DRUG PRESCRIBING PATTERN IN NEONATAL INTENSIVE CARE UNIT AT TERTIARY CARE HOSPITAL, MANDYA: A RECORD BASED STUDY.

Dr. Divya Shree N.*[1], Rose Rebecca T.[2] and Rasigai Priya S.[3]

[1]Assistant Professor, Department of Pharmacy Practice, Bharathi College of Pharmacy, Mandya, Karnataka, India.
[2,3]5th Year Pharm. D student, Bharathi College of pharmacy, Mandya, Karnataka, India.

*Corresponding Author: Dr. Divya Shree N.

Assistant Professor, Department of Pharmacy Practice, Bharathi College of Pharmacy, Mandya, Karnataka, India.

ABSTRACT

Background: As per WHO definition, a newborn infant or neonate is a child under 28 days of age. The neonatal period (≤28 days old) is a critical phase of human development with the newborn having to adjust considerably to various physiological states in its new environment. A neonatal intensive care unit (NICU) is a highly specialized unit that provides high-quality skilled care to critically ill newborn infants and premature and low birth weight infants. Apart from facilities for continuous clinical and biochemical monitoring, the neonatal intensive care unit involves the use of a wide range of medications. Neonatal drug handling is significantly different from that of adults. Such differences are due to rapid physiological changes that take place during the early months of life leading to alterations in various pharmacokinetic and pharmacodynamic variables, which leads to various adverse drug reactions. Prescribing pattern studies are powerful exploratory tools to ascertain the role of drugs in society. In a tertiary care center, prescribing is expected to be judicious, appropriate, safe, effective, and economical. **Objective:** To describe the prescribing pattern of drugs in the neonatal intensive care unit at MIMS, Mandya. **Methodology:** This was a record-based study on drug prescribing patterns in the neonatal intensive care unit at MIMS, Mandya. The information about drug prescribing patterns was obtained from patients' case sheets and details are documented and subjected to suitable statistical methods. **Results:** Among 200 neonates under study, 56% were males and 44% were females. There were 15% preterm born neonates. Neonatal sepsis (23.5%), low birth weight (17%), and jaundice (13.6%) were the common indications for admission. The total number of drugs prescribed was 982 with an average number of drugs per neonate at 4.91. In that, anti-infectives (43.07%) were more frequently prescribed drug class followed by nervous system drugs (5.80%) according to the WHO-ATC classification system. Among anti-infectives more commonly prescribed drug was amikacin (38.6%) followed by amikacin and clavulonic acid combination (26.2%). Among 200 prescriptions 181 contained antibiotics, and 75 % of prescriptions contain 2 antibiotics. The parenteral route of administration is frequently used (44%), followed by oral (26.6%). 42% of drugs were prescribed by generic names 61.9% were drugs prescribed from the essential medicine list (Children) and59.5% were drugs prescribed from the National list of essential medicine of India. **Conclusion:** Our study was mainly focused on prescribing patterns of drugs in the Neonatal Intensive care unit (NICU) and common diseases in neonates. Evaluation of the prescription pattern of drugs can improve the quality of prescription therefore they need to be done periodically.

KEYWORDS: Neonates, Neonatal intensive care unit, Prescription pattern, Rational drug use.

INTRODUCTION

As per WHO definition a newborn infant, or neonate, is a child under 28 days of age.[1] The neonatal period (≤28 days old) is a critical phase of human development with the newborn having to adjust considerably to various physiological states in its new environment.[2]

Gestational age was defined as preterm if the baby was delivered before 37 completed weeks of gestation and term if the birth occurred ≥37 completed weeks of gestation as defined by the American College of Obstetricians and Gynecologists.[3]

As per WHO, Preterm is defined as babies born alive before 37 weeks of pregnancy are completed.[1]

A neonatal intensive care unit (NICU) is a highly specialized unit that provides high-quality skilled care to critically ill newborn infants and premature and low birth weight infants. Apart from facilities for continuous clinical and biochemical monitoring, the neonatal intensive care unit involves the use of a wide range of medications.[4] Since the establishment of the first US neonatal intensive care unit (NICU) in 1960, the neonatal mortality rate has fallen more than 4-fold. Much of this decline can be attributed to the highly specialized care

provided to premature and sick infants by neonatologists and multidisciplinary teams working in NICUs.[5]

Prescribing drugs to newborn infants, particularly those born preterms, is a challenge fraught with complexities including a lack of evidence-based information about pharmacokinetics and pharmacodynamics of drugs, efficacy and side-effect profiles for some of the most frequently used drugs.[6]

Prescribing pattern studies are powerful exploratory tools to ascertain the role of drugs in society. In a tertiary care center, prescribing is expected to be judicious, appropriate, safe, effective, and economical.[7] Drug prescribing studies in pediatric patients have been limited when compared to the Epidemiological evaluation of medicine use in the elderly. The need for safe and effective drugs for use in sick neonates, infants, children, and adolescents requires the establishment of thoughtful drug therapy strategies.[8]

In recent years, major advances have been made in the pharmacological treatment of pre-term neonates, the average number of drugs administered per infant in neonatal intensive care units has been increasing over the last 40 years. Survival of very preterm newborns has improved; thus, clinicians face more patients with complications in this group, and strategies to reduce long-term morbidity have to be developed.[9]

In the Anatomical Therapeutic Chemical (ATC) classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological, and chemical properties.[1]

The drugs prescribed in the NICU department are mainly, anti-infectives, nervous system drugs, respiratory system drugs, Cardiovascular system drugs, Alimentary tract drugs, and Corticosteroids.
Antibiotics are the key drugs for the treatment of infections and are among the most commonly prescribed drugs in the pediatrics department. Commonly prescribed antibiotics in neonatal intensive care unit are amikacin, amoxicillin and clavulonic acid combination, piperacillin, cefotaxime, ampicillin, meropenem, ciprofloxacin, vancomycin, linezolid, azithromycin, ceftriaxone, and metronidazole. These drugs are commonly prescribed to treat diseases like neonatal sepsis, meconium aspiration syndrome, bronchopneumonia, and bronchiolitis.

METHODS
This was a record-based study conducted in the Neonatal Intensive care unit. Case sheets of about 200 cases of 12 months period (Jan 2021- Jan 2022) collected and details collected from case sheets, investigation reports, and treatment given to all inborn and outborn babies of age 0-2 months, admitted during the study period in NICU of MIMS teaching hospital, Mandya after getting approval from Ethics committee. A data extraction sheet was used to collect details like the gender of the patients, maternal and delivery details, the indication of admission, final diagnosis, and all the drugs administered except vaccines, minerals, oxygen, and blood products. Drugs prescribed were categorized using the WHO-ATC classification system, which categorizes drugs into different classes according to the organ or system on which they act.

Statistical analysis
Data will be entered in Microsoft excel worksheet and word to generate graphs, tables, and descriptive statistics like percentage, mean, etc. will be used.

RESULTS
PATIENT DISTRUBUTION BASED ON GENDER
A total of 200 patients were included in the present study. Overall 200 prescriptions were analyzed. Table.1 provides the details of the Gender distribution of the patients. The number of males was 112 (56%) while the number of females was 88 (44%). This shows that the male patient population has more than the female patient population.

Table 1: Patients distribution based on Gender (n=200).

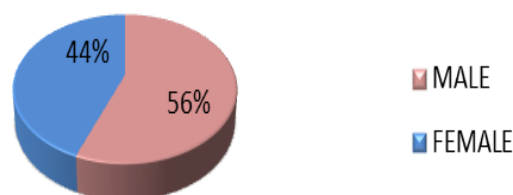| GENDER	NO.OF PATIENTS (n=200)	PERCENTAGE
MALE	112	56%
FEMALE	88	44%

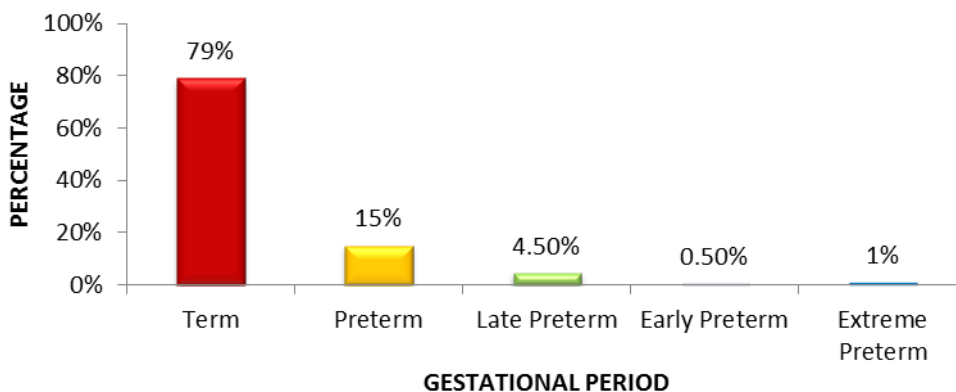**Figure 1: Patients distribution based on gender (n=200).**

NEONATES BASED ON GESTATIONAL AGE

A total number of 200 neonates enrolled in the study. In that 158 neonates (79%) were term babies (39-40 weeks), preterm babies were 30 (15%), late preterm babies were 9(4.5%), early preterm babies 1(0.5%) and extreme preterm babies were 2(1%). This indicates the majority of the neonates admitted to the NICU were term babies.

Table 2: Neonates distribution based on gestational age.

GESTATIONAL AGE	NO.OF PATIENTS	PERCENTAGE
Term	158	79%
Preterm	30	15%
Late Preterm	9	4.5%
Early Preterm	1	0.5%
Extreme Preterm	2	1%

Figure 2: Neonates distribution based on gestational age.

MORBIDITY PATTERN OBSERVED IN NICU

The spectrum of morbidity patterns depicted in table 3, included neonatal sepsis (23.5%), Low birth weight (17%), jaundice (13.6%), transient tachypnea of newborn, Small for gestational age, respiratory distress syndrome, birth asphyxia, meconium aspiration syndrome, Convulsions, Bronchopneumonia, Brochiolitics, Seizure, Very low birth weight, Hypoxic ischemic encephalopathy, Acute Kidney injury, etc.

Table 3: Spectrum of morbidity pattern.

| MORBID CONDITIONS	FREQUENCY	PERCENTAGE
Neonatal sepsis	74	23.5%
Low birth weight	54	17%
Jaundice	43	13.6%
Transient tachypnea of newborn (TTNB)	18	5.7%
Small for gestational age	18	5.7%
Respiratory distress syndrome (RDS)	12	3.8%
Birth asphyxia	12	3.8%
Meconium aspiration syndrome	8	2.5%
Convulsions	7	2.2%
Bronchopneumonia	7	2.2%
Brochiolitics	7	2.2%
Seizure	6	1.9%
Very low birth weight	6	1.9%
Hypoxic ischemic encephalopathy	6	1.9%
Acute Kidney injury	6	1.9%
Miscellaneous <1%	10	3%
Others	20	6.3%
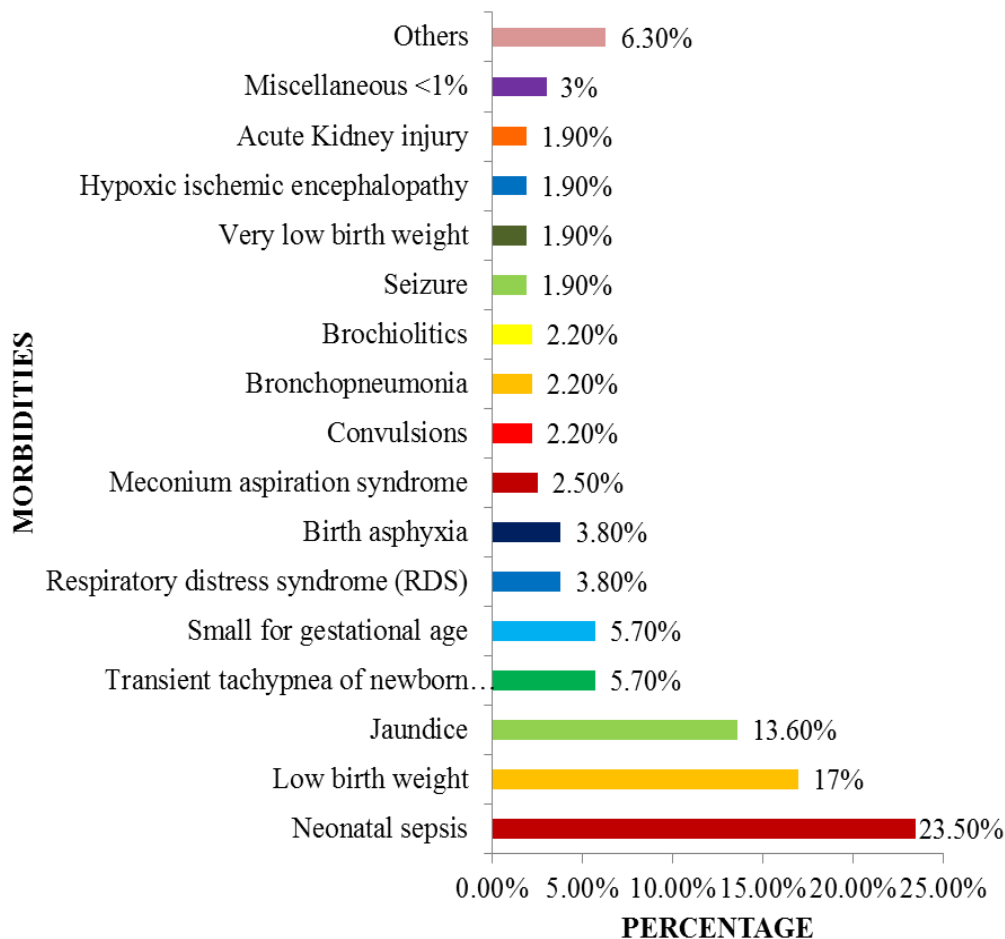
Figure 3: Distribution of spectrum of morbidity pattern.

DRUG USE ACCORDING TO WHO- ATC CLASSIFICATION SYSTEM

Table 4 shows the drug use in the NICU according to the WHO- ATC classification system.

The most used drugs were anti-infectives(43.07%) followed by nervous system drugs (5.80%), cardiovascular drugs (3.86%), respiratory system drugs(3.15%), corticosteroids (1.73%), alimentary tract drugs (1.32%) and other drugs including mineral and vitamin supplements, intra venous fluid, etc were found to be 41.03%.

Table 4: Drug use in NICU according to WHO-ATC classification.

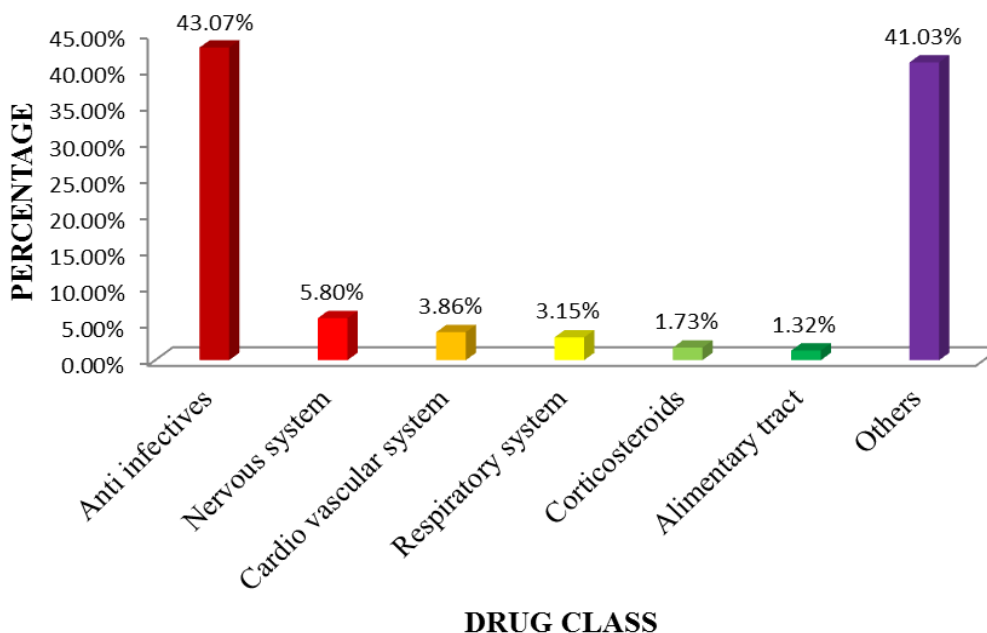| DRUG CLASS	NO.OF DRUGS	PERCENTAGE
Anti infectives	423	43.07%
Nervous system	57	5.80%
Cardio vascular system	38	3.86%
Respiratory system	31	3.15%
Corticosteroids	17	1.73%
Alimentary tract	13	1.32%
Others	403	41.03%

Figure 4: Drug use in NICU according to WHO-ATC classification.

ANTI-INFECTIVES PRESCRIBED IN NICU

This class of drugs is used to treat diseases like neonatal sepsis, meconium aspiration syndrome, bronchopneumonia, and bronchiolitis. Most frequently prescribed anti-infective drug is Amikacin (38.6%) followed by Amoxicillin and Clavulonic acid combination (26.2%), Piperacillin (6.4%), Cefotaxime (6.2%), Ampicillin(4.5%), Meropenem (4.5%), Flucanazole (4.3%), Ciprofloxacin (4%), Vancomycin (2.4%), Linezolid(1.2%), Azithromycin(0.7%) and the least prescribed drugs are ceftriaxone (5%) and metronidazole(5%).

Table 5: Anti-infectives prescribed in NICU.

ANTI-INFECTIVES	NUMBER OF NEONATES RECEIVING ANTI-INFECTIVES	PERCENTAGE
Amikacin	162	38.6%
Amoxicillin+ Clavulonic acid	110	26.2%
Piperacillin	27	6.4%
Cefotaxime	26	6.2%
Ampicillin	19	4.5%
Meropenem	19	4.5%
Flucanazole	18	4.3%
Ciprofloxacin	17	4%
Vancomycin	10	2.4%
Linezolid	5	1.2%
Azithromycin	3	0.7%
Ceftriaxone	2	0.5%
Metronidazole	2	0.5%
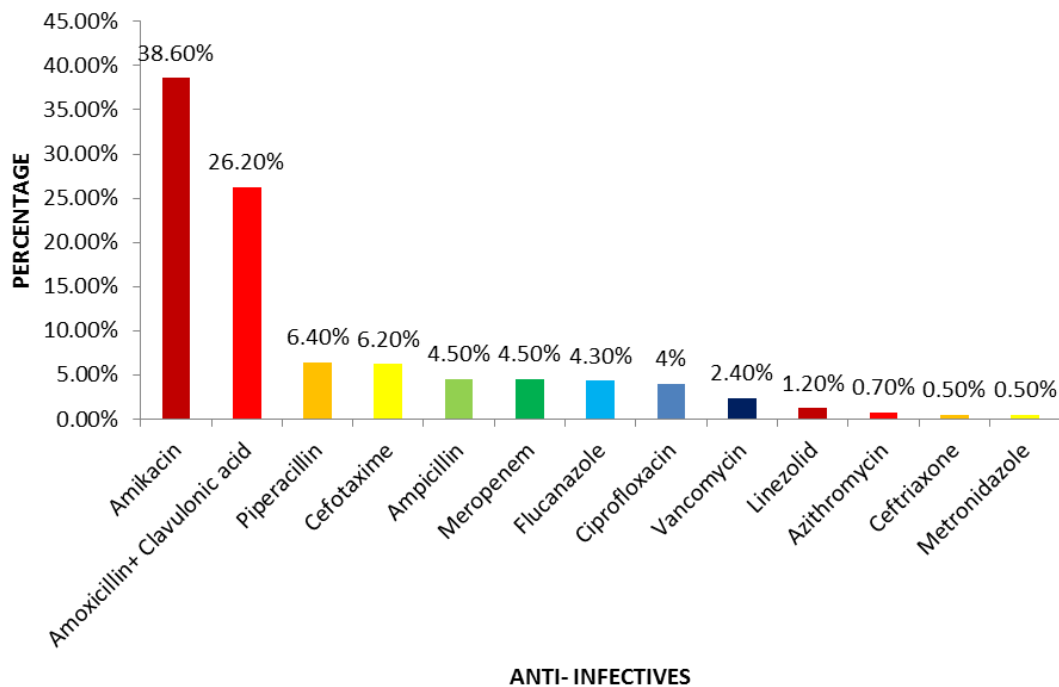
Figure 5: Anti- infectives prescribed in NICU.

NUMBER OF ANTIBIOTICS PER PRESCRIPTION

In this study, more patients received two antibiotics (75%), followed by three antibiotics (12.7%), a single antibiotic (8.2%), and four antibiotics(3.8%).

Out of 200 neonates 181 neonates have received antibiotics.

Table 6: Number of antibiotics per prescription.

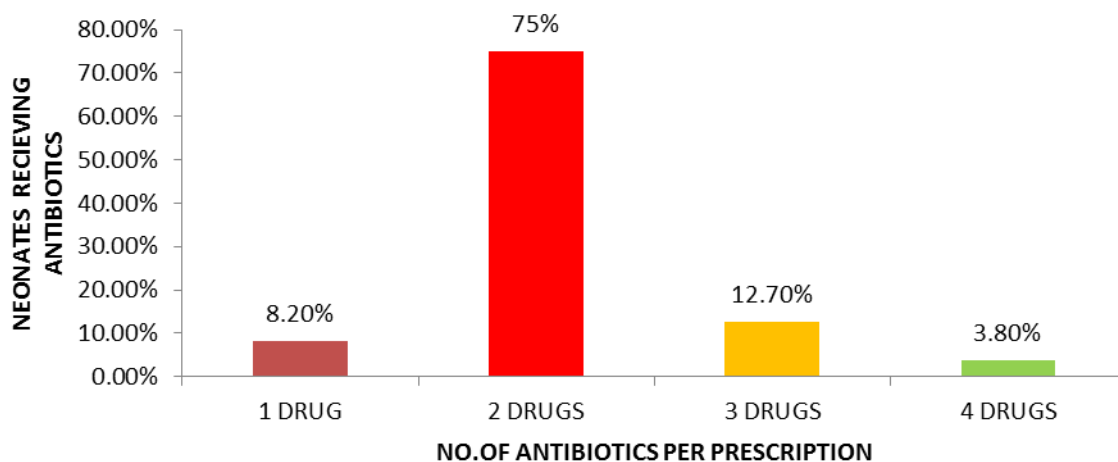| No.Of Antibiotics Per Prescription	No.Of Neonates Receiving Antibiotics	Percentage
1 DRUG	15	8.2%
2 DRUGS	136	75%
3 DRUGS	23	12.7%
4 DRUGS	7	3.8%

**Figure 6: Number of antibiotics per prescription.**

NERVOUS SYSTEM DRUGS PRESCRIBED IN NICU

This class of drugs is used to treat diseases like convulsions, and seizures in neonates.

The most frequently prescribed nervous system drug is Phenobarbitone (44.6%) followed by Levetiracetam (17.8%), Phenytoin (16%) and the least prescribe drugs are Paracetamol (10.7%) and Midazolam (10.7%).

Table 7: Nervous system drugs prescribed in NICU.

| NERVOUS SYSTEM DRUGS	NO. OF NEONATES RECIEVING DRUG	PERCENTAGE
Phenobarbitone	25	44.6%
Levitriacetam	10	17.8%
Phenytoin	9	16%
Paracetamol	6	10.7%
Midazolam	6	10.7%
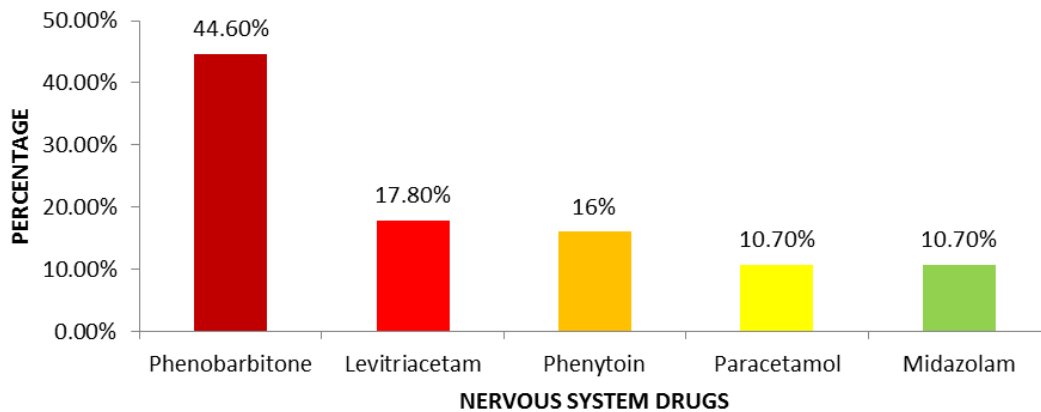
Figure 7: Nervous system drugs prescribed in NICU.

CARDIO VASCULAR SYSTEM DRUGS PRESCRIBED IN NICU

This class of drugs used to treat acute kidney injury, low birth weight, pulmonary hypertension.

Most frequently prescribed cardiovascular drug was Dopamine (29.7%) followed by Sildenafil (21.6%), Dobutamine (18.9%), Adrenaline (16.2%) and Furosemide (13.5%).

Table 8: Cardio vascular system drugs prescribed in NICU.

CARDIOVASCULAR DRUGS	NO. OF NEONATES RECIEVING DRUG	PERCENTAGE
Dopamine	11	29.7%
Sildenafil	8	21.6%
Dobutamine	7	18.9%
Adrenaline	6	16.2%
Furosemide	5	13.5%
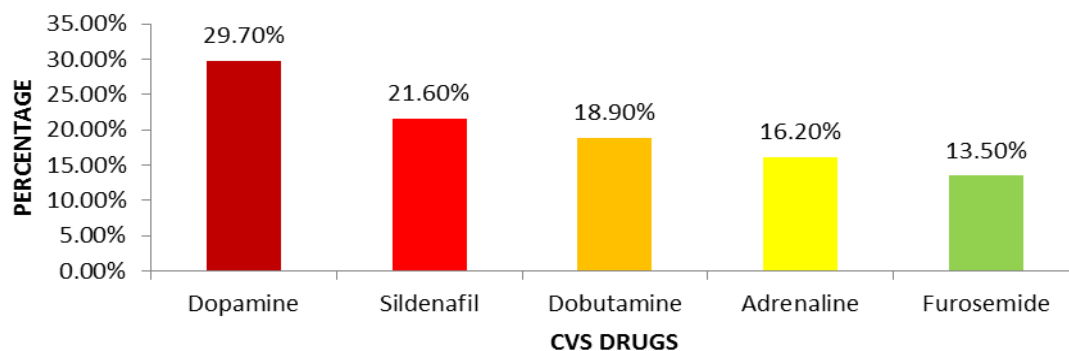
Figure 8: Cardio vascular system drugs prescribed in NICU.

RESPIRATORY SYSTEM DRUGS PRESCRIBED IN NICU

This class of drugs used to treat neonatal apnea of prematurity, broncholitics, transient tachypnea of newborns etc.

Most frequently prescribed respiratory system drugs is caffeine citrate (31%) followed by Salbutamol (24.1), Budesonide (20.7%), Aminophyliine (17.2%) and least prescribed is Terbutaline + Ambroxol (6.9%).

Table 9: Respiratory system drugs used in NICU.

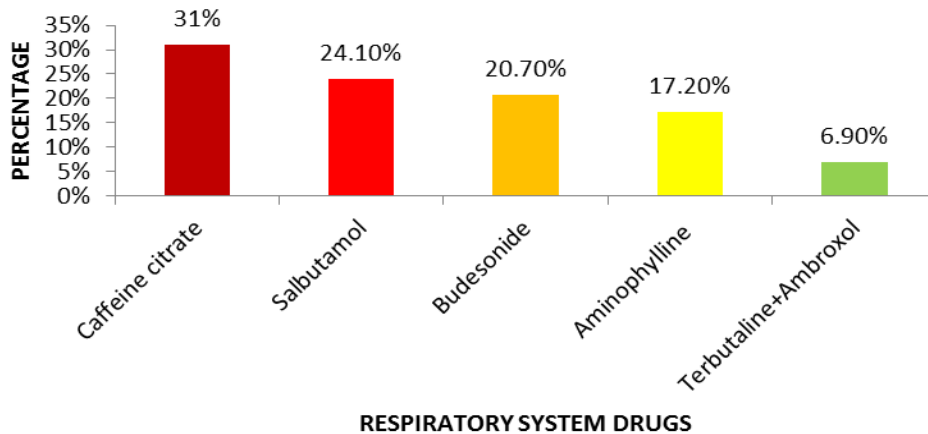| RESPIRATORY SYSTEM DRUGS	NO. OF NEONATES RECIEVING DRUG	PERCENTAGE
Caffeine citrate	9	31%
Salbutamol	7	24.1%
Budesonide	6	20.7%
Aminophylline	5	17.2%
Terbutaline+Ambroxol	2	6.9%

Figure 9: Respiratory system drugs used in NICU.

CORTICOSTEROIDS PRESCRIBED IN NICU

This class of drugs used to treat bronchopneumonia, cough.

Most frequently prescribed corticosteroid is Dexamethasone (64.7%) and Hydrocortisone (35.2%).

Table 10: Cortico steroids prescribed in NICU.

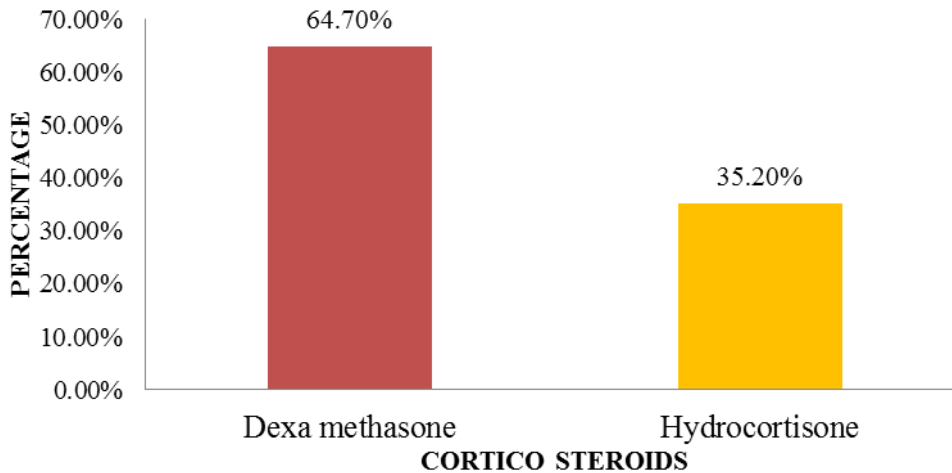| CORTICOSTERIOD DRUGS	NO. OF NEONATES RECIEVING DRUG	PERCENTAGE
Dexa methasone	11	64.7%
Hydrocortisone	6	35.2%

Figure 10: Corticosteroids prescribed in NICU.

ALIMENTARY TRACT DRUGS PRESCRIBED IN NICU
This class of drug used to treat GERD, Preterm neonates etc.

Most frequently prescribed alimentary tract drugs is Ranitidine (63.6%) followed by Ondansetron (18.2%) and Domperidone (18.2%).

Table 11: Alimentary tract drugs prescribed in NICU.

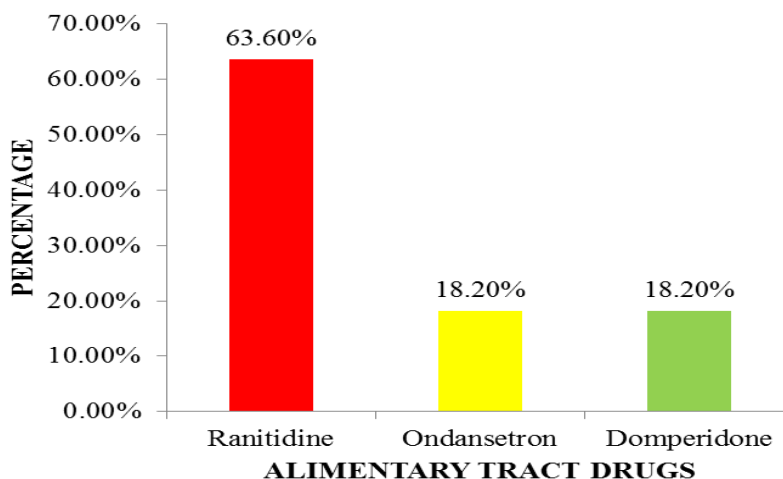| ALIMENTARY TRACT DRUGS	NO. OF NEONATES RECIEVING DRUG	PERCENTAGE
Ranitidine	7	63.6%
Ondansetron	2	18.2%
Domperidone	2	18.2%

Figure 11: Alimentary tract drugs prescribed in NICU.

ROUTE OF ADMINISTRATION OF DRUGS
Different routes of drug administration was observed among 200 case records. The study shows that mainly there are 4 different routes are used for drug administration in NICU. In that parenteral route is more frequently used (44%), followed by oral (26.6%), nebulisation (18.6%), and topical route (10.6%).

Table 12: Distribution of drugs based on route of administration.

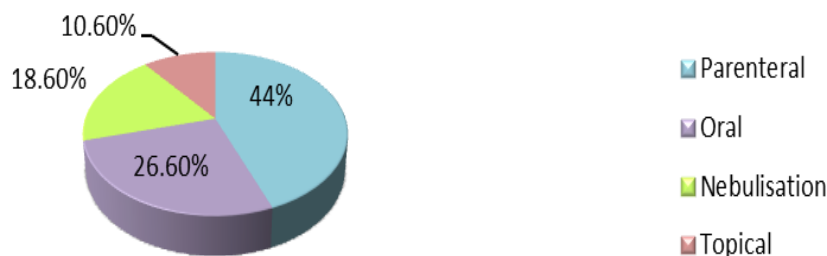| ROUTES OF DRUG ADMINISTRATION	NO.OF DRUGS
Parenteral	33 (44%)
Oral	20 (26.6%)
Nebulisation	14 (18.6%)
Topical	8 (10.6%)

Figure 12: Distribution of drugs based on route of administration.

WHO - PRESCRIBING INDICATORS
A total number of 982 drugs were prescribed for 200 neonates. Average number of drugs per neonates was found to be 4.91. In that 90.5% prescriptions was with antibiotics and 96% prescriptions was with injections.

Only 42% drugs were prescribed by the generic name.61.9% drugs were prescribed from essential medicine list (children) and 59.5% drugs were prescribed from National list of essential medicine of India.

Table 13: WHO-Prescribing indicators.

WHO PRESCRIBING INDICATORS	PERCENTAGE
Total number of drugs in prescriptions	982
Average number of drugs per neonates	4.91
Prescription with antibiotics	90.5%
Prescription with injection	96%
Percentage of drugs prescribed by generic name	42%
Percentage of drugs prescribed from essential medicine list (Children)	61.9%
Percentage of drugs prescribed from National list of essential medicine of India	59.5%

DISCUSSION
The present study of describing the prescription pattern of 200 prescriptions, that were collected from the NICU department of Tertiary care hospital, Mandya. It was found that the total number of male newborns was more than the female newborns these results were in concordance with the studies conducted by Anita Kumari et al.[10] A total of 200 neonates were included in the study. According to gestational age, more neonates were term babies followed by Preterm, Late Preterm, similar to the study conducted by Farshad Namdarifar et al[11] and different from the study conducted by Dr.Jigar Katwala et al where more preterm babies were found than term babies.[12]

According to morbidity pattern in NICU, neonatal sepsis was mostly observed in our study followed by Low birth weight, jaundice, transient tachypnea of newborn, respiratory distress syndrome, birth asphyxia, Meconium aspiration syndrome, Convulsions, Bronchopneumonia, Brochiolitics, Seizure, Very low birth weight, Hypoxic ischemic encephalopathy similar to the study done by Keerti Budnoor Jayram et al[3] and where Sepsis, birth asphyxia, GI problems were common in a study conducted by Kwame Opare et al.[13]

According to the WHO-ATC classification system, in our study, the most commonly prescribed drug class is anti-infectives, nervous system drugs, cardiovascular system drugs, respiratory system drugs, corticosteroids, and alimentary tract drugs this is similar to the study conducted by Anje Neubert[8] different from the study conducted by Inge Mesek et al in which more commonly prescribed drugs were alimentary tract drugs followed by anti-infectives, nervous system drugs, respiratory system drugs, and cardiovascular system drugs.[2]

In our study, the most commonly prescribed antibiotics in NICU are amikacin, amikacin+ clavulonic acid combination, piperacillin, and cefotaxime. This is different from the study conducted by D. Sharad Gedam et al[14] in the middle part of India in which more commonly prescribed antibiotics are ofloxacin+ metronidazole combination and similar to the study conducted by Suparna Chatterjee et al in the eastern part of India.[15] This discrepancy occurred due to the differences in ecology.

Different routes of drug administration were used for the treatment in NICU. The most frequently used route of administration is the parenteral route same as the study conducted by Shailesh Atmaram Chauthankar et al.[16]

A total of 982 drugs were prescribed in the NICU department. In that only 42% is prescribed by generic names this shows a lack of good prescribing pattern in NICU and this result was contrast when compared with the study conducted by Suparna Chatterjee et al[15] in which 79.9 % of drugs were prescribed with the generic name. Our study reports around 61.9% of drugs were prescribed from the essential drug list for children by WHO and 59.5 % of drugs were prescribed from the national list of essential drugs this is due to many vitamins and mineral supplements are not included in the essential list of medicine.

CONCLUSION
Our study was mainly focused on prescribing patterns of drugs in the Neonatal Intensive care unit (NICU) and common diseases in neonates. This study reveals that most of the drugs were prescribed from the WHO essential drug list (Children) 2022. The number of drugs prescribed by their generic name was less compared to the brand name. Most of the drugs were dispensed to the patient from the Hospital free of cost. Neonatal sepsis was most common among the neonate population. This may be due to the less screening of women during pregnancy, low birth weight, intravascular catheters, prematurity, and abnormal amniotic fluid. This can be reduced by providing patient counseling for pregnant women on diet and hygiene. Comprised of a strict sterile technique for line changes and minimizing the administration of other medications or fluids through the parenteral route would reduce catheter contamination and minimizing breaches would reduce the incidence of LOS. Evaluation of the prescription pattern of drugs can improve the quality of prescription therefore they need to be done periodically.

REFERENCES
1. World health organization[Internet]; Place unknown ;2010 [cited 2022 January 29]. Available from https://www.who.int/Inge Mesek, Georgi Nellis, et al. Drug prescription pattern in European neonatal units.Department of Microbiology.DOI: https://doi.org/10.1101/463240.

2. ACOG Committee Opinion No 579: Definition of term pregnancy.
3. Obstet Gynecol, 2013; 122: 1139-40.
4. Keerthi Budnoor Jayaram, Usha D, Prem Bhushal. Drug Utilization pattern in a neonatal intensive care unit at tertiary care hospital attached to a medical college in southern Karnataka, India. International Journal of Contemporary Pediatrics, 2019; 6(3): 1-5.
5. Wade Harrison et al. Epidemiologic Trends in Neonatal Intensive Care, 2007-2012. JAMA Pediatr, 2015; 169(9): 855-862.
6. Asma Al-Turkait, Lisa Szatkowski, et al. Review of Drug Utilization Studies in Neonatal Units: A Global Perspective. International Journal Environmental Research Public Health, 2020; 17: 5669.
7. Ghai OP. Essential Pediatrics, published by interprint A-16, Narain all, New Delhi, India. 4th edition, 1998.
8. Surender Kagitapu, Alekhya Nune, et al. Prescribing Patterns of Drugs in Pediatrics Outpatient Department in Tertiary Care Hospital. IOSR Journal of Dental and Medical Sciences, 2016; 15: 92-95.
9. Antje Neubert, Kristin Lukas, et al. Drug utilization on a preterm and neonatal intensive care unit in Germany: a prospective, Cohort-based analysis. Eur J Clin Pharmacol, 2010; 66: 87–95.
10. Anita Kumari et al. Drug Utilization Pattern in Neonatal Intensive Care Unit of a Tertiary Care Hospital with Particular Emphasis on Off-Label Drug Use. J Clin Neonatol, 2019; 8: 15-8.
11. Farshad Namdarifar et al. Drug utilization study in neonatal intensive care unit at tertiary care hospital. Rev Assoc Med Bras, 2022; 68(2): 212-216.
12. Jigar Katwala, Aksha Memon et al. Study of Drug Pattern and Their Regime Composition in the Neonatal Intensive Care Unit. European Journal of Biomedical and Pharmaceutical Sciences, 2022; 9(8): 321-327.
13. Kwame Opare-Asamoah et al. Clinical Characteristics, Medication Prescription Pattern, and Treatment Outcomes at the Neonatal Intensive Care Unit of a Tertiary Health-Care Facility in Ghana. J Res Pharm Pract, 2021; 10: 30-7.
14. Sharad Gedam, Umesh Patel, et al. Drug Prescription Pattern in Pediatric Out Patient Department in a Teaching Hospital in Central India. Int. J. Pharm. Sci. Rev. Res, 2012; 17(2): 07, 42-45.
15. Suparna Chatterjee, Ananya Mandal, et al. Drug utilization study in a neonatology unit of a tertiary care hospital in eastern India. pharmacoepidemiology and drug safety, 2007; 16: 1141–1145.
16. Shailesh Atmaram Chauthankar et al. Drug Utilization in Neonatal Intensive Care Unit of a Tertiary Care Hospital in Mumbai, India. Indian Pediatrics, 2017; 5: 1-4.