

# A Prospective Cross-sectional Descriptive Study Identifying the Predictors of Antibiotic Prescription Dynamics in Febrile Paediatric Patients

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## ABSTRACT

**BACKGROUND:** Antibiotics are administered as a response to certain triggers and segregating the appropriate catalyst aids in improving practice patterns on both clinical and socioeconomic fronts. This study aimed to investigate healthcare providers' decision-making processes when prescribing antibiotics for febrile children and assess prescription appropriateness.

**METHODS:** A prospective cross-sectional study was conducted from March to September 2023 at SSIMS&RC in Karnataka India. Data were collected from febrile children aged 1 month to 13 years admitted to pediatric wards, Pediatric Intensive Care Unit and Neonatal Intensive Care Unit, excluding nonbacterial etiologies and complex medical conditions. Patient data including demographics, clinical signs and symptoms, vaccination status, and Body Mass Index were compared to antibiotic prescription details. Statistical analysis was done using SPSS Version 28 for Windows, Statistical significance was defined as  $p < 0.05$ .

**RESULTS:** The study enrolled 300 pediatric patients with a male predominance especially affecting infants. Most patients were admitted by virtue of respiratory and urinary system illnesses. Various factors influencing antibiotic prescription were assessed and a statistically significant association appeared

between clinical diagnosis, chief complaints, and aberrant vitals. The study found an augmented average number of antibiotics in patients with improper vaccination status and malnourishment or obesity.

**CONCLUSION:** The rationality of prescribing antibiotics can be assessed effectively by analyzing and assimilating the reasons for which it is prescribed. This study highlights critical factors influencing antibiotic prescription, emphasizing the need for targeted interventions and adherence to clinical guidelines to mitigate antibiotic resistance. Furthermore, identifying factors implicated in prescription can aid physician in reflecting critically on their practices and offers resources for interventions and policymaking.

**Keywords:** antibiotics, antibiotic resistance, body mass index, pediatric population, prescription, prevalence

## INTRODUCTION

Antibiotic resistance has become a critical global health concern, especially in pediatric populations where inappropriate antibiotic use is prevalent <sup>[1]</sup>. Febrile illnesses encountered in pediatrics, especially those under the age of 5 years, constitute the primary rationale for pediatric consultations in emergency and primary care settings <sup>[2]</sup>. Even though the majority is attributable to presumed viral etiologies and typically

resolves on its own, gratuitous prescription of antibiotics is often recurrent. The misuse of antibiotics in such scenarios accelerates the development of resistant bacterial strains, posing a significant public health concern at individual and population levels <sup>[3, 4]</sup>. Recognizing the critical need to address this issue, this study was conceived to explore the decision-making processes of healthcare providers when prescribing antibiotics for febrile children.

The appropriateness of antibiotic prescription has been assessed in previous studies by comparing given therapy with empirical therapy and using criteria such as The International Network for Rational Use of Drugs (INRUD) by the World Health Organization (WHO) and Kunin's criteria to analyze the rationality of prescriptions. Many studies show deviation from standards set by W.H.O and Kunin when it comes to the practical use of antibiotics. This deviation necessitates introducing newer tools that allow the evaluation of prescriptions from often unexplored yet important angles, such as the predictors of antibiotic prescriptions. Each sign or symptom that leads to the prescription of an antimicrobial must be weighed against its chance of being an indicator of a serious bacterial illness that does not resolve on its own and could cause serious complications <sup>[5, 6]</sup>.

In the realm of pediatric medicine, a meticulous examination of the predictors influencing antibiotic prescription in children holds paramount significance. Such a study is imperative for advancing the understanding of clinical decision-making processes, optimizing therapeutic strategies, and addressing the escalating global concern of antimicrobial resistance. Identifying the predictors of antibiotic prescription dynamics allows for the filtering of less significant factors, thereby improving the rationality of prescriptions. This ensures the deployment of appropriate treatment for specific conditions, reduces the chance of antibiotic overuse, and, in a broader perspective, can reduce the incidence of antimicrobial resistance, which can

jeopardize a child's health throughout their life.

Prescribing practices are influenced by a variety of factors, including patient factors like deprivation and comorbidities, clinician factors such as previous experience, training, and attitudes towards antibiotics, the doctor-patient relationship, perceived patient anticipation, and other factors such as time and workload pressures. The identification of predictors, encompassing clinical presentations, age-specific considerations, immunization statuses, and socioeconomic factors, among others, contributes to the refinement of evidence-based guidelines and facilitates the development of targeted interventions <sup>[7]</sup>. Moreover, insights into antibiotic prescription determinants inform antibiotic stewardship initiatives, promoting judicious use and mitigating the risks associated with overuse, such as the emergence of antibiotic-resistant strains.

It is imperative to understand that while seeking to avoid antimicrobial resistance (AMR), we should not lead ourselves into the under-prescription of antibiotics. Insufficient prescription of antibiotics, characterized by inadequate dosing, delayed initiation, or premature cessation of treatment, poses a critical risk for the progression of bacterial infections to sepsis. In the absence of effective antibiotic intervention, the infection can breach local tissue barriers, entering the bloodstream and triggering an exacerbated systemic inflammatory response <sup>[8, 9]</sup>.

By unraveling certain factors guiding antibiotic prescription in pediatric populations, this research not only enhances patient care but also lays the foundation for local prescribing practices/behavior aimed at preserving the efficacy of antibiotics for future generations. This study aims to identify the clinical and non-clinical predictors of antibiotic prescription in pediatric patients and to evaluate the appropriateness of these prescription patterns, providing a robust foundation for improved clinical guidelines.

## **MATERIALS & METHODS**

### **STUDY CENTER**

The study was undertaken at SSIMS & RC, a tertiary care teaching hospital in Davangere, Karnataka, India, with a bed capacity exceeding 720. The facility includes a comprehensive pediatric department, Intensive Care Unit (ICU), outpatient services, and adequately ventilated general and isolation wards. It serves as a primary pediatric referral center, addressing the healthcare requirements of approximately 20-25 adjacent villages, and receives referrals from primary healthcare centers, private clinics, nursing homes, and neighboring districts.

### **STUDY DESIGN**

The study adopted a prospective cross-sectional descriptive methodology, encompassing febrile children admitted to the pediatric ward, Pediatric Intensive Care Unit (PICU), and Neonatal Intensive Care Unit (NICU) over six months from March 2023 to September 2023.

### **STUDY SAMPLE**

The study included all patients ranging from 1 month to 13 years of age, who presented with fever and had a confirmed bacterial cause, leading to antibiotic therapy.

### **EXCLUSION CRITERIA**

Exclusion criteria encompassed patients older than 13 years, attendees of the outpatient department, pediatric patients with intricate medical backgrounds including tuberculosis and cancer, and individuals presenting with suspected or proven non-bacterial etiologies.

### **DATA COLLECTION AND DATA ANALYSIS**

Data were collected using a custom-designed tool approved by the Head of the Pediatric Department at SSIMS and RC. Information acquired encompassed patient demographics (age, gender, body weight, IP number), chief complaints, diagnosis, laboratory investigations, and findings from general and

systemic examinations. Details regarding the antibiotics prescribed (drug name, category, dosage, duration, frequency, and potency) and the total count of the medications prescribed were also recorded.

### **ETHICAL CONSIDERATIONS**

The study protocol was reviewed and approved by the institutional ethics committee. Informed consent was obtained from parents or guardians of all participating children.

### **STATISTICAL METHODS**

All data were meticulously recorded and analyzed using MS Excel 2010 and SPSS version 28. Descriptive statistics, including frequency, percentage, and mean were computed to summarize the data. The Fisher's Exact test was used to determine the statistical significance of associations between antibiotic prescriptions and various clinical parameters. Statistical significance was defined as  $p < 0.05$ .

### **RESULT**

A cohort of 300 febrile pediatric patients receiving antibiotic therapy was enrolled in the investigation. Gender distribution revealed 180 (60%) males and 120 (40%) females. The predominant age bracket ranged from 1 month to 1 year 135(45%), succeeded by ages 2 to 5 years 87 (29%), and a smaller representation in the 6 to 13 years 78 (26%) category. Most patients were initially admitted to pediatric wards 211(70.3%), with subsequent transfers to the Pediatric Intensive Care Unit (PICU) 69 (23%) and Neonatal Intensive Care Unit (NICU) 20 (6.7%). Duration of hospital stay varied, with 156 (52%) patients staying for 6-10 days, 129 (43%) for  $\leq 5$  days, and the remainder 15 (5%) for  $\geq 11$  days. The cohort receiving antibiotic prescriptions had a mean age range of 2 to 5 years, whereas those without fell within 1 month to 1 year. The highest antibiotic prescription rates were observed in children aged 6-13 years and 2 to 5 years followed by 1 month to 1 year.

Initially, the study investigated the effect of various diagnoses on antibiotic prescription. Respiratory tract infections prompted 187 (62%) consultations, with pneumonia being the predominant diagnosis. Urinary Tract Infections (UTI) accounted for 15% of cases, followed by gastrointestinal diseases at 11.33%, as in Figure 1. Antibiotics were commonly prescribed for all cases of acute gastroenteritis, acute otitis media, bronchitis, lower respiratory tract infections (LRTIs), and enteric fever. Pneumonia accounted for 76 out of 277 (27.4%) antibiotic

prescriptions, while respiratory tract infections collectively comprised 172 (62%) as given in Table 1. Scrutinizing the severity of infection was found imperative to support antibiotic prescription based on physician diagnosis. Hence the National Institute for Health and Care Excellence (NICE) risk stratification tool for early recognition of sepsis in pediatrics was leveraged and found that pneumonia, bronchiolitis, UTI, and gastroenteritis posed the highest risk of sepsis [10].

**TABLE 1: Association between general physician diagnosis and antibiotic prescription**

GP Diagnosis	CHILDREN WITH DIAGNOSIS	ANTIBIOTICS PRESCRIBED	PROPORTION OF ANTIBIOTIC PRESCRIPTION %
Acute Colitis	1	1.0	100
Acute Gastroenteritis	32	32.0	100
Acute Glomerulonephritis	1	1.0	100
Acute Otitis Media	5	5.0	100
Acute Post Streptococcal Glomerulonephritis	1	1.0	100
Respiratory Tract Infection	17	11.0	64.71
Bacillary Dysentery	1	1.0	100
Bacterial Appendicitis	1	1.0	100
Bronchiolitis	32	29.0	90.625
Bronchitis	15	15.0	100
Pneumonia	79	76.0	96.20
Cervical Lymphadenitis	2	2.0	100
Croup	1	1.0	100
Enteric Fever	11	11.0	100
Infective Diarrhea	7	5.0	71.43
Lower Respiratory Tract Infection	10	10.0	100
Meningitis	5	5.0	100
Orbital Cellulitis	5	5.0	100
Pharyngitis	9	9.0	100
Rickettsia Fever	3	3.0	100
Sinusitis	1	1.0	100
Tonsillitis	5	2.0	40
Upper Respiratory Tract Infection	15	15.0	100
Urinary Tract Infection	40	40.0	100
Whooping Cough	1	1.0	100

Following diagnosis, abnormal findings in routine clinical parameters, including heart rate, respiratory rate, anomalous chest examinations, and abdominal examinations and imaging studies correlated significantly with antibiotic prescriptions. Pulse and respiratory rates were analyzed as binary variables, with considerations for tachycardia, or normal heart rate adjusted for age, and tachypnea, or normal respiratory

rate adjusted for age. 49% of the children exhibited tachycardia and 63% tachypnoea. Table 2 depicts statistical analysis, utilizing Fisher's exact, identified a significant association between tachypnoea, tachycardia, and antibiotic prescriptions. Among those with tachycardia, 144 out of 147 received antibiotic prescriptions, and among those with tachypnoea, 187 out of 190 were prescribed antibiotics, indicating a

noteworthy relationship. All the patients with abnormal chest examinations and abnormal imaging studies received antibiotics.

Moreover, 17 out of 23 patients with abnormal abdominal examination also received antibiotics.

**TABLE 2: Association between abnormal findings and antibiotic prescription**

PARAMETERS	CHILDREN with abnormalities	Children prescribed with antibiotics	Fisher's exact Test
Heart Rate	147	144/147	0.001
Respiratory Rate	190	187/190	0.001
Chest examination	53	53/53	0.001
Abdominal examinations	23	17/23	0.001
Imaging studies	11	11/11	0.001
A result below p<0.05 was considered significant.			

Analysis revealed 26 specific complaints and symptoms associated with an elevated likelihood of antibiotic prescription, including blood in stools or urine, burning micturition, chest indrawing, noisy breathing, respiratory distress, ear discharge, and dizziness. Categorical data were presented using frequency and percentage

distributions, and associations between variables were assessed through Fischer's exact test; Table 3. Despite the significant statistical correlation, a notable number of cases with complaints of throat pain, runny nose, decreased activity, and poor sleep were deprived of antibiotic treatment.

**TABLE 3: Association between chief complaints and antibiotic prescription**

Chief Complaints	children affected	Prescribed Antibiotics, n%	Fisher's Exact Test
Blood In Stools	6	6/6	0.001
Blood In Urine	5	5/5	0.001
Burning Micturition	9	9/9	0.001
Chest Indrawing	32	32/32	0.001
Cold	123	117/123	0.001
Cough	155	140/155	0.001
Crying While Micturition/ Painful Micturition	14	14/14	0.001
Decreased Activity	247	218/247	0.001
Discharge From Ear	5	5/5	0.001
Dizziness	15	15/15	0.001
Fever	300	280/300	0.001
Headache	9	7/9	0.001
Hurried Breathing	38	37/38	0.001
Joint Pain	3	2/3	0.001
Loose Stools	41	38/41	0.001
Noisy Breathing	30	30/30	0.001
Pain In Abdomen	32	27/32	0.001
Pain In Ear	7	6/7	0.001
Febrile Seizures	52	52/52	0.001
Poor Feeding / Loss Of Appetite	84	71/84	0.001
Poor Sleep	6	2/6	0.001
Rashes	20	16/20	0.001
Respiratory Distress	56	56/56	0.001
Runny Nose	8	5/8	0.001
Swelling Of Limbs And Face	19	17/19	0.001
Throat Pain	14	3/14	0.001
A result below p<0.05 was considered significant.			

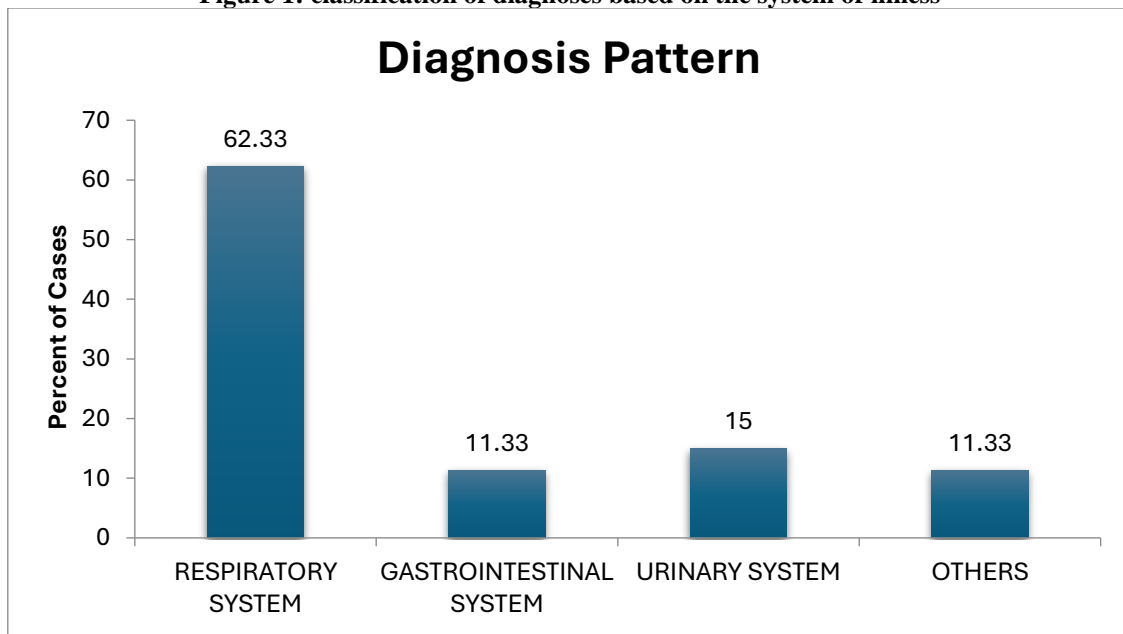
As seen from Table 4, unvaccinated children exhibited a significantly higher propensity for antibiotic prescriptions compared to vaccinated counterparts. On average, unvaccinated or partially vaccinated children received 2.35 antibiotic prescriptions, while vaccinated children received an average of 1.05, highlighting a statistically significant

difference in infection management and prescribing practices. When the Body Mass Index (BMI) of the patients was compared against the average number of antibiotics prescribed, we found that the management of obese and malnourished children demanded augmented antimicrobial therapy.

**Table 4: Influence of vaccination status and BMI on antibiotic prescription**

	Number (n=300)	The average number of antibiotics prescribed
<b>Immunization Status</b>		
Immunized	286	2.05
Unimmunized/ partially immunized	14	2.35
<b>BMI</b>		
Underweight	193	2.07
Normal	76	2
Overweight	11	2.18
Obese	17	2.29

**Figure 1: classification of diagnoses based on the system of illness**



No comprehensive study on antibiotics is considered exhaustive without a thorough analysis of the trends in antibiotic prescription. Among the total 590 prescribed antibiotics, 3<sup>rd</sup> generation Cephalosporins constituted the primary antibiotic class, accounting for 218 out of 590 prescriptions (36%). This was followed by penicillins, representing 89 out of 590 (15%), and aminoglycosides with 81 out of 590 (13%). Subsequently, macrolides accounted for 56 (9.4%) while carbapenems were prescribed

in 39 of 590 (6.6%). Fluoroquinolones and glycopeptides each comprised 29 (4.9%) and 24 (4%) of 590, respectively, alongside nitroimidazoles. Tetracyclines constituted 14 of 590 (2.3%) while Trimethoprim Sulfamethoxazole (TMP-SMX) and nitrofurans represented 9 (1.52%) and 7(1.18%) respectively.

## DISCUSSION

Antibiotics epitomize the foremost pharmacotherapeutic modality, frequently

prescribed within medical practice, with scrutiny directed towards their administration in the pediatric demographic due to pronounced apprehension. Investigations have elucidated a prevalent trend of antibiotic overutilization among pediatric cohorts, highlighting a pertinent clinical concern. Patterns of antibiotic prescription for specific diseases vary from country to country but also from one hospital to another [11]. However there are studies endorsing physician, patient, and/or environmental factors as reliable justification for antibiotic prescription.

The administration of antibiotics is predominantly contingent upon the precise diagnosis of the patient. Our investigation, informed by seminal works such as studies conducted by several other researchers also yielded congruent outcomes [2, 12]. Among the 300 patients enrolled, we identified 25 infectious diseases, each contributing to disease progression and possible complications in varying degrees based on inference from NICE published risk stratification tool. This was attributed to distinct demands in antibiotic prescription. Clinicians deem antibiotic therapy imperative for certain diagnoses. When all the patients presented with acute gastroenteritis, pharyngitis, UTI, and meningitis as well as most cases of pneumonia and bronchiolitis prescribed antibiotics, some patients with tonsillitis, infective diarrhea, and respiratory tract infections were deprived of the same. These findings were in agreement with index studies performed elsewhere.

Furthermore, our findings delineate that aberrations in respiratory and heart exert a discernible influence on antibiotic prescription, mirroring the conclusions drawn by Kathryn O'Brien et al. in 2015 [7]. Moreover, notable pathological manifestations during chest examinations, encompassing chest indrawing, wheezing, crepitations, and rhonchi, exhibit a marked association with an antibiotic prescription, as echoed in studies by Holmes et al. and Akkeraman et al. [13,14]. We also unearthed a

significant correlation between abnormal chest X-ray findings and antibiotic prescription, resonating with the observations elucidated by a US study [15]. Similarly, our investigation revealed that abnormalities detected during abdominal examinations, such as percussion dullness, elicit a notable impact on antibiotic prescription, akin to the findings reported by index literature interestingly, although some research posits a relationship between patient age and antibiotic prescription, our analysis did not yield statistically significant associations in this regard. [16]

We were able to segregate chief complaints which were the perceived predictors of antibiotic therapy according to physicians in our study site. Our study led to the conclusion that symptoms and signs or complaints of the patients had a significant impact on influencing clinician's decisions on antibiotic prescription. Overlapping findings were published by a study conducted in Wales and also suggested that often the diagnosis outweighs the presenting complaints as predictors of antibiotic prescription [7]. In the opinion of McKay R et al, the explanation for physical findings affecting antibiotic prescription was the possibility that these are suggestive of bacterial etiology [17]. Also, we identified a deficiency in our study by comparing it with existing literature being not able to compare the influence of parent expectation and physician specialty on starting antibiotics.

The immunization status of patients emerges as a pivotal determinant in disease progression and severity, thereby necessitating extensive antibiotic therapy. Noteworthy disparities in antibiotic prescription are observed among immunized versus unimmunized or partially immunized individuals, a trend substantiated by research conducted worldwide [2, 18].

In addition, our study underscores the influence of patient nutritional status on antibiotic prescription patterns. Notably, patients with obesity, overweight, or underweight status exhibit a heightened propensity for antibiotic prescriptions

compared to those with normal BMI. This observation, consistent with the findings of Jyotsna Mishra et al. and S. Shah et al., underscores the multifaceted impact of nutritional status on immune function and antibiotic susceptibility.<sup>[19, 20]</sup> Thus our results advocate for nuanced consideration of patient-specific factors in antibiotic prescribing practices, thereby optimizing therapeutic outcomes and mitigating antimicrobial resistance.

There are only a few Indian studies on predictors of antibiotic prescription. A comprehensive summary of relevant factors implicated in antibiotic prescription will encourage physicians to reflect critically on their practice and will provide an evidence-based resource for intervention and policy design.<sup>[17]</sup> Meanwhile similar to many recent studies on the prescription pattern of antibiotics, our study also found evidence of superfluous use of antibiotics delineating from prior set WHO standards. CH Quack states that antibiotic use is a modifiable driver of antibiotic resistance<sup>[11]</sup>. Antibiotics are administered as a response to certain triggers, and segregating the appropriate catalyst aids in improving practice patterns on both clinical and socioeconomic fronts.

## **CONCLUSION**

In conclusion, our comprehensive investigation delves into the intricate interplay between patient-specific factors and antibiotic prescribing practices, drawing upon seminal studies and robust statistical analysis. Through meticulous examinations, we elucidate the profound influence of various clinical parameters on antibiotic prescription patterns, notably highlighting the pivotal roles of patient symptoms, respiratory and heart rate aberrations, pathologic manifestations, and immunization status. Additionally, our findings underscore the nuanced impact of patient nutritional status on antibiotic susceptibility, emphasizing the importance of a holistic approach to therapeutic decision-making.

By synthesizing evidence from diverse sources, including studies by renowned

researchers, we contribute to the evolving understanding of antibiotic utilization and its implications for therapeutic efficacy and antimicrobial resistance. Our results advocate for tailored antibiotic prescribing practices informed by a thorough consideration of patient-specific factors, ultimately aiming to optimize therapeutic outcomes while mitigating the burgeoning challenge of antimicrobial resistance. As we navigate the complex landscape of infectious disease management, our research underscores the imperative for continued vigilance and adaptation in antibiotic prescribing practices to safeguard public health.

It is important to focus on new ways of diagnosing infections quickly and accurately using methods like point-of-care testing and molecular diagnostics. Understanding how things like people's income, the quality of healthcare, and programs to promote careful antibiotic use affect when and how doctors prescribe antibiotics can help make policies to fight antibiotic resistance on a large scale. Using new technologies and computer programs to predict which antibiotic will work best for each patient based on their characteristics could improve treatment results and make global health safer by bringing together different experts to share knowledge and work together.

## **Declaration by Authors**

**Ethical Approval:** Approved

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