

**AN OBSERVATIONAL PROSPECTIVE STUDY OF PRESCRIPTION PATTERN OF  
ANTIMICROBIALS USED IN NEONATAL SEPSIS IN TERTIARY CARE HOSPITAL IN  
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**ABSTRACT**

**Background:** Neonatal sepsis is a Clinical syndrome manifested by systemic signs of infection and isolation of bacterial pathogens from bloodstream. Sepsis is the 3<sup>rd</sup> commonest cause of neonatal death. Neonatal mortality rate in Rajasthan is quite high and data on utilization of antimicrobials for neonatal sepsis is scanty therefore we planned to conduct this study. **Method:** Study was conducted in NICU of Umaid Hospital, a tertiary care teaching hospital associated with Dr. S. N. Medical College, Jodhpur, Rajasthan. 250 Neonates of either sex admitted to NICU with suspected or confirmed sepsis were included in the study while those neonates admitted in other wards were excluded from study. Appropriate patients were selected by regular visits to NICU and were followed till discharge from NICU. EPI-INFO version 7 software was used for statistical analysis of data. **Result:** Total 250 cases of neonatal sepsis were studied, of which 148(59.2%) were suspected and 102(40.8%) were confirmed (culture positive) cases. Majority of patients received 2 or 3 antibiotics during the course of therapy. Almost all (97.95%) antibiotics were prescribed by generic names and 77.7% were prescribed from EDL. Most commonly prescribed antibiotics were Ampicillin, Cefotaxime and Amikacin. 85.21% patients were discharged and mortality was 7.6%. **Conclusion:** Most commonly prescribed antibiotics were Ampicillin, Cefotaxime and Amikacin. Antibiotic utilization studies are good exploratory tools to know the role of drugs in society and they also create a basis for health care decision making.

**KEYWORDS:** Drug utilization pattern, Neonatal sepsis.**INTRODUCTION**

Globally, sepsis is still one of the major causes of morbidity and mortality in neonates, in spite of recent advances in health care units.<sup>[1]</sup> More than 40% of under five deaths globally occur in neonatal period, resulting in 3.1 million newborn deaths each year.<sup>[2]</sup> The majority of these deaths usually occur in low income countries and almost 1 millions of these deaths are attributed to infectious causes including neonatal sepsis, meningitis and pneumonia.<sup>[3]</sup> The incidence of neonatal sepsis according to National Neonatal Perinatal Database is 30 per 1000 live births. Neonatal sepsis is defined as a clinical syndrome in an infant 28days of life or younger, manifested by systemic signs of infections and isolation of a bacterial pathogen from the bloodstream.<sup>[4]</sup> Neonatal sepsis is caused by gram positive and gram negative bacteria and candida. Drug utilization studies are found to be useful tool to facilitate rational use of drugs in healthcare delivery systems. Drug utilization research was defined by WHO in 1977 as "The marketing, distribution, prescription and use of drug in society with

special emphasis on the resulting medical, social and economic consequences.<sup>[5]</sup> Antibiotics are among the most common drugs prescribed in hospital today.<sup>[6]</sup> As consumption of antibacterial rises, resistance to antibacterials becomes a major threat to public health. Existing evidence suggests that there is a casual association between antimicrobial usage in hospital and antimicrobial resistance. Some authors recommend that hospitals should monitor both antimicrobial use and susceptibility trends in an attempt to reduce emergence and spread of antimicrobial resistant pathogens.<sup>[7]</sup> Drug utilization research can provide useful information to health care providers and policy makers. It offers prospect of improving the quality of pharmacotherapy gaining insight in volume and cost development of drug use and estimating prevalence and incidence of disease rather than drug use. We planned to conduct this study because the data for antimicrobial use in neonatal sepsis in our region is scanty and further it would help us to know the present scenario of antibiotic utilization pattern

in our hospital and also help us to evaluate the factors effecting sepsis and mortality in sepsis.

## MATERIALS AND METHODS

The study was conducted in the department of pharmacology in collaboration with department of pediatrics (NICU) at Umaid hospital, a tertiary care hospital associated with Dr. S. N. Medical College, Jodhpur, Rajasthan.

### Study design

It is a prospective, observational and single centre study for duration of 1 year in NICU at Umaid hospital, Jodhpur.

### Sample size and study population

The study population included neonates (0-4 weeks) admitted to NICU at Umaid hospital, suspected /diagnosed as having neonatal sepsis. The study population included 250 cases of neonatal sepsis.

### Data collection

Period of data collection: It was for 1 year, from January 2018 to December 2018.

### Inclusion Criteria

1. All patients (0-4 weeks) of suspected/diagnosed neonatal sepsis of either sex admitted to NICU after starting date of the study.
2. Only those patients, whose parents gave informed consent were included in the study.

### Exclusion criteria

1. OPD patients or patients from other wards

### Study Method

Prior permission was taken from Institutional Ethics Committee. The NICU was visited regularly, appropriate patients were selected and enrolled according to inclusion and exclusion criteria. Data was collected from indoor case sheets and recorded on a pre structured case reporting form.

### Following data were collected

- Classes of antimicrobials used,
- Total number of antibiotics prescribed
- Antibiotics prescribed by generic names,
- Antibiotics given by parenteral route,
- Frequency of individual antibiotic used,
- Outcome of treatment
- Duration of treatment.

## STATISTICAL ANALYSIS

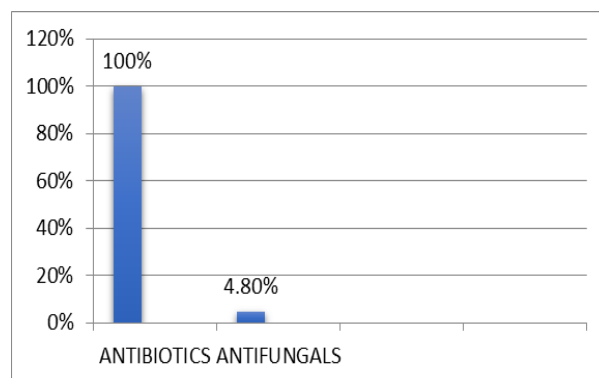
Average number of antimicrobials prescribed per patient was calculated by using mean. EPI-INFO version 7, which is a statistical software developed by Centres for Disease Control and Prevention (CDC) in Atlanta, Georgia (US) was used for statistical analysis.

## RESULTS

1. **Classes of Antimicrobials Used:** Antibiotics were prescribed in 100% patients and antifungals were used in 12 (4.8%) cases.

**Table 1: Classes of Antimicrobials Used.**

Antimicrobials	Number	Percentage
Antibiotics	250	100%
Antifungals	12	4.8%



**Figure 1: Classes of Antimicrobials Used.**

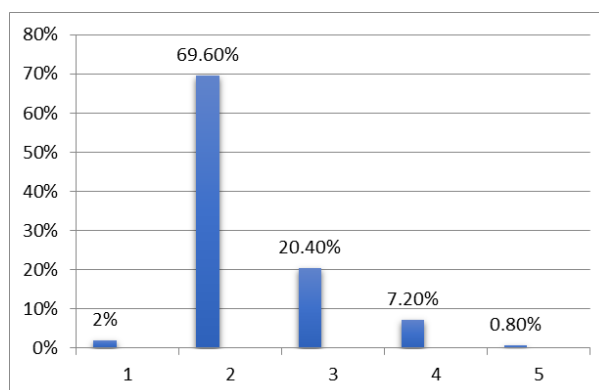
2. **Total Number of Antibiotics Prescribed**

Number of antibiotics prescribed to a patient during course of therapy ranged from 1 to 5, highest number of patients i.e 174 (69.6%) received 2 antibiotics, followed by 51 patients (20.4%) receiving 3 antibiotics, 18 patients (7.2%) receiving 4 antibiotics, 2 patients (0.8%) receiving 5 antibiotics and 5 patients (2%) receiving 1 antibiotic. Mean number of antibiotics prescribed to patients was 2.35.

**Table 2: Total Number of Antibiotics Per Encounter.**

No. Of antibiotics	No. of Encounters	Percentage
1	5	2%
2	174	69.6%
3	51	20.4%
4	18	7.2%
5	2	0.8%

Mean: 2.35.



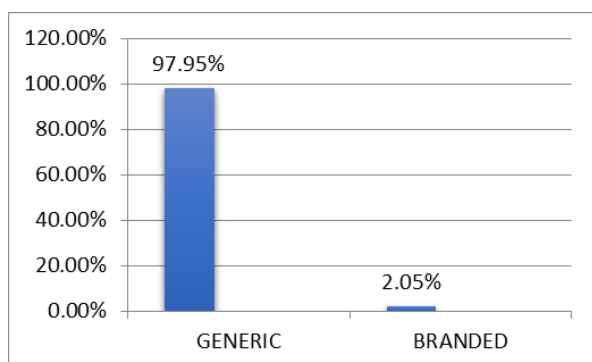
**Figure 2: Number of Antibiotics Prescribed.**

### 3. Percentage of Antibiotics Prescribed By Generic Names

Total 588 antibiotics were prescribed, of which, 576(97.95%) were prescribed by generic names and 12 (2.05%) were prescribed by trade name.

**Table 3: Drugs Prescribed By Generic Names.**

Drugs	Number	Percentage
Generic	576	97.95%
Branded	12	2.05%



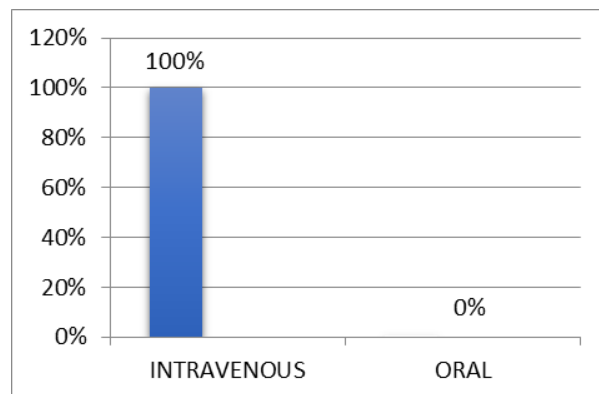
**Figure 3: Percentage of Drugs Prescribed By Generic and Trade Names.**

### 4. Percentage of Antibiotics Prescribed By Parenteral Route

100% drugs were prescribed by intravenous route.

**Table 4: Route of Administration of Drugs.**

Route	Number of Drugs	Percentage
Intravenous	588	100%
Oral	0	0%



**Figure 4: Percentage of Drugs Prescribed By I.V/Oral Route.**

### 5. Frequency of Individual Antibiotic Prescribed

Most commonly prescribed antibiotics were ampicillin and cefotaxime, both were prescribed in 67.2% patients. Amikacin was prescribed in 36.4% patients, Linezolid 12%, Vancomycin in 6.4%, Meropenem 3.2%, Aztreonam 2.8%, Amoxyclav and Ceftriaxone in 1.2% respectively, Cefoperazone + sulbactam, metronidazole and gentamicin in 0.8% respectively and Levofloxacin, ofloxacin and Tobramycin in 0.4% respectively.

**Table 5: Frequency of Individual Antimicrobial Drug Used.**

Drug	No. Of times prescribed	Percentage
Ampicillin	168	67.2%
Cefotaxime	168	67.2%
Amikacin	91	36.4%
Linezolid	30	12%
Piperacillin+tazobactam	26	10.4%
Vancomycin	16	6.4%
Meropenem	8	3.2%
Aztreonam	7	2.8%
Amphoterecin-b	7	2.8%
Fluconazole	5	2%
Amoxyclav	3	1.2%
Ceftriaxone	3	1.2%
Cefoperazone+sulbactam	2	0.8%
Gentamicin	2	0.8%
Metronidazole	2	0.8%
Tobramycin	1	0.4%
Levofloxacin	1	0.4%
Ofloxacin	1	0.4%

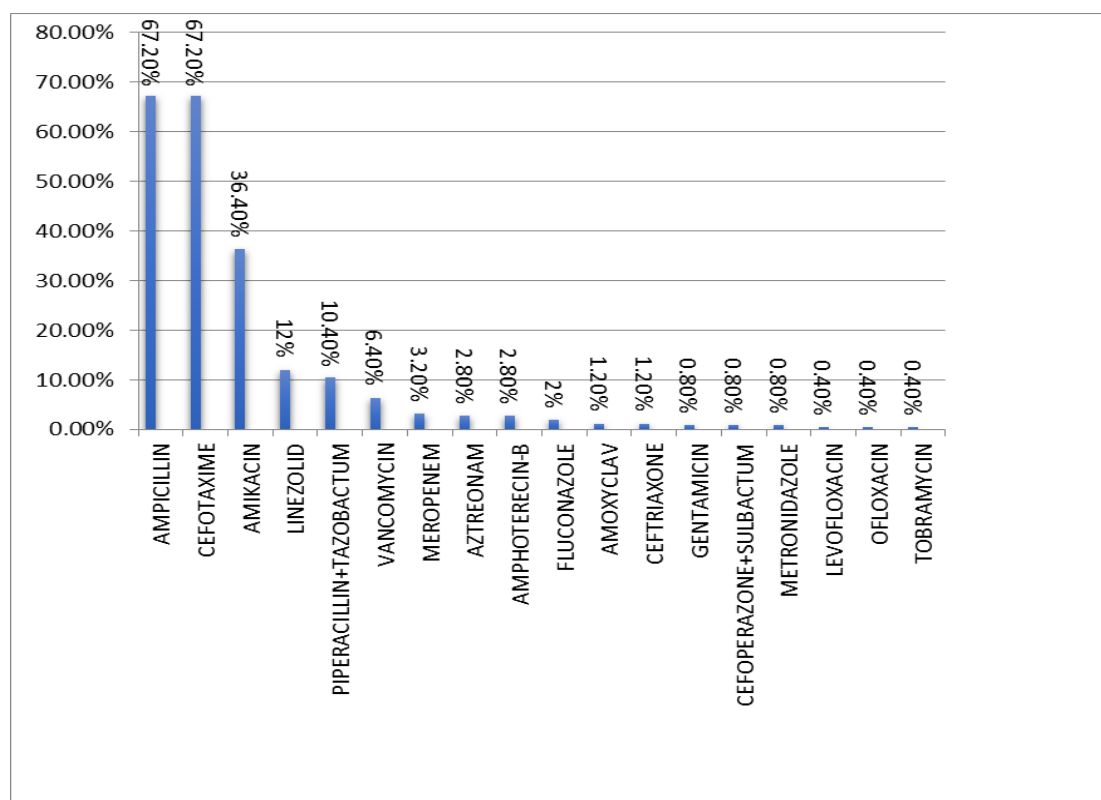


Figure 5: Frequency Of Individual Antibiotics Prescribed.

## 6. OUTCOME OF ANTIMICROBIAL THERAPY

On analysis of total (n= 250) cases of neonatal sepsis, who received antibiotics, 213 (85.2%) were discharged after completion of treatment, 19 (7.6%) cases expired during the course of treatment, 16 (6.4%) cases left the treatment in middle of the course against medical advice and 2 cases (0.8%) absconded.

Table 6: Outcome of Antimicrobial Therapy.

Outcomes	Number	Percentage
discharged	213	85.2%
Expired	19	7.6%
LAMA	16	6.4%
Absconded	2	0.8%
Referred	0	0%

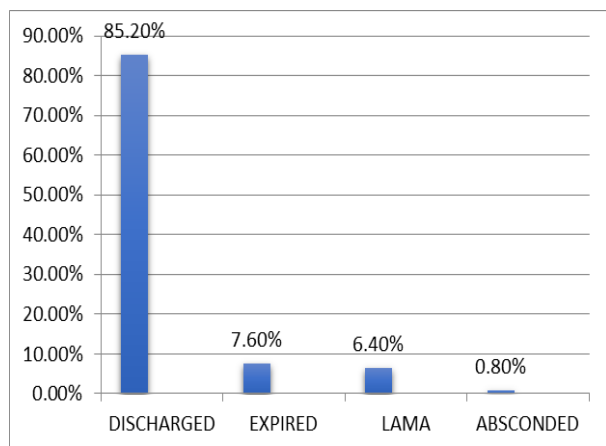


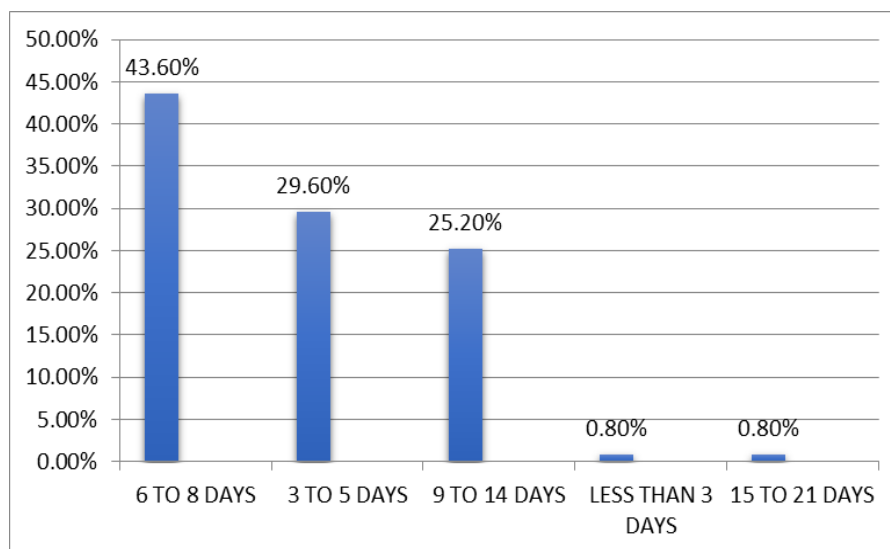
Figure 6: Outcome of Antimicrobial Therapy.

## 7. DURATION OF TREATMENT

It was observed that, maximum i.e 109 (43.6%) cases received antibiotics for 6 to 8 days, followed by 74 (29.6%) cases, who received antibiotics for duration of 3 to 5 days and 63 (25.2%) cases received antibiotics for 9 to 14 days. Only 2 (0.8%) patients received antibiotics for less than 3 days and more than 15 days respectively. The average duration of therapy was  $7.3 \pm 2.1$  days.

Table 7: Duration of Treatment.

Duration of Treatment	No. of Encounters	Percentage
6 TO 8 DAYS	109	43.6%
3 TO 5 DAYS	74	29.6%
9 TO 14 DAYS	63	25.2%
LESS THAN 3 DAYS	2	0.8%
15 TO 21 DAYS	2	0.8%



**Figure 7: Percentage Wise Distribution of Duration of Treatment.**

## DISCUSSION

The average number of antibiotics per encounter were 2.35 with range of 1 to 7. Majority of neonates were prescribed 2 to 3 antibiotics. In study done by Vaniya et al, average 3.74 antibiotics were used per patient and in study done by ShellackN.et al. 3.4 antibiotics were used on an average. All antibiotics were given by parenteral route (intravenous). 97.95% antibiotics were prescribed by generic names and only 2.05% drugs were prescribed by branded names. In previous studies done by Amin AJ et al 50% of the drugs were prescribed by brand names<sup>[8,9]</sup>, and in study done by Vaniya et al 27% drugs were prescribed by brand names. This increase in prescription of drugs by generic names reduces the unnecessary cost of therapy. As severely ill patients are admitted in NICU with multiple causative organisms, multiple antibiotic use by parenteral route is quite relevant. Most commonly prescribed antibiotics were Ampicillin (67.2%) and Cefotaxime (67.2%) followed by amikacin (36.4%), Linezolid (12%), piperacillin +Tazobactam (10.4%), Vancomycin (6.4%) and Meropenem (3.2%). The frequency and intensity of drugs used were directly related to severity of clinical status. Number of neonates exposed to Ampicillin and Cefotaxime were highest in study done by Warriar et al<sup>10</sup>. Previous studies done by Italian collaborative study group and Lesko et al, showed that Penicillin and Aminoglycosides were most commonly used antibiotics<sup>11</sup> and gentamicin was most commonly used in study done by Clark et al<sup>12</sup>. It is evident from this study that in our hospital, most of the neonates with symptoms of sepsis were started on combination therapy of Ampicillin and Amikacin or Cefotaxime and Amikacin or Ampicillin and Cefotaxime and cefotaxime alone in few cases depending on the clinical status and presence of comorbid conditions. Antibiotics were changed or continued as per culture reports. The average duration of therapy was  $7.3 \pm 2.1$  days. This treatment policy is in accordance with current WHO guidelines, which advocates use of Ampicillin and aminoglycoside

combination in hospitalised neonates with possible severe bacterial infections for a duration of 7 to 10 days. Due to increasing resistance to Ampicillin, Cefotaxime has been preferred as first line therapy in many cases. The average duration of NICU stay was  $7.42 \pm 1.33$  days, which is in accordance with study done by Vaniya et al where the average duration of stay was  $7.50 \pm 1.28$  days.<sup>[13]</sup>

## CONCLUSION

The present study was carried out at Department of Pharmacology in collaboration with Department of Pediatrics (NICU), Umaid hospital, a tertiary care teaching hospital associated with Dr. S. N. Medical College, Jodhpur. Total 250 cases of neonatal sepsis were studied, of which 148(59.2%) were suspected and 102(40.8%) were confirmed (culture positive) cases. It was seen that home delivery, rural background, prematurity, low birth weight and early onset sepsis were significantly associated with higher culture positivity rates. Majority of patients received 2 or 3 antibiotics during the course of therapy. Average number of antibiotics prescribed was 2.35. Almost all (97.95%) antibiotics were prescribed by generic names. 77.77% of the total antimicrobials prescribed were from list of essential medicines for state of Rajasthan (2019-2020). Most commonly prescribed antibiotics were Ampicillin, Cefotaxime and Amikacin. In outcome, 85.21% patients were discharged and mortality was 7.6%. Further scanty information is available regarding the pattern of use of antimicrobial drug use in NICU. Results of our study are in accordance with WHO guidelines. Such types of studies are good exploratory tools to know the role of drugs in society and they also create a basis for health care decision making.

## LIMITATION OF THE STUDY

- Shorter duration of study
- Study was conducted in single center only.

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