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Antibiotic Prescription Patterns And Disease Trends In The NICU Of A South Indian Tertiary Care Hospital

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ABSTRACT

Background: Neonate refers to an infant in the first 28 days after birth. They are special group of population who are more susceptible to nosocomial infections due to underdeveloped immunity. The study was conducted to identify the disease spectrum and also to analyze the prescription pattern of antibiotics at our neonatal intensive care unit. Antibiotics are one of the most prescribing drugs in Neonatal Intensive Care Units (NICU).

Objectives: To assess the prescription pattern of antibiotics and disease pattern in in Neonatal Intensive Care Units (NICU).

Materials and Methods: This is a prospective observational study conducted at Basaveshwara Medical College& Hospital, Chitradurga. a period of six months in Neonatal intensive care unit.

Results: A total of 100 patient's data were collected from neonatal intensive care unit, Majority of diseases occurs in 1-10 days age group (76%). 24 were diagnosed with respiratory distress syndrome, 20 patients with low birth weight, 15 patients having birth asphyxia,13 patients were small for gestational age,12 patients had intra uterine growth retardation,12 were diagnosed with sepsis,6 cases were meconium aspiration syndrome. Out of 195 antibiotics prescribed 97 drugs are Penicillins, 89 Cephalosporins, 6 Aminoglycosides and 3 Meropenems.

Conclusion: The study concludes that most commonly occurring disease in NICU is respiratory distress syndrome (RDS) and low birth weight (LBW). Penicillins and Cephalosporins are commonly prescribed antibiotics rarely Aminoglycosides and Meropenems.

Keywords: *NICU, antibiotics, Drug prescriptions, length of stay, Gestational age.*

1. INTRODUCTION

Antibiotics are substances produced by microorganisms which suppress the growth of or destroy other microorganisms at low concentrations[1]. They are powerful and effective drugs in the fight against infectious diseases caused by bacteria and have been frequently used for decades worldwide for effective treatment of a variety of bacterial infections.[2]They are an essential part of modern medicine and play a major role both in the prophylaxis and treatment of infectious diseases.[3]

Neonate refers to an infant in the first 28 days after birth. Those are the special group whom are more susceptible to nosocomial infections due to the underdeveloped immunity.4 Antimicrobial agents are the commonly prescribed drugs in NICU.[4] Health care associated infections are an important problem in neonatal intensive care unit (NICU) in which environmental and host factors often contribute to higher rates of these infections.[5] Infections with gram negative bacilli that are resistant to many commonly used antibacterial drugs are increasingly reported in NICUs.[6]Hence, prompt management with antibiotic therapy and supportive care will serve as benefit for the cases of neonatal cases.

Antibiotics used in the NICU have undoubtedly played an important role in their improved survival. Some studies have demonstrated that resistance is directly associated with selection of inappropriate antimicrobials and increased patients' mortality.[7] Rational antibiotic prescription is very important to avoid multiple drug resistance, treatment failure, non-

compliance and increase in the cost of treatment[8]. While prescribing, not only the knowledge of Pharmacology (Pharmacokinetics – Absorption, Distribution, Metabolism, Excretion and drug interactions) but also that of Gestational maturity and weight of neonate, pathophysiology of disease, correct

diagnosis, microbiological pattern, adverse drug reaction and approach in selecting cost effective drug matters are also important.[9]Apart from the therapeutically significant aspects, antibiotics results in emergence of microbial resistance.[10] This additionally increases the cost of treatment along with morbidity and mortality resulting from drugs.

Infections remain as one of the major problems in NICU and are the leading cause not only of admissions but also of mortality in developing countries.[11] It is estimated that 130 million neonates are born each year and out of these, 4 million die in first 28 days of their life.[7] In neonatal period, 50% of all deaths are within first 24 hours while 75% are within first 7 days of life.[12] The major causes of neonatal deaths globally are estimated to be infections (35%), pre-term births (28%) and asphyxia (23%). Sepsis is the commonest cause of neonatal mortality and is probably responsible for 30-50% of the total neonatal deaths each year in developing countries.[13] India is accounting to 1.2 million or nearly 30% of global neonatal mortality. Three neonates are dying every minute in India and every 4th baby born is low birth weight.[14] The use of drugs in newborns admitted to Neonatal Intensive Care Units (NICUs) is characterized by a great variability in the management of the most common diseases and is a widespread phenomenon observed both within and between different countries.[15] Neonates are a special group of population for dosing because they have a rapidly changing body surface area and weight; a rapidly developing system of drug absorption, metabolism and excretion and inability to communicate with the provider.[16]

The prescription pattern of antibiotics in neonatal intensive care unit is assessed to study the appropriate or rational use of antibiotics in neonates and the disease pattern is analyzed to see the relative incidence of neonatal diseases. These studies are useful for obtaining information about drug usage patterns and data for future reference to streamline antibiotic policy.[17]

Antibiotic regimens would commonly include broad-spectrum penicillins, such as ampicillin or amoxicillin, often combined with an aminoglycoside or a third-generation cephalosporin to provide empirical cover against the micro-organisms in neonatal intensive care unit.[18]Among which Amikacin, Cefotaxime, Ampicillin and Gentamicin were commonly prescribed drugs. Inappropriate use of antibiotics leads to emergence of resistance. So antibiotic surveillance is mandatory to optimize antibiotic therapy especially in culture negative patients with infection like symptoms.[19]

2. METHODS

It was an observational, prospective study conducted for 6 months (November 2015 - April 2016) at Basaveshwara Medical College & Hospital, Chitradurga, Karnataka. 100 neonates, following approval from the Institutional Ethics Committee. The study included 100 neonates admitted and managed in the Neonatal Intensive Care Unit (NICU) during this timeframe.

1. **Exclusion Criteria**

Neonates meeting any of the following criteria were excluded from the study:

2. Discharged, transferred to another ward or hospital, or deceased within the first 48 hours of NICU admission.
3. Diagnosed with malignancy.
4. Identified with congenital or surgically correctable conditions requiring operative intervention.
5. Post-operative neonates admitted to the NICU.
6. Neonates receiving phototherapy exclusively for neonatal jaundice.

Data Collection

The data were systematically recorded by the principal investigator using a pre-designed, structured proforma. The proforma captured demographic details, including: Date of birth, Birth weight, Gestational age in weeks , Gender, Diagnosis, Clinical outcome (discharge, transfer, or mortality)Additionally, data on ,diseases pattern, prescribed antibiotics, including drug name, dosage, frequency, and route of administration, were documented from the day of NICU admission until the final outcome. Neonates were categorized into different gestational age groups based on weeks of gestation at birth.

Data Management and Analysis

Once neonates were discharged or transferred to another facility, no further data were collected. Information regarding maternal drug history was not available in the study. The collected data were entered into MS Excel and analyzed using descriptive statistics. Frequency distributions and percentages were calculated and presented in tabular and graphical formats to summarize key findings.

Ethical consideration After obtaining permission from the institutional ethics committee (IEC) the study was carried out in the NICU of the tertiary care hospital Vide number: SJMCP/IEC/18/2015-16.

Results:

All the patients who were present in the NICU department of hospital viewed daily to identify the disease and prescription pattern of various diseases.

All the patients who were present in the NICU department of hospital viewed daily to identify the disease and prescription pattern of various diseases. The patients were identified and collected their demographic details, chief complaints, clinical data, clinical condition, therapeutic data such as name of the drug, dose, route, frequency, duration of therapy would collect and other relevant details collected by reviewing each prescription, medical records. A total of 100 patients data were collected in Neonatal intensive care unit. All patients were prescribed with antibiotics.

3. DISTRIBUTION OF PATIENTS ACCORDING TO GENDER

Among the whole patients about 58 were males and 42 were females. The results are shown in Table 1 and graphically represented in Figure 1

Table 1: Distribution according to gender

Gender	Total	Percentage
Male	58	58%
Female	42	42%

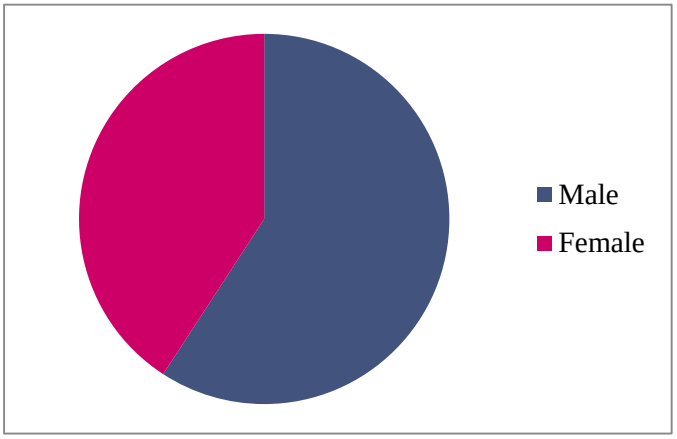

Figure 1: Distribution according to gender

4. DISTRIBUTION OF PATIENTS ACCORDING TO AGE:

The total patients were categorised into three age groups. In total, 36 patients were tern and 64 were pre term. Mean gestational age was 36.3 weeks. In neonates the age was 1-28 days. Majority of diseases occurred in 1-10 days (76%), and least in 10-20 days of age group (9%). 15% admitted 20-30 days age group. The results are shown in Table 2 and graphically represented in Figure 2.

Table 2: Distribution of patients according to age

Age in days	Total	Percentage
0-10 days	76	76%
10-20 days	9	9%
20-30 days	15	15%

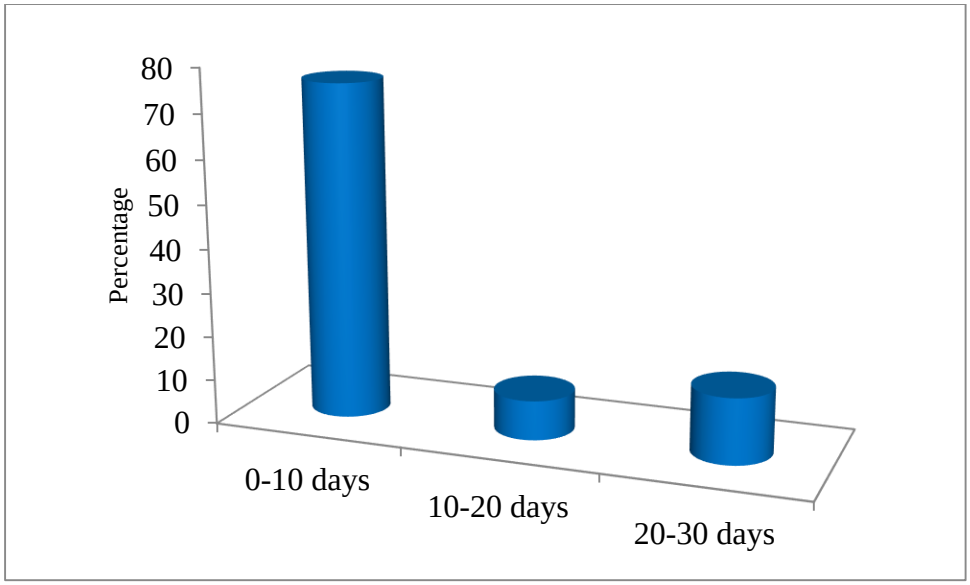

Figure 2: Distribution of patients according to age

5. DISTRIBUTION OF PATIENTS ACCORDING TO WEIGHT

The total patients were categorized into five groups. Less than 2 kg of weight was considered as low birth weight (29%). 38 were in between 2-2.5kg, 21were 2.6-3kg and12 patients were more than 3kg. Average birth weight was 2.3 kg. The results are shown in Table 3 and graphically represented in Figure 3.

Table 3: Distribution of patients according to weight

Weight	Total	Percentage
1-1.5 kg	7	7%
1.6-2 kg	22	22%
2.1-2.5 kg	38	38%
2.6-3 kg	21	21%
>3kg	12	12%

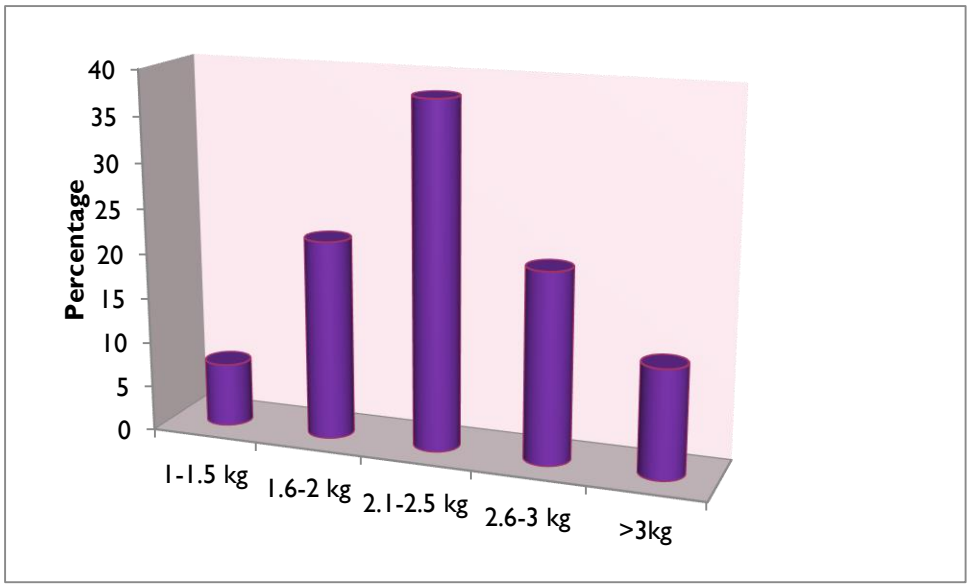

Figure 3: Distribution of patients according to weight

6. DISTRIBUTION OF PATIENTS ACCORDING TO DURATION OF HOSPITALIZATION

The total cases were categorized into three groups. 30 patients stayed in hospital between 1-5 days, 64 were stayed 6-10 days and 6 patients admitted for more than 10 days. The results are shown in Table 4 and graphically represented in Figure 4

Table 4: Distribution of patients according to duration of hospitalization

Duration of hospital stay	Total	Percentage
0-5 days	64	64%
6-10 days	30	30%
11-15 days	6	6%

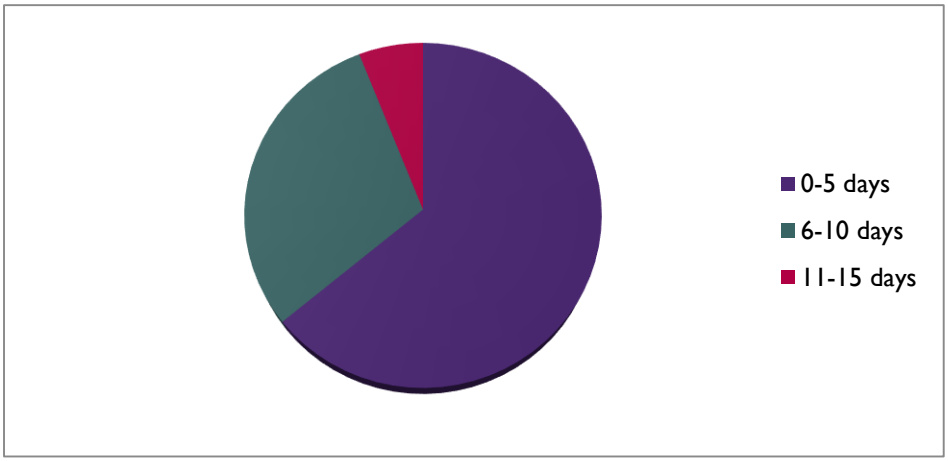

Figure 4: Distribution of patients according to duration of hospitalization

7. DISTRIBUTION OF PATIENTS ACCORDING TO DISEASE

In the study the diseases diagnosed were recorded. Most common disease present in neonatal intensive care unit was respiratory distress syndrome. Among total patients 24 patients were diagnosed with respiratory distress syndrome, 20 patients with low birth weight, 15 patients having birth asphyxia,13 patients were small for gestational age,12 patients had intra uterine growth retardation,12 were diagnosed with sepsis,6 cases were meconium aspiration syndrome,5 patients had neonatal jaundice 5 had pneumonia,3 were diagnosed with meningitis,2 patients were identified with failure to thrive and 2 with congenital pyloric stenosis, one having Edward's syndrome and one with Transient tachypnea of new born. The results are shown in Table 5 and graphically represented in Figure 5

Table 5: Distribution of patients according to disease

Disease	Total	Percentage
Respiratory distress syndrome	24	18.18%
Low birth weight	20	15.15%
Birth asphyxia	15	11.36%
Small for gestational age	13	9.8%
Intra uterine growth retardation	12	9.09%
Hypoxic ischemic encephalopathy	12	9.09%
Sepsis	11	8.33%
Meconium aspiration syndrome	6	4.54%

Pneumonia	5	3.78%
Meningitis	3	2.27%
Failure to thrive	2	1.51%
Neonatal jaundice	5	3.78%
Congenital Pyloric Stenosis	2	1.51%
Edward's syndrome	1	0.75%
Transient tachypnea of new born	1	0.75%

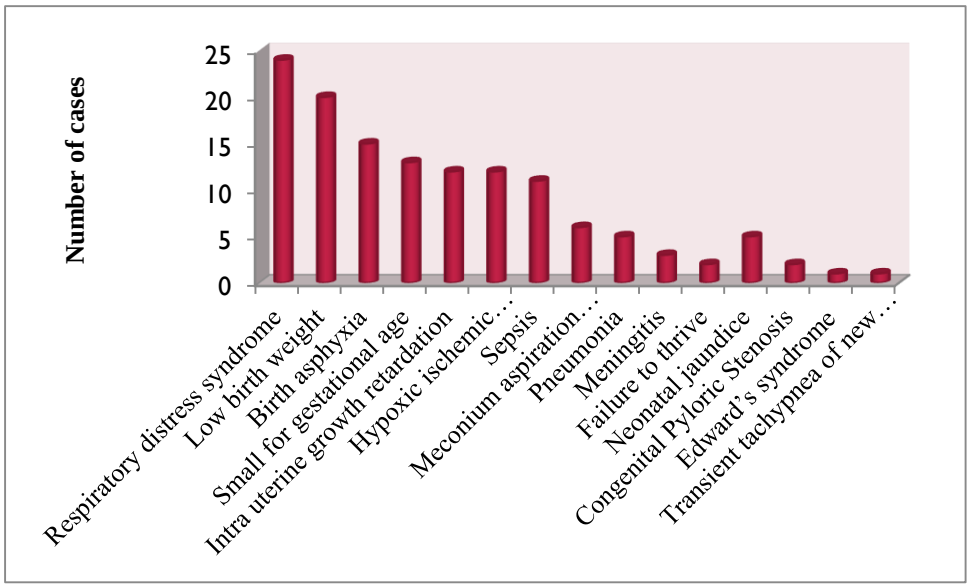

Figure 5: Distribution of patients according to disease

8. DISTRIBUTION ACCORDING TO CLASS OF ANTIBIOTICS PRESCRIBED

In the study period four types of antibiotics were prescribed that are cephalosporins, penicillins, amino glycosides and carbapenems. Most commonly prescribed antibiotics classes were penicillins and third generation cephalosporins and less prescribed antibiotics were aminoglycosides and carbapenems

Table 6: Distribution according to class of antibiotics prescribed

Classes of antibiotics	Total	Percentage
Penicillins	97	49.74%
Cephalosporins	89	45.64%
Amino glycosides	6	3.07%
Carbapenems	3	1.53%

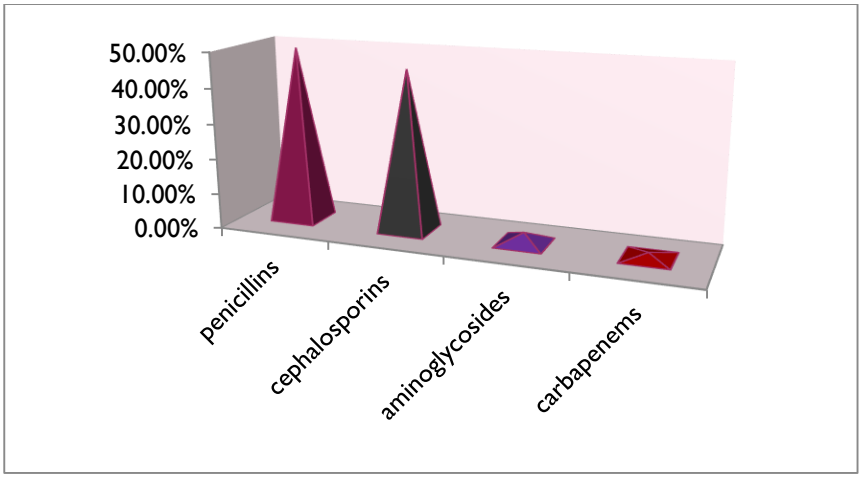

Figure 6: Distribution according to class of antibiotics prescribed

9. DISTRIBUTION ACCORDING ANTIBIOTICS PRESCRIBED

In neonates antibiotics were common drug prescribed for infections. In combination therapy mostly cefotaxime and ampicillin prescribed during study period and these antibiotics were commonly prescribed. The total patient's prescription containing antibiotics were Cefotaxime, Ampicillin, Amikacin, Piperacillin and Meropenem. About 90 prescription contained Ampicillin and 89 had Cefotaxime. Amikacin was prescribed in 6 patients, 7 prescriptions had piperacillin and very less prescriptions had meropenem of about 3.

Table 7: Distribution according antibiotics prescribed

Sl no	Antibiotics	Total in number	Percentage
1	Cefotaxim	89	45.64%
2	Amikacin	6	3.07%
3	Ampicillin	90	46.15
4	Piperacillin	7	3.58%
5	Meropenem	3	1.53%

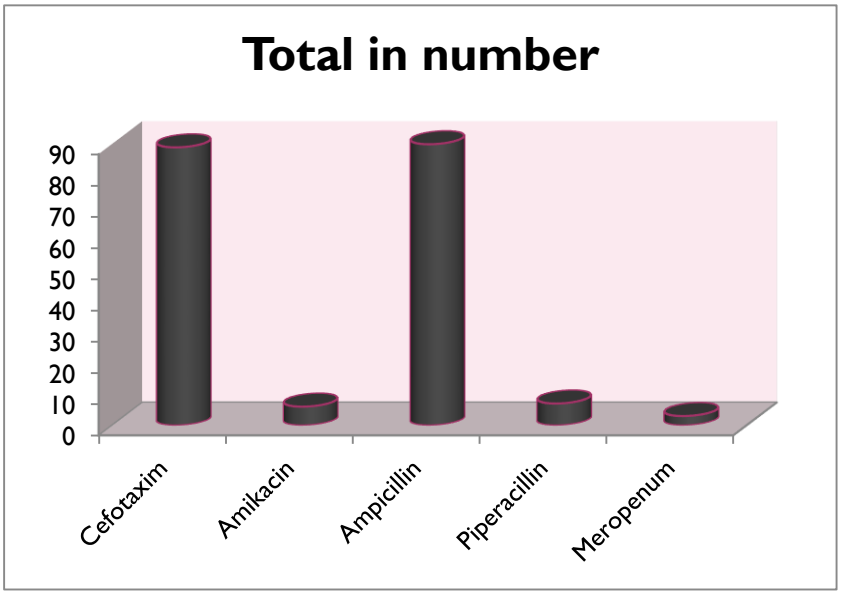

Figure 7. Distribution according antibiotics prescribed

10. DISCUSSION

26 million babies are born in India each year accounting for 20% of global births. Of these, 1.2 million dies before completing the first four weeks of life. This accounts for nearly 30% of the total 3.9 million neonatal deaths worldwide.[31] Among neonatal deaths mortality is highest in the first seven days this accounts for nearly 30% of the total 3.9million neonatal deaths worldwide. Among neonatal deaths mortality is highest in the first seven days. [32,33]

Antibiotics are the mainstay drugs in neonatal intensive care unit. The principle target of the prescription pattern is to promote the rational prescribing of the drugs. Prescription pattern of antibiotics is to assess the prescribing, dispensing and distribution of antibiotics. [34,35]

In my study I have enrolled 100 patients among which the patients belonging to the age group of 1-10 days were more (76%) followed by patients belonging to 10-20 days (9%) and 15% belonging to 20-30 days. A similar study conducted by Sharanappa *et al.,* a study on pattern of drug utilization in neonatal intensive care unit in a tertiary care hospital reveals that the most common age at presentation was on the day of birth (57%), around 34% were presented 2-7 days after birth.[29]

Raghvendra N *et al.* conducted a study of the pattern of admissions and outcome in a neonatal intensive care unit shows that 58% were male and 42% female.[24] In my study about 58 were males and 42 were females. As per Onyaye E *et al*., the prevalence and outcome of preterm admissions at the neonatal unit of a tertiary health centre in southern Nigeria reveals that 71 males and 67females.[12]

Borade S *et al***.** conducted a study on evaluation of antimicrobial prescription pattern in neonatal intensive care unit of tertiary care teaching hospital revealing that the mean gestational age was 36.3 (wks.) and mean birth wt. was 2.1(kg.).[21] In my study average birth weight was 2.3 kg, average gestational age was 36 weeks.[41] Zeb Jan A *et al.* conducted a study revealing the clinical audit of admission pattern and its outcome in a neonatal intensive care unit showing that in total 4800 patients 48 (0.97%) patients were in the weight range of 1-1.5 kg, 1201 (24.5%), 2008 (40.9%) and 1641 (33.5%) patients were in the range of 1.6-2.5 kg, 2.6-3.0 kg and above 3.1 kg respectively.[20] In my study 7 patients having birth weight between 1-1.5, 22 were in 1.6-2, 38 were in between 2-2.5kg, 21were 2.6-3kg and12 patients were more than 3kg.[26]

In my study it was observed that 64 patients stayed in hospital between 1-5 days, 30 had stayed for 6-10 days and 6 patients were admitted for more than 10 days and in Gauchan E *et al* reveals that 57% patients were admitted in hospital for1-5 days24%, 10%, and9% patients admitted for 6-10 days, ii-15 days and more than 15days.[25]

In the study it is observed that some patients had more than one disease. Among total patients 24 patients were diagnosed with respiratory distress syndrome(18.18%), 20 patients with low birth weight(15.15%), 15 patients having birth asphyxia(11.36%),13 patients were small for gestational age(9.8%),12 patients had intra uterine growth retardation(9.09%),12 were diagnosed with sepsis(9.09%),6 cases were meconium aspiration syndrome(4.54%),5 patients had neonatal jaundice(3.78%) 5 had pneumonia(3.78%),3 were diagnosed with meningitis(2.27%),2 patients were identified with failure to thrive(1.51%) and 2 with congenital pyloric stenosis(1.51%), one having Edward's syndrome(0.75%) and one with Transient tachypnea of new born(0.75%).and Aijaz N *et al.* shows that low birth weight (LBW) babies (24.6%) followed by sepsis (19.9%), Respiratory distress Syndrome (RDS) (18.9%), birth asphyxia (17.02), meconium aspiration syndrome (15.2%), neonatal jaundice (9.44%), pneumonias (3.46),hyaline membrane disease (3.4%), congenital malformations (2.8%) and (4.3%). Out of 1069 patients, 148 expired (13.8%).[23]

In another study conducted by Zeb Jan A *et al.* reveals that Sepsis neonatorum (NNS) accounted for 2027 (41.36%), Neonatal Jaundice (NNJ) 1777 (36.2%), intrauterine growth retardation (IUGR) 941 (19.2%), prematurity 515 (10.5%), birth asphyxia (BA) 446 (9.1%) and meconium aspiration syndrome (MAS) 362 (7.3%) accounted of total admissions. The study on drug utilization study in neonatal intensive care unit at tertiary care hospital, Rajkot, Gujarat : A prospective study concluded that most common causes for death were Respiratory distress syndrome [48.6%] followed by Birth asphyxia [25%] and Meconium aspiration syndrome [7.89%].[38]Hussain *S et al* showed in their study that prematurity 646(32.30%), sepsis 578(28.91%), birth asphyxia 220(11%), meconium aspiration syndrome (MAS) 100(5%), congenital malformations 100(5%), Transient tachypnea of newborn (TTN) 100(5%), neonatal jaundice(NNJ) 100(5%), Intrauterine growth restriction (IUGR) 60(3%), Infant of diabetic mother (IDM) 50 (2.5%) , seizure disorder 36(1.80%) and bleeding diathesis 10(0.50%).[30]

Antibiotics are important in neonates because they are susceptible for infections. Out of 100 patients all were prescribed with antibiotics. In the study period four types of antibiotics were prescribed as cephalosporins, penicillins, amino glycosides and carbapenems. Most commonly prescribed antibiotics classes are penicillins and third generation cephalosporins and less prescribed antibiotics are aminoglycosides and carbapenems. The total patient's prescription containing antibiotics were Cefotaxime, Ampicillin, Amikacin, Piperacillin and Meropenem. About 90 prescription contained Ampicillin (46.15%) 89 were had Cefotaxime (45.64%). Amikacin was prescribed in 6 patients (3.07%), 7 prescriptions had piperacillin (3.58%) and very less prescriptions had meropenem about 3(1.53%). Anand J *et al.,* (2003) had conducted a study on drug utilization study of antimicrobial agents in patients in neonatal intensive care unit at a tertiary care hospital in western part of India.in this study Amikacin was used in 73.01% cases while cefotaxime was used in 64.55% of cases. Piperacillin + tazobactam combination was used in 41.26% cases.[29] In another study of Hardik V *et al* shows that most frequently used antibiotics in

decreasing frequency were: Amikacin (97.19%), ampicillin + sulbactam (60.17%), vancomycin (57.64%), ceftazidime (38.71%), cefotaxime (34.22%), ciprofloxacin (26.23%), piperacillin + tazobactam (19.07%).[27]

After performing the study, it is identified that prescription pattern is to find out the appropriateness and rational use of drugs. Rational prescription is important. This study shows penicillins and cephalosporins were more used in the neonatal intensive care unit.

11. CONCLUSION

As per the facts and findings of my research I am concluded that antibiotics are very important drugs. They should be administered in neonatal units with great precautions, taking into account gestational age, weight on admission, severity of infection-judged by clinical assessment, hematologic data, and microbiologic data. In calculating doses, pharmacokinetics of different gestational ages must be taken into consideration which greatly affects the dose and frequency of administration. Most of the studies and literature define rationality on the basis of dose, frequency and duration. No well-defined guidelines are available to define appropriateness of clinical condition. In this study Out of 100 neonates admitted and treated with antibiotics and other supportive care. Most neonates received more than one antibiotic.

In the study more patients were admitted in the hospital within 10 days of their birth.

Most commonly observed diseases in neonatal intensive care unit were respiratory distress syndrome, low birth weight, birth asphyxia, sepsis, pneumonia, hypoxic ischemic encephalopathy and jaundice.

Cephalosporins, penicillins, aminoglycosides and meropenem were the antibiotics prescribed more in the neonatal intensive care unit during study period.

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