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Evaluation of the Epidemiologic Features of Early-Onset Sepsis in the Neonatal Ward of Shabih-Khani Hospital in Kashan, Iran

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ABSTRACT

Background: Neonatal sepsis is defined as the presence of clinical signs in association with positive blood culture in newborns less than one month of age. Sepsis is a common cause of hospital admission in neonates and is known as one of the main causes of neonatal mortality in both developed and developing countries. Delays in diagnosis and initiation of appropriate antibiotic therapy could result in neonatal death. The aim of this study was to find the main pathogens of sepsis and evaluate the changes in the antibiotic susceptibility of organisms in comparison with the past.

Methods: In this descriptive study, medical records of 104 neonates with positive blood culture, admitted to the neonatal ward of Shabih-Khani Hospital, were assessed over two years (2005-2007). Data were extracted for statistical analysis.

Results: In this 2-year study on 104 neonates with sepsis, the most common organisms included flavobacterium (43.3%), pseudomonas (33.3%), coagulase-negative staphylococcus (17.3%), and coagulase-positive staphylococcus (5.9%), followed by enterobacter, Escherichia coli, beta-haemolytic streptococcus, klebsiella, diphtheroid, and listeria.

Conclusion: In this study, flavobacterium was found to be the most common organism in early sepsis. Although infection with flavobacterium is rare, the associated mortality rate is high due to the resistance of this organism to the majority of common antibiotics. Therefore, early diagnosis and appropriate antibiotic treatments can help reduce the associated complications.

Keywords: Early-onset sepsis, Neonatal sepsis, Neonate

Introduction

Bacterial sepsis is one of the most important causes of neonatal morbidity and mortality (1). Prevalence of this disease varies in different geographical regions; in fact, even in a single region, the prevalence and type of pathogens vary from time to time.

Sepsis is known as a neonatal infection and is categorized as early- and late-onset. Early-onset sepsis occurs within the first week of birth, especially during the first three days and is manifested as bacterial pneumonia and meningitis, which can result in death or severe complications (2).

Prevalence of sepsis varies in different regions. As statistics have indicated, neonatal mortality due to sepsis (per 1000 live births) is 0.3-3 in Europe, 1-4 in North America, 1.4 in Jamaica, 8.9 in Guadeloupe, and 10 in South Trinidad (3). The most common signs of this disease include hypotonia, lethargy, poor feeding, reduced neonatal reflexes, unstable body temperature, hypothermia, hyperthermia, apnea, respiratory distress, vomiting, abdominal distension, and jaundice (4).

Early sepsis is inversely correlated with birth weight, gestational age, and socio-economic status. Fever in different stages of labor, maternal urinary infection, prematurity, tachycardia during the second stage of labor, Apgar score <7 (56 times), and rupture of membrane longer than 18 hours are among the factors increasing the risk of sepsis (5, 6).

The most common pathogens of this disease include group B streptococcus, Escherichia coli (E. coli), haemophilus influenza, and klebsiella. Moreover, syphilis and listeria monocytogenes are among the acquired infections, transmitted through placenta (7).

Given the high prevalence of neonatal sepsis and its prohibitive costs, early diagnosis is vital.

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Besides, any effort to reduce neonatal mortality due to sepsis requires an accurate detection of the common germs, etiologic pattern, and prevalence of this disease within a geographical region with a specific socio-cultural status.

In this retrospective study, medical records of neonates with sepsis, admitted to our hospital, were studied in order to gather the results of blood culture, antibiotic susceptibility (according to antibiogram), and microbial resistance (2005-2007). The aim of this study was to detect the most important pathogens.

Material and Method

This cross-sectional, descriptive, retrospective study was conducted on all neonates with sepsis, admitted to the neonatal ward of Shabih-Khani Hospital from June 2005 to July 2007. All the medical records were studied, and cases with signs of sepsis (according to references) and positive blood culture were included in the study. On the whole, 104 neonates with positive blood culture were evaluated. Data including age, gender, gestational age, weight, disease signs, blood group, mode of delivery, neonatal outcomes, type of microorganism, and antibiogram were extracted from the records.

Parents of all the evaluated neonates were fully informed about the aim of the study and their participation in the research. All the cases received appropriate treatment and care, and no unnecessary costs were imposed on the families. Also, no interventions, which would interfere with the treatment process, were performed.

Data were analyzed using SPSS version 15, and descriptive statistics were extracted according to the objectives of the study. Ethical and moral considerations were taken into account, and patients' data were kept confidential. This study was scientifically and ethically approved by the ethics committee and research council of Kashan University of Medical Sciences.

Results

During 2 years (June 2005-July 2007), 1126 neonates with suspected early-sepsis were admitted to the neonatal ward of Shabih-Khani Hospital, among whom 104 cases (9.2%) had confirmed positive blood cultures. Sixteen cases (15.4%) with early sepsis died during the study period.

Overall, 63 male (61%) and 41 female (39%) neonates were affected by early sepsis. As the results indicated, 44% of the neonates were term infants, and 56% were preterm; no post-term infant was included in the study. Moreover, 65.4% of the neonates were born by caesarian section (CS), and 42.1% (44 cases) were low-birth weight (LBW) infants (< 2500 g).

The most prevalent blood group was A+ (36 cases, 34.6%). Clinical manifestations are presented in Table 1. As it is shown, respiratory distress was the most prevalent sign among patients, affected by early sepsis.

As it is shown in Table 2, flavobacterium and listeria were the most and least prevalent pathogens, respectively.

As indicated in Table 3, the highest degrees of sensitivity were as follows: flavobacterium to amikacin (100%), pseudomonas to ceftazidime (93.4%), coagulase-positive staphylococcus to vancomycin (100%), and coagulase-negative staphylococcus to vancomycin (83.4%).

Discussion

This descriptive cross-sectional study was conducted on 104 neonates with positive blood culture, admitted to the neonatal ward of Shabih-Khani Hospital from June 2005 to July 2007. Of all positive cultures, flavobacterium was the most prevalent pathogen (43.3%), followed by pseudomonas (17.3%) and coagulase-positive staphylococcus (17.3%); listeria was the least prevalent pathogen (1.9%).

According to a study performed in Kuala Lumpur, Malaysia (1971-1977) on 16 cases of infection by flavobacterium, only 19% of blood cultures were positive, and others had positive cerebrospinal or peritoneal fluid cultures (8). In the current research, sepsis was the only disease caused by flavobacterium, and no cases of pneumonia or meningitis were reported. The

Table 1. Frequency distribution of clinical signs of the under-study-group according to the patient's

Symptoms	Respiratory distress (percent)	Poor feeding (percent)	Lethargy (percent)	Fever (percent)	Jaundice (percent)	Jaundice (percent)	Others* (percent)	Number (percent)
Female	12 (29.2)	9 (19.5)	5 (12.4)	4 (9.9)	6 (14.6)	2 (4.8)	4 (9.9)	41
Male	16 (25.4)	10 (15.8)	10 (15.8)	11 (17.5)	7 (11.1)	4 (6.4)	5 (8)	63
Total	28 (26/9)	18 (17/3)	15 (14/5)	15 (14/5)	13 (12/5)	6 (5/7)	9 (8/6)	104

*Other clinical signs included diarrhea, sleepiness, etc.

Table 2. Frequency distribution of micro organism

Micro organisms	Flavia bacterium (percent)	Pseudomonas (percent)	Coagulase-positive staphyloccus (percent)	Coagulase-Negative staphyloccus (percent)	Enterobacteria (percent)	Ecoli (percent)	Sterptoccous (percent)	Dipthoroid (percent)	Klebsialla (percent)	Listeria (percent)	Number (percent)
Female	22 (58.1)	5 (8)	8 (19.5)	2 (4.8)	1 (2.4)	1 (2.4)	1 (2.4)	1 (2.4)	---	-----	4
Male	23 (36.4)	13 (20.6)	10 (15.8)	4 (6.4)	3 (4.8)	3 (4.8)	2 (3.2)	1 (1.6)	2 (3.2)	2 (3.2)	63
Total	45 (43.3)	18 (17.3)	18 (17.3)	6 (5.9)	4 (3.8)	4 (3.8)	3 (2.9)	2 (1.9)	2 (1.9))	2 (1.9)	104

Table 3. Frequency distribution of microbial factors according to the antibiotic resistance in neonates affected by sepsis in the neonatal

Antibiotics Organisms	Ampicillin			Gentamicin			Amikacin			Ceftriaxone			Cloxacillin			Vancomycin			Ceftazidime		
	Resistant	%	n	Resistant	%	n	Resistant	%	n	Resistant	%	n	Resistant	%	n	Resistant	%	n	Resistant	%	n
Flavia bacterium	10	100	10	6	24	25	0	0	26	1	10	10	*	*	*	3	25	12	8	47	17
Pseudomonas	*	*	*	4	44.4	9	4	40	10	3	42.9	7	*	*	*	*	*	*	1	6.6	15
Coagulase-positive staphyloccus	*	*	*	6	75	8	4	57.1	7	*	*	*	9	75	12	5	41.6	12	*	*	*
Coagulase-Negative staphyloccus	*	*	*	2	66.6	2	50	0	4	*	*	*	1	33.3	3	1	16.6	6	1	10	1

*antibiograms don't perform

reason for such a difference in the obtained results could be variations in the distribution of this organism in target populations.

In a similar study in Iran, 111 neonates with positive blood culture were evaluated in Shahid Beheshti Hospital in Kashan. Pseudomonas was the most prevalent pathogen (33.3%), followed by other organisms including klebsiella, staphylococcus aureus, E. coli, pseudomonas, serratia, and acinetobacter (9). Moreover, in a study by Mosayebi (1977-1980) at Shahid Beheshti Hospital of Kashan, among 75 neonates with positive blood cultures, the most frequent pathogen was coagulase-positive staphylococcus (34.5%), followed by klebsiella (25.4%); non-haemolytic streptococcus was the least prevalent pathogen (1.8%).

In an Indian study (2001), staphylococcus aureus was the most prevalent pathogen, followed by klebsiella pneumoniae, E. coli, and streptococci (10). Similarly, in a study in Japan, methicillin-resistant staphylococcus aureus was the most prevalent germ (11). Moreover, in a study at a pediatric hospital in Lahore (2003), 288 neonates with positive blood culture were evaluated. In contrast with our study results, E. coli was the most prevalent microorganism (47.3%) (9).

A study performed in Uganda (2006) showed that staphylococcus aureus was the most prevalent pathogen (69.2%), followed by E. coli and streptococcus type B (13). In another study on 1598 neonates in Peshawar, Pakistan (2002), 1003 cases of positive blood culture were evaluated, and E. coli was the most prevalent pathogen (36.6%) (14).

The existing discrepancies between the results obtained in different countries or different regions within a country are due to differences of these regions in terms of culture, sexual habits, nursing care methods, contaminated tools in gynecology and neonatal wards, and antibiotic administration methods; besides, sensitivity and accuracy of laboratory techniques, devices, and kits differed in these regions.

Furthermore, differences in the results of previous studies conducted in one center could be related to the epidemiologic changes happening over time and alterations in the antibiotic response of microorganisms. In addition, the discrepancy between the results of this study and other articles may be related to the fact that in the current research, responsible pathogens were limited to early-onset sepsis, whereas in other studies, both types of sepsis (early- and late-onset) were considered.

In the present research, flavobacterium was the most prevalent pathogen for sepsis. Infection with this organism is considered a nosocomial infection, and detecting the source of contamination is necessary for evaluating its epidemics. In nosocomial infections, blood culture has to be obtained in accordance with microbiological test results and types of infection reported in the neonatal ward. In this study, distilled water, prepared outside the hospital, was detected as the source of infection; however, this organism had been separated from water in other studies (15).

In the current study, 61% of cases were male infants. Similarly, in a study conducted in Trinidad

(2006), 63% of cases were male (16), while in the study by Mosayebi in Shahid Beheshti Hospital of Kashan (1997-2000), 54.2% of the affected neonates were male (3). Also, according to a study in Saudi Arabia, prevalence of neonatal sepsis in male infants was estimated at 53% (17).

In the study conducted in Trinidad (2006), 58% of neonates were preterm (16), which is similar to the rate reported in the current research (56%). Moreover, according to a study conducted in Iran (at Shahid Beheshti Hospital of Kashan, 2003), about 73% of neonates with sepsis were preterm (9).

In the present research, 15.4% of cases with sepsis died, while in a study in Bangladesh (2002), the mortality rate due to sepsis was 30% among the neonates (18). Also, based on the study conducted in Trinidad in 2006, mortality rate was estimated at 37% (16). The low mortality rate in the current study is probably associated with the evaluation of only early-onset cases.

In this study, 65.4% of neonates with sepsis were born via CS. Due to the high prevalence of sepsis in neonates born by CS, findings of this study were compatible with other previous articles (7, 13). For instance, in a study conducted by Clinger et al., CS was considered as one of the predisposing factors for neonatal sepsis (5).

In our study, 42.1% of neonates affected by sepsis weighed less than 2500 g (LBW), and only 5.9% were above 4000 g. In an Indian study in 2006, sepsis was mostly reported in LBW neonates (19). Also, according to the study conducted in Trinidad, 58% of neonates affected by sepsis were preterm and weighed less than 2500 g (16).

In the current study, respiratory distress (26.9%) was known as the most prevalent sign of neonatal sepsis, followed by poor feeding (17.3%). In Mosayebi's research (1997-2000), respiratory distress, poor feeding, lethargy, jaundice, and vomiting were reported as the most prevalent signs of neonatal sepsis (9). Moreover, based on the results of a study conducted in Nigeria in 2006, respiratory distress, fever, and jaundice were the most prevalent signs of neonatal sepsis (20). Additionally, Martin et al. (2003) showed that nutritional disturbance (25.6%) and jaundice (16.2%) were the most prevalent signs of neonatal sepsis (18). In the current study, flavobacterium was resistant to ampicillin, vancomycin, and gentamicin, but not amikacin. Pseudomonas was resistant to gentamicin, ceftriaxone, and amikacin. Coagulase-positive staphylococcus showed resistance to gentamicin, cloxacillin, amikacin, and vancomycin. Also, coagulase-negative staphylococcus was resistant to ceftazidime, gentamicin, amikacin, and cloxacillin.

In a study conducted in Taiwan, flavobacterium was resistant to common antibiotics, while being susceptible to piperacillin, ceftazidime, cefoperazone, and the fourth generation of cephalosporins (21). In a study conducted in the city of Peshawar in Pakistan in 2002, E. coli and pseudomonas showed high degrees of resistance to common antibiotics such as ampicillin and gentamicin. Also, cefotaxime, ceftazidime, and ceftriaxone showed average resistance to cephalosporins. These germs showed mild resistance to drugs such as ofloxacin and ciprofloxacin, which are not administered for neonates (14).

In Mosayebi's study in Kashan, coagulase-negative staphylococcus showed 11.2% resistance to ceftriaxone, ceftizoxime, cefazolin, and ceftazidime. All three types of pseudomonas in this study were 100% sensitive to ceftazidime, gentamicin, and amikacin, and two of them were 66.6% sensitive to ceftriaxone; also, two cases were resistant to ampicillin (3).

In the present study, coagulase-negative staphylococcus showed no resistance to amikacin or vancomycin, and its positive type was not resistant to vancomycin. In 37 cases of pseudomonas, resistance to cefteriaxone and amikacin was at the highest and lowest levels, respectively (9).

Comparison between the findings of this study and other articles showed the increased frequency of hospital-acquired organisms such as pseudomonas and indicated a considerable rise in resistance to common antibiotics such as the third generation of cephalosporins. This increase could be due to the inappropriate and unnecessary use of antibiotics.

Conclusion

In this study, the most common cause of sepsis was flavobacterium. This organism was transmitted from distilled water, contaminated with flavobaterium, to neonates; in other studies, this organism had been separated from water. Given the resistance of this organism to common antibiotics, early diagnosis, performance of antibiogram, and administration of appropriate antibiotics are of paramount importance for reducing the mortality rates. Due to the high resistance of staphylococci to oxacillin and cloxacillin, vancomycin administration seems to be a suitable treatment in cases of sepsis caused by staphylococcus.

Given the high prevalence of pseudomonas, its high resistance to ceftriaxone, and its

susceptibility to ceftazidime, administration of ceftazidime is considered an appropriate treatment. Considering the increasing use of the third generation of cephalosporins, resistance to cefteriaxone has been at a high level. In aminoglycosides, resistance to gentamicin has increased, and amikacin has been used more extensively. Therefore, amikacin should not be administered in cases of antibiotic resistance, and its use should be limited (7).

Suggestions

1) Since the overt and unnecessary use of antibiotics results in the increased resistance of organisms, administration of broad-spectrum antibiotics, in particular the third generation of cephalosporins, should be limited to necessary cases. Also, for the treatment of infections, narrow-spectrum antibiotics should be administered.
2) Detection of the ways through which nosocomial organisms are transmitted is of high importance for controlling infection in neonatal wards. Hand washing before and after physical examination, as well as disinfection methods, especially suctioning on a daily basis, is advised for reducing infection.
3) Due to changes of microbiological flora in neonatal wards, conducting intermittent studies is recommended to find the responsible organisms for septicemia and detect the most prevalent organisms. This can help with the selection of appropriate antibiotic treatments in suspected cases of neonatal septicemia.

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