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Gender-based analysis of antibiotic prescribing trends for pediatric patients with respiratory tract infections admitted to a tertiary care hospital in Lahore

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Abstract

Respiratory tract infections (RTIs), caused by microorganisms such as bacteria and viruses, are a leading cause of morbidity and mortality in children worldwide. Antibiotic resistance is a serious concern, and proper prescribing practices are necessary to avoid life-threatening situations. Thus, this study aims to conduct a gender-based analysis and compare antibiotic prescribing patterns for pediatric patients with respiratory tract infections admitted to a tertiary care hospital in Lahore. This comparative cross-sectional study was conducted at Children's Hospital in Lahore, Pakistan, for three months and enrolled 250 pediatric patients who met the inclusion criteria, including 155 males and 95 females. Data were collected through face-to-face interviews and reviewing hospital records. The results of the study showed that the average number of drugs per prescription was 3.06 ± 1.29 (male) and 3.12 ± 1.5 (female), while the average number of antibiotics per prescription was 2.25 ± 0.60 (male) and 2.17 ± 0.58 (female). The most prevalent medical conditions were bronchopneumonia (53.55% males and 58.95% females), followed by respiratory distress (20.00% males) and pneumonia (16.13% males and 16.84% females). The most commonly prescribed drugs were J01DD04: Ceftriaxone (78.71% males and 71.58% females), J01CR02: Amoxicillin/Clavulanate (59.35% males and 56.84% females), and J01GB06: Amikacin (41.29% males and 45.26% females). A low percentage of prescriptions had major drug–drug interactions (8.39% males and 10.53% females), while most prescriptions had no drug–drug interactions (81.94% males and 84.21% females). There was no significant difference between male and female patients for caregiver, indications for antibiotic prescriptions, the class of active agent prescribed, and drug interactions. Our study findings indicate that most male and female patients admitted to the hospital with lower respiratory tract infections were prescribed antibiotics alongside analgesics and antipyretics. Furthermore, our analysis revealed minimal drug interactions among the prescribed medications. Importantly, we observed a similar antibiotic prescribing trend among male and female pediatric patients, highlighting the consistency in treatment approaches.

Keywords

Respiratory tract infections; Irrational drug use; Antibiotic use in pediatrics; Antibiotic resistance; Intravenous drug use; Drug-drug interactions

1. Introduction

Respiratory tract infections (RTIs) caused by microorganisms such as bacteria and viruses are a major cause of morbidity and mortality in the pediatric population [1]. Children from developing countries are at higher risk of RTIs due to low birth weight, lack of breastfeeding, limited parental education, and limited household income [2]. The symp-

toms of RTIs vary with age and causative agent but typically include earache, sore throat, croup, bronchiolitis, acute cough, and common cold [3]. However, it is challenging to differentiate between viral and bacterial RTIs based solely on symptoms [4]. Globally, RTIs account for 19% of deaths and 8.2% of disabilities in children under the age of 5 years [5]. Among children under the age of 2 years, lower respiratory tract infections account for 20% to 30% of all hospital admissions and 30% to 60% of healthcare facility visits [5, 6].

Antimicrobial agents, such as antivirals and antibiotics, are effective remedies for RTIs. However, a treating physician needs to assess the risk-to-benefit ratio before prescribing them, considering factors such as the causative agent, patient age, infection severity, need for the antibacterial, route of administration, and clinical outcomes [7, 8, 9, 10]. Generally, viruses typically cause acute RTIs that do not require antibiotic treatment. However, antibiotics are often inappropriately prescribed for these infections, contributing to antibiotic resistance, waste of financial resources, poor clinical outcomes, and increased mortality rates [1, 11, 12, 13]. In Europe, antibiotic-resistant microorganisms cause approximately 25,000 deaths each year and result in a loss of €1.5 billion [14].

In Uganda, 43% of antibiotics are prescribed to children under the age of 5 years who visit healthcare facilities for RTIs [15]. Similarly, in developed countries such as Canada and the United States, antibiotics are overprescribed for pediatric patients with RTIs. In Canadian healthcare facilities, antibiotics are prescribed to 74% of children under 5 with RTIs, and 85% do not require antibiotics. In US hospitals, 35% of antibiotics are prescribed to children with RTIs, but only 50% need antibiotic therapy [16]. Similarly, in United States (US) hospitals, 35% of antibiotics are prescribed to children for RTIs; only 50% need antibiotic therapy [16]. Meanwhile, in New Zealand, 97% of children receive at least one course of antibiotics before the age of 5 years [17]. The irrational use of antimicrobial agents can be attributed to various factors, including limited financial resources, poor access to healthcare, lack of diagnostic facilities, noncompliance with treatment guidelines, and the influence of pharmaceutical companies on healthcare professionals [18, 19, 20]. If the irrational use of antibiotics is not controlled by 2050, it is estimated that it could lead to a global health crisis, causing an alarming 10 million deaths annually [21].

The prescribing practices of healthcare professionals in hospitals reveal a concerning trend: approximately 70% of antibiotics used in these settings are prescribed for respiratory tract infections (RTIs) [22]. This overuse of antibiotics has contributed to the emergence of Streptococcus pneumoniae resistance, particularly among young adults. Interestingly, the prescribing patterns of antibiotics vary between pediatric and nonpediatric practitioners. Research indicates that pediatric practitioners adhere more to antibiotic-prescribing guidelines than their nonpediatric counterparts [23]. Notably, amoxicillin prescription declines as children age, while the use of macrolides and third-generation cephalosporins increases in developed countries [24]. Additionally, injectable antibiotics are favored over oral administration [25]. Studies conducted in developed countries have also reported gender differences in antibiotic use among patients seeking treatment for various respiratory tract infections at primary healthcare facilities [26]. Moreover, the nature and type of infection have been found to influence antibiotic prescribing trends among male and female patients in these regions [27].

This situation challenges healthcare professionals to treat infectious diseases with better clinical outcomes. Thus, this study aims to conduct a gender-based analysis and compare antibiotic prescribing patterns for pediatric patients with respiratory tract infections admitted to a tertiary care hospital in Lahore. Moreover, the study also determined trends in prescribing and classified the prescribed drug according to pharmacological groups as well as determined drug-drug interactions.

2. Materials and methods

2.1. Study design

This comparative cross-sectional study comparing antibiotic prescribing patterns between male and female pediatric patients was conducted for three months, from January 2019 to March 2019, in Lahore, Pakistan.

2.2. Ethical approval

Ethical approval for the study was obtained from the review board and ethical committee of the Akson College of Pharmacy, Mirpur University of Science and Technology, Mirpur, Azad Jammu and Kashmir, Pakistan (229/09/EX/ACP/18).

2.3. Study setting

The study was conducted in Lahore, a city with a population of 11,126,285. The target location was Children's Hospital, one of the area's major public tertiary healthcare hospitals specializing in children's healthcare and operating since 1995 [28, 29].

2.4. Participant recruitment

The study included male and female pediatric patients admitted to the targeted healthcare facility under two years old. A pediatric consultant diagnosed them with upper or lower RTIs who received treatment for 3 to 5 days. However, the study excluded ambulatory patients with asthma or other respiratory allergies and those suffering from respiratory diseases other than RTIs.

2.5. Sampling technique and sample size

The sample size of this study was determined through a comprehensive literature review, which identified similar studies in terms of methodology and population. The authors also considered the desired margin of error, confidence interval, and expected distribution rate [30]. After adjusting for nonrespondents, 250 patients were recruited, including 95 female and 155 male patients. Purposive sampling was employed to select participants who met the inclusion criteria, and their parents provided consent for their participation.

2.6. Study tool

This study employed a modified questionnaire consisting of several sections, including demographic information about the children and caregivers, the number of drugs and antibiotics prescribed, indications for antibiotic prescriptions, and the class of active substances prescribed [31]. In addition, field experts reviewed the data collection tool before final use.

2.7. Data collection

The principal investigator collected data using an English questionnaire and conducted face-to-face interviews with caregivers and parents of the children who consented to participate in the study. The patients' medical records were also reviewed to gather information about their infection management at the healthcare facility.

2.8. Study measures

The study questionnaire gathered demographic information about the patients and caregivers, including age, area of residence, education level of the caregiver, and their

relationship with the patient. Detailed information was also gathered from the patient's medical records, focusing on the number and types of drugs and antibiotics prescribed, indications for antibiotic prescriptions, and specific active agents. The drug prescribing patterns were determined using the Anatomical Therapeutic Chemical (ATC) classification system developed by the World Health Organization (WHO) [32]. The drugs were categorized into three levels based on their frequency of use: drugs prescribed to less than 10% of patients were classified as low, drugs prescribed to 10 – 40% of patients were classified as moderate, and drugs prescribed to more than 40% of patients were considered highly used. Additionally, the drugs were classified based on their pharmacological groups according to the ATC classification system [31]. Finally, drug-drug interactions were identified using an authentic website with reliable drug databases and categorized as major, moderate, or minor interactions [33].

2.9. Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (IBM, SPSS Statistics for Windows, version 22.0. Armonk, NY: IBM Corp.). Descriptive statistics were calculated for male and female patients, including mean, standard deviation, frequencies, and percentages. Additionally, a chi-square test was used to assess the difference between male and female patients regarding age, residence, caregiver, caregiver's education, indications for antibiotic prescriptions, trends in active substance prescribed, and drug interactions.

3. Results

Table 1 shows that most male patients (29.68%) were between 7 and 14 months, followed by 21.94% in the 19 to 24 months age group. For female patients, the largest age group was 1 to 6 months (33.59%), followed by 7 to 12 months (27.37%). Most of the patients (75.58% males and 78.85% females) were from urban areas, and most of them were cared for by their mothers (82.58% males and 82.11% females). The majority of caregivers for both male (40.00%) and female (36.84%) patients had an intermediate level of education. There was no significant difference between male and female patients regarding their sociodemographic characteristics.

Table 1. Sociodemographic characteristics of the patients and their caregivers (n = 250).

Variables		Male Patients n = 155		Female Patients n = 95		*p* value
		N	%	N	%	
Age of patients (in months)	1 – 6	43	27.74	32	33.68	0.527
	7 – 12	46	29.68	26	27.37	
	13 – 18	32	20.65	20	21.05	
	19 – 24	34	21.94	17	17.89	
Residence of patients	Rural	38	24.52	20	21.05	0.529
	Urban	117	75.58	75	78.95	
Caregiver	Mother	128	82.58	78	82.11	0.500
	Father	16	10.32	7	7.37	
	Others	11	7.10	10	10.53	
Education of caregiver	No formal education	28	18.06	12	12.63	0.495
	Matriculation	27	17.42	18	18.95	
	Intermediate	62	40.00	35	36.84	
	Graduation	38	24.52	30	31.58	

* Variables are compared using the chi-square test.

The average number of drugs and antibiotics prescribed to male patients was 3.06 ± 1.29 and 2.25 ± 0.60, respectively, while for female patients, it was 3.12 ± 1.5 and 2.17 ± 0.58. Table 2 shows that nearly half of the patients were diagnosed with bronchopneumonia (53.55% males and 58.95% females), followed by respiratory distress among male patients (20.00%) and pneumonia (16.13% males and 16.84% females). Tuberculosis was observed in only a small number of male patients (0.65%).

Table 2. Indications for antibiotic prescriptions among male and female patients.

Disease of Patient	Male Patients n = 155		Female Patients n = 95		*p* value
	N	%	N	%	
Pneumonia	25	16.13	16	16.84	0.869
Respiratory distress	31	20.00	15	15.79	
Bronchopneumonia	83	53.55	56	58.95	
Bronchitis	5	3.23	4	4.21	
Tachypnea	2	1.29	0	0.00	
Pleural effusion	5	3.23	2	2.11	
Pulmonary tuberculosis	1	0.65	0	0.00	
Bronchiectasis	3	1.94	2	2.11	

* Variables are compared using the chi-square test.

Table 3. ATC Classification and trends of active substances prescribed.

Name of Active Agents	ATC Code	Male Patients n = 155		Female Patients n = 95		Prescription Trend	*p* value
		N	%	N	%		
Ceftriaxone	J01DD04	122	78.71	68	71.58	High	0.200
Amoxicillin/Clavulanate	J01CR02	92	59.35	54	56.84	High	0.422
Ampicillin	J01CA01	4	2.58	2	2.11	Low	0.812
Piperacillin/Tazobactam	J01CR05	5	3.23	1	1.05	Low	0.276
Ciprofloxacin	J01MA02	16	10.32	12	12.63	Moderate	0.574
Amikacin	J01JB06	64	41.29	43	45.26	High	0.538
Vancomycin	J01XA01	29	18.71	15	15.79	Moderate	0.556
Linezolid	J01XX08	2	1.29	3	3.16	Low	0.306
Clarithromycin	J01FA09	10	6.45	3	3.16	Low	0.255
Meropenem	J01DH02	3	1.94	2	2.11	Low	0.926
Phenytoin	N03AB02	17	10.97	12	12.63	Moderate	0.690
Hydrocortisone Sodium Succinate	H02AB09	46	29.68	30	31.58	Moderate	0.750
Levetiracetam	N03AX14	4	2.58	2	2.11	Low	0.812
Omeprazole	A02BC01	4	2.58	1	1.05	Low	0.402
Ranitidine	A02BA02	13	8.39	7	7.37	Low	0.773
Paracetamol	N02BE01	22	14.19	17	17.89	Moderate	0.447
Fluconazole	J02AC01	1	0.65	0	0.00	Low	0.433
Midazolam	N05CD08	3	1.94	1	1.05	Low	0.589
Terbutaline	R03A03	1	0.65	1	1.05	Low	0.726
Adrenaline	C01CA24	3	1.94	1	1.05	Low	0.589
Dexamethasone	S02BA06	9	5.81	8	8.42	Low	0.425
Acyclovir	J05AB01	1	0.65	4	4.21	Low	0.051
Dopamine	C01CA04	3	1.94	4	4.21	Low	0.290
Dobutamine	C01CA07	2	1.29	2	2.11	Low	0.618

* Variables are compared using the chi-square test.

Table 4. Prescribed drug classification according to pharmacological groups.

Pharmacological Group	Male Patients n = 155		Female Patients n = 95	
	N	%	N	%
J = Anti-Infective for Systemic Use J01 = Antibacterial for Systemic Use				
Third-generation cephalosporin	122	78.71	68	71.58
Penicillin + beta-lactamase inhibitor	103	66.45	64	67.37
Fluoroquinolones	16	10.32	12	12.63
Aminoglycoside	64	41.29	43	45.26
Glycopeptide antibiotic	29	18.71	15	15.79
Oxazidione (antibacterial)	2	1.29	3	3.16
Macrolide	10	6.45	3	3.16
Penicillin	4	2.58	2	2.11
Carbapenems	3	1.94	2	2.11
J02 = Antimycotics for Systemic Use				
Azole	1	0.65	0	0.00
J05 = Antivirals for Systemic Use				
Purine analog	1	0.65	4	4.21
N = Nervous System N02 = Analgesic				
Analgesic & antipyretic	22	14.19	17	17.89
N03 = Antiepileptic				
Anti-Convulsant	17	10.97	12	12.63
Anti-epileptic	4	2.58	2	2.11
N05 = Psycholeptics				
Benzodiazepines	3	1.94	1	1.05
A= Alimentary Tract and Metabolism A02 = Drug for Acid-Related Disorders				
Proton pump inhibitor	4	2.58	1	1.05
H2 blocker	13	8.39	7	7.37
C = Cardiovascular System C01 = Cardiac Therapy				
Sympathomimetic agent (alpha and beta-adrenergic agonist)	3	1.94	1	1.05
Catecholamine	5	3.23	6	6.32
H = Systemic Hormonal Preparation, excluding Sex Hormones and Insulins H02 = Corticosteroid for Systemic Use				
Anti-inflammatory	46	29.68	30	31.58
R = Respiratory Tract R03 = Drugs for Obstructive Airway Disease				
Beta-adrenergic receptor agonist	1	0.65	1	1.05
S = Sensory Organs S02 = Otologics				
Steroids	9	5.81	8	8.42

Table 3 shows that active substances that were highly prescribed included J01DD04: Ceftriaxone (78.70% males and 71.57% females), J01CR02: Amoxicillin/Clavulanate (59.35% males and 56.84% females), and J01GB06: Amikacin (41.29% males and 45.26% females). Conversely, active substances that were observed to be prescribed on a moderate basis included J01CR05: ciprofloxacin (10.32% males and 12.63% females), J01XA01: vancomycin (18.71% males and 15.79% females), N03AB02: phenytoin (10.97% males and

12.63% females), H02AB09: hydrocortisone sodium succinate (29.68% males and 31.58% females) and N02BE01: paracetamol (14.19% males and 17.89% females). Furthermore, no significant difference was found between male and female patients for any active ingredient prescribed ($p > 0.05$).

Table 4 shows that third-generation cephalosporins were highly prescribed (78.71% males and 71.58% females), followed by penicillin + beta-lactamase inhibitor (66.45% males and 67.37% females) and aminoglycosides (41.29% males and 45.26% females). Corticosteroids for systemic use were the second-largest group of drugs, with anti-inflammatory drugs being prescribed (29.68% males and 31.58% females). A meager number of prescriptions also contained drugs for obstructive airway disease, including beta-adrenergic receptor agonists (0.65% males and 1.05% females), followed by antifungal agents for systemic use, including azoles (0.65% males).

Table 5 shows that a meager number of prescriptions contained minor drug-drug interactions (2.58% males and 2.11% females), limited prescriptions contained major drug-drug interactions (8.39% males and 10.53% females), and a majority of the prescriptions contained no drug-drug interaction (81.94% males and female = 84.21% females).

Table 5. Drug-drug interactions among male and female patients' prescriptions.

Type of drug-drug interactions	Male Patients n = 155		Female Patients n = 95		*p* value
	N	%	N	%	
Minor	4	2.58	2	2.11	0.569
Moderate	11	7.10	3	3.16	
Major	13	8.39	10	10.53	
No interaction	127	81.94	80	84.21	

* Variables are compared using the chi-square test.

4. Discussion

Our study found that the majority of patients recruited were male, resided in urban areas, and received care from their mothers. The most commonly diagnosed conditions were bronchopneumonia and pneumonia, with male and female patients receiving prescriptions for ceftriaxone, amoxicillin/clavulanate, and amikacin. Pharmacologically, antibacterial drugs for systemic use, including third-generation cephalosporin and penicillin + beta-lactamase inhibitor, were the most commonly prescribed, followed by corticosteroids for systematic use. There were limited instances of major drug–drug interactions, with most prescriptions having none. Additionally, no significant differences were found between male and female patients regarding caregiver, number of drugs prescribed, antibiotics prescribed, active ingredient type, or drug–drug interactions.

The study's findings are consistent with an Ethiopian study that examined antibiotic prescriptions for children using hospital records. The study revealed that the most commonly prescribed antibiotics were a combination of ampicillin and gentamicin (43.3%), which were used to treat severe pneumonia (18.82%), severe acute malnutrition (13.97%), and meningitis (13.56%). In addition, 84.33% of the antibiotics were administered through the paracentral route, while only 20.03% and 4.21% of the prescriptions recorded the strength and duration of the antibiotics, respectively [13]. Furthermore, antibacterials were found to be frequently used in treating acute RTIs among children under five years of age in Uganda (60.2%) [15].

A study from Pakistan found that cephalosporins were prescribed to pediatric patients for the treatment of pneumonia (23.4%), diarrhea (11.6%), and bronchitis (11.2%), with 68.83% of prescriptions being administered parenterally and 20.39% orally, with

cefotaxime being prescribed in 20.39% of cases [34]. This overuse of antimicrobial agents has been attributed to the influence of promotional activities and incentives offered by pharmaceutical companies to prescribers [35, 36]. In Saudi Arabia, a study found that cephalosporins were the most commonly prescribed antibiotics for 1 – 5 days in pediatric patients, with 83.33% adherence to standard treatment guidelines and no significant drug interactions in the prescriptions [37].

The study's findings are consistent with research from other countries. A study in Pakistan found that cephalosporins and cefotaxime were commonly prescribed through both oral and parenteral routes for conditions such as pneumonia, bronchitis, and diarrhea. This irrational use of antibiotics can be attributed to promotional activities and incentives offered by pharmaceutical companies. In Saudi Arabia, cephalosporins were also commonly prescribed to pediatric patients for short durations without significant drug interactions. A study in Nigeria found that hospitalized children received an average of 2.1 medicines per prescription, and nearly half of the prescriptions included antibiotics. The most commonly prescribed antibiotics were aminoglycosides, cephalosporins, and penicillin. The study also reported an Index of Rational Drug Prescribing (IRDP) of 2.99, below the standard of 5 [38].

Recent scientific evidence has shown that broad-spectrum antibiotic prescriptions have increased over time, even for medical conditions where narrower-spectrum antibiotics are available [39]. Despite increasing costs and microbial resistance, healthcare providers often prescribe third-generation cephalosporin and macrolides as first-line agents. In addition, clinical guidelines recommend using narrow-spectrum antibiotics as the first-line agent and broad-spectrum antibiotics only when necessary [40, 41]. However, healthcare professionals' lack of knowledge and awareness regarding antibiotics, microorganisms, and standard treatment guidelines can cause irrational prescribing of antibiotics [42].

The study used the ATC classification system to compare antibiotic utilization patterns between male and female pediatric patients. This analysis addressed a sensitive topic within pharmacy practices. Therefore, it contributed valuable insights from the local context, complementing the literature. However, it is important to acknowledge certain limitations of the study. First, the research was conducted solely in one hospital specializing in children's healthcare, limiting the generalizability of the findings. Additionally, the study did not include information on the specific causative agents responsible for the infections or details regarding frequencies, dosages, dosage forms, and durations of antibiotic use. These limitations should be considered when interpreting the results and designing future research.

5. Conclusions

Our study findings indicate that most male and female patients admitted to the hospital with lower respiratory tract infections were prescribed antibiotics alongside analgesics and antipyretics. Furthermore, our analysis revealed minimal drug interactions among the prescribed medications. Importantly, we observed a similar antibiotic prescribing trend among male and female pediatric patients, highlighting the consistency in treatment approaches.

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Consent to participate: All participants who participated in this study provided informed consent prior to data collection.

Data availability: The data supporting this study's findings are available from Sidra upon reasonable request.

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Conflicts of interest: The authors declare no conflicts of interest.

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