

## Research Article

# Neonatal septicemia: isolates and their sensitivity pattern with emergence of *Citrobacter* septicemia

Ram Sunder Sharma<sup>1\*</sup>, Manali Tiwari<sup>2</sup>, Ram Pratap Bansal<sup>1</sup>

<sup>1</sup>Department of Pediatrics, SNCU, G. R. Medical College Gwalior, Madhya Pradesh, India

<sup>2</sup>Department of Pediatrics, AMRI Hospital, Kolkata, India

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### \*Correspondence:

Dr. Ram Sunder Sharma,

E-mail: [dr.ramsundersharma@gmail.com](mailto:dr.ramsundersharma@gmail.com)

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### ABSTRACT

**Background:** Septicemia in neonates refers to bacterial infection documented by positive blood culture in the first 28 days of life and is one of the leading causes of neonatal mortality and morbidity in India. The aim of the study was to identify clinical neonatal sepsis cases and isolate responsible microorganism by blood culture and determine sensitivity pattern of isolates in a tertiary care hospital.

**Methods:** It is a hospital based retrospective study involving neonates admitted in department of paediatrics at a medical college hospital. Two hundred twenty five blood samples were collected for blood culture from neonates with clinical sepsis with standard protocol. Isolation of microorganism and antibiotic sensitivity testing was done with disc diffusion method.

**Results:** Blood culture reports were positive in 43.55% cases of clinical sepsis. Among positive blood culture reports gram negative isolates were more frequent (75.51%). Most commonly isolated was *Klebsiella* species (34.70%), most common gram positive isolate was *Streptococcus* (10.20%). Prevalence of *Citrobacter* species isolation was 16.12%. Among gram negative isolates best overall sensitivity was towards levofloxacin (97.3%) followed by amikacin (60.8%). Sensitivity to piperacillin+tazobactam (20.3%) and cefoperazone+sulbactam (23%) were very low. Gram positive isolates had best sensitivity to vancomycin and linezolid.

**Conclusions:** Gram negative organisms (*Klebsiella* species, *Citrobacter* species), *Streptococcus*, *Staphylococcus* are leading cause of neonatal sepsis. There are high levels of resistance to routinely used antibiotics among them. Therefore results of this study suggest that we should revise our antibiotic treatment policy and emphasize on rationale antibiotic use.

**Keywords:** Neonatal septicemia, Antibiotic resistance, *Citrobacter*

### INTRODUCTION

Neonatal sepsis is a significant cause of neonatal morbidity and mortality in neonates, particularly in preterm, low birth weight babies.<sup>1,2</sup> Neonatal mortality rate in India in year 2010 was 33 per 1000 live births which is a great burden to society<sup>3</sup>. Sepsis is commonest cause of neonatal mortality in India and responsible for 30 - 50% of mortality.<sup>4,5</sup> Septicemia in neonates refers to

generalized bacterial infection documented by a positive blood culture in the first 4 week of life. Neonatal sepsis can be classified as early onset neonatal sepsis (EONS) within 72 hours of birth and late onset neonatal sepsis (LONS) after 72 hours of birth.

The spectrum of organisms that causes neonatal sepsis changes over times and varies from region to region. This

is due to the changing pattern of antibiotic use and changes in life style.

In developed countries, group B streptococci and coagulase negative Staphylococci are the most common microbial agents for early onset and late onset sepsis (EOS & LOS) respectively. However, in the developing countries, these organisms are less frequently isolated. Resistance to commonly used antibiotics is increasing. Formulation of appropriate rational antibiotic policy is essential to control this growing problem. There is an urgent need to do longitudinal surveillance of the microbial flora in every hospital.<sup>6</sup> With this background, the present study was undertaken to study the incidence of neonatal septicemia, and bacteriological profile of neonatal septicemia and their antimicrobial sensitivity pattern in a Government Medical college and hospital.

### METHODS

The present study was carried out to study the bacteriological profile of neonatal septicemia and their antibiotic susceptibility pattern for planning strategy for the management of these cases from July 2015 to December 2015 in a Government medical college and hospital.

**Inclusion criteria:** All neonates presenting with birth asphyxia convulsion, respiratory distress (respiratory rate >60 breaths/min, nasal flaring, severe chest indrawing, grunting, crepitations) bulging fontanelle, redness around umbilicus, temperature >37.7°C or <35.5°C, lethargic or unconsciousness, reduced movements, not able to feed, not sucking at all, increased capillary refill time (>3 seconds) were included in the study.

**Exclusion criteria:** Surgical cases, patients with congenital anomalies, birth weight less than 1000 gm and

age more than 28 days at the time of diagnosis were excluded from the study.

**Method:** Blood sample were collected either before starting antimicrobial therapy or in patients already on antibiotic therapy, blood sample was collected just before the next dose of antibiotic therapy. One ml of blood was withdrawn from all neonates aseptically and inoculated in blood culture bottle containing 10 ml brain heart infusion broth. These culture bottles were transferred to department of microbiology immediately for isolation of pathogen and to know their antimicrobial susceptibility pattern. Antimicrobial susceptibility pattern was done by disc diffusion method. All blood culture reports were analyzed and those neonates with positive blood culture reports were evaluated.

### RESULTS

During study period total 225 newborns were admitted with clinical sepsis. Blood culture was positive in 98 (43.55%) cases. Details of positive blood culture are provided in Table 1. Gram negative organisms were isolated more frequently (75.51%) than gram positive organisms (24.48%).

**Table 1: Frequency of organism isolation.**

| Organism              | Frequency of isolation (N=98) |
|-----------------------|-------------------------------|
| <i>Klebsiella</i>     | 34 (34.70%)                   |
| <i>Citrobacter</i>    | 16 (16.12%)                   |
| <i>E. Coli</i>        | 10 (10.20%)                   |
| <i>Streptococcus</i>  | 10 (10.20%)                   |
| <i>Enterobacter</i>   | 09 (09.18%)                   |
| <i>Staphylococcus</i> | 08 (08.16%)                   |
| CONS                  | 06 (06.12%)                   |
| <i>Acinotobacter</i>  | 04 (04.08%)                   |
| <i>Pseudomonas</i>    | 01 (01.02%)                   |

**Table 2: Antibiotic sensitivity pattern of enterobacteriaceae organisms.**

| Drug                     | <i>Klebsiella</i> sp. (n=34) | <i>Citrobacter</i> sp. (n=16) | <i>Enterobacter</i> sp. (n=09) | <i>E. coli</i> (n=10) | <i>Acinotobacter</i> sp. (n=04) | <i>Pseudomonas</i> sp. (n=01) | Total (n=74) |
|--------------------------|------------------------------|-------------------------------|--------------------------------|-----------------------|---------------------------------|-------------------------------|--------------|
| Amikacin                 | 18 (52.94%)                  | 09 (55.2%)                    | 05 (55.5%)                     | 10 (100%)             | 02 (50%)                        | 01(100%)                      | 45 (60.8%)   |
| Ampicillin               | 04 (11.76%)                  | 00 (00%)                      | 04 (44.4%)                     | 00 (00%)              | 00 (00%)                        | 00 (00%)                      | 08 (10.8%)   |
| Cefoperazone + Sulbactam | 04 (11.76%)                  | 03 (18.7%)                    | 04 (44.4%)                     | 06 (60%)              | 00 (00%)                        | 00 (00%)                      | 17 (23%)     |
| Cefixime                 | 07 (20.58%)                  | 02 (12.5%)                    | 01 (11.1%)                     | 07 (70%)              | 00 (00%)                        | 00 (00%)                      | 17 (23%)     |
| Cefotaxim                | 14 (41.17%)                  | 07 (43.7%)                    | 06 (66.6%)                     | 05 (50%)              | 02 (50%)                        | 00 (00%)                      | 34 (46%)     |
| Ceftazidime + cv         | 15 (44.11%)                  | 05 (31.2%)                    | 07 (77.7%)                     | 05 (50%)              | 00 (00%)                        | 00 (00%)                      | 32 (43.2%)   |
| Ceftriaxone              | 20 (58.82%)                  | 06 (37.5%)                    | 06 (66.6%)                     | 06 (60%)              | 02 (50%)                        | 00 (00%)                      | 40 (54%)     |
| Gentamycin               | 11 (32.35%)                  | 08(50%)                       | 04 (44.4%)                     | 06 (60%)              | 00 (00%)                        | 00 (00%)                      | 29 (39.2%)   |
| Levofloxacin             | 34 (100%)                    | 16(100%)                      | 08 (88.8%)                     | 10 (100%)             | 04 (100%)                       | 00 (00%)                      | 72 (97.3%)   |
| Piperacillin/tazo.       | 03 (08.82%)                  | 09 (55.2%)                    | 03 (33.3%)                     | 00 (00%)              | 00 (00%)                        | 00 (00%)                      | 15 (20.3%)   |

Most common gram negative isolates (total 74) were *Klebsiella* species (34.70%) followed by *Citrobacter* species (16.12%) and *E coli* (10.20%). Other organisms isolated were *Enterobacter* species (9.18%), *Acinabacter* species (4.08%) and *Pseudomonas* (1.02%).

Among gram positive isolates (total 24) most frequently found organism was *Streptococcus* species (10.20%) followed by *staphylococcus* (8.16%) and CONS (6.12%).

Table 2 and 3 provides antibiotic sensitivity testing of isolated organism's gram negative and gram positive respectively. Among gram negative isolates best overall sensitivity was reported towards levofloxacin (97.3%) followed by amikacin (60.8%) and ceftriaxone (54%). These organisms showed poor sensitivity against antimicrobials like cefixime (23%), cefoperazone +sulbactam (23%) and Piperacillin+tazobactam (20.3%).

**Table 3: Antibiotic sensitivity pattern of gram positive isolates.**

| Drug                     | <i>Staphylococcus</i> (n= 08) | CONS (n=06) | <i>Streptococcus</i> (n=10) | Total (n=24) |
|--------------------------|-------------------------------|-------------|-----------------------------|--------------|
| Amikacin                 | 04 (50%)                      | 02 (33.3%)  | 06 (60%)                    | 12 (50%)     |
| Amoxyclav                | 02 (25%)                      | 00 (00%)    | 04 (40%)                    | 06 (25%)     |
| Ampicillin               | 00 (00%)                      | 00 (00%)    | 00 (00%)                    | 00 (00%)     |
| Azithromycin             | 00 (00%)                      | 02 (33.3%)  | 00 (00%)                    | 02 (8.3%)    |
| Cefoperazone + Sulbactam | 00 (00%)                      | 00 (00%)    | 00 (00%)                    | 00 (00%)     |
| Ceftazidime + cv         | 00 (00%)                      | 01 (16.6%)  | 00 (00%)                    | 01 (4.1%)    |
| Piperacillin/tazo.       | 01(12.5%)                     | 02 (33.3%)  | 01 (10%)                    | 04 (16.6%)   |
| Vancomycin               | 08 (100%)                     | 06 (100%)   | 04 (40%)                    | 18 (75%)     |
| Linezolid                | 08 (100%)                     | --          | --                          | --           |
| Nitrofurantoin           | --                            | --          | 06 (60%)                    | --           |

Among gram positive isolates best overall sensitivity in staphylococcus was towards vancomycin and linezolid. No organism showed resistance against towards these antimicrobial agents. 50% strains shows sensitivity against amikacin. In *Streptococcus* species best sensitivity was against amikacin and nitrofurantoin, 60% strain showed sensitivity against these agents. Among CONS all strains were sensitive to vancomycin

Among gram positive isolates overall sensitivity towards piperacillin + tazobactam is very low (16.6%) most of isolates showed resistance towards it.

## DISCUSSION

For effective management and empirical treatment of neonatal sepsis knowledge of bacteriological profile and sensitivity pattern is essential. Bacteriological profile and their sensitivity pattern vary in different geographical area and different institution. In present study blood culture positivity rate of clinical neonatal sepsis cases were 43.55%. Similar rates were also found by Desai et al and also by Jain et al, Chandel et al.<sup>7-9</sup>

In present study gram negative organisms constitutes a major portion which correlates with findings of Kamble et al and Jain et al.<sup>8,10</sup> Among gram negative organisms most frequently isolated organism was *Klebsiella* species similar results were also found by Jyothi et al.<sup>11</sup> A total 24.48% of gram positive organisms were isolated in our

study similar to Desai et al.<sup>7</sup> In this group streptococcus species was predominant organism.

Among gram negative isolates prevalence of *Citrobacter species* was 16.32% which was considerably high compared to other studies done previously by Nayar et al (2.1%), Bhat et al (3.05%).<sup>12,13</sup> Antimicrobial resistance among *Citrobacter* species was high and only levofloxacin was effective against all bacteria. Resistance pattern is illustrated in Table 2. This high prevalence of *Citrobacter* species might be attributed to selective growth of this nosocomial organism.

Results of antimicrobial sensitivity pattern revealed that majority of gram negative microorganism were resistant to commonly used antimicrobial agents. In recent past due to widespread misuse and over the counter medication, resistance to antibiotics like cefixime, piperacillin+tazobactam, cephaloperazone+sulbactam have emerged as a big threat in patient care and to society and many a times leads to treatment failures. Similar results on resistance also obtained by Chandel et al, Bhat et al.<sup>9,13</sup>

Among gram positive isolates *Staphylococcus* was sensitive to vancomycin and linezolid. No organism showed resistance to these agents. Sensitivity to amoxyclav was 50% and only one organism was sensitive to Piperacillin+tazobactam. *Streptococcus* and CONS also showed similar pattern of resistance. Among gram positive organism no one was sensitive to ampicillin and only 25% sensitive to amoxyclav. Surprisingly resistance

to piperacillin+tazobacram was very high among both gram positive and gram negative organisms and only 16.6% and 20.3% organisms were sensitive to it respectively. Similar results was also obtained by Bhat et al.<sup>2</sup> This high level of resistance to piperacillin+tazobacram might be due to excessive use of this agent in our unit being second line agent.

Keeping in mind this high level of resistance among organisms and selective growth of resistant strains we feel that it is extremely important to revise our antibiotic policy and should emphasize on rationale use of these agents to prevent further emergence of resistance. Second and third line antimicrobial should not be used as empirical treatment especially in low income countries like India where culture and sensitivity facilities not easily available.

## CONCLUSION

Gram negative organisms (*Klebsiella* species, *Citrobacter* species), *Streptococcus*, *Staphylococcus* are leading cause of neonatal sepsis. There are high levels of resistance to routinely used antibiotics among them. Therefore results of this study suggest that we should revise our antibiotic treatment policy and emphasize on rationale antibiotic use.

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