ORIGINAL ARTICLE

NEONATAL SEPSIS: CAUSATIVE BACTERIA AND THEIR RESISTANCE TO ANTIBIOTICS

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Background: Neonatal sepsis is one of the major causes of neonatal morbidity and mortality, particularly in developing countries. The objective of this study was to determine the causative bacteria and level of their resistance to commonly used antibiotics. **Methods:** This descriptive study was carried out at Ayub Teaching Hospital, Abbottabad from April 2009 to January 2010. All neonates of either gender admitted in neonatology unit with clinical sepsis and positive blood culture were included in the study. Neonatal period was defined as 28 days of life at term and up to 44 weeks of gestational age in preterm babies. One hundred and thirty neonates of either gender were studied during the period. Blood sample for culture was taken from a peripheral vein or an artery ensuring standard anti-septic measures. BACTEC technique was used for obtaining bacterial growth and drug sensitivity after incubation of 24–48 hours. Second blood culture was also performed in few cases which were not showing improvement after initial treatment. **Results:** Male to female ratio was 1.3:1. Early and late onset sepsis was found in 29.2% and 70.8% respectively. Gram-negative bacteria were more frequent than gram-positive bacteria with a frequency of 54.6% and 45.4% respectively. Gram-positive and gram-negative bacteria showed high resistance against commonly used antibiotics such as ampicillin, amoxicillin, cefotaxime, ceftriazone and gentamicin. **Conclusion:** *Staph. aureus* is the most common gram-positive bacterium and *E. coli* is the most common gram-negative bacterium causing neonatal sepsis. Gram-positive and gram-negative bacteria are highly resistant against commonly used antibiotics such as ampicillin, amoxicillin, cefotaxime, ceftriazone and gentamicin, and are relatively more sensitive to less commonly used drugs like amikacin and ceftazidime.

Keywords: Neonatal sepsis, antibacterial resistance, gram-positive, gram-negative

INTRODUCTION

Neonatal sepsis is characterised by bacteraemia and clinical symptoms caused by micro-organisms and their toxic products.[1] Early onset (within first week of life) neonatal sepsis is generally acquired from pathogens of maternal genital tract, whereas late onset sepsis (after first week till 28 days of life) has its environmental origin either in the community or in hospital.[2] Neonatal sepsis or sepsis neonatorum has considerable contribution in the high neonatal morbidity and mortality. World over, nearly 1.6 million neonatal deaths are caused by neonatal infections.[3] Bacterial sepsis is considered to be an important cause of neonatal mortality.[4] Depending upon the type of micro-organism the mortality rate ranges between 20 to 50% being highest with gram-negative and enterococcus.[5] The spectrum of bacteria most commonly implicated in neonatal sepsis are quite different in industrialised countries compared with middle and low income countries.[3]

Millennium Development Goal-4 aspires to reduce under-5 mortality close to 30 child deaths[6] per 1000 live births by 2015 and worldwide neonatal deaths share about 41% of all deaths in children below 5 years of age.[7] Of the estimated 130 million annual births worldwide, 4 million die in the first 28 days of life, and nearly half of them on the first day. Developing countries share 99% of neonatal deaths and up to 1 million deaths are attributed to infectious causes including neonatal sepsis, meningitis and pneumonia.[8]

Among Asian countries, Thailand and Sri Lanka have managed to reduce their neonatal mortality rate (NMR) to under 10 deaths per 1000 live births.[9] Pakistan is one of the five countries contributing 49% (4.294 million) of child deaths[10] and has one of the highest neonatal mortality (53/1000 live births).[11] World over, two-third of the global neonatal deaths are contributed by just ten countries, mostly in Asia[12] and Pakistan ranks at third position with a share of 7%. A cohort study conducted in Pakistan showed that 45% of the neonatal deaths occurred within 48 hours of birth and 73% within 1st week. Preterm birth, birth asphyxia and infections were observed in 34%, 26% and 23% of the neonatal deaths respectively.[13]

The greatest challenge of the day to the practicing paediatrician is the emerging threat of neonatal sepsis coupled with antimicrobial resistance to the commonly used antibiotics.[14,15] This cross-sectional descriptive study was designed to find common causative bacteria implicated in neonatal sepsis along with their sensitivity to different antimicrobial drugs.

The objectives of the study were to determine the causative bacteria responsible for neonatal sepsis and level of their resistance to commonly used antibiotics.

MATERIAL AND METHODS

This cross-sectional descriptive study was conducted in collaboration with Neonatal Unit, Department of Paediatrics, Ayub Teaching Hospital, Abbottabad from April 2009 to January 2010. Neonatal period was defined as 28 days of life at term and up to 44 weeks of gestational age in preterm babies.[16] Gestational age was confirmed from the mother by the last date of menstrual period (LMP), obstetrical ultrasonography or from clinical assessment using New Ballard Score sheet.[17]

All neonates of either gender admitted in neonatology unit with clinical sepsis and positive blood culture were included in the study. Babies who had received antibiotics prior to admission or had surgical, chromosomal or congenital anomalies or dysmorphism were excluded from the study.

One hundred and thirty neonates of either gender were studied during the period. Fully informed and voluntary consents were obtained from the parents or attendants. Detailed history and complete physical examination was carried out on each patient. Blood sample for culture was taken from a peripheral vein or an artery ensuring standard antiseptic measures. Blood sample amounting 3–5 ml was taken in 5 ml disposable syringe using butterfly cannula in all cases. BACTEC technique was used for obtaining bacterial growth and drug sensitivity after incubation of 24 to 48 hours. Second blood culture was also performed in few cases which were not showing improvement after initial treatment. Other investigations including relevant haematological, biochemical and radiological were also performed.

Data was entered, cleaned and analysed using SPSS-10.

RESULTS

Out of 130 patients, 74 (56.9%) were male and 56 (43.1%) were female babies. The ages of all the neonates were in the range of 2–28 days with 95% CI of 13.14–17.32 days for males, and 10.4–14.3 days for females. Late onset sepsis (LOS) was found in 92 (70.8%) cases, whereas early onset sepsis (EOS) was present in 38 (29.2%) cases.

Gram-negative bacteria were more frequent than gram-positive bacteria with a frequency of 71 (54.6%) and 59 (45.4%) respectively.

Staphylococcus aureus and *E. coli* were the commonest causative bacteria responsible for neonatal sepsis in 35 (26.9%) and 30 (23.1%) respectively. *Streptococcus* species were only found in EOS, whereas *Klebseila* and *Moraxella* species were found only in LOS. Table 1 shows various bacteria found to be responsible for sepsis neonatorum in our settings.

Table-1: Frequency of various bacteria causing neonatal sepsis

Causative bacteria	Number	Percentage
Staphylococcus aureus	35	26.9%
Escherichia coli	30	23.1%
Staphylococcus epidermidis	17	13.1%
Acinetobacter spp	17	13.1%
Klebseila	13	10%
Streptococci spp	7	5.4%
Enterobacter cloacae	6	4.6%
Moraxella	5	3.8%
Total	**130**	**100%**

The bacteria responsible for the sepsis showed variable pattern of resistance to commonly used antibiotics. Table 2 shows the levels of resistance of various bacteria responsible for neonatal sepsis to commonly used antibiotics.

Table-2: Levels of resistance of various bacteria to commonly used antibiotics

Antibiotics	Causative Bacteria (%)						
	S. aureus	***S. epidermidis***	***Streptococcus***	***E. coli***	***Acinetobacter***	***Klebseila***	***Enterobacter***
Ampicillin	77.0	82.6	14.3	73.3	98.1	92.3	80.3
Amoxicillin	77.0	85.0	20.8	76.6	98.1	100	80.3
Gentamicin	-	-	-	60.0	66.6	46.0	66.6
Amikacin	-	-	-	3.3	46.6	26.6	0
Cefotaxime	70.1	82.3	14.6	63.4	74.3	62.5	66.6
Ceftriaxone	74.3	98.0	14.6	60.0	74.3	46.5	80.0
Ceftazidime	80.0	70.5	0	50.3	59.5	46.5	66.6
Ciprofloxacin	30.4	58.8	20.8	40.3	70.5	26.3	0
Ofloxacin	30.5	70.5	13.5	20.0	52.9	7.6	0
Imipenem	74.0	70.5	13.5	2.9	0	0	0

DISCUSSION

Developing countries share 99% of the estimated 4 million neonatal deaths world over, and infections such as sepsis, pneumonia, diarrhoea and tetanus are major contributor to it[18] being responsible for about 34/1,000 live births compared to developed countries where neonatal mortality due to sepsis is around 5/1,000 live births.[19]

This study was conducted on 130 neonates with confirmed sepsis on blood culture. Male babies were 74 (56.9%) and female babies were 56 (43.1%) with a ratio of 1.3 to 1, which is consistent with the study by Shaw *et al.*[20]

Although gram-positive and gram-negative bacteria have been isolated from different cases, gram-negative bacteria were more common (54.6%) than gram-positive (45.4%). These results are consistent with international and local studies conducted by Movahedian *et al*,[4] Awoniyi *et al*[18] and Waseem *et al*[21]. Some studies such as Karlowicz *et al*[22] found gram-positive as the main organisms responsible for neonatal sepsis. This could be due to the fact that spectrum of different bacteria responsible for neonatal sepsis varies between countries and even within the country.[3,4]

Bacterial resistance to commonly used antibiotics such as ampicillin and amoxicillin in our settings was found quite high. These antibiotics showed high resistance of 77%, 98.1%, 92.3% and 73.3% in cases of *Staph aureus*, *Acinetobacter*, *Klebseila* and *E. coli* respectively. The study by Waseem *et al*[21] found almost similar resistance pattern being present in 83.3%, 50%, 100% and 83.3% respectively against these bacteria.

Gram-positive and negative bacteria have demonstrated high resistance against 3rd generation cephalosporins. In our study, cefotaxime and ceftriaxone were found to be resistant in 63.1% and 66.9% of cases respectively, whereas ceftazidime was resistant in 56.9% of the cases. Aminoglycosides have shown variable pattern of resistance against different bacteria. Gentamicin was resistant to *E.coli*, *Acinetobacter*, *Klebseila* and *Enterobacter* in 60%, 66.9%, 48.9% and 66.9% of cases respectively. These findings are similar to many other studies.[18,20,21]

Resistance against quinolones, although found low compared to commonly used antibiotics, is emerging due to their indiscriminate use. Shaw *et al*[20] found ciprofloxacin to be highly resistant against *Staph. aureus*, *Streptococcus* and *Enterobacter*, whereas the present study showed 100% sensitivity of ciprofloxacin and ofloxacin against *Enterobacter*.

Our study demonstrated high resistance of imipenem against *Staphylococcus*, but 100% sensitivity against *Acinetobacter, Klebseila and Enterobacter*. Studies by Shaw *et al*[20] and Waseem *et al*[21] have described 100% sensitivity of imipenem against *Staphylococcus* in addition to *Acinetobacter, Klebseila, E.coli and Enterobacter*. The high resistance of imipenem against *Staphylococcus* found in our study may be due to its improper use.

CONCLUSION

The present study revealed that *Staph.aureus* is the most common gram-positive bacterium and *E.coli* is the most common gram-negative bacterium causing neonatal sepsis. The commonly used antibiotics such as ampicillin, amoxacillin, cefotaxime, ceftriazone and gentamicin are highly resistant against gram-positive and gram-negative bacteria. Less commonly used drugs like amikacin and ceftazidime are relatively more sensitive than commonly used antibiotics.

RECOMMENDATIONS

Physicians, particularly paediatricians should manage the case of neonatal sepsis keeping in view the causative bacteria and level of resistance, particularly against the commonly used drugs. Large scale, multicentre studies should be carried out to identify the changing patterns of the prevailing flora and susceptibility to various antibiotics in the region.

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