ORIGINAL RESEARCH article

Drug utilization pattern in the NICU: A World Health Organization-Anatomical Therapeutic Chemical Classification-based cross-sectional study

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Abstract: Drug utilization in Neonatal Intensive Care Units is complex due to the immaturity of neonates and the critical nature of their ailments. Understanding prescribing patterns is essential for promoting rational pharmacotherapy and improving neonatal outcomes. To evaluate drug utilization patterns in the Neonatal Intensive Care Unit at Aljala Maternity and Gynecology Hospital, Tripoli, Libya. A prospective, cross-sectional observational study was conducted from September to December 2023. Data were collected from 503 neonates who received at least one medication. Drug use was analyzed based on the World Health Organization-Anatomical Therapeutic Chemical classification. Of 739 neonates admitted, 503 met the inclusion criteria. Males accounted for 57.3% and 73.0% were born at term. The average hospital stay was 5.61 days. Neonatal sepsis (87.5%) and respiratory distress (65.2%) were the most common diagnoses. A total of 1,443 medications were prescribed, with an average of 2.9 drugs per neonate. Anti-infective agents represented 79.8% of all prescriptions, with benzyl penicillin, gentamicin, and cefotaxime being the most common. Injections were used in 93.1% of cases, and 97.4% of drugs were from the Libyan Essential Medicines List. The findings reveal high antibiotic use and empirical prescribing practices in response to infectious morbidities. There is a critical need for improved diagnostic support, therapeutic drug monitoring, and antimicrobial stewardship to ensure safe and effective pharmacotherapy in the Neonatal Intensive Care Unit.

Introduction

The Neonatal Intensive Care Unit (NICU) plays a critical role in the survival and treatment of high-risk neonates, particularly those born prematurely or with serious medical conditions. Due to their physiological immaturity, neonates are especially vulnerable to infections, respiratory complications, and other morbidities that often require complex pharmacological interventions [1]. The World Health Organization (WHO) emphasizes the use of drug utilization studies as a vital tool for evaluating prescribing trends and informing policy [2, 3]. This study aims to

assess the patterns of drug use among neonates admitted to the NICU at Aljalaa Maternity and Gynecology Hospital in Tripoli, Libya, with a focus on evaluating the types, frequency, and indications of prescribed medications using the WHO-Anatomical Therapeutic Chemical (WHO-ATC) classification system and WHO-core prescribing indicators. Despite global efforts to optimize neonatal pharmacotherapy, there is a notable lack of published data on drug utilization in neonates in Libya, limiting data-driven improvements in prescribing practices and policy development.

Materials and methods

This cross-sectional, observational, prospective study was conducted at Aljalaa Maternity and Gynecology Hospital in Tripoli, Libya, from September to December 2023, to assess drug utilization in the NICU. All neonates admitted to the NICU and prescribed at least one medication were included. Those receiving only fluids, parenteral nutrition, blood products, oxygen, phototherapy, or vaccinations were excluded except for those administered ferrous sulfate and phytonadione, due to their defined therapeutic use. Non-therapeutic items such as intravenous solutions, blood products (except albumin), oxygen, and electrolytes were also excluded from the drug utilization analysis, in line with previous research [4]. Data were extracted from medical records, including demographics, delivery mode, admission reasons, clinical outcomes (length of stay and mortality), laboratory results, and medication details. Drug classification followed the WHO-ATC system and WHO-core prescribing indicators.

Ethical approval: The approval was obtained from the Scientific Research Ethics Committee at the University of Tripoli (SREC/010/73).

Data presentation: Data were analyzed using SPSS version 27 with descriptive statistics such as mean, median, standard deviation, and frequency distributions.

Results

Demographic and clinical characteristics of neonates: A total of 503 neonates were included in the study (**Table 1**). The majority were male (57.3%) and term neonates (73%), while moderate to late preterm constituted 21.9%, and extremely preterm 1.2%. Most neonates had normal birth weight (78.9%), with 17.1% classified as low birth weight and 1.0% as extremely low birth weight. Cesarean section (C/S) was the predominant mode of delivery (65%). The majority of neonates were discharged (92.2%), while the mortality rate was 4.4%. The average length of hospital stay was 5.61 days, ranging from one to 49 days.

Morbidities observed in NICU: Regarding clinical morbidities (**Table 2**), neonatal sepsis was the most frequent condition, affecting 87.5% of neonates, followed by respiratory distress (RDs) (65.2%) and neonatal jaundice (33.8%). Other conditions included prematurity (27.0%), low birth weight (21.1%), birth asphyxia (11.3%), infants of diabetic mothers (IDM) (10.9%), and neonatal convulsions (4.6%). Less frequently reported morbidities were hypocalcemia (3.2%), anemia (3.0%), intrauterine growth restriction (IUGR) (2.8%), and necrotizing enterocolitis (NEC) (1.2%).

Medications prescribed to the neonates: A total of 1,443 medications were prescribed during the study period (**Table 3**). Anti-infective agents were the most commonly prescribed drug class (79.8%), followed by drugs targeting the nervous system (6.79%), cardiovascular system (5.19%), and respiratory system (3.6%). **Table 4** details drug distribution by WHO-ATC code. Benzyl penicillin was the most frequently prescribed medication

(97.8%), followed by gentamicin (57.5%) and cefotaxime (40.8%). Among nervous system drugs, phenobarbital (5.8%) and caffeine citrate (5.2%) were commonly used. For cardiovascular support, dopamine was most frequently prescribed (9.5%). Surfactant therapy was administered in 8.7% of neonates, while hydrocortisone, supplements, and other supportive medications were prescribed as needed.

Table 1: Demographic and clinical characteristics of the neonates

Variables	Total number = 503	
	Frequency	Percentage
Male	288	57.3%
Female	215	42.7%
Term ≥ 37 weeks	367	73.0%
Moderate to late preterm 32-36 weeks	110	21.9%
Very preterm 28-31 weeks	20	04.0%
Extremely preterm < 28 weeks	06	01.2%
Normal birth weight ≥ 2500 g	397	78.9%
Low birth weight 1500-2499 g	86	17.1%
Very low birth weight < 1500 g	15	03.0%
Extremely low birth weight < 1000 g	05	01.0%
NVD	176	35.0%
C/S	327	65.0%
Discharge	464	92.2%
Death	22	04.4%
Discharge against medical advice	07	01.4%
Transfer	10	02.0%
Mean length of stay	5.61	01.0 - 49.0

Table 2: Morbidities observed in the Neonatal Intensive Care Unit

Morbid condition	Frequency	Percentage
Neonatal sepsis	442	87.5%
RDs	328	65.2%
Neonatal jaundice	170	33.8%
Preterm	136	27.0%
Low birth weight	106	21.1%
Birth asphyxia	57	11.3%
IDM	55	10.9%
Neonatal convulsions	23	04.6%
Hypocalcemia	16	03.2%
Anemia	15	03.0%
IUGR	14	02.8%
NEC	06	01.2%

Table 3: Drugs used according to the WHO-ATC classification system

Total medicines	WHO-ATC category					
1443	Anti-infective	Nervous system	Cardiovascular system	Respiratory system	Alimentary tract	Others
n	1151	98	75	52	02	64
%	79.8%	6.79%	5.19%	3.60%	0.14%	4.44%

Table 4: Distribution of drugs used categorized according to WHO-ATC Codes

Drug category	ATC code	Drug	Neonates (n)	Percentage
Anti-infective	J01CE01	Benzyl Penicillin	492	97.8%
	J01GB03	Gentamicin	289	57.5%
	JO1DD01	Cefotaxime	205	40.8%
	J01DH02	Meropenem	50	09.9%
	J01GB06	Amikacin	40	08.0%
	J01CF02	Cloxacin	31	06.2%
	J01XA01	Vancomycin	27	05.4%
	J01XD01	Metronidazole	06	01.2%
	J01MA02	Ciprofloxacin	05	01.0%
	J02AC01	Fluconazole	03	00.6%
	J01CR02	Co-amoxiclav	01	00.2%
	J01CR05	Piperacillin tazobactam	01	00.2%
	J01DD02	Ceftazidime	01	00.2%
Central Nervous system	N03AA02	Phenobarbital	29	05.8%
	N03AB02	Phenytoin	19	03.8%
	N02AA01	Morphine	06	01.2%
	N01AH01	Fentanyl	12	02.4%
	N05CD08	Midazolam	02	00.4%
	N02BE01	Paracetamol	04	00.8%
	N06BC01	Caffeine citrate	26	05.2%
Cardiovascular system	C03CA01	Furosemide	14	02.8%
	C01CA04	Dopamine	48	09.5%
	C01CA24	Adrenaline	09	01.8%
	C01CA07	Dobutamine	03	00.2%
	C02DB02	Hydralazine	01	00.6%
	C04BE03	Sildenafil	01	00.2%
Alimentary tract	A03FA03	Domperidone	01	00.2%
	A02BC01	Omeprazole	01	00.2%
Respiratory system	R07AA	Surfactant	44	08.7%
	R03BB01	Ipratropium bromide Nebulizer	08	01.6%
Endocrine system	H02AB09	Hydrocortisone	03	00.6%
Others		Supplement	43	08.6%

Prescribing pattern according to WHO-Core indicators: Based on WHO-core prescribing indicators (**Table 5**), the average number of drugs prescribed per neonate was 2.9. Antibiotics were included in 79.8% of prescriptions, and 93.1% of drugs were administered via injection. Importantly, 97.4% of prescribed drugs were from the Libyan Essential Drugs List.

Table 5: Prescribing pattern based on WHO-core indicators

WHO-core indicators	Value
Total number of drugs prescribed	1443
Average number of drugs per neonate	02.9
Percentage of prescription with antibiotics	79.8%
Percentage of prescription with injection	93.1%
Percentage of drug prescribed from the Libyan Essential Drugs List	97.4%

Discussion

This study investigated neonatal care patterns in a NICU, highlighting key demographic, clinical, and pharmacological trends. A predominance of male neonates was observed, consistent with global. These data suggest that male neonates are more frequently admitted to the NICU, possibly due to biological or environmental factors that increase their vulnerability to conditions requiring intensive care. This pattern underscores the need for further research to understand the underlying causes of this increased risk among male neonates. The rate of C/S delivery was higher than normal vaginal delivery (NVD), in line with studies conducted in China (64.3% C/S and 35.7% NVD) and Iran (64.2% C/S and 35.8% NVD). The high prevalence of C/S deliveries may reflect underlying maternal or fetal complications such as maternal hypertension, gestational diabetes, or fetal distress, contributing to the higher NICU admission rates in this population [4-12]. Neonatal sepsis emerged as the most prevalent condition affecting admitted neonates; this high incidence is concerning, as sepsis is a leading cause of neonatal morbidity and mortality [13]. Neonates are especially vulnerable due to their immature immune systems and the challenges in diagnosing sepsis early. Several cases were suspected of early-onset sepsis (EOS), occurring within the first 72 hours of life, often due to maternal infections transmitted during labor or delivery. In the current study, the EOS was frequently associated with inadequate prenatal care, especially notable during the COVID-19 pandemic, when antenatal services were closed. These findings emphasize the need for improved prenatal infection screening and continuity of maternal care [14]. According to various studies utilizing the WHO-ATC classification system, anti-infective agents for systemic use were consistently identified as the most frequently prescribed pharmacological group [15]. This trend was also observed in the NICU analyzed in this study. This high utilization of anti-infective agents aligns with the critical need to manage infections in neonates, in agreement with findings that emphasize the high prevalence of infectious conditions in the NICUs [6, 16-18].

Several factors contribute to the increased use of anti-infective agents in NICUs. One key factor is empirical use, where healthcare providers often initiate broad-spectrum antibiotics to address suspected infections in neonates before identifying specific pathogens. While this approach is necessary in many cases and can curtail mortality by about 70.0%, it can lead to the overuse of anti-infective agents. The time required to obtain culture and sensitivity results further exacerbates this issue, leading to prolonged use of broad-spectrum antibiotics while awaiting pathogen confirmation. This delay, coupled with the lack of rapid diagnostic tools, contributes to the extended or sometimes unnecessary use of these medications [17, 19]. In this study, empirical treatment was commonly initiated due to limited access to culture diagnostics, leading to extended use of broad-spectrum antibiotics. The NICU relied primarily on C-reactive protein levels for infection monitoring, highlighting the urgent need for better diagnostic tools and access to microbiological testing [20]. The consistent use of similar antibiotics, such as aminoglycosides and penicillin, across neonatal units in various countries highlights the global reliance on these drugs used as first line treatments of infections in neonates [16]. Narrow therapeutic index drugs (NTDs) like gentamicin and vancomycin were widely used without therapeutic drug monitoring (TDM), increasing the risk of toxicity. Additionally, cefotaxime and meropenem were frequently prescribed for severe infections, while high-risk agents such as ciprofloxacin and omeprazole were used selectively due to safety concerns in neonates [21]. In the absence of TDM, clinicians must rely on indirect methods to monitor the effects of NTDs, such as observing clinical signs of efficacy or toxicity and tracking laboratory parameters like serum creatinine for nephrotoxicity. However, these methods are less sensitive and can result in delayed detection of adverse effects or treatment failures. Neonates, especially those who are preterm or have low birth weight, exhibit significant variability in drug metabolism and excretion [22]. Factors such as immature renal function, hepatic enzyme activity, and fluctuating plasma protein levels can affect drug pharmacokinetics, making standardized

dosing unreliable. TDM helps tailor drug doses to the individual neonate's pharmacokinetics profile, but without it, clinicians are left to rely on less precise dosing guidelines [21, 22, 23]. According to WHO-core prescribing indicators, the average number of drugs per neonate may reflect the complexity of clinical cases, a tendency toward over prescription, or a potential risk of polypharmacy. Polypharmacy increases the tendency towards drug-drug interactions and adverse drug reactions [22, 24], both of which can complicate neonatal care and negatively impact outcomes. This highlights the need for more rational and evidence-based prescribing practices [23]. In comparison with international data (**Figure 1**), which reports an average of 2 to 9 drugs per neonate across various countries, the observed value falls within the global range. This suggests relatively conservative prescribing practices [25-28]. However, the frequent use of antibiotics and the absence of TDM underscore the urgent need for antimicrobial stewardship programs, improved diagnostic tools, and safer prescribing protocols to optimize neonatal outcomes. When interpreting these drug utilization patterns, it is important to consider factors such as the prevalence of specific conditions, the availability of medications, and adherence to local treatment guidelines [4, 5, 16, 17, 29, 30].
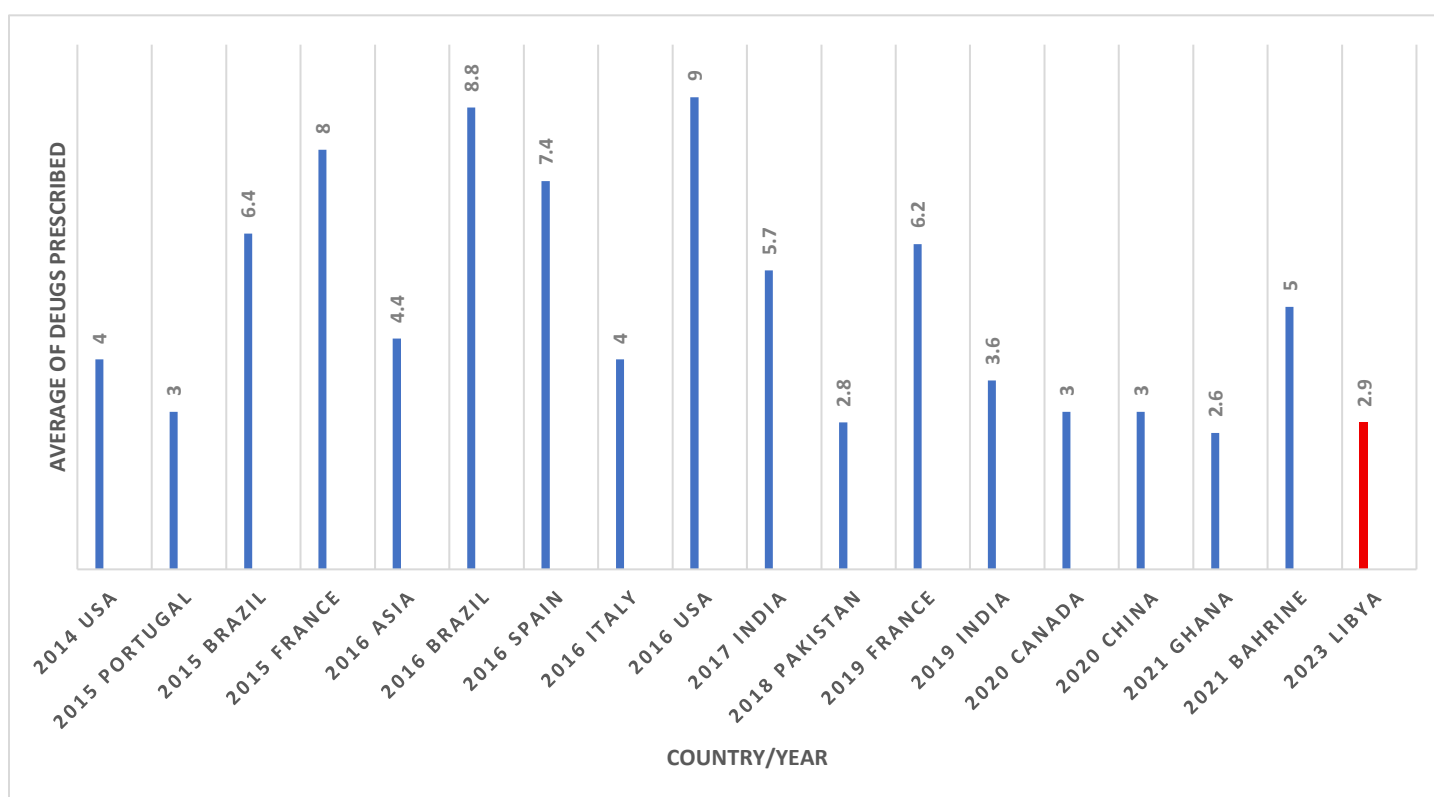

Figure 1: Average number of drugs per neonate from various countries

Conclusion: This study highlights significant patterns in drug utilization within the NICU, marked by a high reliance on anti-infective agents, largely driven by the high incidence of neonatal sepsis. These findings emphasize the urgent need to implement antimicrobial stewardship programs and improve diagnostic capabilities to promote safer and more rational drug use in neonates. While prescribing practices generally adhered to the national essential medicines list and WHO guidelines, several challenges persist, including the absence of TDM, limited access to diagnostic tools, and a continued dependence on empirical treatment. Future efforts should focus on optimizing evidence-based treatment protocols and strengthening neonatal pharmacovigilance to enhance clinical outcomes in this vulnerable population.

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