Original Article

Evaluation of Some Biomarkers in Diagnosis of Bacterial Bloodstream Infection in Children

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Abstract

Background: Bloodstream infection (BSI) is a life-threatening condition caused by the presence of microorganisms, generally caused by a range of bacteria in the blood. **Objectives:** The aim of this study was to evaluate the possible role of procalcitonin (PCT) and C-reactive protein (CRP) as biomarkers of pediatric BSI. **Methodology:** The study was conducted on 150 blood samples collected from the patient who admitted to Children Welfare Teaching Hospital, Medical City, Baghdad. During the period from November 2020 to March 2021, ninety blood samples from them were positive culture and 60 blood samples were negative culture (control group). The isolates were identified depending on the morphological, microscopic examination, and biochemical tests. Moreover, serum was obtained from all participants for the determination of the screening level of human PCT measured by enzyme-linked immunosorbent assay and CRP by slide agglutination test. **Results:** The results in this study revealed that the mean levels of serum PCT and CRP in Gram-negative group and Gram-positive group were significantly difference from the control group. **Conclusions:** The adoption of these biomarkers as routine diagnostic tests for sepsis may help in the early diagnosis of pediatric sepsis.

Keywords: Bacterial bloodstream infection, biomarkers, children

Introduction

Bloodstream infections (BSIs) are characterized as severe disorders since they are acute events and usually result in serious life-threatening organ dysfunctions such as sepsis and septic shock.[1,2] Sepsis is considered to be a public health issue and is a leading cause of mortality worldwide, being recently listed as a global health priority by the World Health Organization.[3] BSI may be transient bacteremia, an indication of true systemic infection (endocarditis, osteomyelitis, and pneumonia), or otherwise, contamination from skin flora. Pediatric patients with BSI may present a diagnostic and therapeutic challenge where they often present with fever; however, sometimes, they may present with normal or even low body temperature.[4,5] Bacteremia refers to any true-positive blood culture, which reflects the presence of viable bacteria in the bloodstream. Gram-negative bacteremia, which often produces sepsis or septic shock associated with their lipopolysaccharide of their cell walls, were at some point the predominant organisms isolated in blood cultures in the hospital setting.[6] Gram-negative organisms such as *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa,* and *Salmonella* spp. played more important roles in children's community-acquired bacteremia.[7,8] Moreover, Gram-positive organisms including (*Staphylococcus aureus*, coagulase-negative staphylococci [CONS], and enterococci) have become an important cause of BSIs.[9]

BSI is a potential life-threatening condition that requires early diagnosis and rapid pathogen identification to initiate the correct antibiotic or antifungal therapy.[10,11] Several biomarkers have been described as either being associated with the presence of BSI or suggested to have prognostic value for the outcome of BSI. The most widely studied marker is C-reactive

Access this article online

Quick Response Code:

Website: http://www.mmjonweb.org

DOI: 10.4103/MJ.MJ_10_21

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Submitted: 26-Jul-2021 **Revised:** 09-Aug-2021 **Accepted:** 14-Aug-2021 **Published:** 15-Dec-2021

How to cite this article: Abood RM, Ashoor ZF, Al Saadi YI. Evaluation of some biomarkers in diagnosis of bacterial bloodstream infection in children. Mustansiriya Med J 2021;20:62-5.

protein (CRP), which is an acute-phase protein released by the liver after the onset of inflammation. CRP is mostly used to assess the presence of infection and sepsis.[12] Moreover, procalcitonin (PCT) is the prohormone of calcitonin and was first reported as a marker of inflammation in 1993,[13] several studies have been published which investigated its clinical value in the diagnosis of bacterial infections, especially sepsis.[14,15]

Methodology

This study includes (150) blood samples of children, their ages ranging from 1 day to 2 years old. Samples were collected from Children Welfare Teaching Hospital/Medical City/Baghdad. Ninety blood samples from them were positive culture and sixty blood samples were negative culture collected to be comparable to positive culture samples.

Five ml of blood specimen collected from patients, 2.5 to 3.0 ml injected immediately in brain heart infusion, and incubated 24 h before cultured on different media (MacConkey agar and Blood agar). After the growth of bacteria, the isolates were identified by microscopic examination, biochemical tests, analytical profile index 20E, and VITEK-2 system. Another 1 ml of blood specimen was collected in a plain tube and centrifuged to get serum for the screening level of PCT (Human procalcitonin enzyme-linked immunosorbent assay [ELISA] kit/BT LAB-China) by ELISA technique and CRP (CRP– Latex kit/SPINREACT-Spain) by slide agglutination test.

Results

A total of 150 blood samples obtained from the patients who were submitted to microbiological culture technique unite, samples were 90 (60%) give a positive culture, whereas 60 (40%) were negative culture result. The samples diagnosed with sepsis as confirmed by blood culture results and 30 (20%) of them were Gram negative and 60 (40%) were gram positive as shown in Figure 1.

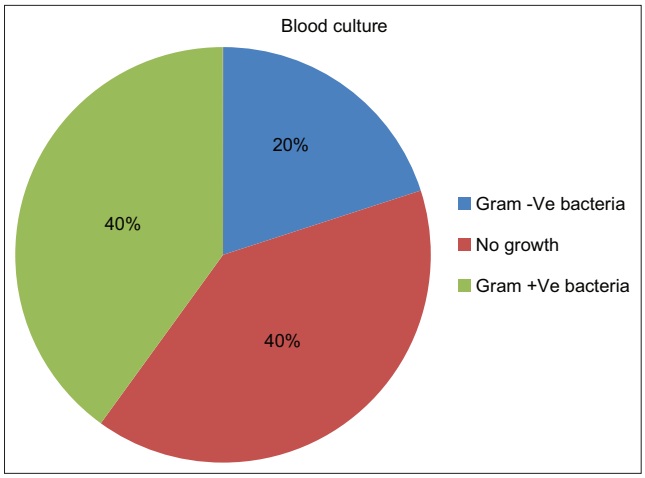

Figure 1: The frequency of culture positive and negative culture cases among study specimens

Table 1 shows the distribution of microorganisms from blood culture. Gram-positive bacteria 60 (66.66%) caused the majority of sepsis as compared with Gram-negative bacteria 30 (33.33%).

Ten bacterial species were isolated from the total of 90 positive blood culture samples. The most common organisms from blood cultures were CoNS 46 (51.11%), 26 male and 20 female. Followed by *Acinetobacters* spp., 16 (17.77%), 10 male and six female, *S. aureus* 10 (11.11%), seven male and three female, *K. pneumonia* 6 (6.66%), two male and four female, *Streptococcus* spp. 4 (4.44%), (one male and three female), *Pseudomonas* spp. 3 (3.33%), (three male), *Citrobacter* spp. 2 (2.22%), (two male), *Proteus* spp. 1 (1.11%), (one male only), *E. coli,* and *Salmonella typhi* 1 (1.11%) (one female) [Table 1].

According to CRP results in the three studied groups, Table 2 shows the distribution of bacterial isolates in these groups. A total of 30 Gram-negative group 21 (70.00%) was with CRP positive test, whereas only 9 (30.00%) with CRP-negative test. The Gram-positive group was 17 (56.67%) with CRP-positive test and 13 (43.33%) with CRP-negative test. The control group (negative culture) give 6 (20.00%) CRP-positive test and 24 (80.00%) CRP-negative test, and these results showed a highly significant difference between the three studied groups.

Table 3 shows the increase in the mean serum level of PCT in Gram-negative group (755.06 ± 56.87) as compared to Gram-positive group, which was (483.05 ± 46.62), whereas in control group was much less (10.52 ± 3.32). A significant difference between three groups was observed.

Discussion

In the present study, 150 blood samples were obtained for culture from the children who admitted in the hospital. The results revealed out of 150 samples, positive culture 90 (60%) higher than negative culture 60 (40%), and the majority of sepsis was caused by Gram-positive bacteria 60 (66.66%), compared with Gram-negative bacteria 30 (33.33%), the current study is similar to a study conducted by Acquah *et al.* on pediatric sepsis, who reported a (25.9%) blood culture positivity rate, Gram-positive was the predominant isolates accounting for 60.9%) of the total isolates and Gram-negative comprised (39.1%) all isolates.[16] Another study conducted by Sakyi *et al.* gives similar results which showed blood culture positivity rate of (23.3%) and the most common bacterial isolates were Gram positive (57.2%), whereas the Gram-negative was 42.8%.[17]

In contrast, much lower positive results were reported from Iran (5.6%)[18] and from Kuwait (8.7%).[19] These variations can be attributed to many different factors, of which antibiotic therapy before the laboratory diagnosis may have had the most important influence on the low culture results, environment factors, and sample collection sites such as general ward, neonatal intensive care unit (NICU,) and pediatric intensive care unit.

In the current study, conduct was showed the most common organisms from blood cultures were coagulase-negative

Table 1: Distribution of organisms isolated from blood culture according gender

Organism isolated	Gender		Total number of organism (%)	*P*
	Male	Female		
Gram-negative organisms (*n*=30)				
Acinetobacters spp	10	6	16 (17.77)	0.036*
Escherichia coli	0	1	1 (1.11)	0.048*
Klebsiella pneumonia	2	4	6 (6.66)	0.027*
Pseudomonas spp	3	0	3 (3.33)	0.0074**
Proteus spp	1	0	1 (1.11)	0.048*
Salmonella typhi	0	1	1 (1.11)	0.048*
Citrobacter spp	2	0	2 (2.22)	0.0073**
P	**	**	**	-
Gram-positive organisms (*n*=60)				
Staphylococcus aureus	7	3	10 (11.11)	0.0006**
Streptococcus spp	1	3	4 (4.44)	0.0094**
CONS	26	20	46 (51.11)	0.0239*
Total number of organisms	52	38	90	0.0063**
P	0.0001**	0.0001**	0.0001**	-

*$P \leq 0.05$, **$P \leq 0.01$. CONS: Coagulase negative staphylococci

Table 2: Distribution of sample study according to C-reactive protein in different groups

Group	Positive, *n* (%)	Negative, *n* (%)	*P*
Control	6 (20.00)	24 (80.00)	0.0001**
Gram negative	21 (70.00)	9 (30.00)	0.0001**
Gram positive	17 (56.67)	13 (43.33)	0.0318*
P	0.0001**	0.0001**	-

*$P \leq 0.05$, **$P \leq 0.01$

Table 3: Comparison between difference groups in procalcitonin

Group	Mean±SE of PCT
Control	10.52±3.32^{c}
Gram negative	755.06±56.87^{a}
Gram positive	483.05±46.62^{b}
t-test	129.73**
P	0.0001

Means having with the different letters in same column differed significantly. **$P \leq 0.01$. PCT: Procalcitonin, SE: Standard error

Staphylococci spp., followed by *Acinetobacter* spp., *S. aureus*, *K. pneumonia*, *Streptococcus* spp., *Pseudomonas* spp., *Citrobacter* spp., *Proteus* spp., *E. coli,* and *Salmonella typhi.* This result resembles to a another study who showed that the most common bacterial isolate was coagulase-negative staphylococcus, followed by coagulase-positive staphylococcus, *Klebsiella* spp., *E. coli*, Methicillin-resistant *S. aureus*, and *P. aeruginosa*.[17] A similar result was reported by Al Mohajer and Darouiche, who found that coagulase-negative *Staphylococcus* species were reported to be the most common pathogens followed by *S. aureus*.[6]

This contrasts with a study in Bangladesh where showed that *Acinetobacter spp.* was the most prevalent organism in NICU patients, followed by *Pseudomonas spp*., CoNS., *Klebsiella,* and *Moraxella spp*. respectively, *S. aureus*, *Enterobacter* spp., *E. coli,* and *Enterococci spp*.[20] Another study in China revealed the *S. aureus* is the most common microorganism isolated from the blood culture-positive cases followed by *A. baumannii*, *K. pneumonia*, *Staphylococcus epidermis*, *Enterococcus spp.*, *P. aeruginosa,* and *E. coli,* respectively.[21]

This may be due to the fact that most CoNS are the normal flora of the skin. Hence, during the blood collection, they may contaminate the blood. And also, it may be the expanding use of intravascular catheters and indwelling prosthetic devices causing the increase of nosocomial bacteremia caused by CoNS because they infect a wide variety of prosthetic medical devices.

Regarding to the CRP, among 30 samples, Gram-negative group was 21 (70.00%), CRP-positive test (+Ve), and 9 (30.00%) CRP-negative test (-Ve), whereas Gram-positive group was 17 (56.67%), CRP-positive test (+Ve) and 13 (43.33%) CRP negative test (-Ve), but control (negative culture) was 6 (20.00%) CRP-positive test (+Ve) and 24 (80.00%) CRP negative test (-Ve). These percentages similar to study conduct in Turkey showed that the median CRP level was (47.8 mg/dl) (10.2–119.5) in the sepsis group and (18.6 mg/dl) (4.9–66.1) in the nonsepsis group.[22] Similar study in Jordan showed that the concentration of CRP was significantly higher in sepsis group (median 44.0 mg/l) than that in probable sepsis group and no sepsis group (medians of 21.5 and 1.0 mg/l, respectively).[23]

The results of this study were in contrasts with another study who found that the mean of CRP levels between both groups (positive and negative blood culture) was similar (105 ± 105 vs. 119 ± 110 mg/L).[1] In addition, CRP cannot be recommended as a sole indicator of neonatal sepsis, but it may be used as part of a sepsis workup and in combination with other laboratory tests.

In this study revealed that the serum level of PCT that determining by ELISA method. The mean of PCT level in Gram-negative group was 755.06 ± 56.87 and 483.05 ± 46.62 in Gram-positive group but in control group was (10.52 ± 3.32). This results in agreement with other study that showed the median values of PCT: 0.56 ng/mL (0.33–1.32) were in control group, 2.69 ng/mL (1.10–5.29) were in group with Gram-positive, and 9.36 ng/mL (3.11–39.35) in patients with Gram-negative group.[24] A similar study in Ghana revealed that the PCT (ng/L) level in sepsis group was 632.8 (465.70–1468.0) whereas in control group was 434.20 (345.0–523.3).[17] In contrasts with others who showed that the median PCT values for Gram-positive versus Gram-negative bacteremia were nearly identical; 15.58 ng/mL (interquartile range 0.67, 35.01) versus 13.72 ng/mL (interquartile range 0.63, 34.13).[25]

Conclusions

The most common cause of BSI was Gram-positive bacteria such as CoNS and *S. aureus* followed by Gram-negative bacteria such as *Acinetobacter* spp. PCT and CRP markers could help the clinicians to diagnose most cases of pediatric sepsis; the rapid diagnosis of sepsis will reduce the morbidity and mortality by starting the antibiotic treatment as soon as possible. Therefore, using of these biomarkers as routine diagnostic tests for sepsis will aid in the early diagnosis of pediatric sepsis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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