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A Study on Drug Resistance and Sensitivity Patterns of Bacteria and Prescribing Patterns of Antibiotics in Neonates and Pediatrics

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ABSTRACT
Infections that are caused by bacteria which leads to main cause of neonatal mortality and also morbidity across the world. Bacterial pathogens and drug resistance are different in different countries and also with in the country. In this study, we determined the bacterial pathogens and drug resistance and sensitivity patterns among the neonatal intensive care unit (NICU) and pediatric intensive care unit in tertiary care hospitals. This prospective observational was done on 210 hospitalized neonates and pediatrics whose samples sent to culture and sensitivity tests. This study was conducted from March 2023 to September 2023. Blood, urine, stool, pus aspirates, and endo tracheal secretions were evaluated. Out of 210 patients, 98(46.6%) cultures showed positive. The major growth was observed in Gram-negative micro-organisms (76.5), of which Pseudomonas aeruginosa (24.5%). Escherichia coli (23.5%). And Klebsiella pneumonia (17.3 %) were the most frequent isolates. Gram-positive organisms constituted (18%), among them Staphylococcus aureus (10%) was the most common followed by CONS (7.1%). Gram-negative group showed high resistance to cefazolin (81%) cefuroxime (76.84%) and cefepime (72%) and high susceptibility to amikacin (62.78%), imipenem (61.73%) and meropenem (61%). Gram-positive organisms had shown high resistance to the drug ampicillin (83.33%) ciprofloxacin (72%) and cefuroxime (66%) but were highly sensitive to levofloxacin, tetracycline (88.86%) and vancomycin (84%). There is a need a progressive evaluation of the sensitivity and resistance patterns of bacterial pathogens by that we can improve the rational use of the antibiotics.
Keywords: *Bacterial infections, Drug resistance, Drug sensitivity, Neonates, Pediatrics.*

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INTRODUCTION

Antibiotics are used to treat infections that are caused by bacteria. Antimicrobial resistance is a worldwide problem. Antibiotics resistance means the ability of bacteria to resist the effects of antibiotics [1]. Irrational use of antibiotics has led to multidrug-resistance infections like Extended -Spectrum Beta-Lactamase (ESBL) urinary tract infections/sepsis, multidrug-resistant tuberculosis [2]. There are several mechanisms are involved in the drug resistance of micro-organisms. It can be due to genetic or non genetic [3]. The increasing resistance will leads to longer hospital stay in addition with it also creates antibiotics related adverse events and increases health care cost [4]. Infections that are commonly occurred in neonates and pediatrics are BSI (bloodstream infections; Sepsis), LRTI (Lower Respiratory Tract Infections), and UTI (urinary tract infection)[7]. Sepsis is a major cause of neonatal death. Neonatal sepsis means a systemic inflammatory response syndrome that is caused by a suspected or proven infection that occurs within the first 28 days of life. Based on the onset time, it was classified as early onset sepsis when seen within 72 hours of birth and late onset sepsis when seen after 72 hours of birth. [8,9]. Commonly isolated bacterial pathogens in sepsis are gram-negative bacteria (*Klebsiella species, E.coli, Pseudomonas species, Acinetobacter, Enterobacter species*.) and gram-positive bacteria (Staphylococcus aureus, Enterococci.). The most common LRTIs are bronchitis and pneumonia [10]. Klebsiella pneumonia and Pseudomonas aeruginosa were commonly isolated pathogens in LRTI [11,12]. UTI is a common bacterial infection in children. *E. coli, Klebsiella* species, *Enterobacter* species, and *Staphylococcus* species were the most isolated bacterial pathogens isolated from UTIs [13]. The world population consists of about 28% of neonates and children were tending to have high infections due to low immune responses [15]. The microbiological pattern of infections in children was changing day by day so there is a necessity in the causative micro-organism and their drug usage patterns [16]. Pathogens encountered in blood culture of neonates and

pediatric varies worldwide and the reports from the developing countries shows gram-negative organisms are commonly seen [18]. Knowledge of the most common micro-organism and their patterns of sensitivity and resistance will helpful in early initiation of the appropriate treatment that provides better outcome for the patient. Therefore, this study was conducted to determine the common bacterial pathogens and their antibiotics sensitivity and resistance patterns from various body samples (blood, urine, stool, ET secretions, and pus aspirates) and identify the prescribing patterns of antibiotics of neonates and pediatrics.

MATERIAL AND METHODS

Aim: to assess the bacterial pathogens and drug resistance and sensitivity patterns among the neonatal intensive care unit (NICU) and pediatric intensive care unit in tertiary care hospitals.

Objectives:

- To assess the most common type of microorganism detected in infected neonates.
- To assess the patterns of antibiotics sensitivity and resistance towards microorganisms
- To assess the prescribing patterns of antibiotics in neonates

Study Site and Population:

A prospective study was conducted in the In-patient set up of Neonatal Intensive Care Unit (NICU) and Pediatric Intensive Care Unit (PICU) at tertiary care hospitals from March to September, 2023.

Inclusion criteria:

All the patients (neonates) who are receiving antibiotics.

Samples of children < 12 years that gone to microbial sensitivity and resistance testing.

Exclusion criteria:

Children parents who are not willing to share their data.

Data Collection:

The study period, neonates (0–28 days of age) and pediatrics (1M-12 years) were investigated. Data collected which includes name; age, gender, and gestational age were collected and recorded in the previously prepared case record form. Various samples (blood, urine, stool, endo tracheal secretions, and pus aspirates) were also collected with proper antiseptic precautions by a pediatrician and sent to a microbiological laboratory for the identification of organisms by culture growth. Informed consent was obtained from all individual participants or attendees of the patients.

Statistical methods:

Data was entered into Microsoft Excel worksheet. All statistical analysis was performed by using Graph Pad Prism Version 8.3.0. Data entered in Excel (version2010). Continuous variables were summarized using standard error of the mean (SEM), minimum, maximum, range, mean (Descriptive statistics).

RESULTS

The total of 210 samples were collected, 98 reports shows positive microorganism growth with 53 male and 45 female with 54% and 46% respectively as shown in the below table 1. According to the age categories, neonates, infants, young child and child were classified in the below table 2. Among all the samples, blood samples were collected in high number when compared to pus aspirates. Based on the type injury and infections site, the collection of sample changes. Source of sample collection and their positive and negative culture results are represented in the below table 3. A total of 210 culture samples were screened in 6 months of period, of which 98 samples (46.6%) were culture positive. Out of these positive microbial growth samples, 75.5 percent (75 isolates) were positive for Gram negative bacteria. Amongst the Gram-negative isolates, 21.9 percent isolates of Klebsiella pneumonia and 19% of E. coli were the most commonly isolated bacteria. Among gram negative bacteria Pseudomonas showed 100% sensitivity to ciprofloxacin and meropenem and least sensitivity towards piperacillin (20%). It was (100%) resistance was noticed with cefazolin followed by ceftriaxone (91%) and *E.coli* showed high sensitivity to ciprofloxacin, levofloxacin and meropenem (56%) and it showed high resistance to cefuroxime (86%) followed by ceftriaxone (69%) shown in the below figure. Among Gram- positive bacteria, Staphylococcus had high sensitivity to amikacin, levofloxacin, tetracycline, and vancomycin (66%). It is more resistance to ampicillin (50%) CONS showed (100%) sensitivity to levofloxacin and tetracycline and it showed 100% resistance to ampicillin, cefuroxime, and ciprofloxacin. Tazobactum/piperacillin (43%) is the highly prescribed antibiotic before culture followed by meropenem (40%) and amikacin (39%). Mostly prescribed antibiotic after culture is amikacin (53%) followed by ciprofloxacin (31%) and meropenam (21%).

DISCUSSION

Bacterial infections are still prevalent in neonates and pediatrics. In this study the most common source was the blood sample isolates (71.4%), followed by urine (11.9%), stool (9.5%) and others include ET secretions and Pus aspirates (7%), whereas isolates in the sputum is most common according to another study (57.7%), followed by urine (16.8%) and blood (10.9%)[18]. The isolation of micro-organisms in blood culture-positive cases were (43.3%) which was different to rates reported in other studies Kerala (22%)[8], New Delhi (42%)[17], Iran (5.1%)[3], Nepal (20.5%)[9], (4.2%)[16], Egypt (42.7%)[18]. The isolation rate of urine cultures was (56%) which was differed from the other studies in which the positive rate is (26.7%)[24] and (7.%)[13]. The isolation rate of stool culture in this study is (45%) these results slightly differ from the results of various studies (43%) [14] and (41.5%)[26]. Variations of results have observed due to differences in geographical areas and methods used to test the samples.

Culture report of organism

In the present study, gram-negative bacteria were the most frequently isolated bacteria these results are consistent with various other studies [3]. This pattern has differed from the results of many other studies where the gram-positive organism was predominant [8]. The results will support those varieties of micro-organisms that cause infections to neonates will vary from one place to another and also changes from time to time within the same place [18]. In this study, gram-negative organism has been documented to a common cause of infections. The probable reasons being, newborns most probably acquire these gram-negative rods from the vaginal and fecal flora of the mother and the environment where the delivery occurs [27]. Among gram-negative bacteria, the most commonly isolated organisms from the culture samples were *Pseudomonas aeruginosa* (25%) followed by *Escherichia coli* (24%), and *Klebsiella pneumonia* (18%), these results are consistent with another study [19].by this we can know that infections that are caused by these agents will have a significant threat to the neonates and children. Among gram-positive bacteria, *Staphylococcus* (11%) is the most commonly isolated organism followed by CONS (7%) but in developed countries group B *Streptococcus* is main infection-causative organism among gram-positive organisms [27].

Sensitivity and resistance patterns of isolated organisms

In our study gram-positive bacteria, was most sensitive to levofloxacin, tetracycline (89%) and vancomycin (84%), but these results differed from another study which shows that gram-positive bacteria was highly sensitive to the drug vancomycin (93.33%) and gentamycin (56.52%)[8]. Gram-positive bacteria, high resistance to ampicillin (83.33%) ciprofloxacin (72%) and cefuroxime (66%) but in another study gram-positive complete resistance to ampicillin and pencillin[8]. Gram-positive bacteria sensitivity to vancomycin has dropped from (100%) to (84%)[26].The patterns of sensitivity was changing rapidly in a short period of time especially in the developing countries where the prescribing patterns of antibiotics are very irrational due to antibiotics are not only prescribed by the doctor but also purchased from the pharmacies without any prescription. Gram-negative bacteria, was most sensitive to amikacin (63%), followed by imipenem (62%) and meropenem (62%) while a high level of resistance was observed to cefazolin (81%) cefuroxime (76.84%) and cefepime (72%) suggesting cautious use of these drugs, these result contradictory to another study in which gram-negative bacteria, most of the resistance was seen in ampicillin (95%), while a high sensitivity was seen in meropenem (88.24%)[8]. The sensitivity of cefperazone/sulbactam sensitivity to gram-negative bacteria has dropped from 100% to 20%[27]. WHO recommends the first line rational treatment in NICU was ampicillin-sulbactam that was combined with cephalosporins or aminoglycosides antibiotics. In this present study, a high resistance was found against ampicillin, which is a 3rd generation cephalosporins and thus, the WHO recommended an empirical combination regimen that may no longer be valid in NICU in this region[18]. Based on these results ciprofloxacin are now largely prescribed to treat the *Pseudomonas aeruginosa* infections in our setups. *Pseudomonas* showed 100% resistance to cefazolin followed by ceftriaxone 92% and cefuroxime 88% but in another study complete resistance is observed to ampicillin[22].

Prescribing patterns of antibiotics

Combinedly before and after culture amikacin was prescribed predominantly these results are consistent with Suryawanshi S et al., (2015) study in which amikacin was the most often prescribed drugs [15]. This study shows that tazobactam/piperacillin was the most commonly prescribed antibiotic drug before culture followed by meropenem and amikacin and mostly prescribed antibiotics after the culture is amikacin followed by ciprofloxacin and meropenem. After performing the analysis of blood culture and sensitivity (CS) results, (65%) of the antibiotic therapy were altered, and (35%) were not altered, because the susceptibility was shown for the empirical treatment so they were not modified but these results are not corelated with another study which is conducted in 2012 in this study only (27%) antibiotic therapy modified and (73%) were not modified [28].

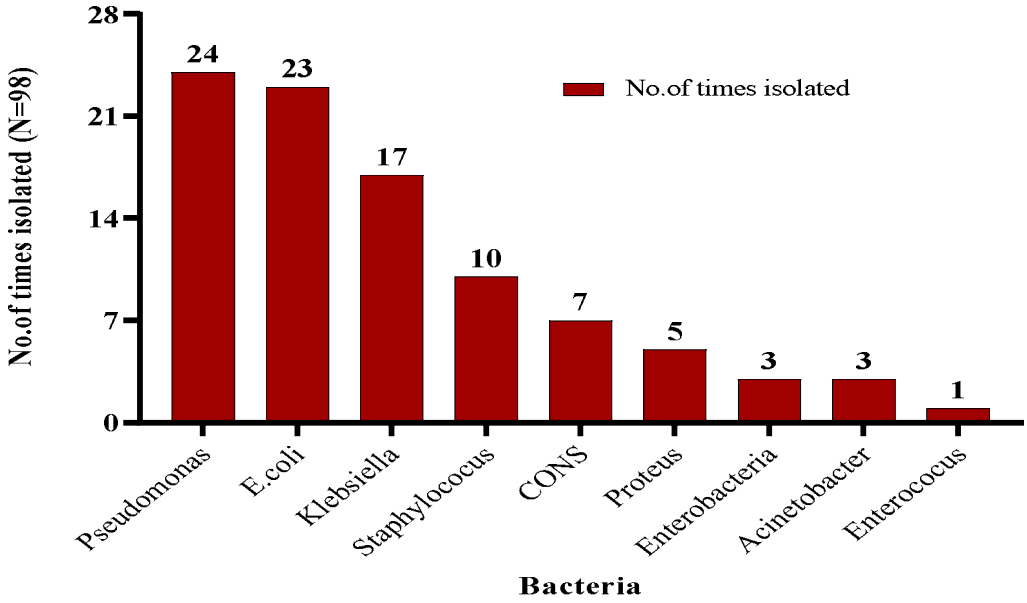

Fig-1: bacterial isolates

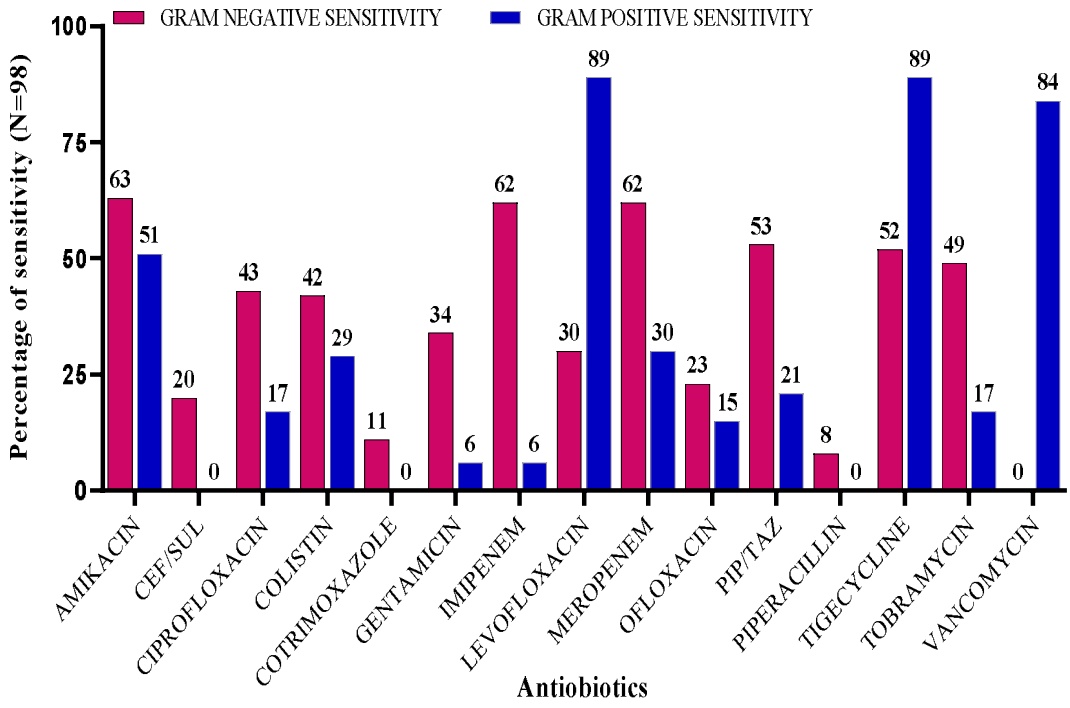

Fig-2: *antibiotics sensitivity*

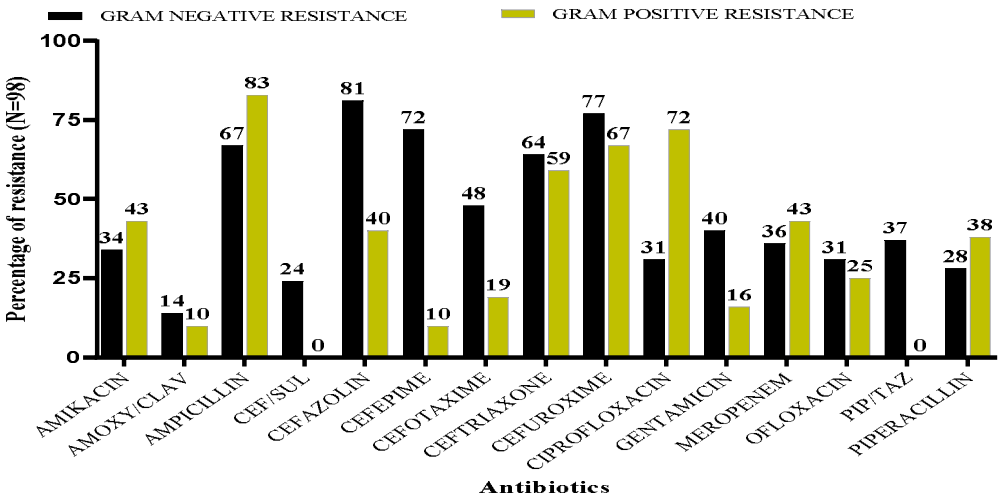

Fig-3: ***antibiotics resistance***

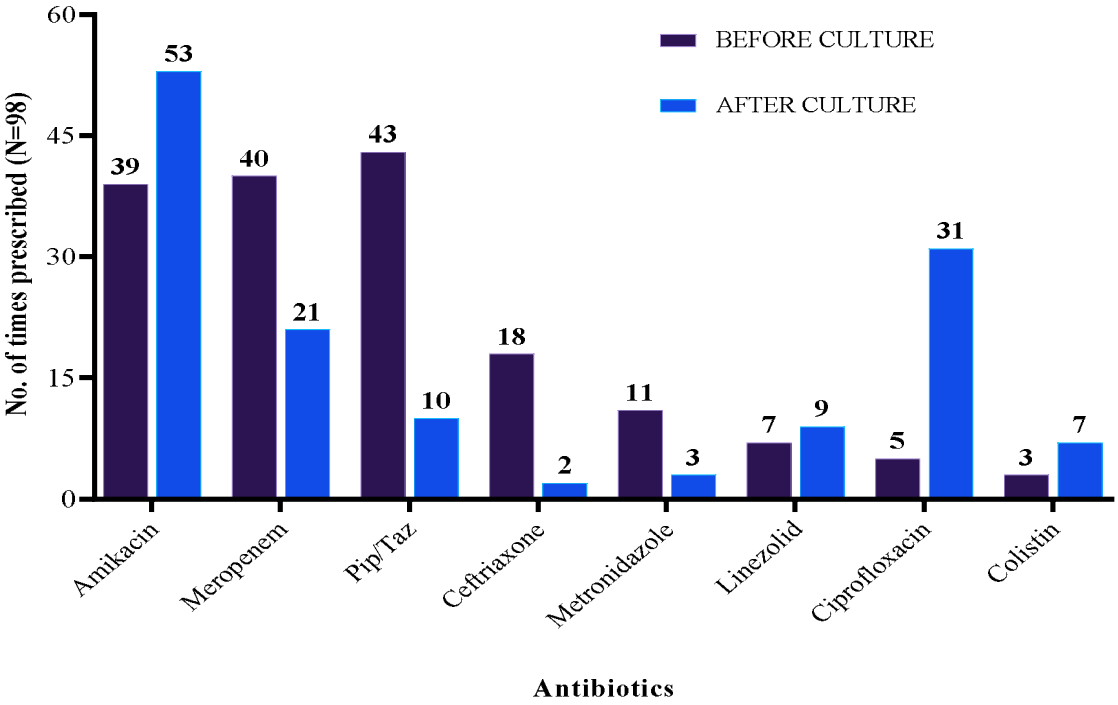

Fig-4: antibiotics prescribed

Table-1: gender

S.No	Gender	Number of Individuals(N=98)	Percentage (%)
1	Male	53	54
2	Female	45	46

Table-2: age category

Category	Age	Number of Individuals(N=98)	Percentage (%)
Neonates	0-30 days	57	58
Infants	1 month-2 years	24	24
Young child	2 years-6 years	5	5
Child	6 years-12 years	12	12

Table-3: Source of culture

SOURCE OF CULTURE	CULTURE RESULTS	
	NEGATIVE	POSITIVE
BLOOD (n = 150)	85 (56.6%)	65 (43.4%)
URINE (n = 25)	11 (44%)	14 (56%)
STOOL (n = 20)	11 (55%)	9 (45%)
OTHER BODY FLUIDS (n = 15) (ET secretions & Pus aspirates)	5 (33.3%)	10 (66.7%)

CONCLUSION

Majority of hospital setups did not make any modifications in their antibiotic therapy, this may increase the resistance of antibiotics. By results and discussion, we concluded that antimicrobials must be administered according to

- Epidemiologic studies in the region
- Confirmed indications
- Based on the results of susceptibility tests.

Antibiotic resistance and sensitivity patterns different in different geographical locations and within the same country as well. Therefore, there is a need to continuously evaluate the sensitivity-resistance pattern of isolates by that we can improve the rational use of antibiotics

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