

Antibiotic Prescription Patterns in Hospitalized Pediatric Patients: An Observational Study

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Abstract:

Background: Antibiotics are generally used in hospitalized children with bacterial infection. Yet, misuse of antibiotics is a major cause of resistance and poor outcomes; hence, analysis of antibiotic prescription patterns becomes imperative.

Aim: To assess the antibiotic prescribing patterns, practices, and outcomes for children admitted to hospitals.

Methodology: An observational study was carried out in the Department of Pediatrics at Prasad Institute of Medical Sciences, Prasad Hospital, Lucknow, Uttar Pradesh for a duration of one year. One hundred and fifty pediatric patients who were admitted to the hospital for systemic antibiotics were recruited in the study. The data were retrieved from the medical record and analyzed using SPSS version 27.0.

Results: The age group that dominated the sample size was the 1-5-year-old patients who comprised 34.7%. The most common diagnosis was respiratory tract infection accounting for 28.0%. The drugs that were mostly prescribed were cephalosporins (37.3%) and penicillin (25.3%). IV administration was used in 74.7% of cases. The other common practice was empirical therapy in 73.3%, and monotherapy in 62.7% of cases. The success.

Conclusion: Prescribing antibiotics empirically, especially cephalosporins, was the most common form of antibiotic prescription for hospitalized children. It is necessary to improve the practice of antimicrobial stewardship and rational prescribing of antibiotics.

Keywords: Antibiotic Prescription Pattern, Hospitalized Pediatric Patients, Antimicrobial Stewardship, Cephalosporins, Empirical Therapy, Antimicrobial Resistance.

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Introduction

Antibiotics have revolutionized the treatment of infectious conditions, and they rank among the most significant treatments used in pediatrics. Children are highly susceptible to bacterial infections due to their immature immune system. Therefore, early and effective treatment with antibiotics is necessary for minimizing the complications and improving the outcome of the treatment. It is common practice to prescribe antibiotics empirically prior to microbiological confirmation in pediatric hospitalized patients due to the severity of the infection [1]. Thus, antibiotics are among the drugs that are most frequently prescribed in pediatric hospitalizations. However, their extensive usage has caused worries about unnecessary prescriptions and potential risks such as adverse drug events and antimicrobial resistance (AMR).

A rational approach to prescribing antibiotics entails choosing an optimal antimicrobial agent, dosage, mode of administration, frequency, and duration according to the patient's age, body weight, clinical status, and suspected causative agent [2].

Prescribing practices in pediatrics are generally much more complicated than those for adults since pharmacodynamics and pharmacokinetics vary significantly with age. Additionally, a shortage of drug forms specially developed for children, and reliance on empirical prescribing practices add up to the risk of irrational prescribing. Irrational prescribing practices such as prescribing of unnecessary broad-spectrum antibiotics, extended courses of antibiotics, and improper combinations of drugs result in resistant pathogens and rising costs [3].

Antimicrobial resistance has become one of the greatest public health problems of the twenty-first century. According to the World Health Organization (WHO), AMR is a serious threat that renders ineffective the available antimicrobials and raises the incidence of infectious diseases across the globe. Unsound use of antibiotics in hospitals is one of the main contributors to the development and propagation of resistant microorganisms [4]. Children are among those who are the most

impacted by AMR due to their increased vulnerability to the infections requiring antibiotic treatment, which involves respiratory, gastrointestinal, urinary, and systemic disorders.

Pediatric respiratory tract infections, gastroenteric infections, urinary tract infections, skin infections, neonatal sepsis, and febrile illness are the causes of significant numbers of hospitalizations that necessitate antimicrobial treatment. In many cases, empirical treatment is administered since microbiological culture data may not be available promptly. While empirical treatment is frequently appropriate from a clinical point of view, wrong choice of antibiotics and not adjusting treatment based on the findings of culture and sensitivity may result in excessive exposure to antimicrobials and poor efficacy of treatment [5]. Thus, assessment of prescribing trends is informative from the perspective of current clinical practice and its conformity to guidelines.

Utilization studies are crucial tools to assess the quality of drug prescriptions and to improve patient care by highlighting the need for enhancement in certain areas. Utilization studies examine the choice, frequency, dosages, routes of administration, and duration of prescribed drugs. This enables physicians and policymakers to make the best use of the available medicines and promotes rational use of drugs [6]. Antibiotics are another class of drugs wherein prescription pattern studies help in determining the frequently prescribed antibiotics, trends in prescription, empirical treatment vs. culture-based treatment, use of monotherapy vs. combination therapy [7].

Many national and international surveys have found that cephalosporins and penicillins are the most commonly used antibiotics in hospitalized children. Intravenous use is the major route of delivery during acute infection. Though such trends indicate that antibiotics are being prescribed according to clinical standards, significant variation exists between health-care facilities concerning choices of antibiotics, length of treatment and compliance with clinical guidelines [8]. Thus, it is important to constantly assess such prescribing trends to detect any deviation from established guidelines.

In spite of rising levels of knowledge concerning antimicrobial stewardship, there is still a lack of information on patterns of antibiotic use in hospitalized children at many of the tertiary care centers. Data specific to each hospital is very necessary since it can be different from one health care center to another in terms of the epidemiology, disease prevalence, bacteria susceptibility and antibiotic prescribing behavior. It is crucial to have an understanding of these patterns to optimize antimicrobial therapy.

Consequently, the current observation study was carried out to investigate the antibiotic prescription practices in hospitalized pediatric patients in the Department of Pediatrics at Prasad Institute of Medical Sciences, Prasad Hospital College. The objectives of this study were to determine the use of antibiotics; to find out which antibiotics were mostly prescribed to patients; to investigate prescribing practices such as route and duration of treatment; and to investigate laboratory and microbiology findings as well as clinical outcomes.

Methodology

Study Design: This research was an observational study performed in the hospital setting with an objective of assessing the patterns of antibiotic prescription in the hospitalized pediatric population. This study was aimed at evaluating the patterns of antibiotic usage, the process of antibiotic prescription, the most frequently used antimicrobials, the indications for antibiotic therapy and the patterns of antibiotic treatment in pediatric inpatients.

Study Area: The study was carried out at the Department of Pediatrics at Prasad Institute of Medical Sciences and Prasad Hospital, Lucknow, Uttar Pradesh, India.

Study Duration: The research study was carried out over a one-year time period. Within this one-year time period, there was a systematic analysis of the medical files of pediatric patients in hospitals on antibiotic therapy.

Study Participants

Inclusion Criteria

- Pediatric patients in the age group 0-18 hospitalized in the Department of Pediatrics at the study site.
- Pediatric patients receiving at least one course of systemic antibiotics during hospitalization.
- Pediatric patients with complete medical charts, including demographics, clinical diagnosis, investigations, and antibiotics used.
- Pediatric patients admitted for more than 24 hours.

Exclusion Criteria

- Patients admitted in the outpatient department alone.
- Patients who did not get any antibiotic while being admitted in the hospital.
- Patients whose files are incomplete.
- Patients who got discharged or referred prior to getting any antibiotics.

Sample Size: In total, 150 children who qualified for inclusion criteria were studied. Selection was done keeping in mind different age categories of the pediatric population and various types of infections

that required antibiotic treatment during the course of the study.

Procedure: The medical files and prescription charts of eligible pediatric patients admitted into the department of pediatrics were retrieved and analyzed using a standardized data collection form. Data on patient characteristics, clinical diagnosis, length of stay, types of antibiotics prescribed, dose of the medication, frequency, mode of administration, length of treatment period, and laboratory tests conducted was extracted. The different types of antibiotics prescribed were classified based on pharmacological class, mode of administration and indication for use. The prescriptions were assessed for whether they were empirical or culture-based, monotherapy or combination therapy, and adherence to treatment protocols where appropriate. Ethical clearance for the study was obtained from the institutional ethics committee prior to data collection.

Statistical Analysis: Data were analyzed by entering it into the SPSS software version 27.0 (IBM Corporation, Armonk, NY, USA). Descriptive statistics such as frequency, percentage, mean, and

standard deviation were computed for demographic profile, clinical diagnosis, and antibiotic prescription patterns. Relationships among categorical variables were analyzed using Chi-square test whereas relationships among continuous variables were analyzed using independent t-test where applicable. The significance level was set at <0.05.

Results

The demographics and clinical details of 150 pediatric patients admitted into the hospital are presented in Table 1. The age composition revealed that the highest number of patients were in the age group of 1-5 years (52, 34.7%), followed by patients less than 1 year of age (40, 26.7%), age group of 6-10 years (32, 21.3%), and 11-18 years (26, 17.3%). There were 86 males (57.3%) and 64 females (42.7%) in the patient population. The most common reason for admitting into the hospital was respiratory infections (42, 28.0%), followed by gastrointestinal infections (30, 20.0%), febrile disease (28, 18.7%), urinary infections (20, 13.3%), skin and soft tissue infection (16, 10.7%), and others (14, 9.3%).

Table 1: Demographic and Clinical Characteristics of Hospitalized Pediatric Patients

Parameter	Frequency (n)	Percentage (%)
Age Group		
<1 year	40	26.7
1-5 years	52	34.7
6-10 years	32	21.3
11-18 years	26	17.3
Gender		
Male	86	57.3
Female	64	42.7
Primary Diagnosis		
Respiratory tract infection	42	28.0
Gastrointestinal infection	30	20.0
Febrile illness	28	18.7
Urinary tract infection	20	13.3
Skin and soft tissue infection	16	10.7
Other infections	14	9.3
Hospital Stay (days)	Mean $\pm$ SD	5.8 $\pm$ 2.4

Distribution of Antibiotic Classes Prescribed to Hospitalized Patients is Presented in Table 2 below. The most common group of antibiotics were cephalosporins which were administered to 56 (37.3%) patients; followed by penicillins (38, 25.3%); aminoglycosides (20, 13.3%); macrolides

(16, 10.7%); carbapenems (12, 8.0%) and others (8, 5.4%). Overall, third generation cephalosporins were the most popular antibiotic drugs used empirically in treatment of bacteria infections. Figure 1 below illustrates distribution of antibiotic classes prescribed to hospitalized pediatric.

Table 2: Pattern of Antibiotics Prescribed Among Hospitalized Pediatric Patients

Antibiotic Class	Frequency (n)	Percentage (%)
Cephalosporins	56	37.3
Penicillins	38	25.3
Aminoglycosides	20	13.3
Macrolides	16	10.7
Carbapenems	12	8.0
Others	8	5.4

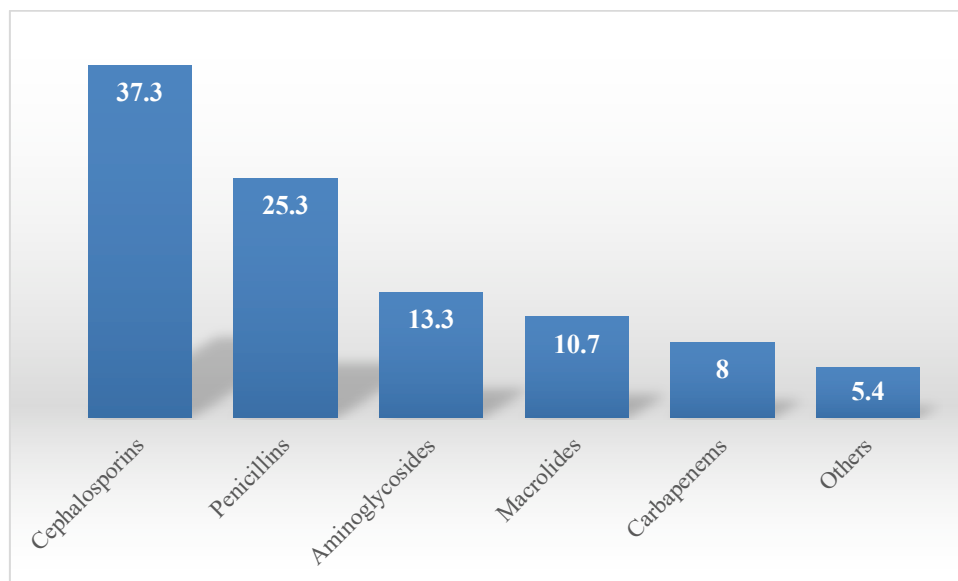


Figure 1: Visual Representation of Pattern of Antibiotics Prescribed Among Hospitalized Pediatric Patients

Table 3 highlights the pattern of antibiotic prescribing among hospitalized children. IV infusion was the main method of delivery of antibiotics in 112 patients (74.7%), while oral antibiotics were prescribed in 38 cases (25.3%). Monotherapy was given to 94 patients (62.7%), and

56 patients (37.3%) were treated using combination therapy with antibiotics. Empiric therapy was followed in 110 patients (73.3%), while culture-based therapy was administered in 40 patients (26.7%). The average course of antibiotic treatment was 6.4 ± 2.3 days.

Table 3: Antibiotic Prescribing Practices

Parameter	Frequency (n)	Percentage (%)
Route of Administration		
Intravenous	112	74.7
Oral	38	25.3
Therapy Type		
Monotherapy	94	62.7
Combination therapy	56	37.3
Treatment Approach		
Empirical therapy	110	73.3
Culture-guided therapy	40	26.7
Duration of Antibiotic Therapy (days)	Mean $\pm$ SD	6.4 ± 2.3

Table 4 illustrates laboratory and microbiological results among the subjects included in this study. An increased WBC count was found in 96 individuals (64.0%), while elevated C-reactive protein was identified in 82 individuals (54.7%). The microbiology culture test was carried out for 68 individuals (45.3%), out of which positive bacterial

growth was detected in 46 patients (30.7%). Blood cultures yielded a positive result for 18 patients (12.0%), which facilitated targeted antimicrobial treatment for some selected patients. Figure 2 is a graphical illustration of laboratory and microbiological results among pediatric patients.

Table 4: Laboratory and Microbiological Findings

Investigation	Frequency (n)	Percentage (%)
Elevated white blood cell count	96	64.0
Elevated C-reactive protein	82	54.7
Culture performed	68	45.3
Positive culture report	46	30.7
Positive blood culture	18	12.0

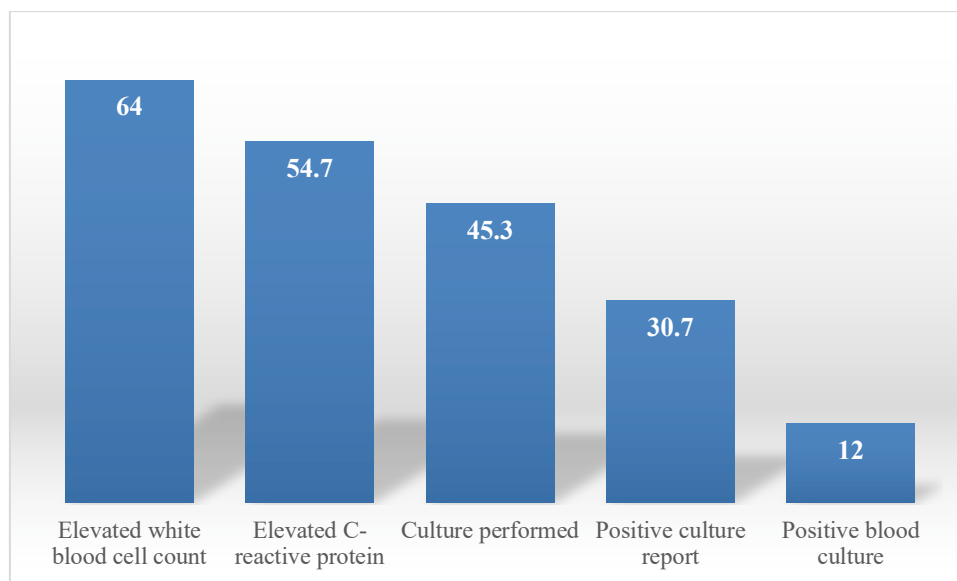


Figure 2: Visual Representation of Laboratory and Microbiological Findings

The clinical outcomes of the antibiotic treatment of hospitalized pediatric patients are demonstrated in Table 5 below. Clinical improvement was noted in 128 (85.3%) patients, while the need for changing antibiotics according to the patient's response or microbiological data was reported for 24 (16.0%) patients. The need for PICU admission was recorded

for 12 (8.0%) patients; for six (4.0%) patients, referral to a higher healthcare facility was noted. In total, 138 (92.0%) patients were successfully discharged after treatment. Figure 3 below shows the clinical outcomes of the hospitalized pediatric patients under antibiotic treatment.

Table 5: Clinical Outcomes of Hospitalized Pediatric Patients

Outcome	Frequency (n)	Percentage (%)
Clinical improvement	128	85.3
Antibiotic modification	24	16.0
PICU admission	12	8.0
Referral to higher center	6	4.0
Successfully discharged	138	92.0

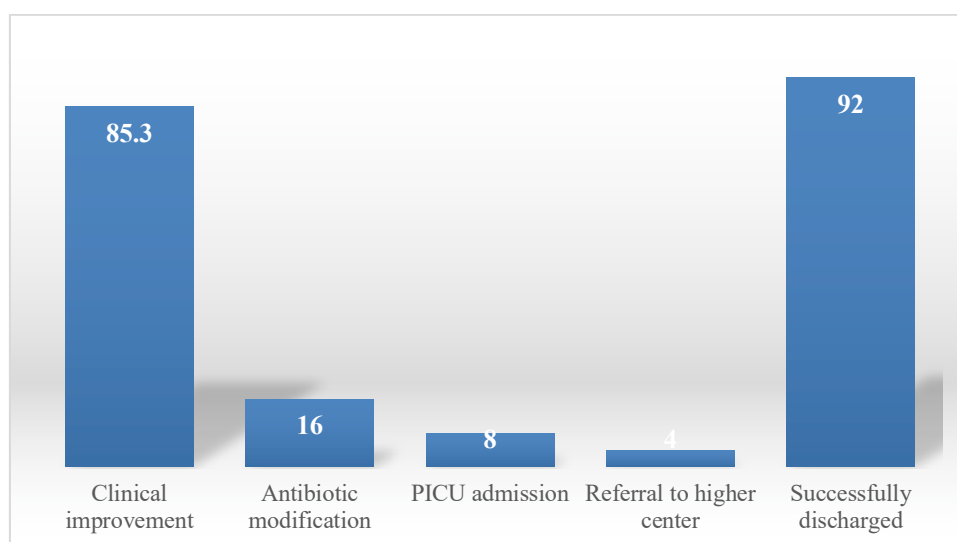


Figure 3: Visual Representation of Clinical Outcomes of Hospitalized Pediatric Patients

The relationship between the primary diagnosis and the type of antibiotic treatment is presented in Table 6. Combination antibiotic treatment was more common among patients diagnosed with respiratory

tract infections and UTIs, while monotherapy was mainly applied for patients suffering from gastrointestinal infections and fever. Chi-square test indicated a statistically significant relationship

between primary diagnosis and antibiotic treatment pattern ($\chi^2 = 9.86$, $p = 0.043$).

Table 6: Association Between Primary Diagnosis and Antibiotic Therapy Type

Primary Diagnosis	Monotherapy n (%)	Combination Therapy n (%)
Respiratory tract infection	24	18
Gastrointestinal infection	22	8
Febrile illness	20	8
Urinary tract infection	10	10
Skin and soft tissue infection	8	8
Other infections	10	4
Chi-square (χ^2)	9.86	
p-value	0.043*	

*Statistically significant ($p < 0.05$).

Table 7 provides a comparison of the length of hospital stay based on the type of antibiotic treatment. The group of patients who underwent combination antibiotic treatment had a significantly

greater length of hospital stay (7.1 ± 2.5 days) than those under monotherapy (5.2 ± 1.8 days). The independent t-test showed that this difference was highly significant ($t = 4.72$, $p < 0.001$).

Table 7: Comparison of Hospital Stay According to Antibiotic Therapy

Therapy Type	Hospital Stay (Mean $\pm$ SD)
Monotherapy	5.2 ± 1.8
Combination therapy	7.1 ± 2.5
t-value	4.72
p-value	<0.001*

*Statistically significant ($p < 0.05$).

Discussion

This current observational study assessed the prescribing pattern of antibiotics in 150 admitted pediatric cases and found that the use of antibiotics was quite prevalent among a variety of infectious disorders. The highest number of pediatric patients was recorded in the age range of 1–5 years, followed by below one year of age category, showing that young children constituted the majority of pediatric admissions that required antibiotic therapy (Kurian et al., 2016) [9]. There were slightly more male pediatric cases as compared to females. Among all other infectious diseases, respiratory tract infection was the most common initial diagnosis, followed by gastro-intestinal infection, febrile illness, UTI, and skin and soft tissue infections (Majhi et al., 2017) [10].

Cephalosporins were the most commonly used antibiotic class comprising 37.3% of the total antibiotic consumption, followed by penicillins, aminoglycosides, macrolides, carbapenems, and other antimicrobials (Malpani et al., 2016) [11]. The predominance of cephalosporins could be explained by their broad antibacterial activity, relatively good safety, and extensive application in the empirical treatment of severe infections in children. But the high consumption of broad-spectrum antibiotics, especially carbapenems, demonstrates that clinicians should have clinical reasons for this type of therapy (Mathew et al., 2021) [12]. Otherwise,

they risk contributing to the emergence of antimicrobial resistance.

The route of choice in antibiotic administration was intravenous therapy, which was applied in 74.7% of the patients, while only fewer patients had received oral administration of the drugs. This trend is understandable in children admitted to hospitals since intravenous therapy is quick and reliable in providing antibiotics to patients with moderate to severe infection. Monotherapy was used in 62.7% of the patients while 37.3% had received antibiotics using combination therapy (Okubo et al., 2021) [13]. The high prevalence of monotherapy therapy implies that there was an attempt to reduce the unnecessary use of multiple antibiotics.

Empirical therapy was used in 73.3% of the subjects, while 26.7% underwent culture-based treatment. Microbiological cultures were done in 45.3% of cases, while 30.7% had positive bacterial cultures in their tests (Olesen et al., 2018, Pradeepkumar et al., 2017) [14,15]. It means that antibiotic administration was primarily done through clinical evaluation and laboratory test results, like high white blood cell count and C-Reactive protein levels. While empirical therapy is sometimes essential among pediatric patients admitted to hospital settings, it may be beneficial to increase the use of culture and sensitivity tests to make a more informed choice of antibiotics (Sharma et al., 2016, Shiva et al., 2018) [16,17].

The outcomes for the patients were mostly favorable, with 85.3% of them demonstrating clinical improvement and 92.0% achieving successful discharge (van de Maat et al., 2019) [18]. Antibiotics changes were necessary in 16.0% of the cases, primarily due to ineffective antibiotic response and microbiological findings. The statistical data analysis revealed a significant relationship between the primary diagnosis and the type of antibiotic therapy prescribed, which means that different types of infections required the application of different methods – either monotherapy or combination therapy (Yackey et al., 2019, Zhao et al., 2021) [19,20]. Patients who took part in combination therapy also demonstrated significantly increased hospital stay time compared to monotherapy, meaning that combination therapy was applied more often in serious cases. All in all, the results of the study indicate that rational antibiotic prescription, the use of microbiological tests, and periodic reassessment should be used.

Conclusion

Observation from the above-mentioned study shows that there is a widespread prescription of antibiotics in pediatric cases admitted to hospitals with respiratory tract infections being the most common condition. Cephalosporins were the most used type of antibiotics while the use of empirical treatment and intravenous administration was the most popular approach. Overall, a high proportion of patients showed positive clinical responses and were discharged successfully with satisfactory rates of clinical improvement. Nevertheless, the low frequency of the application of culture-based approach to antibiotic treatment and the tendency to prescribe broad-spectrum agents underline the necessity of more appropriate prescribing approaches. It is crucial to enhance antimicrobial stewardship programs and encourage culture and sensitivity tests.

References

1. Alekaw, H., Derebe, D., Melese, W. M., & Yismaw, M. B. (2022). Antibiotic prescription pattern, appropriateness, and associated factors in patients admitted to pediatric wards of Tibebe ghion specialized hospital, Bahir dar, North West Ethiopia. *Infection and Drug Resistance*, 6659-6669.
2. Antony, L. J., Maharani, B., Jaikumar, S., & Somasundaram, G. (2021). Prescription pattern of drugs used in pediatric patients of a tertiary care hospital in Puducherry. *National Journal of Physiology, Pharmacy & Pharmacology*, 11(4), 380.
3. Bryce, A., Hay, A. D., Lane, I. F., Thornton, H. V., Wootton, M., & Costelloe, C. (2016). Global prevalence of antibiotic resistance in paediatric urinary tract infections caused by *Escherichia coli* and association with routine use of antibiotics in primary care: systematic review and meta-analysis. *bmj*, 352.
4. Butler, A. M., Brown, D. S., Durkin, M. J., Sahrman, J. M., Nickel, K. B., O'Neil, C. A., ... & Newland, J. G. (2022). Association of inappropriate outpatient pediatric antibiotic prescriptions with adverse drug events and health care expenditures. *JAMA network open*, 5(5), e2214153.
5. Demoz, G. T., Kasahun, G. G., Hagazy, K., Woldu, G., Wahdey, S., Tadesse, D. B., & Niraiyo, Y. L. (2020). Prescribing pattern of antibiotics using WHO prescribing indicators among inpatients in Ethiopia: a need for antibiotic stewardship program. *Infection and Drug Resistance*, 2783-2794.
6. Di Salvo, M., Santi Laurini, G., Motola, D., Valpiani, G., Sapigni, E., Pompilio, A., ... & Marra, A. (2024). Pattern of drug use in Pediatrics: An observational study in Italian hOSpitals (the PAPEOS study). *British Journal of Clinical Pharmacology*, 90(4), 1050-1057.
7. El-Dahiyat, F., Salah, D., Alomari, M., Elrefae, A., & Jairoun, A. A. (2022). Antibiotic prescribing patterns for outpatient pediatrics at a private hospital in Abu Dhabi: A clinical audit study. *Antibiotics*, 11(12), 1676.
8. Hagedoorn, N. N., Borensztajn, D. M., Nijman, R., Balode, A., von Both, U., Carrol, E. D., ... & PERFORM consortium. (2020). Variation in antibiotic prescription rates in febrile children presenting to emergency departments across Europe (MOFICHE): a multicentre observational study. *PLoS medicine*, 17(8), e1003208.
9. Kurian, J., Mathew, J., Sowjanya, K., Chaitanya, K. R. K., Ramesh, M., Sebastian, J., & Narayanappa, D. (2016). Adverse drug reactions in hospitalized pediatric patients: a prospective observational study. *The Indian Journal of Pediatrics*, 83(5), 414-419.
10. Majhi, B., Panda, A., & Barma, S. K. (2017). Antibiotic prescribing pattern in paediatrics outpatient in a tertiary care hospital. *J Evid Based Med Healthc*, 4, 3048-51.
11. Malpani, A. K., Waggi, M., Rajbhandari, A., Kumar, G. A., Nikitha, R., & Chakravarthy, A. K. (2016). Study on prescribing pattern of antibiotics in a pediatric out-patient department in a tertiary care teaching and non-teaching hospital. *Indian Journal of Pharmacy Practice*, 9(4), 253.
12. Mathew, R., Sayyed, H., Behera, S., Maleki, K., & Pawar, S. (2021). Evaluation of antibiotic prescribing pattern in pediatrics in a tertiary care hospital. *Avicenna Journal of Medicine*, 11(01), 15-19.
13. Okubo, Y., Nariai, H., Michels, K. B., Kim-Farley, R. J., Nishi, A., Arah, O. A., ... &

- Miyairi, I. (2021). Change in clinical practice variations for antibiotic prescriptions across different pediatric clinics: a Japan's nationwide observational study. *Journal of Infection and Chemotherapy*, 27(11), 1621-1625.
14. Olesen, S. W., Barnett, M. L., MacFadden, D. R., Lipsitch, M., & Grad, Y. H. (2018). Trends in outpatient antibiotic use and prescribing practice among US older adults, 2011-15: observational study. *Bmj*, 362.
 15. Pradeepkumar, B., Alameri, T., Narayana, G., Reddy, Y. P., & Ramaiah, J. D. (2017). Assessment of antibiotic prescribing pattern in pediatric patients: A cross-sectional hospital-based survey. *CHRISMED Journal of Health and Research*, 4(4), 235-237.
 16. Sharma, S., Bowman, C., Alladin-Karan, B., & Singh, N. (2016). Antibiotic prescribing patterns in the pediatric emergency department at Georgetown Public Hospital Corporation: a retrospective chart review. *BMC infectious diseases*, 16(1), 170.
 17. Shiva, F., Ghanaie, R., Shirvani, F., Armin, S., Rafiei Tabatabaei, S., Fahimzad, S. A., ... & Karimi, A. (2018). Pattern of antibiotic usage in children hospitalized for common infectious diseases. *Arch Pediatr Infect Dis*, 6(1), e34474.
 18. van de Maat, J., van de Voort, E., Mintegi, S., Gervaix, A., Nieboer, D., Moll, H., ... & Gökay, S. S. (2019). Antibiotic prescription for febrile children in European emergency departments: a cross-sectional, observational study. *The Lancet infectious diseases*, 19(4), 382-391.
 19. Yackey, K., Stukus, K., Cohen, D., Kline, D., Zhao, S., & Stanley, R. (2019). Off-label medication prescribing patterns in pediatrics: an update. *Hospital pediatrics*, 9(3), 186-193.
 20. Zhao, H., Wei, L., Li, H., Zhang, M., Cao, B., Bian, J., & Zhan, S. (2021). Appropriateness of antibiotic prescriptions in ambulatory care in China: a nationwide descriptive database study. *The Lancet Infectious Diseases*, 21(6), 847-857.