

Profile of Bacterial Sepsis in Neonates from Kashan in Iran

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ABSTRACT

Background: Neonatal sepsis is serious and often life threatening.

Objectives: To investigate the spectrum of organisms causing neonatal sepsis in Kashan and to assess sensitivity to various groups of antimicrobial drugs.

Materials and methods: Blood taken from neonates admitted to the neonatal unit at the Beheshti Teaching Hospital with a clinical diagnosis of sepsis was cultured.

Results: Of 529 neonates with suspected sepsis, 72 had positive blood cultures. The most common causative organisms were *Klebsiella*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas*, *Serratia* and *Acinetobacter*. Most of the gram-negative organisms and all the *S. aureus* were resistant to ampicillin. The gram-negative organisms were sensitive to amikacin and third generation cephalosporins. *S. aureus* was highly sensitive to vancomycin.

Conclusions: Gram-negative organisms are the major cause of neonatal sepsis in Kashan. The data must be periodically reviewed and antibiotic policy revised accordingly. (*J Infect Dis Antimicrob Agents* 2003;20:97-102.)

INTRODUCTION

Neonatal sepsis is one of the most common reasons for admission to neonatal units.^{1,2} Despite the development of newer and more potent antimicrobial agent³, infections are still important cause of neonatal morbidity and mortality.^{3,4}

The spectrum of organisms that cause neonatal

sepsis changes over time and varies from region to region. In the past, gram-positive cocci, were the most common pathogens in the United States but this predominance shifted to gram-negative enteric bacilli after antimicrobial agents were common used. In the early 1960s, *Staphylococcus aureus* and *Escherichia coli* were the most organism. In the late 1960s, group

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B streptococci (GBS) emerged as a perinatal pathogen and continues to be an important organism in neonatal sepsis in Europe and North America^{3,5}, but gram-negative organisms remain the major cause of neonatal sepsis in developing countries.⁶⁻¹²

Neonatal sepsis is a major cause of mortality in both developed and developing countries and delay in diagnosis and treatment with appropriate antibiotics may result in death.^{2,6,7} Therefore, surveillance is needed to identify the common signs and pathogens of neonatal sepsis as well as the antibiotic sensitivity patterns for the agents of sepsis in a particular area. The purpose of this study was to identify the most common organisms causing neonatal sepsis along with their antibiotic sensitivity profiles and compare it with other developing countries to point out the differences.

PATIENTS AND METHODS

From September 1999 to September 2002, all babies aged under one month admitted to the neonatal units of Beheshti Hospital, a tertiary level care hospital in Kashan, Iran, were enrolled.

Neonates with clinical signs of sepsis including poor feeding, vomiting, lethargy, respiratory distress, jaundice and temperature instability were enrolled in this study. A thorough history taking and physical examination were performed. Patients who received antibiotics before admission, had surgical problems, respiratory distress syndrome (RDS) or major gross congenital anomalies were excluded.

Blood culture was taken in all cases by standard method and inoculated into BACTEC (Becton Dickinson) bottles.

Sepsis was defined by a single positive blood culture associated with appropriate clinical finding as judged by a neonatologist. Sepsis was categorized as early (occurring within 4 days of life) or late (occurring within 5 to 28 days of life) onset.

RESULTS

During the study period (36 months), 529 neonates

with suspected sepsis were admitted to our unit. Of 529 neonates, 72 had positive blood cultures. The most common organisms were *Klebsiella* (25/72, 34.7%), *S. aureus* (24/72, 33.3%), *E. coli* (14/72, 19.3%), *Pseudomonas aeruginosa* (6/72, 8.3%), *Serratia* (2/72, 2.8%), and *Acinetobacter* (1/72, 1.4%). Nearly two-thirds (48/72, 66.7%) of the 72 organisms were gram-negative bacilli and one-third (24/72, 33.3%) was gram-positive. Blood culture positivity was lower in those with early onset (29/72, 40.3%) compared to late onset (43/72, 59.7%) sepsis.

Klebsiella was the most common (48.3%) infecting organisms causing early onset sepsis and *S. aureus* the most common (46.5%) organism causing late onset sepsis (Table 1). There were more males with positive blood cultures compared with females (male 49/72, 68%; female 23/72, 31.9%). Nearly two-thirds of neonates (53/72, 73.6%) were preterm, 18 (25.0%) were term and 1 (1.4%) was post-term. There was not difference in bacterial profile between term and preterm infants.

The most frequent clinical presentation of patients with culture proven sepsis were respiratory distress (30/72, 41.7%), poor feeding (27/72, 37.5%), lethargy (14/72, 19.4%), jaundice (14/72, 19.4%) and vomiting (12/72, 16.6%) (Table 2).

Most gram-negative organisms were resistant to ampicillin (92.9-100%), 50.0-66.7 percent and 52.0-85.7 percent of isolates were sensitive to gentamicin and amikacin respectively, whereas 40-100 percent were sensitive to third generation cephalosporins.

Most of the *S. aureus* were sensitive to vancomycin (83.3%) and all were resistant to ampicillin (Table 3).

DISCUSSION

Despite great improvements in infant mortality rate in recent years, it is estimated that approximately five million neonatal deaths occur in developing countries each year. Infections such as respiratory infections, sepsis, neonatal tetanus and diarrhea account

Table 1. Main pathogens causing neonatal sepsis according to time of onset.

Organism	Timing of sepsis		Total
	Early onset (< 4 days)	Late onset (> 4 days)	
Klebsiella	14	11	25
<i>S.aureus</i>	4	20	24
<i>E.coli</i>	5	9	14
Pseudomonas	4	2	6
Serratia	2	-	2
Acinetobacter	-	1	1
Total (%)	29 (40.3)	43 (59.7)	72 (100)

Table 2. Common clinical manifestations of the 72 blood culture positive cases of neonatal sepsis.

Organism Clinical features	Organism						Total (%)
	<i>S. aureus</i>	Klebsiella	<i>E. coli</i>	Pseudomonas	Serratia	Acinetobacter	
Respiratory distress	9	12	5	2	1	1	30 (41.7)
Poor feeding	13	6	4	3	-	1	27 (37.5)
Lethargy	5	2	3	3	1	-	14 (19.4)
Jaundice	6	4	4	-	-	-	14 (19.4)
Vomiting	6	4	1	1	-	-	12 (16.7)
Fever	5	1	-	1	-	-	7 (9.7)
Hypothermia	-	2	2	-	-	1	5 (6.9)
Convulsion	2	1	-	1	-	-	3 (4.2)
Apnea	-	-	1	-	-	-	1 (1.4)

Table 3. Pattern of antibiotic susceptibility in common pathogens.

Organism	Antibiotics						Number tested
	Ampicillin	Gentamicin	Amikacin	Cloxacillin	Vancomycin	Third generation cephalosporins	
Klebsiella	1 (4.0%)	5 (20.0%)	13 (52.0%)	0	0	10 (40.0%)	25
<i>S. aureus</i>	0	10 (41.7%)	2 (8.3%)	8 (33.3%)	20 (83.3%)	6 (25.0%)	24
<i>E. coli</i>	1 (7.1%)	7 (50.0%)	12 (85.7%)	0	0	10 (71.4%)	14
Pseudomonas	0	4 (66.7%)	4 (66.7%)	0	0	6 (100%)	6
Serratia	0	0	0	0	0	2 (100%)	2
Acinetobacter	0	0	0	0	0	1 (100%)	1

for an estimated 30 to 40 percent of neonatal deaths in developing countries. In contrast, neonatal mortality rates in developed countries are about 5/1,000 livebirths and most are due to prematurity.¹⁴ The outcome of neonatal infections can be improved if illness is recognized early and appropriate antimicrobial agents are administered promptly.⁴

The spectrum of organisms causing neonatal sepsis in our study is similar to that reported for other neonatal units in developing countries, with gram-negative organisms being responsible for most cases, particularly early onset. Increased prevalence of gram-negative sepsis as found in our study could be due to invasive medical procedures (e.g. endotracheal intubation, umbilical catheterization), indiscriminate and inappropriate use of antibiotics, poor sanitation conditions and ineffective infection control in the maternity services.

Almost 67 percent of episodes of neonatal sepsis in our unit were caused by gram-negative organisms, with *Klebsiella* being the most common (34.7%) and *E. coli* the second most common (19.4%) followed by *Pseudomonas* (8.3%). A similar pattern was reported by Bhutta and Yusuf in which *Klebsiella* was the most common cause of neonatal sepsis in Karachi, Pakistan.⁶ In India, Joshi et al reported gram-negative sepsis in 67.2 percent of their cases with *Pseudomonas aeruginosa* being the most common organisms (38.3%) followed by *Klebsiella* (30.4%) and *E. coli* (15.6%).¹⁰

S. aureus was the second most common organism in our study. Anwer et al found gram-positive organism to be the main cause of neonatal sepsis in a hospital in Karachi, Pakistan.¹ Gram-negative organisms were responsible for almost half of the episodes of early onset neonatal sepsis in their series. Dawodu et al and Kilani and Basamad have reported similar results from Riyadh, Saudi Arabia.^{2,12}

GBS was not isolated from any culture in our study. The same has been reported in most studies from India, Pakistan, Ethiopia and other developing

countries.^{1,2,6,10,11,15-17} Robbilard et al from Guadeloupe reported GBS in 46 percent of positive blood cultures and 52 percent of gastric aspirates.¹⁸ Koutouly and Habib Ullah found that GBS was the most common organism (23%) particularly in early onset sepsis in 106 culture positive cases.¹⁹ The insignificance of GBS as a pathogen in our study may be attributable to low prevalence of GBS colonization of pregnant mothers in this area, or possibly, to the presence of strains with low virulence and also intrapartum antibiotic administration.

In this study, late onset sepsis was more common than early onset disease, in contrast to other reports in which early onset sepsis generally has been more common.^{5,20} Perhaps this discrepancy may be due to high mortality rate in early onset disease, and occurrence of death prior to arrival at the hospital.

Other studies have shown that males have been reported to be 2-6 times more likely than females to develop sepsis.²¹ Nearly 2:1 ratio of male to female infant in our study is consistent with this data.

Our study shows a very high degree of resistance of gram-negative organisms to ampicillin. There is low degree of resistance to aminoglycosides especially amikacin and third generation cephalosporins. The data of Anwer et al from Karachi show 80 percent resistance to ampicillin, 11-13 percent resistance to cefotaxime and 0-10 percent resistance to amikacin.¹ Bhutta et al also reported a high degree of resistance to ampicillin and gentamicin among gram-negative organisms.²²

In this study, all the *S. aureus* were resistant to ampicillin but sensitive to vancomycin, gentamicin and cloxacillin. The data of Orrett and Shurland from Trinidad show 85 percent of *S. aureus* were resistant to ampicillin.⁷

Antibiotic resistance is increasing worldwide and has become a serious health problem in hospitals and the community. Infection with resistant organisms has been associated with treatment failure, higher morbidity and mortality and increased costs. This has necessi-

tated the development, implementation and evaluation of policies on the use of antibiotics.²³⁻²⁵ Routine bacterial surveillance and study of their resistance patterns must be an essential component of neonatal care.

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