

Clinical Manifestation and Laboratory Findings of Positive Blood Culture in Neonatal Septicemia

Ahmad Shah Farhat¹, Ashraf Mohammadzadeh¹, Farid Mirzaie¹, Gholamreza Khademi^{2*}, Mahboubeh Naderi Nasab³

1. Neonatal Research Center, Imam Reza Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

2. Department of Pediatrics, Imam Reza Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

3. Department of Microbiology, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

ABSTRACT

Background: Neonatal septicemia is a major cause of mortality and morbidity in newborns. This study aimed to evaluate the clinical manifestation and laboratory findings of positive blood culture in neonatal septicemia.

Methods: In this retrospective study, we investigated 100 positive blood culture records of neonates suffering from septicemia. A questionnaire was completed for each patient regarding their age at admission, gender, birth weight, admission time, type of delivery, pre-term or post-term delivery and the clinical symptoms. Types of organism causing sepsis and their resistance to antibiotics were evaluated and empirical treatment was the method of choice.

Results: Respiratory distress, cyanosis and lethargy were more prevalent among the patients. The antibiogram was indicative of Ampicillin resistance in 86% and Gentamicin resistance in 66% of the studied records. Moreover, it was observed that 36% of the positive blood culture cases had gram-negative and 64% had gram-positive bacteria. The most frequent bacteria in blood cultures were coagulase-negative *Staphylococcus* (35%), *Staphylococcus Aureus* (24%) and *Klebsiella* (18%), respectively. Other prevalent bacteria were *Enterobacter*, *E. coli* and *Enterococcus* (5%), *Acinetobacter* (3%), *Pseudomonas aeruginosa* and gram-negative Bacilli (2%) and *Serratia* (1%). According to the antibiogram, the most effective antibiotics against bacterial growth were Vancomycin, Cephalosporin, Amikacin, Cotrimoxazole and Gentamicin.

Conclusion: Since the most frequent bacteria in neonatal septicemia cases were coagulase-negative *Staphylococcus*, *Staphylococcus Aureus* and *Klebsiella*, pediatricians need to select regimens able to cover the gram-negative bacteria for empirical antibiotic treatment.

Keywords: Blood culture, Laboratory findings, Neonatal septicemia

Introduction

Nowadays, neonatal health is of paramount importance whereas in the past, neonatal mortality accounted for more than one-third of the deaths among children (1). Neonatal mortality rate is an indicator of the efficacy of the health care system in every country (2, 3) and neonatal septicemia is a major cause of neonatal mortality and morbidity across the world (4, 5).

World Health Organization (WHO) has estimated that 1.6 million neonates die from neonatal infections each year globally (6). The incidence of sepsis in neonates is 0.1-1% in live births with a mortality rate of 0.016-0.2% (4) while in developed countries, the mortality rate of sepsis in Neonatal Intensive Care Units (NICU) is about 20% (7).

Neonatal septicemia is defined as the presence of systemic symptoms of bacteremia in the first 28 days of the infant's life (8). In developed countries,

the main causes of neonatal sepsis are Group B *streptococcus* (GBS), *E. coli* and *Listeria monocytogenes* while in developing countries, gram-negative bacilli, Coagulase-negative *staphylococcus* (CONS) and other bacteria are responsible (9).

Prominent symptoms of septicemia are respiratory distress, cyanosis, lethargy, poor feeding, apnea, jaundice, convulsion, fever, irritability, vomiting and hypothermia (10). As a matter of priority, neonatal septicemia needs to be managed effectually by appropriate antibiotics as to minimize the risk of severe mortality and morbidity and diminish the emergence of multidrug-resistant organisms (11).

This study aimed to evaluate the clinical manifestation and laboratory findings of positive blood culture in neonatal septicemia in a teaching hospital in the Northeast of Iran.

* Corresponding author: Gholamreza Khademi, Department of Pediatrics, Imam Reza Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Tel: 05137276580; E-mail: khademigh@mums.ac.ir

Materials and Methods

This retrospective study was conducted on neonates selected from the NICU of Imam Reza Hospital affiliated with Mashhad University of Medical Science from March 2005 to March 2009.

We collected 100 records of positive blood culture in the neonates suffering from septicemia. The subjects had been admitted with the condition or were referred from other wards due to hospital-acquired sepsis. Patients with incomplete files were excluded from the study (with the exception of the ones with only one missing laboratory test, e.g. Erythrocyte sedimentation rate (ESR) or human C-reactive protein (CRP)).

This study was approved by the Ethics Committee of Mashhad University of Medical Sciences. A questionnaire was completed for each patient consisting of the following information:

age at admission (in days), gender (male/female), birth weight (Kg), weight at admission (Kg), type of delivery (Cesarean section/natural vaginal delivery), pre-term delivery (less than 37 weeks of gestational age (GA) or post-term delivery (more than 42 weeks of GA) and symptoms (respiratory distress, cyanosis, lethargy, poor feeding, apnea, jaundice, convulsion, fever, irritability, vomiting, hypothermia).

Furthermore, the laboratory records of the subjects were investigated with regards to bacteria in blood culture (2), effective medications according to antibiogram and their sensitivity to

Ampicillin and Gentamicin in a routine blood culture. Hemoglobin, ESR, platelet and white blood cell count (WBC), polymorphonuclear neutrophils (PMN) and lymphedema (LYM) were measured as well.

The collected data were analyzed by SPSS software version 15 (SPSS Inc., Chicago, IL, USA). To compare the results of the studied variables, we used Chi-square and Fisher's exact test and P-value (≤ 0.05) was considered as statistically significant.

Results

In total, 100 septicemic neonates who had been admitted in the NICU were included in the present study (57 male and 43 female). There were 72 pre-term cases and 28 term neonates. Low birth weight (LBW) was observed in 75 cases while others were normal. Forty-four subjects had been born via natural vaginal delivery and 56 cases were born via Cesarean section. Moreover, 67 neonates were admitted within the first 24 hours of birth and 31 cases had a normal ESR.

The hemoglobin level was normal in 58 cases while it declined in 42 neonates. WBC was normal in 85 cases, while it saw an increase and a decrease in 11 and 4 cases, respectively. In the blood culture, Ampicillin and Gentamicin resistance were observed in 86 and 66 patients, respectively. In positive blood culture cases, 36% were found to be gram-negative and 64% were gram-positive.

Table 1. Comparison between grams positive / negative in terms of time of delivery, birth weight, weight of admission, age at admission, platelet count and symptoms

Variables		Gram -Positive		Gram -Negative	
		N	%	N	%
Time of delivery	Premature	30	83.3	42	65.6
	Mature	6	16.7	22	34.4
Birth weight	Low	32	88.9	43	67.2
	Normal	4	11.1	21	32.8
Weight of admission	Low	29	87.9	43	69.4
	Normal	4	12.1	19	30.6
Age at admission	First 24 hours	30	83.3	37	57.8
	More than 2 days	6	16.7	27	42.2
Platelet Count	Less than Normal	16	14.4	8	12.5
	Normal	20	55.6	56	87.5
Symptoms	Respiratory distress	22	61.1	33	51.6
	Cyanosis	6	16.7	18	28.1
	Lethargy	4	11.1	19	29.7
	Poor feeding	3	8.3	12	18.8
	Apnea	5	13.9	8	12.5
	Jaundice	2	5.6	8	12.5
	Convulsion	2	5.6	8	12.5
	Fever	0	0	5	7.8
	Irritability	0	0	5	7.8
	Vomiting	1	2.8	0	0
	Hypothermia	0	0	1	1.6
	Without symptom	3	8.3	4	6.3

Table 2. Birth weight and Hemoglobin rate in Positive and Negative Urine Culture

		Positive Urine Culture		Negative Urine Culture	
		N	%	N	%
Birth weight	Low	8	100	67	72.8
	Normal	0	0	25	27.2
Hemoglobin	Less of Normal	6	75.0	36	39.1
	Normal	2	25.0	56	60.9

Table 3. The effective antibiotics on germs as reported in Antibigram

Drugs	N	%
Vancomycin	50	50
Cephalosporin	23	23
Amikacin	23	23
Co-trimoxazole	16	16
Gentamycin	16	16
Ciprofloxacin	13	13
Nitrofurantoin	9	9
Imipenem	9	9
Chloramphenicol	7	7
Tetracycline	5	5
Ampicillin	4	4
Erythromycin	4	4
Amoxicillin	2	2
Cloxacillin	1	1
Doxycycline	1	1

Out of 8 cases of positive blood and urine culture, 7 were pre-term and only one was term (6 male and 2 female). In addition, the platelet count in 6 cases was normal while it declined in 2 cases and WBC in 7 neonates was normal which decreased in one case. The analysis of antibiogram revealed that 3 cases (50%) were ciprofloxacin-sensitive while only one case (16.7%) was sensitive to other antibiotics (e.g. Amikacin, Co-trimoxazole or Erythromycin-sensitive).

The most frequent bacteria in the blood culture were coagulase-negative *Staphylococcus* (35%), *Staphylococcus Aureus* (24%), *Klebsiella* (18%), *Enterobacter*, *E. coli* and *Enterococcus* (5%), *Acinetobacter* (3%), *Pseudomonas aeruginosa* and gram-negative *Bacilli* (2%) and *Serratia* (1%).

Premature cases accounted for 30 (83.3%) and 42 (65.6%) subjects in the gram-positive and gram-negative group, respectively ($P=0.05$).

In the comparison of the gram-positive and gram-negative group respectively, the rate of LBW was 32 (88.9%) and 43 (67.2%) ($P=0.01$), low weight at admission was 29 (87.9%) and 43 (69.4%) ($P=0.04$), admission within the first 24 hours of birth was 30 (83.3%) and 37 (57.8%) ($P=0.009$) and reduced platelet count was 16 (14.4%) and 8 (12.5%) ($P=0.001$) (Table 1).

In the groups of the same blood culture type, the rate of LBW was 8 (100%) and 67 (72.8%) and low hemoglobin rate was 6 (75.0%) and 36

(39.1%) ($P=0.06$) in the positive and negative urine culture, respectively (Table 2). The most effective antibiotics were Vancomycin, Cephalosporin, Amikacin, Co-trimoxazole and Gentamicin (Table 3).

Discussion

In this study, respiratory distress, cyanosis and lethargy were found to be more prevalent among the patients. Moreover, the antibiogram was indicative of ampicillin resistance in 86% and gentamicin resistance in 66% of the studied records.

The most frequent bacteria in the blood cultures were coagulase-negative *Staphylococcus* (35%), *Staphylococcus Aureus* (24%) and *Klebsiella* (18%), respectively. Other prevalent bacteria were *Enterobacter*, *E. coli* and *Enterococcus* (5%), *Acinetobacter* (3%), *Pseudomonas aeruginosa* and gram-negative *Bacilli* (2%) and *Serratia* (1%). Accordingly, the most effective antibiotics against bacterial growth in antibiogram were Vancomycin, Cephalosporin, Amikacin, Co-trimoxazole and Gentamicin.

In their research, Hammoud et al. evaluated the incidence, etiology and anti-microbial resistance of late-onset neonatal infections over a period of five years. They realized that the most frequent pathogen was coagulase-negative *Staphylococcus* which was observed in 339 cases (35.7%), while *Klebsiella* was the most prevalent gram-negative infection as observed in 178 cases (18.8%). *E. coli*, *Enterococcus* and *Enterobacter* spp were each responsible for 6% of all the detected infections. Furthermore, *Candida* was found to have caused 104 (11.0%) cases of the infections (12). Their findings are in accordance with the results of the current study.

In our study, we also found that 36% of the positive blood culture cases had gram-negative while 64% had gram-positive bacteria.

In their research, Mokaddas et al. investigated 3408 pediatric surgical neonates with septicemia for a period of 4 years. They realized that gram-positive and gram-negative bacteria accounted for 54% and 39% of the septicemia cases, respectively, while *Candida* spp was responsible for only 7% (11 cases) (13).

In the present study, respiratory distress, cyanosis, lethargy and poor feeding were among the frequent symptoms observed in the patients while in the study of Matloub et al., the most prevalent clinical features were feeding reluctance (83.75%), lethargy (70%), pallor (47.5%), irritability (38.75%) and hypothermia (32.5%) (14). A noticeable frequency has been reported in the literature for such clinical presentations as respiratory distress, cyanosis and lethargy (15).

In the present study, the highest prevalence of septicemia-causing bacteria was attributed to coagulase-negative *Staphylococcus*, *Staphylococcus Aureus* and *Klebsiella*, respectively. In a study conducted by Orrett et al. on the neonatal sepsis and its mortality in a regional hospital in Trinidad, *Pseudomonas aeruginosa* and *Staphylococcus aureus* were found to be the most frequently isolated organisms (43%) (16). However, coagulase-negative *Staphylococcus*, *E. coli* and *Klebsiella* have been recognized as the most responsible organisms in other studies (17).

With respect to the frequency of gram-negative and gram-positive bacteria, our findings revealed the prevalence to be 36% and 64%, respectively.

Pre-term, septicemic neonates as well as those admitted within the first 24 hours of life are likely to manifest lethargy as the first presentation of the condition. Therefore, gram-positive bacteria was found to be most probable to cause the neonates' germ. We also realized that ESR could not be as efficient a diagnostic criterion for septicemia in neonates as it was known before (18). Additionally, WBC count and hemoglobin level were not considered as effective diagnostic factors for septicemia which is a finding compatible with the study of Zamora et al. (19).

In the current study, it was also discovered that 82% of bacterial septicemia cases were amoxicillin-resistant and 66% were gentamicin-resistant which is consistent with the findings of Gheibi et al. (11).

Another study performed in the Tertiary Care Centre of Eastern India claimed that resistance to common antibiotics like ampicillin (98.5%), gentamicin (84.4%), amikacin (65.6%) and cefotaxime (81.3%) was relatively high (20).

One of the limitations of the present study was using data extracted from hospital records which were specifically for routine diagnosis and not for research purposes. Consequently, the authors highly recommend that this study be repeated in a nested cohort design.

Conclusion

If neonates demonstrate signs of septicemia within the first days of birth, the responsible organism is most probably gram-negative bacteria. Thus, this type of bacteria needs to be covered in the empirical antibiotic treatments. Since most of the infecting bacteria in septicemia were resistant to amoxicillin and gentamicin, these antibiotics could not be effective components of the treatment. Furthermore, if the WBC count and ESR are in the normal range, these tests are not likely to affect neonatal septicemia.

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