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CURRENT PATTERNS AND UTILIZATION OF HIGH-END ANTIBIOTIC IN THE PEDIATRIC POPULATION: A COMPREHENSIVE EVALUATION

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ABSTRACT

Antibiotics are essential for managing bacterial infections, but the increasing threat of antimicrobial resistance (AMR) necessitates their prudent use through restricted antibiotic policies and antimicrobial stewardship programs. This study analyzed the utilization of high-end antibiotics in pediatric patients at Tertiary Care Hospital, Hyderabad, over six months (July 2023 to January 2023). Patient data, categorized by age, revealed a higher prevalence of antibiotic use in infants and children aged 0–12 years, with a slight male predominance. Meropenem was identified as the most frequently used restricted antibiotic, administered primarily via the intravenous route. Commonly prescribed alternative antibiotics included penicillins and cephalosporins. Elevated C-reactive protein levels were a notable finding in culture reports, which also highlighted diverse microbial strains with generally low susceptibility rates. Statistical analysis using IBM SPSS indicated a positive correlation between the use of alternative and restricted antibiotics. These findings emphasize the critical role of antimicrobial stewardship programs, interdisciplinary collaboration, the implementation of restricted antibiotic justification forms, and continuous surveillance to optimize antibiotic use and address resistance in pediatric care.

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INTRODUCTION

Antibiotics are cornerstone medications in modern healthcare, particularly in managing bacterial infections across diverse patient populations. They function by targeting specific bacterial mechanisms, achieving bacteriostatic (inhibiting bacterial growth) or bactericidal (killing bacteria) effects. This has made them indispensable tools for combating severe infections. However, the misuse and overuse of antibiotics have facilitated the alarming rise of antimicrobial resistance (AMR), where microorganisms adapt to render these medications ineffective. As AMR continues to pose a grave global health threat, strategies for optimizing antibiotic use are becoming more critical than ever.(1)

The concept of restricted antibiotics emerged as a targeted response to AMR. These high-end antibiotics are reserved for specific, severe infections that fail to respond to first-line therapies. Their use is governed by institutional policies and often requires consultation with infectious disease specialists or antimicrobial stewardship (AMS) teams.(2) In pediatric settings, where infections are a leading cause of hospitalization, ensuring the rational use of antibiotics is particularly crucial. Recent surveys report that restricted antibiotics account for 37% of pediatric inpatient prescriptions globally, underscoring the need for stringent monitoring and stewardship practices.(3)

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Pediatrics as a discipline involves unique challenges due to the physiological and immunological differences between children and adults. Neonates and infants, for instance, exhibit immature renal and hepatic functions, which directly influence drug absorption, metabolism, and clearance. Consequently, antibiotic therapy in children requires careful consideration of factors such as age, weight, organ function, and the nature of the infection.(4)The evolving practices in pediatric pharmacotherapy emphasize the critical role of tailored dosing strategies and therapeutic drug monitoring to minimize adverse effects and maximize efficacy.(5)

The history of antibiotic development is both a triumph and a cautionary tale. Since the discovery of penicillin by Alexander Fleming in 1928, antibiotics have revolutionized healthcare. However, the subsequent emergence of resistance, first documented against drugs like Salvarsan and penicillin, has challenged their long-term utility.(6) By the 1990s, resistant strains such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus had become widespread. This growing crisis prompted the World Health Organization (WHO) to declare AMR a global health emergency and advocate for a coordinated international response.(7)

In light of these developments, antimicrobial stewardship programs (ASPs) have gained prominence. These programs aim to optimize antibiotic use by selecting the appropriate agent, dose, route, and duration of therapy while minimizing the risks of resistance and adverse events.(8) Pediatric ASPs, in particular, focus on improving patient outcomes and ensuring the judicious use of high-end antibiotics in hospital settings. Collaborative global initiatives, including the "One Health" approach and high-level ministerial conferences, further underscore the importance of unified efforts to combat AMR.[9]

This article delves into the patterns and utilization of high-end antibiotics in the pediatric population, exploring key aspects such as restricted antibiotic policies, pharmacotherapeutic considerations, and the role of stewardship programs in addressing AMR. By evaluating current practices and proposing actionable recommendations, it aims to contribute to the collective effort of safeguarding antibiotics for future generations.

MATERIALS AND METHODS

Study Site: The research was conducted at Tertiary Care Hospital located in Banjara Hills, Hyderabad, Telangana

Study Period: The investigation spanned 6 months, commencing in July 2023 and concluding in January 2023.

Study Design: This research adopted a prospective observational study design to observe and analyse antibiotic prescription patterns.

Sample Size: The sample size, calculated based on a prevalence rate of 77.1% from a previous study, was determined to be 106 with a 5% two-sided alpha error, an 8% margin of error, and a 95% confidence interval. To account for potential non-participation or loss to follow-up (15%), an additional 20 subjects were included, bringing the final required sample size to 126.

Ethical Consideration: Approval for the study was obtained from the Institutional Ethical Committee of Hospital.

Data Collection: A prospective observational study was conducted in the Pediatric department at Tertiary Care Hospital in Banjara Hills, Hyderabad. A minimum of 126 eligible participants were recruited based on specified inclusion and exclusion criteria. Demographic data, including age and gender, were gathered from patient records. Detailed information on antibiotic prescriptions, focusing on types, frequencies, and combinations of primary and restricted high-end antibiotics, with an emphasis on dosage and duration, was extracted. Before initiation, formal permission and research consent were obtained from the Ethical Committee. Data confidentiality and privacy were strictly maintained, with access restricted solely to the researcher to ensure participant anonymity.

Inclusion Criteria:

1. Pediatric Patients:

- Age: Children aged 0 to 18 years.
- Patients with suspected or confirmed bacterial or fungal infections requiring high-end antibiotic therapy using specified antibiotics.

2. Diagnosis:

- Pediatric patients with conditions necessitating high-end antibiotic treatment, including severe infections caused by multidrug-resistant pathogens.

Exclusion Criteria:

1. Non-infectious Conditions:

- Patients with non-infectious medical conditions that do not require high-end antibiotics.

Statistical Analysis:

The statistical analysis employed IBM SPSS (version 24). Continuous and discrete variables were presented as Mean+/- Standard deviation and frequency with percentage (N), respectively. Data were presented as mean with standard deviation for normal distribution/scale data and as frequency with proportion N (%) for categorical data. The Chi-square test was used to test different groups among variables given in different categories. All statistical analyses were conducted at a 5% significance level or 95% confidence interval, considering a P value less than 0.05 as statistically significant.

RESULT

I. Patient Demographics

Age Distribution

The dataset predominantly comprises infants (0–2 years, 49%) and children (3–12 years, 48%), collectively representing the majority of the sample. Early (13–14 years) and middle adolescence (15–17 years) have minimal representation, contributing only 1% and 2%, respectively, while late adolescence (18–19 years) is entirely absent. This distribution underscores the significant focus on infancy and childhood within the dataset as shown in (figure 1).

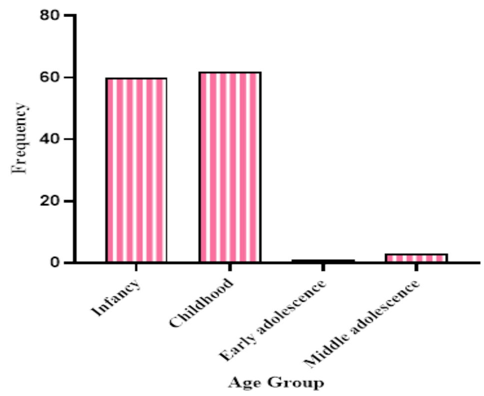

Figure 1. Age Distribution

Gender Distribution

The dataset reveals a gender distribution with 69 males (55%) and 57 females (45%), highlighting a slightly higher male representation. This breakdown underscores a near-balanced but male-skewed gender composition in the sample as shown in the (figure 2)

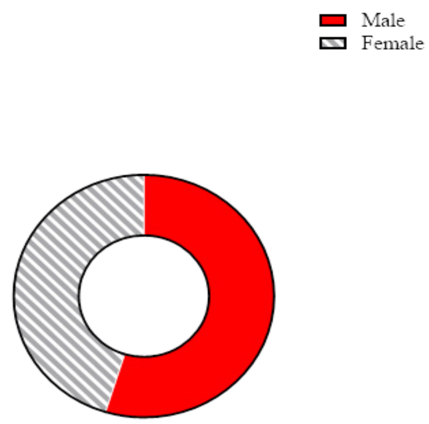

Figure 2. Gender Distribution

Weight Distribution

The dataset categorizes individuals by weight, highlighting a mean weight of 14.36 kg with a standard deviation of 9.94 kg, reflecting moderate variability. Most individuals fall in the 6–10 kg range (21%), closely followed by the 1–5 kg (18%), and 16–20 kg (18%) categories. The representation decreases in higher weight brackets, with the 31–35 kg and >35 kg categories contributing only 5% and 2%, respectively as shown in (figure 3)

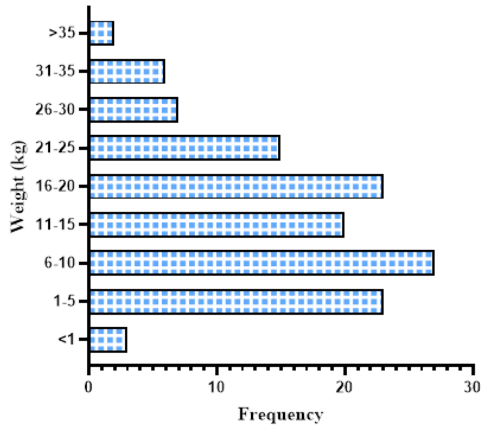

Figure 3. Weight Distribution

II. Medical Details

Department Wise Distribution of Restricted Antibiotics

The dataset reveals the allocation of restricted antibiotics among individuals in various departments. In the General department, 104 individuals, representing 83% of the total sample, received these specialized antibiotics. The Surgery department follows, with 13 individuals accounting for 10% of the dataset, who were administered restricted antibiotics. Hemato-oncology, while having a smaller representation, included 9 individuals (7%) receiving these specialized medications. This breakdown highlights the distribution patterns of individuals receiving restricted antibiotics across different departments, offering insights into the department-wise utilization of these medications within the analyzed as shown in (figure 4)

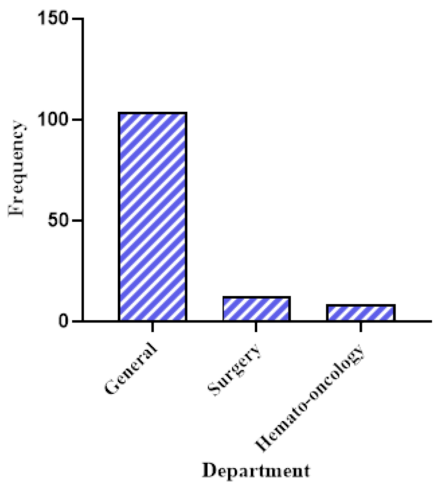

Figure 4. Department Wise Distribution of Restricted Antibiotics.

Class of Alternate Antibiotics Usage Pattern

The dataset outlines the distribution of individuals across different classes of antibiotics, presenting both the absolute number of individuals (N) and the corresponding percentages for each antibiotic class. Among the analyzed sample, Penicillin emerges as the most prevalent class, with 56 individuals, constituting 44% of the total. Cephalosporins closely follow, with 49 individuals and a 39% representation. Macrolides exhibit a notable presence with 35 individuals, making up 28% of the dataset. Aminoglycosides, Sulphonamides, and Nitroimidazoles contribute to the distribution, each comprising 16%, 7%, and 5%, respectively. Tetracyclines have the smallest representation, accounting for 6% of the total as shown in (figure 5)

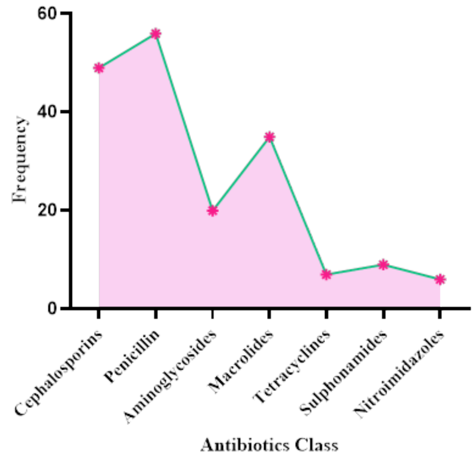

Figure 5. Class of Alternate Antibiotic Usage Pattern

Department Wise Alternate Antibiotic Usage Pattern

The data set provides a statistical overview of antibiotic usage across different departments, presenting the absolute number of individuals (N), corresponding percentages, and the p-value indicating the overall significance. Notably, Cephalosporins were significantly more prevalent in the Surgery department (46%) compared to the General (38%) and Hemato-oncology (44%) departments ($p=0.0009$). Penicillin usage varied slightly, with the Hemato-oncology department showing a higher percentage (56%) compared to the General (44%) and Surgery (38%) departments. Aminoglycosides were most frequently used in the Hemato-oncology department (33%), while Macrolides were more common in the General medicine (32%). Tetracyclines showed minimal usage, and Sulphonamides were notably higher in the Hemato oncology department (44%). Nitroimidazoles were more prevalent in the Surgery department (23%). This data provides insights into the significant differences in antibiotic class usage across departments, helping to identify patterns and potential areas for further investigation as shown in (figure 6)

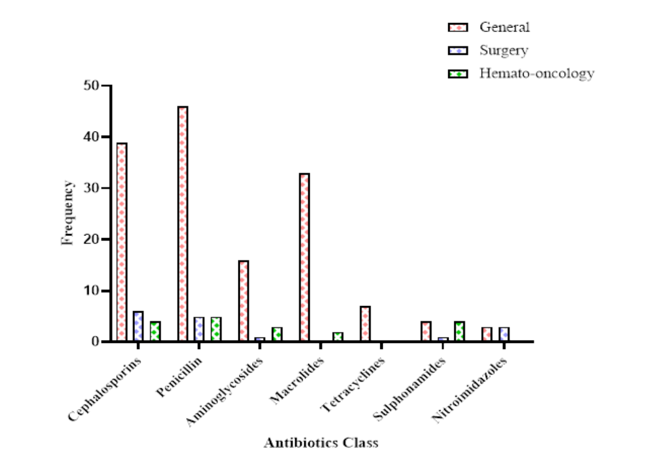

Figure 6. Class of Alternate Antibiotics Used based on Department

CRP (C-reactive protein) Levels Distribution

The dataset delineates the distribution of individuals based on C-reactive protein (CRP) levels, presenting both the absolute number of individuals (N) and the corresponding percentages for each CRP category. Among the analyzed sample, a significant majority, comprising 100 individuals or 79%, exhibits increased CRP levels. In contrast, 26 individuals, constituting 21%, fall within the normal range for CRP. This breakdown underscores a predominant occurrence of elevated CRP levels in the dataset, potentially indicating an inflammatory response and other health conditions associated with increased CRP as shown in (figure 7)

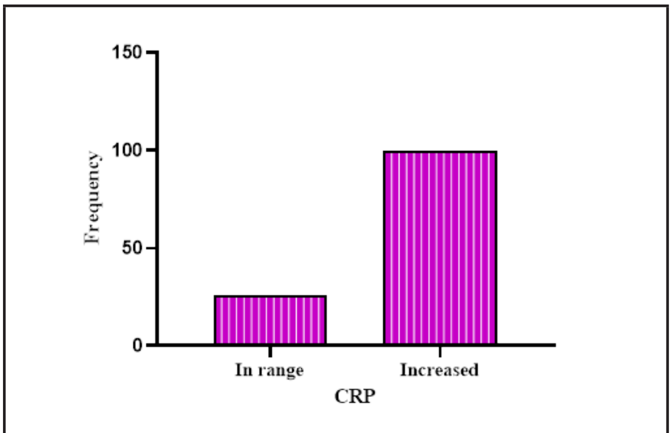

Figure 7. CRP (C-reactive protein) Levels Distribution

Route of Administration Trends

The dataset provides insight into the distribution of individuals based on the administration route of medications, presenting both the absolute number of individuals (N) and the corresponding percentages for each route. Among the analyzed sample, the intravenous (IV) route stands out prominently, with 204 individuals, constituting 89.1% of the total. Oral administration is the second most prevalent route, with 21 individuals and a representation of 9.2%. Ophthalmic, intranasal (IN), per nasal (PN), and nasogastric (NG) routes each have a minimal presence, each accounting for 0.4% of the dataset with one individual each. This breakdown emphasizes the predominant use of the IV route for medication administration in the analyzed sample as shown in (figure 8).

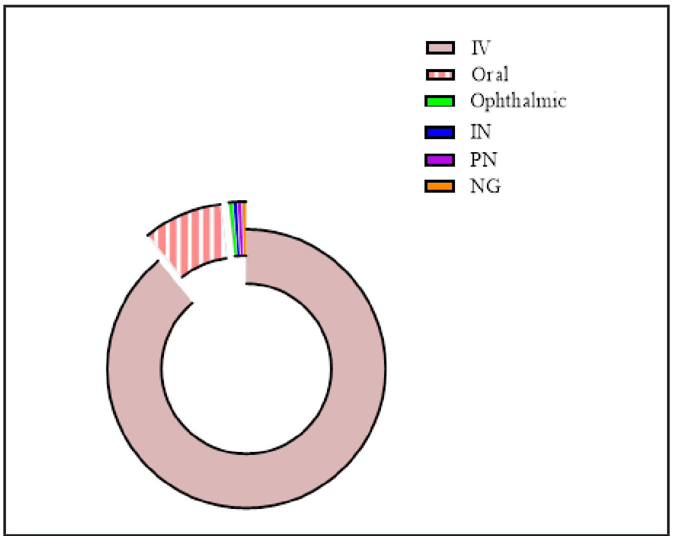

Figure 8. Route of Administration Trends

III. Antibiotic Usage Pattern

Restricted Antibiotics Usage

The dataset reveals the distribution of individuals across various drugs, specifying the absolute number (N) and the corresponding percentages for each drug category. Meropenem is the most frequently administered drug, accounting for 73% of the sample, followed by Linezolid at 41%. Other drugs, including Vancomycin, Polymyxin B, Teicoplanin, and several antifungals and antibiotics, show varying levels of representation. Notably, Ceftaroline, Daptomycin, and Doripenem have zero occurrences in the dataset as shown in (figure 9)

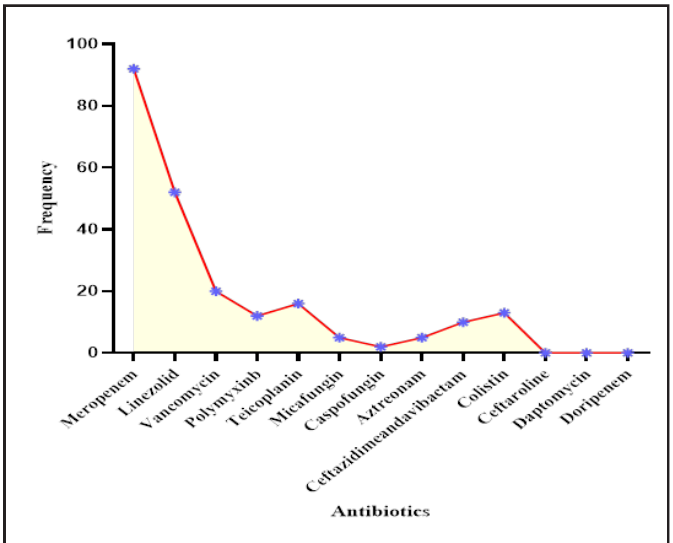

Figure 9. Restricted Antibiotics Usage

Number of Restricted Antibiotics Used per Patient

The data illustrates the usage patterns of Restricted Antibiotics (RA) among patients. It shows that 47% of cases involved the use of a single restricted antibiotic, while 36% included two antibiotics. A smaller percentage of cases involved three (10%), four (4%), or five (3%) restricted antibiotics. The average number of restricted antibiotics prescribed was 1.81, with a moderate variability (SD ±0.99). These findings emphasize the importance of adopting a more tailored approach to antibiotic prescriptions. Further research is recommended to explore the factors influencing these prescribing trends and to improve patient outcomes while reducing the risk of antibiotic resistance, as depicted in Figure 10.

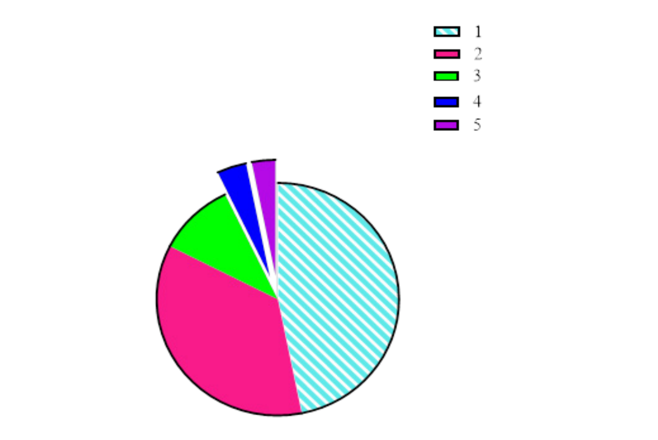

Figure 10. Number of Restricted Antibiotics Used per Patient.

IV Microbial Analysis

Prevalence of culture test

The dataset provides a comprehensive overview of the distribution of culture tests conducted on various specimens, offering insights into the frequency of testing for each specimen type. In the case of blood cultures, 67 patients underwent a single test, constituting 54% of the sample, while 14 patients had two tests (11%), and 2 patients had three tests (2%). For COVID tests, 1 patient had a single test (0.8%), and another had two tests (0.8%). In the case of cerebrospinal fluid (CSF) cultures, 2 patients underwent a single test (1.6%). Other specimens, including Et culture, Flu panel, Nasopharyngeal, PCR, Peritoneal fluid, Pleural fluid, Pus, Sputum, Stool, Throat swab, and Urine, exhibited varying testing frequencies. Notably, 8% of patients had no culture tests, 36% had one test, 36% had two tests, and 50% had three tests among the combined "Others" category.

Table 1. Prevalence of Culture Test

Specimen	Culture Test		
	1	2	3
Blood	67	14	02
Covid	01	01	0
CSF	02	0	0
Et culture	04	01	01
Flu panel	06	02	02
Nasopharyngeal	02	0	0
PCR	02	01	01
Peritoneal fluid	01	0	0
Pleural fluid	01	01	0
Pus	02	02	0
Sputum	01	0	01
Stool	03	01	0
Throat swab	01	0	0
Urine	16	16	02
Others	07	07	05
Not taken	10	80	112

Type of organisms identified in culture

The dataset examines culture testing patterns, showing that in the first round, most patients had single tests for Gram-positive bacteria (54%), with others showing combinations of Gram-positive and Gram-negative bacteria (21%), viral organisms (13%), or fungal organisms (8%). A significant number of patients (46%) did not show identifiable organisms. Subsequent testing revealed more complex combinations of organisms, but many patients continued to show no identifiable organisms in later rounds (107, 103%; 116, 112%). This highlights the evolving nature of culture testing patterns and the variability in identified organisms across multiple instances as shown in (figure.11).

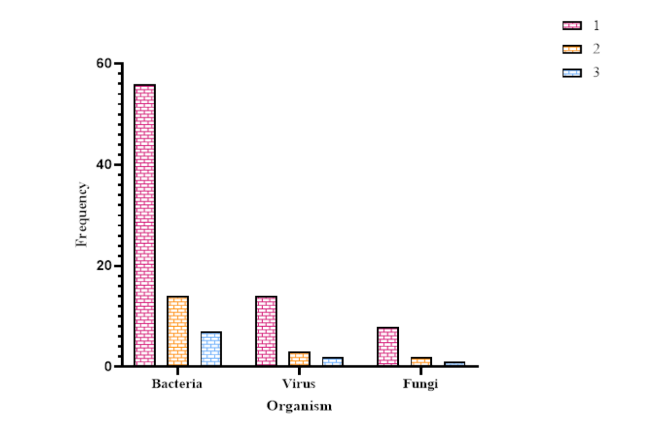

Figure 11. Type of organism identified in culture

Correlation and trends

Number of Restricted Antibiotics Used based on Department

Table 2. Number of Restricted Antibiotics Used based on Department

No. of RA	Department						P value
	General		Surgery		Hemato-oncology		
	N	%	N	%	N	%	
1	52	50	04	31	03	33	0.2081
2	34	33	08	62	03	33	
3	09	09	01	08	03	33	
4	05	05	0	0	0	0	
5	04	04	0	0	0	0	

No notable difference is found in the no. of RA used based on the department.

Correlation of No. of Alternate Antibiotics Used and No. of Restricted Antibiotics Used

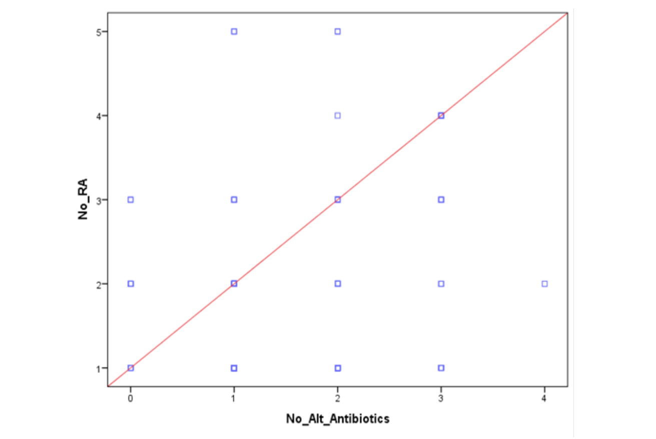

Figure 12. Correlation of No. of Alternate Antibiotics Used and No. of Restricted Antibiotics Used

r= 0.195* p= 0.028. A significant positive correlation was found between No. of alternate antibiotics used and No. of restricted antibiotics used.

DISCUSSION

Our investigation involved an in-depth analysis of prescription patterns within our hospital, specifically focusing on the utilization of restricted high-end antibiotics in the pediatric demographic. Notably, children constituted the largest cohort receiving both primary and high-end antibiotics, likely attributed to the gravity and urgency of their medical conditions, necessitating the use of restricted antibiotics in conjunction with standard ones. Gender-based analysis revealed a higher incidence among males, a phenomenon influenced by intricate interactions among biological, social, and environmental factors. This underscores the imperative for a nuanced comprehension to guide targeted interventions and practices. The heightened prevalence of restricted antibiotic use in the general pediatric department, as opposed to surgery and oncology cases, is linked to the broader spectrum of infectious conditions encountered in general pediatric care. This results in more frequent and diverse applications of primary antibiotics in tandem with restricted antibiotics. Primary antibiotics, particularly penicillins, were prominently employed across departments (general=44%, surgery=38%, hemato-oncology=56%), underscoring their broad-spectrum effectiveness as a preferred choice for managing a diverse array of common pediatric infections. Elevated C-reactive protein levels (79%) indicated a prevalent inflammatory response in the study population. Meropenem emerged as the most frequently prescribed restricted antibiotic, followed by linezolid. A detailed breakdown revealed varying degrees of escalation, with some patients receiving multiple restricted antibiotics. This escalation was linked to the prior administration of primary antibiotics outside the hospital, necessitating the use of high-end antibiotics upon admission to the tertiary care hospital. The range of isolated organisms, spanning one to three samples in different patients, signified the severity of sepsis cases, justifying the use of high-end antibiotics to address diverse microorganisms. Despite some instances where high-end antibiotics were prescribed without conducting culture and potential resistance to the prescribed antibiotic, the urgency of clinical situations and evident clinical signs justified their use. The time lag of 48 to 72 hours to obtain microbiological evidence contributed to the empirical rather than therapeutic and prophylactic use of high-end antibiotics, particularly in cancer and surgery cases. Furthermore, the likelihood of relapse after treatment with lower-tier antibiotics necessitates the utilization of restricted high-end antibiotics. Drawing on the study by Thuong et al. (2000) in France, the implementation of antibiotic order forms for restricted antibiotics, along with subsequent follow-up, demonstrated a significant reduction in antibiotic consumption. This approach facilitated the acceptable and appropriate use of such drugs. A comprehensive strategy involving both restrictive and educational measures is imperative to enhance overall antibiotic usage in hospitals. This multifaceted approach should engage clinicians, clinical microbiologists, pharmacists, and infectious disease experts. Additionally, studies underscore the efficacy of audit and feedback strategies in promoting adherence to policy guidelines.

CONCLUSION

In conclusion, the findings of our investigation into pediatric antibiotic prescription practices at our hospital underscore the complexity inherent in the administration of both primary and restricted high-end antibiotics. The preponderance of infants within the recipient cohort underscores the imperative for a judicious amalgamation of standard and potent antimicrobial agents, reflecting the severity and urgency of their clinical conditions. Gender-based variations, particularly the heightened incidence among males, suggest the influence of intricate biological, social, and environmental determinants, underscoring the necessity for nuanced interventions. The observed heterogeneity in restricted antibiotic utilization across departments reflects the diverse spectrum of infectious conditions encountered in general pediatric care. Notably, penicillins emerge as a preferred choice due to their broad-spectrum efficacy. Elevated C-reactive protein levels further affirm the prevalent inflammatory responses within the studied population. Prescription patterns, inclusive of frequent meropenem and linezolid usage, as well as the escalation to multiple restricted antibiotics, highlight the challenges associated with managing cases that have undergone prior primary antibiotic administration outside the hospital milieu. The variability in isolated organisms and the exigency of clinical situations contribute to the empirical utilization of high-end antibiotics, particularly in cancer and surgery cases where delayed microbiological evidence acquisition may compromise therapeutic precision.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation.

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