Original Article

Neonatal Sepsis : *Staphylococcus aureus* as the Predominant Pathogen

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Abstract. 96 consecutive inborn neonates with blood culture proven bacterial sepsis during the period January to June 1997 were studied. Lethargy with refusal of feeds (28%), fever (28%) and respiratory distress (31.3%) were the major presenting features. Half of them (n=48) were of early onset (< 48 hours) and the remaining half were of late onset (> 48 hours). Staphylococcus aureus (n=59, 61.5%) was the predominant pathogen and 66% of them were methicillin resistant followed by Klebsiella pnemoniae (n=24, 21.9), Escherichia coli (n=13, 13.5%) and streptococci (n=3, 3.1%). Antibiotic resistance was common, with the sensitivity to various antibiotics being ampicillin 19%, gentamicin 21.6%, cefotaxime 32.8%, amikacin 50%, chloromycetin 59.6% and ciprofloxacin 90.3%. **[Indian J Pediatr 2001; 68 (8) : 715-717]**

Key words : *Neonatal sepsis; Staphylococcus aureus; Antimicrobial resistance*

Neonatal septicemia either acquired from the mother (vertical transmission) or nosocomial (horizontal transmission) continues to haunt the neonatologists all over the world as a formidable problem with considerable morbidity and mortality and significant economic costs. Blood culture remains as the gold standard for the diagnosis of neonatal sepsis. Only 54.4% of neonates with clinical diagnosis of sepsis had positive blood cultures. (National Neonatal Perinatal Database, 1995).[1] This could be due to the neonatal sepsis being a great mimicker giving rise to symptoms and signs compatible with almost every other neonatal problem or problem in growing the organism *in vitro* due to the fastidious nature of the organism itself, prior antibiotic therapy and/or lack of improvised microbiological techniques.[2] Government Kasturba Gandhi Hospital for Women and Children, Chennai is a large teaching maternity hospital affiliated to the Chennai Medical College and Research Institute with an annual delivery rate of more than 10,000. An audit of microbiological profile of babies with neonatal sepsis over the years 1994 to 1996 showed that staphylococcus aureus is the predominant pathogen in our centre (136 of 155, 87.7% in 1994, 126 of 260, 48.5% in 1995 and 139 of 242, 57.4% in 1996). In view of this, we planned to study the clinical and microbiological profile of neonates with blood culture positive sepsis over the six months period January to June 1997 to gain some insight into the reasons and possible solutions to the predominance of Staphylococcus aureus in our centre.

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MATERIALS AND METHODS

Neonates with culture proven sepsis amongst all the consecutive live born neonates delivered during January–June, 1997 constitute the study. At the end of each month, all the neonates with sepsis during that month were reviewed and their clinical data and bacteriological profile recorded. Since we analyzed each month separately in the first instance, results from data analysis were used in subsequent months for clinical decisions like using ciprofloxacin for neonates not responding to standard antibiotics. Standard culture techniques for aerobes and facultative anaerobes were used. No specific anaerobic culture media were used during the study period. Neonates becoming symptomatic within 48 hours of life were classified as early onset sepsis (vertical transmission) and those becoming symptomatic after 48 hours termed as late onset sepsis (horizontal transmission). Outborn babies with sepsis admitted during this period (n = 24) are excluded from this communication.

RESULTS

Of 4907 live born neonates during the study period, 96 had culture proven sepsis giving an incidence of 1.96%.

They accounted for 16.5% (96 of 581) of nursery admissions during this period. The culture positive rate was 51.34% (96 of 187). 48 of them (50%) had early onset sepsis while the remaining 48 (50%) had late onset neonatal sepsis. Lethargy with refusal of feeds (n=26, 28%), fever (n=26, 28%) and respiratory distress (n=29, 31.3%) were the major presenting features. Necrotizing enterocolitis was seen in 2 neonates of whom 1 died, sclerema in 5 (3 died) and arthritis in 2 (none died). Respiratory distress was significantly more likely to be the presentation of early onset neonatal sepsis (25 of 48 in early onset group Vs 4 of 48 in late onset group, $\chi^2 = 19.8$, $p < 0.0001$) whereas fever was more likely to be the presenting feature of late onset sepsis (4 of 44 in early onset group Vs 22 of 48 in late onset group, $\chi^2 = 15.2$, $p<0.0001$). Lethargy with refusal of feeds as a presenting feature was not different in early onset and late onset groups (12 of 48 in early onset group Vs 14 of 48 in late onset group, $\chi^2 = 0.21$, $p = 0.6$).

Staphylococcus aureus was the predominant pathogen accounting for 61.5% of cases (n =59), Klebsiella pneumoniae accounted for 21.9% (n = 21), Escherichia coli (E.coli) 13.5% (n = 13) and streptococcal species for the remaining 3.1% (n = 3). Streptococcal isolates were not typed for Lancefield's grouping. 50% of (n = 48) of cases were of early onset and remaining 50% (n = 48) were of late onset and presumably nosocomially acquired. While E.coli was acquired vertically in majority of cases (11 vertical Vs 2 nosocomial), the mode of acquisition did not seem to differ significantly in the S.aureus group (24 vertical Vs 35 nosocomial) and the Klebsiella group (13 vertical Vs 8 nosocomial). The antibiotic sensitivities of the organisms is represented in Table 1.

13 of the 96 neonates with sepsis died giving a case fatality rate of 13.53%. There were 8 deaths in the *S.aureus* group (13.6%), 4 deaths in the Klebsiella group (19%) and 1 death in the *E.coli* group (7.7%). 9 of the 48 neonates with early sepsis had died as opposed to 4 out of 48 neonates with late onset sepsis ($X^2 = 2.22$, $p=0.1$). When analyzed according to birth weight, 8 of 12 septic neonates with birth weight less than 1500g had died as against 2 of 15 neonates weighing 1500g to 2000g and 3 of the 69 neonates weighing more than 2000g. (X^2 for linear trend = 18.8, $p<0.0001$).

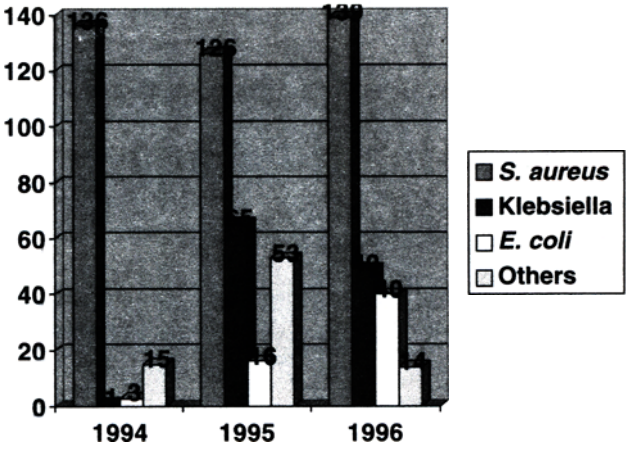

Fig. 1. Causative organisms in neonatal sepsis

DISCUSSION

The 1.96% incidence of culture proven sepsis and the culture positive rate of 51.34% are comparable to previously published studies in Indian literature.[3-6] 50% of our neonates had early onset sepsis which is much higher than the 25% incidence of early onset sepsis reported by the Australian Study group for Neonatal infections.[7] This high incidence of early onset sepsis creates a reservoir of infected neonates who pose a significant risk of nosocomial transmission to other neonates in the nursery. This underscores the necessity for studying the bacterial colonization of the maternal genital tract and the role of intrapartum antibiotic prophylaxis to bring about a reduction of early onset sepsis.

TABLE 1. Sensitivity Pattern of the Organisms Isolated

Antibiotics	*S. aureus* % (n)	Klebsiella % (n)	*E. coli* % (n)	Overall % (n)
Gentamicin	24.4 (41)	25 (20)	7.7 (13)	21.6 (74)
Ampicillin	28 (50)	9.5 (21)	0 (13)	19 (84)
Cefotaxime	33.3 (42)	33.3 (12)	25 (4)	32.8 (58)
Amikacin	38.1 (42)	83.3 (12)	60 (10)	50 (64)
Cloxacillin	34 (47)	—	—	—
Chloromycetin	73.8 (42)	45 (20)	33.3 (12)	59.5 (74)
Ciprofloxacin	88.1 (59)	100 (21)	84.6 (13)	90.3 (93)

Figures outside parenthesis represent the per cent sensitivity of the organisms to the particular antibiotic and the figures in parenthesis indicate the number of strains tested for the particular antibiotic. (e.g) number of strains sensitive to gentamicin is 10 of 41 = 24.4 (41).

Lethargy, fever and respiratory distress were the three frequently presenting features in septic neonates. Respiratory distress was more likely to be the presenting feature of early onset sepsis probably because the mode of acquisition involves aspiration from maternal genital tract. It is worth noting that 28% of septic neonates presented with fever in a city with tropical climate like Chennai where one expects to find environmental fever (the so called dehydration fever). The message is that any neonate with fever has to be evaluated for sepsis to avoid preventable catastrophies. Despite our unit following an exclusive breastfeeding policy, there were two definite cases of necrotizing enterocolitis (with pneumatosis intestinalis). Lumbar punctures are not done routinely before starting antibiotics in our centre because of logistic problems (non-availability of 24h laboratory support). In the 15 neonates in whom CSF analysis was done in the study group, only one had positive culture (*S. aureus*).

S. aureus is the predominant pathogen of neonatal sepsis in our centre (61.5%) followed by Klebsiella (21.9%) and *E. coli* (13.5%). This is different from that reported by the National Neonatal Perinatal Database wherein Klebsiella is the predominant pathogen (29%) followed by *S. aureus* (13%) and *E. coli* (12%).[1] A recent study from Coimbatore has also found S.aureus as the predominant pathogen accounting for 50.6% of the isolates.[8] Majority of the *S. aureus* strains in our study (66%) are Methicillin resistant (MRSA). No clustering of MRSA strains were noticed during study period and a significant proportion of *S. aureus* cases were acquired early (24 of 59, 40.7%), presumably by vertical transmission thereby implying maternal colonization. Efforts to decrease *S. aureus* colonization by cord and skin care have been studied before but whether this will reduce the incidence of systemic sepsis is still unproven.[9,10] Aggressive microbiological surveillance and carrier elimination which are traditionally instituted for control of MRSA have been questioned in recent articles.[11,12]

Antimicrobial drug resistance is an important issue to tackle. For *S. aureus* only chloromycetin (73.8%) and ciprofloxacin (88.1%) had more than 50% sensitivities and amikacin was the next best with sensitivity of 38.1%. Amikacin remains as a good drug for Klebsiella and *E. coli* in our centre. National Neonatal Perinatal Database also identifies antimicrobial resistance in Klebsiella and enterobacter species as a major problem.[13] Vancomycin is not available in our hospital because of its cost. Among the three neonates with more than 2 kg who died of sepsis, two were term neonates with MRSA sepsis. These deaths made us to offer ciprofloxacin with the informed consent of the parents in four neonates in this study group with gratifying results. Multidrug resistant MRSA has been accepted as an indication for ciprofloxacin treatment in pediatric age group but its use in neonates is still experimental because of lack of safety data.[14]

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