

Original Research Article

THERAPEUTIC EVALUATION OF VARIOUS ANTIBIOTICS USE IN PAEDIATRIC INPATIENTS: INSIGHTS FROM A TERTIARY CARE TEACHING HOSPITAL

ABSTRACT: Background: Antimicrobial consumption has led to the development of antimicrobial resistance, a major concern to the healthcare system as it has severe consequences, including loss of life. Antimicrobial resistance predicts 4.7 million deaths in Asia by 2050. **Objective:** To reduce, the risk of antimicrobial resistance, misuse of antibiotics and prevent the possible drug interactions. **Methodology:** A prospective observational study was conducted in paediatric department for 6 months. In-patients who were under antibiotic therapy and patients with co-morbid conditions were included in the study. **Results:** A total of 160 patients were enrolled in this study among which males (56.25%) were more predominant than females (43.75%). Majority of the subjects were aged between 1-11years which accounts 56.25%. Respiratory tract infections (RTI) (33%) were the most common. Ceftriaxone was the commonly prescribed antibiotic 24.64%. The common dosage form of antibiotics were injectables in 91.39% cases. A total of 40 drug-drug interactions were found among which 80% were antibiotics interacting with other drugs. In this study 6.87% subjects underwent antibiotic sensitivity testing, whereas remaining 93.12% did not undergo any such. **Conclusion:** We conclude that the development of institutional guidelines for diagnosing and treating common infectious diseases can minimize the risk of antibiotic resistance in paediatric patients. In addition, implementing antibiotic stewardship strategies can help in avoiding unintended consequences.

Key Words: Antimicrobial resistance, Rational use, Respiratory Tract Infections, Empirical therapy, Definitive therapy, Paediatrics.

INTRODUCTION: Paediatrics is a fascinating specialty which encompasses care of premature neonates and adolescents. It covers the age group less than 18 years of age. ¹ The paediatric population are often prone to various infectious diseases and in order to treat them antibiotics are commonly used, which are produced by microorganism or of biological origin or produced partially or wholly through synthetic means which at low concentrations can inhibit the growth of, or kill the other microorganisms. The antibiotics act by various mechanisms such as Inhibition of Cell wall synthesis, Breakdown of cell membrane structure or function, Inhibition of the structure and function of nucleic acid, Inhibition of protein synthesis and by blockage of key metabolic pathways. ²

Several studies reported that 50-85% of children receive antibiotics in developed and developing countries. ³ Misuse of antibiotics has an impact on health care costs, antibiotic resistance, treatment failure, hospitalization time and increased return visits to the physician. Children are at a greater risk for medication errors than adults and these errors are preventable when the antibiotics are used judiciously. ⁴

Antimicrobial resistance is associated with high mortality, frequent health-care visits, prolonged hospital stay and a huge economic burden on health care and hence it is a major threat to health care system. The main cause of antimicrobial resistance is the misuse of antimicrobials both in animal and human medicine globally. One of the primary causes of high incidence of antimicrobial resistance is thought to be the frequent use of antibiotics. ⁵

Different bacteria use different mechanisms to exhibit antibiotic resistance such as chemical alteration by modifying the antibiotic molecule there by leading to destruction of the antibiotic, Preventing the antibiotic from reaching the target site, by decreasing antibiotic penetration and increasing efflux, by modifying target site, and by the global cell adaptive process. ⁶

The Center for Disease Control and Prevention has identified drug resistant organisms as a particular threat and recommended increased surveillance, risk factor identification, and

promotion of judicious antibiotic prescribing.⁷ The use of antibiotics is said to be rational when patients receive the drugs for right indication, the right dose, the right duration, the right route and at an affordable cost.⁸

A current, high-level report estimates that by 2050 ten million people will die every year due to antimicrobial resistance⁹ and 700,000 deaths per year globally are due to drug resistant infections.¹⁰ Misuse or overdose of antibiotics may also result in adverse drug reactions and high treatment cost.

The global action plan on antimicrobial resistance by WHO outlines five main objectives:

- To develop the economic case for sustainable investments that takes account of the needs of all countries.
- To strengthen the knowledge and evidence base through surveillance and research
- To reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures
- To improve awareness and understanding of antimicrobial resistance through effective communication, education and training
- To optimize the use of antimicrobial medicines in human and animal health¹¹

This study is planned to evaluate the usage of various antibiotics in paediatrics and also to reduce the risk of resistance, drug interactions, adverse reactions associated with their use and also to promote the importance of antimicrobial stewardship.

MATERIALS AND METHODS:

STUDY DESIGN: A Prospective observational study, was carried out in the Department of Paediatrics, VIMS, Ballari District, Karnataka for a period of six months (From March 2023- August 2023).

STUDY SAMPLE SIZE: The sample size was calculated by using the formula $n=Z^2pq/d^2$

$$n = (1.96)^2 * 0.9 * 0.1 / (0.05)^2$$

n- Required sample size, Z-Reliability coefficient

$$n = 138$$

p-estimated proportion, d- Margin of error

The required minimum sample size was 138 Paediatric patients. 160 was the achieved sample size.

SOURCE OF DATA: Data was collected from patient case sheets.

STUDY CRITERIA:

The study was carried out by considering the following inclusion and exclusion criteria.

INCLUSION CRITERIA: Patient of either sex, patient aged under 16, In-patients under antibiotic therapy, cases with co morbid conditions and patients on antimicrobial therapy. **EXCLUSION CRITERIA:** Patients who are treated in an outpatient department, patients whose caretakers are not willing to give informed consent to participate in the study, and prescription with insufficient and incomplete data.

MATERIALS USED: Patients information sheet, Informed consent form, and Data collection form, Micromedex to look for drug interactions.

STUDY PROCEDURE: Regarding this project pilot study was done. Various articles were collected and reviewed pertaining to the project. A study protocol, including study design and design of Performa was prepared. The ethical consent prior to study was obtained. Patients were enrolled according to the inclusion and exclusion criteria. The Patient's details were collected from the case sheet and were evaluated for various antibiotics usage from patient treatment chart. The obtained information was represented in the form of graphs and tables by using MS Excel sheets, and the report was submitted.

RESULTS

1. DEMOGRAPHICS OF THE STUDY POPULATION

1.1 Age and Gender wise distribution of the study population

In this study a total of 160 study subjects receiving antimicrobial therapy were recruited. Of these 90 (56.25%) were male and 70 (43.75%) were female as shown in the figure 01 which shows that males were very much prone to infections, and most of the study subjects were belonging to the age group of children (>1-11 years) 90 (56.25%) followed by infants (1-12 months) 48 (30%), adolescents (>11-19 years) 20 (12.5%) and neonates (0-28 days) 02 (1.25%)

Figure 01: Gender distribution

2. TYPE OF DISEASE AND CLINICAL PRESENTATION:

2.1 Distribution of patients according to type of disease

Among 160 patients, 53 (33%) were suffering from respiratory tract infections, 27 (16%) had neurologic disorders, 24 (15%) were having other disease, 20 (13%) had infectious diseases, 10 (6%) had neurological disorders, 8 (5 %) had renal disorders, 8 (5%) had liver diseases ,6 (4%) had hematologic disorders,6 (4%) had nutritional disorders, 4 (3%) had cardiovascular disease, and 4 (3%) had lymphatic disease as shown in table 01. The other diseases were 24 (15%) which included dengue, dengue like illness, acute febrile illness, pyrexia of unknown origin hydrocarbon consumption and snake bites etc.

Table 01: Distribution Of Patients According to Type of Disease

SL .N O	TYPE OF DISEASE	MALE	FEMALE	No. OF PATIENTS	PERCENTAGE
1	Respiratory Tract Infections	28	25	53	33%
2	Others	14	10	24	15%
3	Infectious Diseases	12	8	20	13%

4	Neurologic Disorders	15	12	27	16%
5	Renal Disorders	3	5	8	5%
6	Liver Diseases	3	5	8	5%
7	Hematologic Disorders	3	3	6	4%
8	Nutritional Disorders	3	3	6	4%
9	Cardiovascular Diseases	2	2	4	3%
10	Lymphatic Disease	2	2	4	3%
	TOTAL	85	75	160	100%

2.2 Distribution of the patients according to clinical presentations

The clinical presentations of the enrolled participants were as follows, 73 (15%) were found with cough, 37 (8%) were found with cold, 109 (23%) were found with fever, 44 (9%) were found with hurried breathing, 17 (4%) were found with convulsions, 48 (10%) were found with vomiting, 27 (6%) were found with loose stools, 12 (2%) were found with pain in abdomen as shown in figure 02, the other clinical presentations included were 111 (23%) in number and included, chest pain, headache, breathlessness and drowsiness.

Figure No 02: Clinical Presentations

2.3 Distribution of patients based on co-morbid conditions

Among 160 patients, 87 (54%) of them did not have any co-morbidities, at least one co-morbid condition was observed in 41 patients (26%), 16 patients (10%) had 2 co-morbidities, 8 (5%) patients had 3 co-morbid conditions and 8 (5%) patients had more than 3 co-morbid conditions as shown in figure 03

Figure No 03: Comorbid Conditions

3.USAGE OF ANTIBIOTICS:

3.1 Distribution of Antibiotics prescribed

In this study the antibiotics prescribed were as follows, Ceftriaxone, Vancomycin, Piperacillin+Tazobactam, Meropenem, Azithromycin, Cefotaxime, Clindamycin, Doxycycline, Ceftazidime, Ciprofloxacin, Amoxicillin + Clavulanic Acid, Linezolid, Cefixime, Ofloxacin, Ampicillin, Clarithromycin, Colistin, Levofloxacin, Moxifloxacin and Penicillin as shown in table 02. The most commonly prescribed antibiotic was Ceftriaxone.

Table 02: Distribution of antibiotics prescribed

SL.NO	NAME OF THE ANTIBIOTIC	FREQUENCY	PERCENTAGE
•	Amikacin	26	6.22%
•	Amoxicillin + clavulanic acid	6	1.43%
•	Ampicillin	1	0.24%
•	Azithromycin	22	5.26%
•	Cefotaxime	17	4.07%
•	Cefixime	2	0.48%
•	Ceftazidime	6	1.43%
•	Ceftriaxone	103	24.64%
•	Ciprofloxacin	6	1.43%
•	Clarithromycin	1	0.24%
•	Clindamycin	16	3.83%
•	Colistin	1	0.24%
•	Doxycycline	15	3.59%
•	Levofloxacin	1	0.24%
•	Linezolid	5	1.21%
•	Meropenem	35	8.37%
•	Metronidazole	22	5.26%
•	Moxifloxacin	1	0.24%
•	Ofloxacin	2	0.48%
•	Penicillin	1	0.24%

•	Pipercillin+Tazobactum	54	12.92%
•	Vancomycin	75	17.94%
	TOTAL	418	100%

3.2 Distribution of Antibiotics based on class

The antibiotics which were prescribed to the study participants were further categorized based on their classes which are as follows, 128 (30.84%) drugs belonged to cephalosporins, 75 (18.07%) drugs were from glycopeptide class, 55 (13.25%) drugs belonged to penicillin, 35 (8.43%) drugs belonged to carbapenem class, 27 (6.50%) drugs belonged to aminoglycosides, 22 (5.30%) drugs belonged to macrolides, 22 (5.30%) were from the nitroimidazole class, 16 (3.85%) drugs belonged to the lincosamide class, 14 (3.13%) drugs were from the tetracycline class, 10 (3.37%) drugs were fluoroquinolones, 6 (1.44%) were from the aminopenicillins, and 5 (1.20%) drugs were from oxazolidinone class as shown in figure 04.

Figure No 04: Distribution Of Antibiotics Based on The Class

3.3 Number of Antibiotics per prescription

The number of antibiotics prescribed to each patient were as follows, 60 (37.5%) patients were treated with 2 agents, 41 (25.63%) patients were treated with 3 agents, 26 (16.25%) patients were treated with one agent, 20 (12.5%) patients were treated with 4 different antibiotics, 11 (6.88%) patients were treated with 5 agents and 2 (1.25%) patients were treated with 6 agents as shown in table 03.

Table no 03: Number of Antibiotics per prescription

SL.NO	No. of antibiotics	No. of antibiotics per prescription	Percentage
1	1 agent	26	16.25%
2	2 agents	60	37.5%
3	3 agents	41	25.63%

4	4 agents	20	12.5%
5	5 agents	11	6.88%
6	6 agents	2	1.25%
	TOTAL	160	100%

3.4 Dosage form of the Antibiotics prescribed

Different dosage forms of antibiotics were prescribed among 160 patients in which injections were 382 (91.39%), syrup 20 (4.78%), tablets 14 (3.35%), capsule 1 (0.24%), eye drop 1 (0.24%) as shown in figure 05.

Figure 05: Dosage forms of the antibiotics prescribed

3.5 Drug- drug interactions associated with antibiotics

A total of 40 drug-drug interactions were found in this study out of which 32 (80%) were antibiotics interacting with other non-antibiotic drugs and 8 (20%) were antibiotics interacting with another antibiotic as shown in table 04.

Table no 04: Drug-drug interactions associated with antibiotics

SL.NO	DRUG -DRUG INTERACTIONS	NO. OF PATIENTS	PERCENTAGE
1	Antibiotics Interacting with Other Antibiotics	8	20%
2	Antibiotics Interacting with Other non-antibiotic Drugs	32	80%
	TOTAL	40	100%

4.ANTIBIOTIC CULTURE AND SENSITIVITY:

4.1 Distribution of patients according to antibiotic culture and sensitivity test

Out of total 160 patients, only 11 (6.87%) subjects underwent antibiotic culture and

sensitivity testing, whereas the remaining 149 (93.12%) subjects did not undergo any such antibiotic culture and sensitivity testing as shown in figure 06. This shows that therapy was not definitive.

Figure 6: Distribution of patients according to antibiotic culture and sensitivity test

5.0 DURATION OF HOSPITAL STAY

Among 160 patients, there were 73 (45.63%) patients who stayed in the hospital for 4-6 days, followed by 43 (26.88%) patients observed for a period of 7-9 days, 19 (11.86%) patients remained under medical care for a duration of 10-12 days, 16 (10%) patients were admitted to the hospital and remained under medical care for a duration ranging from 1-3 days and 9 (5.63%) patients remained hospitalized for a duration exceeding 12 days as shown in figure 07.

Figure No 07: Duration of Hospital Stay

DISCUSSION: Our aim of the study was to evaluate the usage of antibiotics in paediatrics in order to avoid irrational use and also to prevent antimicrobial resistance which has become a challenging threat globally.

A total of 160 patients who satisfied inclusion criteria were enrolled for the study. Among 160 study subjects analyzed, 90 (56.2%) were male and 70 (43.75%) were female. These results were similar to the study done by **Avanthi Bandela et al**,¹² gender distribution reveals that the overall study population were predominantly male.

In the current study, out of 160 patients the highest age group of patients observed were children of age group (>1-11years) were 90 (56.25%), followed by infants (1-12 months) were 48 (30%), adolescents (>11-19years) were 20 (12.5%) and neonates (0-28days) were 2 (1.25%). This shows that children of age group between 1-11 years are more prone to infections in the particular study region. This was similar to the results of the

study conducted by **Sachin Vahadane et al;**⁷

In the current study, distribution of patients according to type of disease out of 160 patients, majority i.e., 33% (55) of study population were found with respiratory tract infections. These results were similar to study conducted by **Rinta Mathew et al;**¹³ and **Majed Al-Armouti**¹⁴ where the distribution of illness in paediatrics with respiratory infections of 112 (37%) were observed during their study period. So, we can conclude that children are very much prone to respiratory tract infections for a number of reasons such as immature immune system, smaller airways, frequent exposure to pathogens, less developed cough reflex etc.

We assessed the frequency of antibiotics prescribed for total 160 study subjects in which Ceftriaxone was observed in 103 (24.64%) followed by vancomycin in 75 (17.94%), Piperacillin+Tazobactam in 54 (12.92%), meropenem in 35 (8.37%), amikacin in 26 (6.22%), metronidazole in 22 (5.26%), azithromycin in 22 (5.26%), cefotaxime in 17 (4.07%), clindamycin in 16 (3.83%), doxycycline in 15 (3.59%), ceftazidime in 6 (1.43%), ciprofloxacin in 6 (1.43%), Amoxicillin + clavulanic acid in 6 (1.43%), linezolid in 5 (1.21%), cefixime in 2 (0.48%), ofloxacin in 2 (0.48%), ampicillin in 1 (0.24%), clarithromycin in 1 (0.24%), colistin in 1 (0.24%), levofloxacin in 1 (0.24%), moxifloxacin in 1 (0.24%), and penicillin in 1 (0.24%). These results were similar to study conducted by **Adane Yehualaw et al;**⁸ whereas the commonly prescribed single antibiotic in paediatric patients was ceftriaxone in 147 (45.91%) during their study period. In the study site ceftriaxone was used as drug of choice for prophylaxis.

In the present study, the distribution of antibiotics based on the class reveals that 128 (30.62%) drugs belonged to cephalosporins, 75 (17.94%) drugs belonged to glycopeptide class, 56 (13.41%) drugs belonged to penicillin, 35 (8.37%) drugs belonged to carbapenem class, 27 (6.46%) drugs belonged to aminoglycosides, 23 (5.49%) drugs belonged to macrolides, 22 (5.26%) were from the nitroimidazole class, 16 (3.83%) drugs belonged to the lincosamide class, 15 (3.59%) drugs were from the tetracycline class 10 (2.41%) drugs were fluoroquinolones, 6 (1.43%) were from the aminopenicillins, and 5 (1.20%) drugs were from oxazolidinone class . These results were similar to the study conducted by **Rinta Mathew et.al;**¹³ where the major distribution of antibiotics by class

observed during their study period in paediatrics was cephalosporins 224 (45%). The reason for use of cephalosporins most commonly might be due to its broad spectrum, high efficacy and low toxicity.

In the current study, we assessed number of antibiotics per prescription, out of 160 study subjects, 60 (37.5%) were treated with 2 agents, 41(25.62%) were treated with 3 agents 26 (16.25%) were treated with one agent, 20 (12.5%) were treated with 4 different antibiotics, 11 (6.88%) were treated with 5 agents and 2 (1.25%) were treated with 6 agents. These results were similar to study conducted by **Mohammed Aamir Khan et.al;**¹⁵ where (65.02%) were treated with two antibiotics and 20.62% were treated with 3 agents. This shows that the therapy was not definitive, in most of the cases the antibiotics were prescribed empirically which can lead to development of antimicrobial resistance.

We also evaluated the dosage forms of antibiotics prescribed among 160 patients in which injections were 382 (91.39%), followed by syrup 20 (4.78%), tablets were 14 (3.35%), capsules were only 1 in number (0.24%) and one eye drop (0.24%) as. This result was similar to the study conducted by **Avanthi Bandela et.al;**¹² where different types of dosage forms of antibiotics were used in patients during their study period such as injections 893 (82.13%) followed by syrups 110 (10.12%), followed by tablets 78 (7.18%) and capsules 5 (0.46%). The injectable antibiotics can provide rapid and effective treatment and also guarantee that full course is completed as compared to oral use.

In the current study around 40 drug-drug interactions associated with antibiotics, out of which we found that 32 (80%) interactions were between antibiotics with other non-antibiotic drugs and 8 (20%) were that of antibiotic interacting with other antibiotics. These results were similar to the study conducted by **Firomsa Bekele et, al;**¹⁶ where they observed that antibiotics interacting with other drugs are 46 (60.53%) and antibiotics interacting with other antibiotics were 30 (39.47%) during their study period. Hence it is necessary to check for possible drug interactions prior to administration and proper prescription auditing can help in prevention of such occurrence.

In the present study, we observed that out of total 160 subjects, only 11 subjects (6.87%) underwent antibiotic culture and sensitivity testing, whereas the remaining 149 subjects

(93.12%) did not undergo any such antibiotic culture and sensitivity testing. The antibiotic culture and sensitivity test helps to identify the exact bacteria causing the infection and allows for most targeted and effective antibiotic use, also minimize the risk on unnecessary broad spectrum antibiotic use and prevent the development of resistance.

The duration of hospital stay of 160 patients was as follows 73 patients (45.62%) had stayed in hospital for 4-6 days, 43 patients (26.87%) were observed for a period of 7-9 days, 19 (11.86%) patients remained under medical care for a duration of 10-12 days, 16 (10%) patients were admitted to the hospital and remained under medical care for a duration ranging from 1-3 days and 9 (5.63%) patients remained in hospital for a duration exceeding 12 days. These results were similar to the study conducted by **Xu Hu et.al.**,¹⁷ where they observed that 4411 (79.65%) of the patients stayed in hospital for 0-10 days during their study period.

CONCLUSION

This study gives an overview of antibiotics use in Paediatric Inpatients in a tertiary care teaching hospital. In this study, assessment based on antibiotic culture and sensitivity test reveals that treatment regimen implemented in most of the cases is without doing any culture sensitivity test which may lead to irrational prescription, development of antimicrobial resistance. As a result, precise monitoring of antimicrobial therapy is required. In order to minimize the risk of antibiotic resistance in paediatric patients, prescriber should restrict empirical therapy and encourage effective diagnosis based definitive therapy. In addition, we advise the physicians to adopt a standard institutional treatment guideline for diagnosing and treating various bacterial infections to prevent antibiotic resistance and also suggest to implement antimicrobial stewardship programme to prevent the misuse of antibiotics, promote use of appropriate agents, dose, duration route and minimize the unintended consequences.

RECOMMENDATIONS:

The American Academy of Paediatrics and the Paediatric infectious diseases society recommend establishing antimicrobial stewardship programme to improve antibiotic

prescribing.¹⁸

CONSENT FOR PUBLICATION:

The authors have given their consent for publication.

ETHICAL APPROVAL AND CONSENT:

This study was conducted after obtaining approval from institutional ethics committee of T.V.M college of Pharmacy Ballari (Ref.no: TVMCP/IEC/VPD/2022-23/01) and Informed consent form (ICF) was obtained from the guardians of the study subjects.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declares that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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