positive blood culture. However, several studies have suggested that these criteria alone should not be used to differentiate true-positive results from contaminants.6,10,11 The quantity of growth of an organism in a given sample may also help determine the clinical significance of a culture result; in conjunction with specific clinical information, this may distinguish a true infection from a contaminated culture. Clinical and laboratory information is therefore essential to appropriately classify positive blood culture results.6,10,11 In recent decades, healthcare institutions increasingly utilise data warehousing technologies with automated classifications to increase the efficiency of blood culture surveillance and reporting systems.6,10,11

Many studies have confirmed the unfavourable impact of FPBC results on clinical management, patient-related costs and available resources.4,5,7,10,12–14 In many cases, the decision to admit a febrile child to hospital depends on blood culture results. In the current study, the rate of blood culture contamination was 46.2%; this result was inconsistent with those of previous studies (4.7–11%), which identified strict blood extraction techniques and culture differentiation criteria as factors contributing to low contamination rates.8,10,14 However, the rate of unnecessary hospital admissions in the current study (47.2%) was higher than rates reported by Segal et al. and Thuler et al. (24.4% and 26%, respectively).4,14 Waltzman et al. reported very low rates of FPBCRs (0.9%) and needless hospital admissions (8.0%), due in part to the exclusion of all patients with a suspected viral illness or a bacterial infection, other than otitis media.7

In the present study, hospital admissions, antibiotic prescriptions and changes in antibiotic regimens during hospital admission were significantly more frequent among children with true-positive cultures. Other studies have reported that FPBC results have a greater impact on unnecessary hospitalisations, antibiotic prescriptions and investigations.6,13,14 This may be because of the high percentage of patients with chronic illnesses in the current study. In addition, the presence of a focus of infection was identified among 67.9% of those with false-positive cultures, thus constituting a high number of unnecessary and unwarranted blood culture extractions.

In contrast to results reported by Thuler et al., the current study found significant associations between true-positive cultures and age, fever and WBC and ANC values.19 Segal et al. also reported

Table 4: Demographic, clinical and laboratory characteristics of cases with positive blood cultures identified at the Sultan Qaboos University Hospital, Muscat, Oman (N = 344)

| Characteristic                              | n (%)          | P value  |
|--------------------------------------------|----------------|----------|
| Median age at blood culture in years (IQR) | 2.6 (1.3–6.8)  | <0.001   |
| Gender                                     |                | 0.314    |
| Male                                       | 90 (48.6)      |          |
| Female                                     | 95 (51.4)      |          |
| Median length of stay in days (IQR)        | 14 (7–37)      | <0.001   |
| Chronic illness                            | 153 (82.7)     | <0.001   |
| Fever                                      |                |          |
| Any documented fever                       | 144 (77.8)     | 0.002    |
| High-grade†                                 | 96 (66.7)      | 0.001    |
| Focus of infection                         | 54 (29.2)      | <0.001   |
| Hospital admission                         | 125 (67.6)     | <0.001   |
| Antibiotics prescription                   |                |          |
| At all                                     | 166 (89.7)     | <0.001   |
| For >7 days†                               | 112 (67.5)     | <0.001   |
| Regimen changes during admission           | 37 (20.0)      | 0.004    |
| WBC in x10^9/L‡                            | 175§ (56.1)    | <0.001   |
| Range                                      | 0–39.8         | 1–29     |
| Median (IQR)                               | 10.9 (7.5–16.2)| 4.9 (1.5–11.2)|
| ANC in x10^9/L§                            | 175§ (56.1)    | <0.001   |
| Range                                      | 0–34           | 0.5–20   |
| Median (IQR)                               | 4.9 (2.5–8.7)  | 1.9 (0.2–6.1) |
| CRP level in mg/L§                         | 160 (64.8)     | 0.791    |
| Range                                      | 1–494          | 1–247    |
| Median (IQR)                               | 19 (0–118)     | 16 (4–64) |

IQR= interquartile range; WBC = white blood cell count; ANC = absolute neutrophil count; CRP = C-reactive protein.
"Among those with any documented fever.† Among those with antibiotic prescriptions. The total dataset for this variable was 312 due to missing data.‡ A total of 10 patients with haematological malignancy and very high cell counts were excluded.§ The total dataset for this variable was 247 due to missing data.
similar results to those of the present study. Lee et al. found a significant negative correlation between high CRP levels and blood culture contamination when comparing groups of adults visiting an emergency department (ED). Chiu et al. also found that WBC and CRP measurements were significant predictors of true-positive cultures among children in an ED setting. However, Shaoul et al. reported that only CRP level was a significant predictor of contamination, with neither WBC nor ANC values allowing differentiation between true-positive results and contaminated blood cultures in children. These three laboratory parameters may therefore help in differentiating true- and false-positive blood cultures, although CRP level was not found to be a statistically significant marker of contamination in the current study.

A possible reason for a high rate of culture contamination is the extraction of blood in overcrowded EDs. As SQUH has no dedicated phlebotomy team, blood extraction is usually the responsibility of nurses. Among young patients, paediatric nurses generally have more experience in extracting blood than ED nurses. In the ED, contamination of blood cultures collected by phlebotomists has been reported to be significantly lower than for those collected by non-phlebotomists (3.1% versus 7.4%). A dedicated and well-trained phlebotomy team is therefore highly recommended, especially for paediatric patients. At SQUH, the extraction of blood from intravenous catheters (IVCs) is common, with blood samples usually taken during the initial insertion or replacement of IVCs to minimise venipuncture among children in the ED or inpatient wards. However, this practice may result in a higher rate of blood culture contamination; Norberg et al. observed that blood culture contamination rates decreased significantly from 9.1% to 2.8% when specimens were drawn from a separate site other than those of newly inserted IVCs (P < 0.001). In addition, a young age was associated with increased contamination rates, regardless of the site of blood extraction; this may explain why patients were significantly younger than those with true-positive results. Interestingly, discarding the initial aliquot of blood (5–10 mL) when obtaining blood cultures from IVCs has not been found to reduce contamination rates.

The current study is subject to some limitations. First, it was performed in a single large tertiary care paediatric hospital; as the incidence of serious infections is higher in tertiary care centres, the results are therefore not generalisable to other types of hospitals or patient populations. Second, the data were sourced from a retrospective analysis of medical patient records. Finally, an estimation of the additional costs due to FPBC results of unnecessary admissions and investigations could not be ascertained.

### Conclusion

As FPBC results can lead to unnecessary hospitalisation, administration of antibiotic therapy and use of microbiological tests, it is essential to differentiate true pathogens from contaminated cultures. Healthcare providers should therefore be aware of preventative measures to reduce FPBC rates. Blood cultures should be taken from a site other than that of an IVC. In addition, a separate, dedicated and well-trained phlebotomy team is mandatory at all hospitals, especially for paediatric patients. In the current study population, CRP levels were not found to adequately differentiate between true- and false-positive blood cultures.

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### CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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