

# Drug Utilisation Study in Neonatal Intensive Care Unit of Tertiary Care Teaching Hospital

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**Abstract:** ***Aims and objectives:** evaluate the drug utilization pattern in the NICU of a tertiary care teaching hospital with the objectives of identifying the pattern of drug use in the NICU to identify problems in drug utilization and suggest any measures if possible. **Materials and Methods:** A Cross-sectional, prospective drug utilization study was carried out in the NICU of the paediatric department of a tertiary care hospital over a period of 12 months. The line of treatment to be given was decided by the physician in charge of the department of paediatrics. **Results:** Out of 660 patients, 32.87% of neonates were pre-term and 44.16% were low birth weight. Neonatal sepsis, neonatal jaundice and RDS were major morbid conditions accounting for 73.78% of total neonates. Amikacin, Cefotaxime, and Vancomycin were the most used antimicrobials. 65.51% of drugs were given by generic name and 34.48% were given by brand name. The average duration of stay in the NICU was about 6–8 days. **Conclusion:** Scant information is available regarding the extent and pattern of drug use in the NICU. As paediatric patients are not simply small adults, there is a great need to study the drug utilization pattern.*

**Keywords:** Neonatal intensive care unit, Drug utilization pattern, Very-low – birth weight, Intrauterine growth restriction, antimicrobial drug

## 1. Introduction

NICU (neonatal intensive care unit) is a unit that provides high quality skilled care to critically ill neonates by offering facilities for continuous, clinical, bio-chemical, and radiological monitoring and use of life support system (ventilator) with the aim of improving survival of these babies.<sup>1</sup>

The term “Intensive care unit” conjures the image of baby surrounded by a variety of beeping monitors and a mesh of wires. The term ‘intensive care’ need not be synonymous ‘invasive care’. Minimizing invasive procedures like vein/arterial puncture, intubation, catheterization, etc. Care to newborn is intensive in nursing skill but conservative in protocol management. Protocol needs to be highly technical; It could include the substitution of radiant warmer and room heater for expensive incubators.<sup>1</sup>

Pediatric medicine differs from adult medicine in many ways, because of the more rapid growth and development of child. The child is not a little adult, infants are not small children, neonates are not small infants and premature are not a small neonate.<sup>2</sup>

According to world health organization (WHO) estimate, there are about 3.2 million neonatal deaths in a year, 98% of that occurring in developing countries. Most of these deaths occur in the first week of life, most are on the first day.<sup>3</sup>

The most common causes of death in the neonatal periods are infections including septicemia, meningitis, respiratory infections, diarrhea, neonatal tetanus, birth asphyxia, injuries, prematurity. All are also common problems or diseases of neonate which required admission in NICU.<sup>3</sup>

Many drugs used for children are not licensed or are used off-label. An increased risk of medication errors and unexpected Adverse drug reaction (ADR) associated with off-label and unlicensed drug prescription has been reported. This risk increases in the newborn who are more likely to be predisposed to and ADR due to their physiological immaturity.<sup>4</sup>

## 2. Methods

A Cross-sectional, prospective drug utilization study was carried out in NICU of paediatric department of a tertiary care hospital. Prior permission of the medical superintendent of hospital, Institutional Ethics Committee and Head of Paediatrics department was obtained for conducting the study.

An appropriate study protocol and Performa were developed and discussed with teaching staff members of the pharmacology department and head of paediatric department.

Selection criteria of patient

### Inclusion criteria

- 1) All the patients with age  $\leq$  28 days
- 2) Either sex

### Exclusion criteria

- 1) Patient's age more than 28 days of life
- 2) Final diagnosis is not made or query

Data extraction sheet was used to collect the data regarding demographic details, maternal and delivery details, indication for admission, final diagnosis and medications administered.

All drugs given to the neonates were recorded except oxygen and blood products. Drugs prescribed were categorized based on WHO - ATC classification system; a pharmaceutical coding system which divides drugs into different groups according to the organ or system on which they act or their therapeutic and chemical characteristics.

**Statistical analysis**

Recorded data was entered in Microsoft excel sheet and analyzed using SPSS - 20. Results were expressed in terms of descriptive statistics

**3. Results**

**Demographic characteristics**

Age and sex wise distribution, which is depicted in Table 1, included, the study includes a total of 660 neonates, comprising 369 (55.90%) male and 291 (44.09%) female. Among them, No. of patients admitted in early neonatal period is 600 and no. of patients admitted in late neonatal period is 60.

**Table 1:** Age and sex wise distribution in neonatal intensive care unit

Category	Early neonatal period (<7 days)	Late neonatal period (7 - 28 days)	Total	Percentage (%)
Male	331	38	369	55.90
Female	269	22	291	44.09
Total	600	60	660	100.00

Birth weight category, which is depicted in Table 2, included, most neonates were term ( $\geq 37$  weeks) accounting for 66.81% followed by preterm 32.87% and 0.30% were extreme preterm. The group maximum exposed to the drugs are neonates weighing more 2.5 kilograms which constitutes 54.84 % of the total prescription followed by weight group of 2.5 - 1.5 kilogram constituting 39.09%, 1.5 - 1kg weight group constitutes 5.90%, and 0.15% less than 1kilogram.

**Table 2:** Birth weight category observed in neonatal intensive care unit

Category	No of neonates	Percentage (%)
Normal birth weight $\geq 2500$ grams	362	54.84
Low birth weight (2499 - 1500 grams)	258	39.09
Very low birth weight (1499 - 1000 grams)	39	5.90
Extremely low birth weight (< 1000 grams)	1	0.15

The spectrum of morbidity pattern, which is depicted in Table 3, included neonatal sepsis (30.60%), neonatal jaundice (26.51%), respiratory distress syndrome (17.57%), Hypoglycemia (5.75%), MSL/MAS (5.15%), Pneumonia (2.42%), Birth asphyxia (2.42%) and Others (10.15%) and the common condition associated with mortality were moderate to severe neonatal sepsis, neonatal jaundice, and respiratory distress syndrome. Neonatal sepsis and neonatal jaundice have the highest admission rate with 30.60% and 26.51% respectively.

**Table 3:** Morbidity pattern observed in neonatal intensive care unit

Morbid condition	Normal birth weight	Low birth weight	Total	Percentage (%)
Neonatal sepsis	98	104	202	30.60
Neonatal jaundice	106	69	175	26.51
Respiratory distress syndrome	88	28	116	17.57
Hypoglycemia	3	35	38	5.75
MSL/MAS	29	5	34	5.15
Pneumonia	10	6	16	2.42
Birth asphyxia	11	1	12	1.81
Others	17	50	67	10.15
Total	362	298	660	100

**Medication/prescription descriptive**

According to WHO - ATC (World health organization anatomical therapeutic committee) classification system, most frequently used drugs in decreasing frequency were Amikacin, Inj. D10, Vit K, NS, Cefotaxime, Ampicillin + sulbactam, Iso P, Injection paracetamol, Calcium Gluconate, Vancomycin, Tazobactam + Piperacillin, Caffeine Citrate and Domperidone as depicted in Table 4.

**Table 4:** Most frequently prescribed drugs in neonatal intensive care unit

Name of drug	No. of neonates receiving drug (no. of encounters)	Percentage (%)
Amikacin	478	72.42
Injection D10	425	64.39
Vit K	383	58.03
NS	359	54.39
Cefotaxime	253	38.33
Ampicillin + sulbactam	233	35.30
Iso P	209	31.66
Injection PCM	174	26.36
Calcium Gluconate	83	12.57
Vancomycin	73	11.06
Tazobactam+ Piperacillin	69	10.45
Caffeine Citrate	63	9.54
Domperidone	33	5.0

The less frequently used drugs which constitutes less than 5% in total prescription has been included in Table 5. It includes high end antibiotics like netilmicin, tobramycin eye drop, Cefoperazone, furosemide, adrenaline, metronidazole, midazolam, phenytoin, digoxin, dopamine, phenobarbitone, meropenem etc.

**Table 5:** Drugs prescribed with a frequency of less than 5%

Name of drug	No. of encounters
Netilmicin	21
Tobramycin eye drops	16
Cefoperazone	22
Furosemide	1
Adrenaline	9
Metronidazole	1
Midazolam	17
Phenytoin	6
Digoxin	2
Dopamine	17
Phenobarbitone	2

**Table 6:** WHO core indicators

WHO core indicators	% of patients
Prescription with antibiotics	81.51
Prescription with injections	92.18
Percentage of drug prescribed by generic name	65.51
Percentage of drug prescribed from EML 2021 (children)	60.00
Percentage of drug prescribed from NLEMI 2021	34.48

Total no. of Diff. Drugs Prescribed	Total no. of encounters	Average no. of drugs per encounters
3833	660	5.80

A total of 3833 drugs were prescribed for 660 study population during the period of hospital stay. The average number of drugs administered per neonate were 5.80

Length of stay in neonatal intensive care unit, which is depicted in Table 7, included, 1.21% of encounters have duration less than 2 days, 34.24% of encounters have duration in range of 3 - 5 days, 26.51% of encounters have duration in range of 6 - 8 days, 12.42% of encounters have duration of 9 to 10 days and 25.60% of encounters have duration of more than 10 days.

Mean  $\pm$  SD of length of stay in NICU of all patients being admitted is  $9.1 \pm 6.79$  days.

**Table 7:** length of stay inneonatal intensive care unit

Duration of stay (In days)	No of encounter	Percentage (%)
< 2	8	1.21
3 to 5	226	34.24
6 to 8	175	26.51
9 to 10	82	12.42
> 10	169	25.60
Total	660	100

#### 4. Discussion

In present study, we have collected data of 660 patients matching inclusion criteria admitted in neonatal intensive care unit (NICU) of a tertiary care hospital. Data of the patients like age, sex, diagnosis, duration of stay in NICU and drug treatment were analyzed. Largest proportion of patients admitted in NICU were males 55.90 % (Table 1). This is in accordance with study done by Smita et al. (2019) in which 64% of patients were male.<sup>5</sup> This shows that the gender discrimination in term of access to public health care and need for immediate awareness against gender discrimination in early stage of life.

In present study, no. of patients admitted in NICU with normal birth weight, low birth weight, very low birth weight and extremely low birth weight was 54.84 %, 39.09 %, 5.90 % and 0.15% respectively. (Table 2). The mean birth weight in our study was  $2465.33 \pm 623.33$  g. This is in accordance with study done by Nepal et al (2020).<sup>6</sup> The mean birth weight was  $2483.96 \pm 812.631$  g. Neonates are hostile to the influences of several septic infection of premature birth in early neonatal period which demands special attention.

Majority of the neonates (30.60%) were admitted in NICU for Neonatal sepsis followed by neonatal jaundice (26.51%),

RDS (17.57%). which is similar to a study done by Hadgu et al. in which the largest number of neonates were in the premature category, birth asphyxia, respiratory distress and jaundice (Table3).<sup>7</sup> In present study it was seen that 51.48 % of babies with neonatal sepsis, 39.42 % of babies with neonatal jaundice and 24.13% of babies with RDS, were. which is similar to a study done by Sara et al. showed 50 - 60% of septic babies are premature babies and VLBW are more vulnerable.<sup>8</sup>

In present study No. of preterm neonates admitted were 32.87%. (Table7) This is in consonance with study done by Flint et al. 2018 in which no. of preterm neonates admitted were 34%.<sup>9</sup> In present study mean duration of stay in NICU for all patients being admitted was  $9.1 \pm 6.79$  days. This is in consonance with study done by Shahidullah et al.2017, mean duration of stay in NICU was  $11.1 \pm 6.7$  days.<sup>10</sup>

In present study the average number of drugs per encounter was 5.80 with range of 1 to 9. The majority of neonates were prescribed 5 to 6 drugs which are similar to a study done by Garrido et al 7.5 drugs were given to neonates on an average. As severely ill patients are admitted in NICU, use of polypharmacy is quite relevant.<sup>11</sup>

Most prescribed drugs were Amikacin (72.42 %), Inj. D10 (64.39%), Vit. K (58.03%), Cefotaxime (38.33%), Ampicillin+salbactam (35.30%), Inj. ISO - P (31.66%), Inj. PCM (26.36%), Inj. Calcium gluconate (12.57%), Vancomycin (11.06%), Tazobactam + piperacillin (10.45%). which is similar to a study done by Garrido et al. The frequency and intensity of the use of these drugs appears to be directly related to the severity of the clinical status, and inversely related to birth weight and gestational age.<sup>1</sup> In present study total encounters with an antibiotic prescribed were 660 which accounts for almost 81.51% of total encounters. Majority of the neonates received at least 2 antibiotics. Around 45% neonates were prescribed 2 or more than 2 antibiotics. It is clear that neonates who did not receive any antibiotic make trivial contribution (18.48%) to data. As antibiotics were given as life saving measures it is difficult to focus on their irrationality. Another similar study, Numbers of neonates exposed to Ampicillin and Cefotaxime were highest in study done by Garrido et al. (2021).<sup>1</sup> and Ampicillin and Gentamicin were commonly prescribed antibiotics in a study done by Bandale et al (2019).<sup>12</sup>

In present study most of neonates received drugs via parenteral route, which is similar to a study done by Costa et al. (2018) <sup>13</sup> who reported most of drugs were given by parenteral route. In our study 38 drugs were prescribed by generic name and 20 drugs were given by brand name. So, 65.51% drugs were given by generic name and 34.48% were given by brand name. Majority of drugs were prescribed by generic name which reduce to the cost of therapy. which is similar to a study done by Roche et al, Hadia RB et al and Singal GL et al which show Increasing generic prescribing would rationalize the use and reduce the cost of drugs.<sup>14, 15, 16</sup>

In present study average drug cost per encounter is Rs 128.25 which is significantly affordable. This was despite not considering cost of phototherapy, exchange transfusion, ventilation, oxygen, and laboratory charges. Direct non -

medical cost i. e., cost incurred by patient in receiving medical care e. g., transportation to and from hospital and lodging of family members were not considered.

Drug utilization studies helps in framing hospital formulary and standard treatment guidelines as per the diagnosis and helpful in rational use of drugs making treatment cost effective and beneficial to patients and to the countries with poorly funded health system. The strength of present study is that it is a step further in the broader evaluation of safety and efficacy of drug prescription in NICU. Sample size, administrative data for analysis is our limitation as this type of study should be broadly studied and present study is confined to only one teaching hospital.

## 5. Conclusion

To conclude, periodic survey should be conducted over the time to facilitate rational usage of drugs in neonates because of their immature body functions and to avoid adverse drug reactions. Most importantly the therapeutic treatment guidelines should be established to control the over usage of antibiotics and to rationalize the drug usage. all though this study had a small sample size it gave us an overall pattern of drug use profile in a tertiary care NICU. This report is also intended to be a step in the broader evaluation of safety and efficacy of drug prescription in NICU. Neonates are a very vulnerable group due to immaturity of their body functions and great care needs to be taken to use the minimum number of drugs. Use of generic medicine reduce the cost of therapy.

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**Ethical approval:** The study was approved by the Institutional Ethics Committee.

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