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Bacteriological Profile and Antibiogram of Neonatal Sepsis in a Tertiary Care Hospital

Londhe A.C.*, Deshmukh L.S., Joshi A.K.*****

Author's Affiliation:
*Assistant Professor, **Professor and Head, ***Associate Professor, Dept. of Neonatology, Government Medical College, Aurangabad, Maharashtra, India.

Reprint Request:
Londhe Atul Chandrakant,
5A, Harikirshna Apartment, Old SBH Colony, Peer Bazaar, Aurangabad -431001, Maharashtra
E-mail:
atul.londhe1982@gmail.com

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Abstract

Introduction: Neonatal sepsis is one of the major causes of neonatal morbidity and mortality. It is responsible for about 30-50% of the total neonatal deaths in developing countries. Delay in diagnosis and treatment of sepsis can have devastating consequences in a neonate. So, surveillance is necessary to identify common signs and the bacterial pathogen as well as its antibiotic sensitivity pattern in a particular area. *Methodology*: This was a retrospective study conducted in Government Medical College and Hospital, Aurangabad from October 2013 to September 2015. Data was collected retrospectively by analyzing case sheet papers of neonates admitted to Neonatal Intensive Care Unit (NICU), GMCH Aurangabad during the study period. *Results:* Out of 3217 babies admitted to NICU, 523 (16%) developed culture positive sepsis. Females and preterm babies were more affected. Gram negative isolates were more common with Enterobacter aerogens being the most common organism followed by Klebsiella pneumoniae. Staphylococcus aureus was the most common gram positive isolate. There was wide spread resistance to cephalosporins among gram negative organisms. *Conclusion:* Early onset sepsis was more common in our set up. Gram negative organisms were predominant. Enterobacter aerogens was the most common isolate followed by Klebsiella pneumoniae. All gram negative organisms were resistant to cephalosporins. Staphylococcus aureus was most common gram positive isolate.

Keywords: Neonate; Sepsis; Culture; Antibiotic Sensitivity.

Introduction

Neonatal sepsis is one of the major causes of neonatal morbidity and mortality. It is responsible for about 30-50% of the total neonatal deaths in developing countries [1,2]. Despite increased awareness of hand hygiene, newer methods of early diagnosis and treatmentandnewer antimicrobial agents, sepsis claims a big life toll in neonates .

Neonatal Sepsis refers to systemic and generalised bacterial infection of neonate documented by positive blood culture. Isolation of organism from blood culture is considered as gold standard for diagnosis of bacterial sepsis. It is the most common diagnosis at referral facilities. According to State of India's Newborn report 2014 (SOIN 2014), the incidence of neonatal sepsis in India is 30 per thousand live birth in hospital based studies while community-based studies indicate an incidence of 2.7% to 17% of all live births [3]. Also Sepsis contributed to 33% of overall neonatal deaths [3]. Delay in diagnosis and treatment of sepsis can have devastating consequences in a neonate. So, surveillance is necessary to identify common signs and the bacterial pathogen as well as its antibiotic sensitivity pattern in a particular area.

Neonatal sepsis is broadly divided in two types according to age of onset. Early onset sepsis (onset of symptoms/signs within 72 hours of life) and Late Onset Sepsis (>72 hours to 28 days of life). This classification is of particular importance for

identification of predominant organisms. Early onset sepsis is caused by microorganisms acquired from mother (vertically transmitted or perinatally acquired). In Late Onset sepsis, infection is acquired in NICU or in community.

In the developed world, Group B Streptococcus (GBS) and Coagulase negative staphylococci (CONS) are the most common causes of Early Onset Sepsis (EOS) and Late Onset Sepsis (LOS) respectively [4]. But same is not true in the developing world. In India, common organisms for neonatal sepsis are Klebsiella and Staphylococcus aureus [3]. The prevalence of the bacterial pathogen and its sensitivity pattern in a particular area can guide for empirical antibiotic treatment for neonatal sepsis.

The aim of the present study is to profile bacteriological spectrum and its sensitivity pattern in neonatal sepsis in a Tertiary care center in Aurangabad.

Aim and Objectives

1. To study pattern of bacterial isolates in neonatal sepsis.
2. To study antibiotic sensitivity pattern of these organisms.
3. To study incidence of meningitis among neonates with culture proven sepsis.

Methodology

This was a retrospective study conducted in Government Medical College and Hospital, Aurangabad from October 2013 to September 2015. It is one of the largest Tertiary Care center serving urban and rural population in Marathwada region. Data was collected retrospectively by analyzing case sheet papers of neonates admitted to Neonatal Intensive Care Unit (NICU), GMCH Aurangabad during the study period. Institutional ethical committee approval was obtained.

The Neonates were suspected having sepsis if one of the following symptoms/signs was present: Hypothermia, poor feeding, lethargy, respiratory distress, apnea, irritability and seizures. Sepsis screen was sent along with blood culture.

Only babies with positive blood culture were enrolled in the study. Details were entered in proforma. Babies with positive blood culture subjected to CSF examination as per unit protocol.

Criteria for Diagnosing Bacterial Meningitis was

a. CSF Proteins > 100 mg/dl in term [15] and >150 mg/dl in preterm [14] and/or
b. CSF sugar < 50% of BSL or < 40 mg/dl
c. CSF microscopy - > 30 cells
d. Positive CSF culture

Antibiotic susceptibility testing was done by disc diffusion method. For Gram positive organisms antibiotics tested were Ampicillin, Amoxicillin-clavulanic acid, Cefoxitin, Gentamicin, Erythromycin, Tetracycline and TMP-SMX. For gram negative organisms Amikacin, Cefepime, Cefotaxime, Ceftazidime, Piperacillin-tazobactum, Meropenem and Ciprofloxacin were tested.

The data obtained was entered into Microsoft Excel. Pearson Chi-square test and Standard Error between two Means were used to test for statistical significance between the parameters and clinical criteria. P value <0.05 was considered to be statistically significant.

Results

During 2 year study period a total of 3217 neonates were admitted in NICU. Of that, 523 (16%) developed culture positive sepsis. More females (59.9%) had sepsis than males. More preterm babies (71%) had culture positive sepsis than term babies (Figure 1).

Gram negative sepsis was more common with Enterobacter aerogens (29.8%) being most common organism followed by Klebsiella pneumoniae (21.4%). Staphylococcus aureus (13.2%) was the most common gram positive isolate followed by Coagulase negative staphylococci (3.6%) (Table 1).

Early onset sepsis (87.2%) was more common in our set up than late. Enterobacter aerogenes was the most common organism in both early (126) and late (30) onset sepsis. This may be chiefly because of outbreak during July 2014 to October 2014 (Table 2).

Out of 523 babies, 29% (152) had bacterial meningitis. Neonates infected with organisms from Enterobacteriaceae family (46%) and E. Coli (45%) were commonly associated with meningitis (Table 3).

Gram negative organisms were sensitive to amikacin, ciprofloxacin and meropenem. There was wide spread resistance to cephalosporins across all gram negative organisms (Table 4).

Gram positive organisms were mostly sensitive to Tetracycline, Gentamicin and cefoxitin (Table 5).

Three hundred and sixteen babies (60.4%) were discharged on successful completion of treatment.

Overall Mortality was 39.6% in culture positive neonatal sepsis. Mean hospital stay was 12.7 days.

(Figure 2).

Table 1: Bacterial isolates in blood culture

Sr. No	Organisms	No.	%
1	Enterobacter aerogenes	156	29.8
2	Klebsiella pneumoniae	112	21.4
3	Staphylococcus aureus	69	13.2
4	Enterobacter cloacae	66	12.6
5	Escherichia coli	51	9.8
6	Enterobacteriaceae family	22	4.2
7	Staphylococcus, coagulase negative	19	3.6
8	Acinetobacter baumannii	13	2.5
9	Pseudomonas aeruginosa	5	1.0
10	Streptococcus pneumoniae	4	0.8
11	Streptococcus, beta-haem. Group A	4	0.8
12	Citrobacter freundii	2	0.4
	Total	**523**	

Table 2: Distribution of cases according to age of onset

Sr. No	Organisms	EOS	LOS
1	Enterobacter aerogenes	126	30
2	Klebsiella pneumoniae	105	7
3	Staphylococcus aureus	62	7
4	Enterobacter cloacae	56	10
5	Escherichia coli	44	7
6	Enterobacteriaceae family	19	3
7	Staphylococcus, coagulase negative	16	3
8	Acinetobacter baumannii	13	0
9	Pseudomonas aeruginosa	5	0
10	Streptococcus pneumoniae	4	0
11	Streptococcus, beta-haem. Group A	4	0
12	Citrobacter freundii	2	0
	Total	456	67

Table 3: Bacterial Meningitis in culture positive sepsis

Sr. No	Organisms	CSF +	CSF -
1	Enterobacter aerogenes	59 (38%)	97
2	Klebsiella pneumoniae	20 (18%)	92
3	Staphylococcus aureus	10 (14%)	59
4	Enterobacter cloacae	24 (36%)	42
5	Escherichia coli	23 (45%)	28
6	Enterobacteriaceae family	10 (46%)	12
7	Staphylococcus, coagulase negative	0 (0%)	19
8	Acinetobacter baumannii	3 (23%)	10
9	Pseudomonas aeruginosa	0 (0%)	5
10	Streptococcus pneumoniae	3 (75%)	1
11	Streptococcus, beta-haem. Group A	0 (0%)	4
12	Citrobacter freundii	0 (0%)	2
	Total	**152 (29%)**	**371**

Table 4: Antibiotic sensitivity pattern in Gram negative organisms

Sr. No	Antibiotic	Eae n=156	Kpn n=112	Ecl n=66	Eco n=51	Ef n=22	Aba N=13	Pae n=5	Cfr n=2
1	Amikacin	102 (65%)	74 (66%)	54 (82%)	37 (73%)	19 (86%)	5 (39%)	3 (60%)	2 (100%)
2	Cefepime	43 (28%)	27 (24%)	07 (11%)	21 (41%)	15 (68%)	02 (15%)	02 (40%)	01 (50%)
3	Cefotaxime	36 (23%)	28 (25%)	02 (0.03%)	22 (43%)	07 (32%)	02 (15%)	01 (20%)	0 (0%)
4	Ceftazidime	40 (26%)	26 (23%)	04 (0.06%)	21 (41%)	10 (46%)	01 (7%)	01 (20%)	01 (50%)
5	Ciprofloxacin	120 (77%)	65 (58%)	62 (94%)	29 (57%)	11 (22%)	04 (30%)	03 (60%)	02 (100%)
6	Meropenem	98 (63%)	76 (68%)	53 (81%)	35 (69%)	16 (73%)	04 (30%)	04 (80%)	02 (100%)
7	Piperacillin+ tazobactum	86 (56%)	61 (55%)	46 (70%)	31 (60%)	12 (54%)	03 (23%)	02 (40%)	02 (100%)

(Eae- Enterobacteraerogenes, Kpn- Klebsiellapneumoniae, Ecl- Enterobacter cloacae, Eco-Escerichia coli, Ef- Enterobactericeae family, Aba-Acinetobacterbaumanii, Pae- Pseudomonas aeruginosa, Cfr- Citrobacterfrenudii)

Table 5: Antibiotic sensitivity pattern in Gram positive organisms

Sr. No	Antibiotics	Staph aureus n = 69	CONS n = 19	Strep pn n = 04	GABHS n = 04
1	Ampicillin	31(45%)	6(31%)	2(50%)	1(25%)
2	AmoxClav	23(33%)	10(53%)	3(75%)	2(50%)
3	Cefoxitin	32(47%)	9(47%)	0(0%)	0(0%)
4	Erythromycin	25(36%)	5(26%)	1(25%)	1(25%)
5	Tetracycline	50(73%)	17(90%)	3(75%)	3(75%)
6	Gentamicin	30(44%)	10(53%)	1(25%)	1(25%)
7	TMP SMX	35(50%)	10(53%)	1(25%)	0(0%)

(CONS-Coagulase negative Staphylococcus, GABHS-Group A beta Hemolytic Streptococcus, TMP-SMX- Trimethoprim-Sulphamethoxazole)

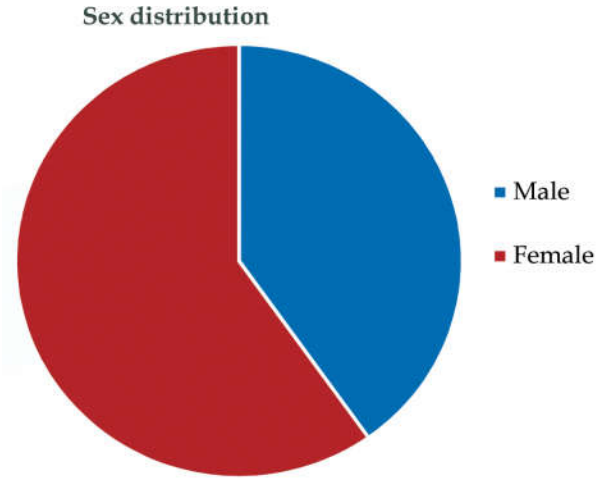

Fig. 1: Sex distribution in culture positive sepsis

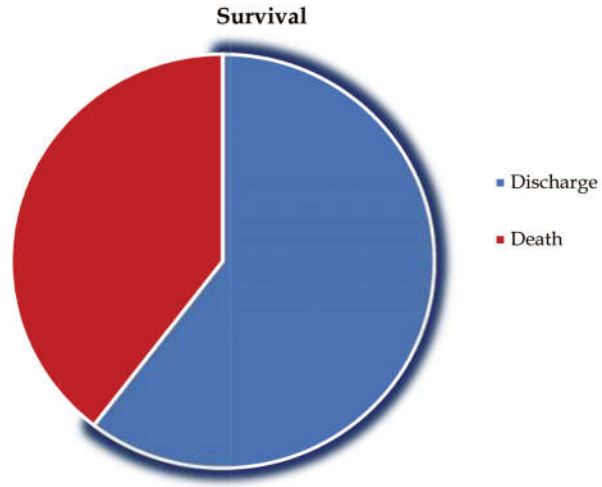

Fig. 2: Survival in culture positive sepsis

Discussion

Neonatal sepsis is a leading cause of death in developing countries like India, followed by prematurity, low birth weight, perinatal asphyxia. So, early diagnosis and appropriate antibiotic therapy is needed to prevent neonatal mortality arising from sepsis. For that, we should know common bacterial isolates and their antibiogram in our setup to aid proper selection of antibiotics.

During the study period, a total of 3217 neonates admitted in our NICU. Of that, 523 (16%) developed culture positive sepsis. This is much lower as compared to other studies like Roy I et al [5] (47.5%) and Kayange N et al [6] (38.9%). But in contrast, Shreshtha NJ et al [7] (6.1%) and KarambinM et al [8] (10.6%) had similar outcomes. The percentage of culture positive sepsis in our study is low as it is against total NICU admissions and not in cases with suspected sepsis just.

Female sex and prematurity were found to be risk factors for neonatal sepsis in our study. Females (59.8%) were more affected than males in our study. This is in contrast with Mustafa M et al [9] (61%), Nawshad ASM et al [10] (63%) and Karambin M et al [8] (58%).

More preterm babies (70.6%) have culture positive sepsis than term (29.4%). This is in accordance with Karambinet al [8] (67%). But Naher BS et al [11] found more term babies (30.6%) were affected than preterm.

Early onset sepsis (87%) was common in our study as this unit caters only to inborn babies. Naher BS et al [11] (73.3%), Roy I et al [5] (71%) and Mustafa M et al [9] (58%) found similar results. But Shreshtha NJ et al [7] (16%), KarambinM et al [8] (23%) and Kuruvilla KA et al [12] (24%) found Late onset sepsis was more common presentation of neonatal sepsis due to outborn admissions.

Gram negative isolates were most common (82%) in our study with Enterobacteraerogens (29.8%) being most common followed by Klebsiellapneumoniae (21.4%). This may be chiefly because of outbreak of enterobacter sepsis during July 2014 to October 2014 in our NICU. Other gram negative organisms were Enterobacter cloacae (12.6%), E coli (9.8%) and organisms from enterobacteriacae family (4.2%). We did not find any case of GBS in our study. In Karambin M et al [8] study from Iran, Enterobacter (78%) was the most common organism causing neonatal sepsis. Other studies demonstrated Klebsiella pneumonia as the most common organism [5,6,9,12,13].

Among gram positive organisms, Staphylococcus

aureus (69/523) contributed the most.

29% neonates developed bacterial meningitis in our study. Only one study reported the incidence of meningitis in neonatal sepsis but it is much lower (<1%) than our study [12].

All gram negative organisms were having considerable sensitivity to amikacin and piperacillin-tazobactum and were highly susceptible to Meropenem and ciprofloxacin. In our study, there was increasing resistance to third-generation cephalosporins, probably attributable to extended spectrum beta-lactamase (ESBL) production by Gram negative bacteria, especially Klebsiellapneumoniae. Our findings correlate with previous studies [5,6,8,9,12].

All gram positive organisms were moderately susceptible to tetracyclines. Staphylococcus aureus was having intermediate susceptibility to ampicillin and gentamicin. We could do antibiotic susceptibility testing on these available drugs only. This is contradictory to previous studies which showed considerable resistance to penicillin group and gentamicin [5,8-10].

Nearly two third babies with sepsis survived despite appropriate antibiotic therapy and good supportive care. It is comparable to Nawshad ASM et al [10] but much higher in comparison with Kuruvilla KA et al [12] (14%) and Kayange N et al [6] (19%).

Conclusion

From our study we noticed that Gram negative bacteria were more commonly the cause of neonatal sepsis and Enterobacter aerogens and Klebsiella pneumoniae were the predominant pathogens. We also noticed that these Gram negative bacteria were resistant to most cephalosporins. The higher antibiotics such as Meropenem should be reserved for multi-drug resistant Gram negative bacteria.

Positive blood culture is considered as gold standard for diagnosis of neonatal sepsis and their antibiogram is the best guide to antimicrobial therapy, as resistance to antibiotics is a common problem that causes ineffectiveness of empirical treatment. Prevention of prematurity, strict infection control practices, adherence to hand hygiene practice combined with judicious use of antibiotic therapy are the main solutions to this problem. Neonatal sepsis remains major cause of morbidity and mortality especially in preterm babies. Every attempt should be made to prevent sepsis by following asepsis protocols designed for one's NICU. Also rational use of antibiotics is necessary to prevent emergence resistant flora.

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