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The Outcome of Blood Cultures in Febrile Children Presenting at the Emergency Department

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Abstract

Background: An unknown number of children who attend an Emergency Department may have a serious underlying, systemic infection as a cause of their fever. Blood culture (BC) remains the gold standard approach to establish the diagnosis and presence of pathogens in a child with a suspected, serious bacterial infection. This study investigated the proportion of positive blood cultures and the correlation with basic laboratory investigations (C-reactive protein, white blood cell count, and absolute neutrophil count), prescription of antibiotics in patients visiting a pediatric emergency department in a primary hospital

Methods: A retrospective study in Qatar- Al Wakra Hospital- Pediatric Emergency Department, over one year. Patients younger than 3 months of age and patients with any form of immune deficiency were excluded.

Results: A total of 828 patients (median age 3.55 years) with fever (>38°C) or a history of fever (>38°C). 121 (14.6%) were later admitted to the pediatric ward; 10 (1.2%) to the pediatric intensive care unit and 4 (0.4%) to pediatric surgery. In total, positive blood culture was present in 20 (2.42%) children. Of these 20,4 (20%) were admitted to the pediatric ward, and 9 (45%) were observed in the hospital for less than 24 hrs and 7 (35.0%) were sent back home after a clinical assessment and the results of the initial laboratory tests. The referrals of patients with negative blood culture were similar. There were no differences in the mean value of absolute neutrophil counts or CRP measurement between patients exhibiting positive or negative BC.

Conclusion: The incidence of a positive BC in routine care of febrile patients in an emergency department setting is low, 2.42%. There were no significant differences in associated clinical laboratory results (WBC, CRP or ANC) or admission to hospital wards between the groups with positive or negative BC.

Keywords: Blood cultures; Bacteremia; CRP; Neutrophils; Antibiotics

Background

Fever is the most frequent reason for presentation at the pediatric emergency department (PED) [1-5]. The percentage of patients who attend the PED due to fever ranges from 10.5 to 25% [3]. Fever is an important clinical sign because of the association of an underlying infection, although most infections are viral. However, a small group of these children may have a serious bacterial infection as the cause of the fever [2,3,5-7]. One of the greatest challenges to physicians caring for febrile children in the PED is therefore the risk of an occult bacteremia (OB) [8,9]. The proportion of occult bacteremia is variable, and for children less than 3 years of age, it was estimated to be 3-10% in the pre-Hemophilus influenzae B (HiB) vaccine era. This figure has dropped after the introduction of the HiB vaccination and is currently 0.5% after the worldwide adoption of this vaccination program [10]. The mortality rate associated with bacteremia may be as high as 30% [11]. The clinical management of children older than 3 months of age, who present in the PED with fever, is still controversial [10,12]. There is great heterogeneity in the evaluation and the management practices of this group of patients, including the need for a complete blood count (CBC), measurement of C-reactive protein (CRP) and blood culture (BC) [2-4,6,7,13]. BC remains still the gold standard approach to determine the presence or absence of pathogens in a child with a suspected serious bacterial infection or fever of unknown origin [10,14-18]. However, the value of BC in febrile children in the ED has been questioned recently [10,19,20]. In hospital-based studies, the proportion of patients with a positive blood culture was less than 3% [16], even reported to be low as 2% [21]. However, another concern is that blood culture contamination rates in the ED are also substantial and may vary from 1 to 9% and may reach as high as 11%. The consequences of a false positive result include the unnecessary administration of antibiotic therapy, admissions to hospital, prolonged duration of hospitalization and the request of more laboratory tests [14,15,17,22]. It has been described that about 17% to 90% of children receive antibiotics for the common cold [23]. Unnecessary administration of antibiotics creates diagnostic confusion and is associated with increased antibiotic resistance [8,24]. In contrast, delayed antibiotic therapy may result in morbidity and mortality for children who do have a serious bacterial infection [16-19]. Consequently, the issue of the value of blood cultures for children presenting to the ED is an important one. Blood cultures are expensive, painful, and false positive results have many adverse consequences. This study will describe the proportion of positive BC in a population

of children with fever or history of fever, the prescription of antibiotics, the association to other markers of infection and the referral to hospital wards.

Subjects and Methods

This was a retrospective study carried out on patients who visited the Pediatric Emergency Department at Al Wakra Hospital (AWH), Qatar - over one year (01-06-2012 to 31-05-2013). The study was approved by the Institutional Review Board of Hamad Medical Corporation, Doha. Following this, a clinical chart review was conducted in order to determine the demographics, clinical presentations, treatment and the blood culture results. The information was entered into an electronic database and subsequently analyzed.

The study population included patients older than 3 months up to 14 years of age. Patients were excluded if they had any of the following: 1) age less than or equal to 3 months, 2) had a congenital or an acquired immune deficiency disease or a malignancy. The criteria to obtain a blood culture was fever (38°>C) or a history of fever and no signs of a focal, localized infection, e.g. pneumonia, UTI or tonsillitis/ear infection. Temperature was evaluated by tympanic measurement. Blood samples were collected under aseptic technique by well trained nurses and send for culture and other analysis [such as white blood cell count (WBC), absolute neutrophil counts ANC and C-reactive protein (CRP).

Statistical Analysis

The statistical analysis was carried out using descriptive statistics, including means and frequencies, and inferential statistics, that included using Student's t test and χ^2 test. Student's t test was used to test the significance of the differences between the mean values of two continuous variables. The χ^2 analysis was performed to test the differences in proportions of categorical variables between ≥2 groups. In 2 × 2 tables, the Fisher exact test replaced the χ^2 test if the assumptions underlying the χ^2 test were violated. The level of $p<0.05$ was considered as the cutoff value for significance. Data analysis was done using SAS software, version 9.4.

Results

The results of blood cultures (BC) taken over one year for 828 patients is presented in Table 1.

Characteristic	Number (%)
Gender	
Male	469 (56.6)
Female	359 (43.4)
Nationality	
Qatari	228 (27.5)
Non-Qatari	600 (72.5)
Age, years	
All, Median, (Range)	3.55 (0.25-13.83)
≤ 3	464 (56.0)
>3 to 6	205 (24.8)
>6 to 10	107 (12.9)
>10	52 (6.3)
Blood culture	
Positive	20 (2.42)
Negative	808 (97.6)
Antibiotic Use	
Before blood culture	83 (10.0)
After blood culture	559 (67.5)
Admissions	
Admission for observation (<24 hrs)	425 (51.3)
Admission to PICU	10 (1.2)

Admission to the pediatric ward	121 (14.6)
Admission to surgical ward	4 (0.4%)
Sent home within 2 hrs	273 (32.9)
Temperature 0C, Median (Range)	38.9 (36-41.4)
Duration of Fever (Days), Median (Range)	2.0 (1-30)
Laboratory Results	
WBC, Median (Range) (x103/ul)	11.5 (2.0-30.8)
ANC, Median (Range) (x103/ul)	6.8 (1.0-37.9)
CRP, Median (Range) (mg/L)	20.0 (1.0-417.0)

Table 1: Patient characteristics.

The ages of the patients range from 0.25 to 13.83 years and the median age was 3.55 years. Temperatures ranged from (36.0-41.4°C), with a mean of 38.82°C. The duration of fever ranged from 1 to 30 days, with a mean of 2.8 days. Those patients with a temperature below 38°C, where considered as febrile if there was a history of fever or a consumption of antipyretics prior to admission. Of the 828, 425 (51.3%) were observed in hospital less than 24 hrs and then discharged home. 121 (14.6%) were admitted to the pediatric ward, and 10 (1.2%) admitted to the pediatric intensive care unit (PICU), while 4 (0.4%) were admitted to pediatric surgery.

273 (22.9%) were sent home within 1-2 h, after the initial investigations' results were available (Figure 1). 83 (10.0%) received oral antibiotic before testing for BC, while 559 (67.5%) were started on empiric antibiotic treatment after the delivery of BC. 808 (97.6%) had negative BC, whereas 20 (2.42%) patients demonstrated a positive BC.

For the group with positive BC, the mean age was 2.90 ± 3.03 years, for negative BC was 3.56 ± 3.17 years, (P=0.3450). The mean temperature in positive and negative BC was 39.27°C and 38.8°C, respectively (P<0.05). 9 of these twenty patients (45.0%) were observed in hospital less than 24 hrs, 4 (20%) were admitted to the pediatric ward, and 2 (10.0%) received oral antibiotic treatment prior to obtaining a BC. 17 (85%) started antibiotic therapy after the BC.

The mean value of WBC in patients with positive BC was 14.97 and in patients with negative BC 12.97, (P=0.4402). The ANC was 8.44 in positive, and 7.87 in negative cultures, (P=0.6484). The CRP was 36.4 in patients with positive BC, while the value in patients with negative BC was higher, 46.99. However, this surprising difference was not significant (P=0.4326).

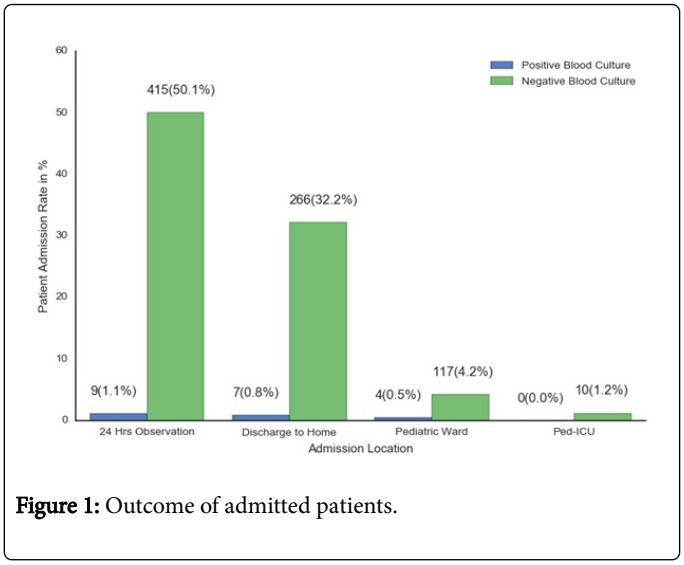

Figure 1: Outcome of admitted patients.

In summary, Table 2 demonstrates the comparison of the results for groups with positive and negative BC.

Characteristic	**Blood Culture**		**P-value**
	Positive Number (%)	**Negative Number (%)**	
Gender			
Male	14 (70.0)	455 (56.4)	0.2599
Female	6 (30.0)	352 (43.6)	
Nationality			

Qatari	5 (25.0)	223 (27.6)	0.7946
Non-Qatari	15 (75.0)	584 (72.4)	
Age			
≤3years	14 (70.0)	449 (55.6)	
>3 to 6 years	4 (20.0)	201 (24.9)	0.5806
>6 to 10 years	1 (5.0)	106 (13.1)	
>10 years	1 (5.0)	51 (6.3)	
Admissions			
Admission for observation <24hrs)	9 (45.0)	415 (51.42)	0.843
Admission to PICU	0.0(0.0)	10 (1.24)	0.6165
Admission to the pediatric ward	4 (20.0)	117 (14.5)	0.4916
Send home within 2hrs	7 (35.0)	266 (32.9)	0.8481
Fever			
Degree of fever, Mean ±SD	39.27 ± 0.91	38.8 ± 1.09	0.0350*
Lab Results			
WBC, Mean ±SD (x103/ul)	14.25 ± 7.00	12.97 ± 12.11	0.4402
ANC, Mean ±SD (x103/ul)	8.44 ± 5.46	7.87 ± 5.17	0.6484
CRP, Mean ±SD (mg/L)	36.4 ± 39.5	46.99 ± 67.36	0.4326
Antibiotic Use			
Before blood culture	2.0 (10.0)	81 (10.0)	0.9956
After blood culture	17 (85.0)	541 (67.4)	0.0903

Table 2: Comparison of positive and negative blood culture groups.

Discussion

Over one year we reviewed 828 patients presented to the PED. The patients age more than 3 months up to 14 years old, with mean age of 3.55 ± 3.17. Only 2.42% (20) exhibited positive blood culture. This is in line with previous studies since most of the reviews on blood culture reports have a positive rate of 4-8% [25-29]. A question that rises is to what extent a positive result did change the management of the patients. For example, current guidelines do not support the use of blood culture for patients with the diagnosis of for example asthma or bronchiolitis [30,31]. A substantial part of all patients (273), 33.0%, were send home within 24 hrs, with no significant difference between the groups with negative or positive blood culture. Interestingly, the same proportion of patients in the two groups, positive and negative blood culture, 35.0% and 33.0%, respectively were sent home within two hours. That suggests there were no differences in their clinical conditions. Almost 15% who required admission after more than 24 hrs, and were send to the pediatric ward or PICU, had negative culture results, whereas 20% of those with positive culture were admitted to the pediatric ward, but none to the PICU. The reason for this lack of difference is most likely due to similar clinical presentations between the two groups, and further emphasis the lack of value for a clinical decision by the BC. Furthermore, there were no significant differences in the admissions to the different types of hospital care between the two groups. That indicate physicians had inappropriately and frequently suspected a bacteremia [32] in the group of negative BC. In our study the temperature was significantly higher in the group with positive BC ($P<0.001$). Therefore, the degree of fever was a clinical feature that was associated with bacteremia. Blood culture investigation in adult ED has been questioned, in particularly in immune-competent patients with a common infection or an infection that can be diagnosed by other means, with the conclusion that the BC was of very limited usefulness [33-35]. In most of the patients that later was confirmed with a positive BC, empiric antibiotic treatment was started more frequently than in patients with a negative BC ($P=0.015$), illustrating that other clinical factors, e.g. presentation and/or fever were used for the guidance of clinical decision making. However, the figures from this study also demonstrate that antibiotics were prescribed to a large proportion of the patients with negative BC, i.e. 67.5%. Altogether, 77.5% of all patients with suspected infection received antibiotics. A surprising finding was the lack of correlations between BC and the additional blood markers for infections, i.e. ANC, WBC and CRP. The results of these additional laboratory investigations were not correlated to the results of positive or negative BC. However, bacteremia can be present even with a normal white blood cell count [36,37]. Our finding is in contrast to Stathakis and

coworkers (2007) who found that a pathological neutrophil count was the strongest predictor to bacteremia in children aged 3-36 months [38]. The difference in results can also be explained by a broader in age range in our study.

CRP has been suggested to be an important predictor of serious bacterial infections [39]. However, in the present study, the analysis of CRP did not demonstrate any difference between the groups with positive and negative blood culture. The most frequent use of CRP has been for respiratory tract infections where its use has demonstrated a reduction in the prescription of antibiotics [40].

Conclusion

Although, blood culture is regarded as the gold standard approach to confirm diagnosis in a child with suspected serious bacterial infection or fever of unknown origin, the rate of bacteremia in a population of children attending an ED is low. This finding questions the policy of blood culture sampling as a "mandatory" measure to obtain diagnosis in this group of patients. Furthermore, the results of BC demonstrated no association with the admission to hospital wards or the prescription of antibiotics.

There is no significant correlation between BC outcome and the result of WBC, ANC and CRP. This is of interest from a practical point view since the results of these laboratories test most often create the foundation for the decision to prescribe antibiotics and/or referral for inpatient care.

Our recommendation is therefore to restrict the ordering of BC to cases where the source of infection is not clear and the clinical picture speaks in favor of a bacterial origin. This is also an important step in order to reduce the costs for laboratory analysis.

Declaration

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Ethics approval and consent to participate: The study was approved by the Institutional Review Board of Hamad Medical Corporation, Doha.

Availability of data and material: The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

Authors' contributions: All authors participated in conceiving and design of the study and helped to draft the manuscript. All conducted the research, and KS coordinated the project. All authors read and approved the final manuscript.

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