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The prevalence of sepsis in neonates caused by multidrug resistant bacteria

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Abstract
The spectrum of organisms that cause neonatal sepsis changes over time and varies from region to region. It can even vary from hospital to hospital in the same city. This is due to the changing pattern of antibiotic use and changes in lifestyle. Gram negative organisms were the most common cause of neonatal sepsis in Europe and America in the 1960s. A prospective hospital based study over a period of one year was carried out at neonatal intensive care unit of our hospital, a tertiary care centre. At least 20% deliveries require nursery admission. All neonates born at the hospital and presenting with signs and symptoms of sepsis or born to mothers with potential risk factors for sepsis were investigated for sepsis. All the neonates diagnosed to have culture positive sepsis or clinical sepsis with multidrug resistant organisms were included as study cases. The most common organism was CONS accounting for 32.79% followed by Klebsiella species (16.39%) Staph aureus (14.75%). All the CONS positive cultures were non MDR (100%). Whereas 70% of the Klebsiella species and 100% of the Staph species were MDR.

Keywords: Neonatal Sepsis, MDR, Staph Aureus

Introduction
In spite of the major advances in antimicrobial therapy, neonatal life support measures and risk factor assessment, neonatal septicemia remains a serious cause of morbidity and mortality among neonates. Septicemia in neonates refers to generalized bacterial infection documented by a positive blood culture in the first 4 weeks of life and is one of the four leading causes of neonatal mortality in India. According to the 2008 WHO data, out of the total 3.1 million neonatal deaths one-third were because of sepsis. In India, the current neonatal mortality rate as per 2012 data is 32 per thousand live birth, out of which 25% is due to infections. It is important to note that 20-30% of the survivors of neonatal sepsis may exhibit neurological sequealae. Sepsis related mortality is however largely preventable with rational antimicrobial therapy and aggressive supportive care [1, 2].

The spectrum of organisms that cause neonatal sepsis changes over time and varies from region to region. It can even vary from hospital to hospital in the same city. This is due to the changing pattern of antibiotic use and changes in lifestyle. Gram negative organisms were the most common cause of neonatal sepsis in Europe and America in the 1960s. It changed to group B streptococcus during the 1970s and coagulase negative *Staphylococcus* during the late 1980s and 1990s. In most of the developing countries, Gram negative organisms remain the major cause of neonatal sepsis, particularly early onset neonatal sepsis. These organisms have developed increasing multidrug resistance over the last two decades, due to the indiscriminate and inappropriate use of antibiotics, over the counter sale of antibiotics, lack of legislation to control their use, poor sanitation, and ineffective infection control in the maternity services [3, 4].

Neonates are particularly vulnerable to infection because of their weak immune barrier. Several risk factors have also been identified in mother and neonates which are known to predispose to sepsis. Advances in management of sick neonates have improved the survival of newborn both the sick and very low birth weight. This has resulted in increased use of broad spectrum antibiotics, resulting in Multi drug resistant bacterial strains becoming a common nosocomial problem. Emergence of resistance to multiple antimicrobial agents in pathogenic bacteria has become a significant public health threat as there are fewer or even sometimes no effective antimicrobial agents available for infections caused by these bacteria (both gram positive and gram negative). So with increasing emergence of antibiotic

resistance among the organisms causing neonatal sepsis the need for bacteriological monitoring and sensitivity profiles cannot be overemphasized [5].

Neonatal sepsis is an important common cause of morbidity and mortality worldwide. According to the World Health Organization (WHO, 2008), it is estimated to cause about 0.9 millions deaths worldwide.

The reported incidence of neonatal sepsis varies from 7 to 38 per 1000 live births in Asia, from 6.5 to 23 per 1000 live births in Africa, and from 3.5 to 8.9 per 1000 live births in South America and the Caribbean.

By comparison, rates reported in the United States and Australia range from 6-9 per 1000 live births and in Europe 0.3-3 per 1000 live births.

However, in developing countries, neonatal sepsis is the most common cause of morbidity and mortality among infants accounting for 30-50% of total deaths each year. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes.

As per National Neonatal Perinatal Database (NNPD) 2002-2003,the incidence of systemic infection is 3% among intramural babies in tertiary care institutions in India, with septicaemia being present in three-fourth of the cases [6].

Methodology

Study design: Prospective cross sectional study design.

Inclusion criteria: All the neonates born in Hospital and presenting with clinical signs and symptoms of sepsis were taken in this study. Also those babies born to mothers with potential risk factors were screened for sepsis were included. Each patient was included as a case patient only once if a culture positive is obtained at more than one occasions i.e. only the first episode of infection was taken into account.

Cases: Neonates admitted in NICU having MDR sepsis.

Controls: Neonates admitted in NICU having non MDR sepsis.

Exclusion criteria: All the culture negative sepsis were excluded from the study.

A prospective hospital based study over a period of one year was carried out at neonatal intensive care unit of our hospital, a tertiary care centre. At least 20% deliveries require nursery admission. All neonates born at the hospital and presenting with signs and symptoms of sepsis or born to mothers with potential risk factors for sepsis were investigated for sepsis. All the neonates diagnosed to have culture positive sepsis or clinical sepsis with multidrug resistant organisms were included as study cases. For each case, the subsequent neonate with sepsis with non-MDR organisms were enrolled as control. Written informed consent was taken from parents of all cases and controls. The data for these participants was obtained by doing retrospective evaluation of medical records following a structured survey (Annexure 1) that indicated mother's age, gestational age, sex, weight at birth, risk factors for infection in newborn, clinical features, laboratory results, treatment given and outcome (discharge/death) of the baby. The diagnosis of sepsis and multidrug resistance was as per CDC criteria. Also, the risk factors which may be significantly associated with multidrug resistance like meconium stained liquor, birth asphyxia, premature rupture of membranes, fever and indiscriminate use of antibiotics in mother were studied. These newborns with sepsis were investigated and managed as per existing unit policy, guided by culture and sensitivity. Blood cultures were processed using the standard technique described by Cruickshank *et al* and the antibiotic sensitivity was performed by Kirby-Bauer's disc diffusion method [13]. The Parameters of morbidity included day of starting feeds after initiating antibiotics and duration of nursery stay. Outcome was taken as whether the neonate got discharged or did not survive.

Results

Table 1: Descriptive data presentation of variables like maternal age, Gestational age, Apgar scores in the study population

Variable(s)	Mean ± SD (n=320)	Median (n=320)	Min-Max
Maternal age	24.63 ± 3.59	24	18-42
Gestational age	35.83 ± 3.6	37	23-41
Birth weight	2160.76 ± 745.64	2100	0.75-4250
Apgar at 1 min	7.26 ± 1.72	8	2-8
Apgar at 5 min	8.37 ± 1.5	9	3-9

In the present study blood culture positivity was reported in 61((19.06%) of the suspected sepsis cases and were further studies for their antibiotic sensitivity profiles and other characteristics.

Out of these 61 cases of culture positive sepsis, MDR sepsis was diagnosed in 30 newborns i.e. 49.18% and 31 newborns had non-MDR sepsis i.e. 50.82%.

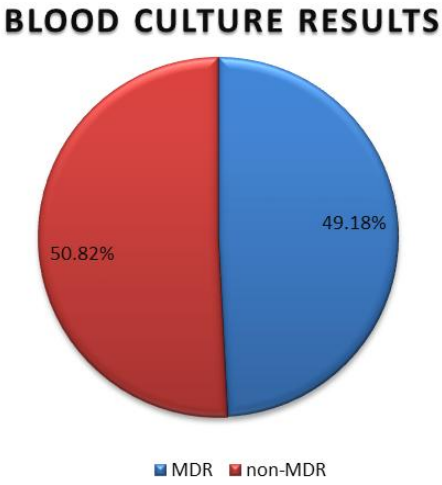

Fig 1: Showing the distribution of multidrug resistant organisms causing sepsis in the culture positive study group

The most common organism was CONS accounting for 32.79% followed by Klebsiella species (16.39%) Staph aureus (14.75%). All the CONS positive cultures were non MDR (100%). Whereas 70% of the Klebsiella species and 100% of the Staph species were MDR**.**

Table 2: Shows the various organisms that were grown in blood culture

	Frequency	Percentage
Acinetobacter spp	5	8.20%
Cons	20	32.79%
E.coli	5	8.20%
Enterobacter spp	3	4.92%
Enterococcus spp	2	3.28%
Group b streptococcus	2	3.28%
Klebsiella spp	10	16.39%
Micrococcus spp Contaminants	32	4.92% 3.28%
Staph aureus	9	14.75%
Total	61	100.00%

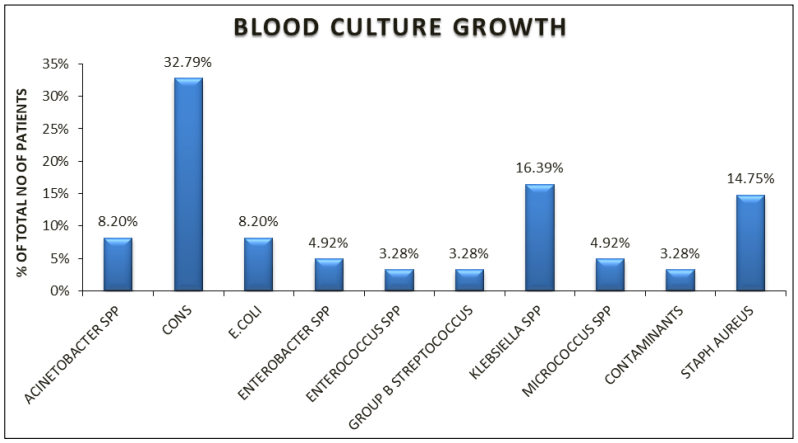

Fig 2: Shows the growth of various organisms in the blood culture

CSF examination was performed in 77.97%, out of which CONS culture positivity was noted in 3.28% while 1.64% showed Staph aureus growth. There were no MDR organisms in CSF culture growths.

Table 3: Showing growth of various organisms in CSF culture

	Percentage
Cons	3.28%
No growth	77.05%
Not done	18.03%
Staph aureus	1.64%
Total	100.00%

Discussion

The mean birth weight of neonates in Group 1 (sepsis with MDR) was 2156.7 and Group 2 (sepsis with non-MDR) was 2162.9. This was slightly lower than the mean birth weight as observed in NNPD 2002-03, which was 2742 $\pm$ 468 gm. In the present study, 216 (67.5%) were low birth weight babies, while in NNPD, it was 21.1%. This shows that there was an increased number of low birth weight babies in our setup. In the present study, the mean gestational age in Group 1 was 36.43 weeks and in Group 2 was 36.08 weeks. Mean maternal age in Group 1 and Group 2 was 24.43 yrs and 24.58 yrs respectively. The male: female ratio in the study was 1.23:1 while in NNPD it was 1.16:1.

The percentage of MDR and non-MDR organisms in neonatal sepsis in our study was found to be 49.18% and 50.82% respectively.

The blood culture positivity rate in our study was 19.06%, which was much higher than the study done by Ni Chungee *et al*. [7] (9.31%). This blood culture positivity was comparable to the positivity rate in the study done by Nalini Agnihotri *et al*. [8]. (19.19%). This indicates a higher blood culture positive sepsis seen in the Indian setting.

In the present study, the univariate analysis of variables such as gender, mean birth weight, mean gestational age, mean maternal age, and resuscitation at birth did not reveal any significant difference in the two groups. This signifies that the two groups were comparable with respect to baseline characteristics.

The commonest symptom at admission to the neonatal ICU in the present study was respiratory distress (54.84%). This is comparable with the results of Jain *et al*. study and other (42.6%) [9, 10].

Conclusion

There is a high prevalence of multidrug resistant organisms in neonatal sepsis (49.18% i.e 1 in every 2 cases of culture positive sepsis)

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