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Research Article

Prescribing trends of Antibiotics among Pediatrics in two tertiary care Hospitals in Lahore, Punjab, Pakistan

Muhammad Rehan Sarwar[2*], Shazia Ayaz[1], Muhammad Kamran Raza[1], Saba Aslam[2], Musfirah Javed[2], Iqra Sakhi[2]

[1]Ghazi Khan Medical College, D.G. Khan, Pakistan

[2]Akhtar Saeed College of Pharmaceutical Sciences, Lahore, Pakistan

ABSTRACT

Objective: To assess the pattern of antibiotics use among pediatrics in two tertiary care hospitals in Lahore, Punjab, Pakistan. **Methods:** The study was conducted from 1st December, 2016 to 30th April, 2017 in two tertiary care hospitals of Lahore, Punjab province of Pakistan. Sampling population consisted of 322 pediatric patients aged <18 years, suffering from any disease. Statistical Package for Social Sciences (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) and Microsoft Excel, 2013 were used to analyze the data. *P*-value < .05 was taken as the mark of significance for statistical tests. **Results:** The most frequently diagnosed infections among the study population were; gastrointestinal tract infections (n = 136, 42.2%), fever (n = 117, 36.3%) and upper respiratory tract infections (n = 79, 24.5%). Cephalosporins (n = 235, 73%), penicillins (n = 80, 24.8%), and fluoroquinolones (n = 76, 23.6%) were most frequently prescribed antibiotic classes. Most frequently prescribed antibiotics agents were; ceftriaxone (n = 235, 73%), ciprofloxacin (n = 76, 23.6%) and co-amoxiclav (n = 71, 22%). Frequently prescribed antibiotics combinations were; co-amoxiclav+ceftriaxone (n = 42, 13%), ceftriaxone+vancomycin (n = 26, 8.1%) and ceftriaxone+ciprofloxacin (n = 12, 3.7%). The parenteral route was most commonly used for the administration of antibiotics. **Conclusions:** Current study concluded that antibiotic prescribing in pediatrics is quite high, an unfavorable trend which paves the way towards antimicrobial resistance.

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***Correspondence to:**
Dr. Muhammad Rehan Sarwar,
Email:
rehansarwaralvi@gmail.com

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INTRODUCTION

Excessive use of antibiotics makes most of the microbes resistant to antibiotics thus leading towards antimicrobial resistance (AMR) [1]. The most commonly prescribed drugs in various countries for pediatrics are the antibiotics, as paediatrics are more prone to have bacterial infections. The main reason for this is that in pediatrics the immune system of the body is in developing stage [2]. The antibiotics use in some infections where there is no need of it, such as those caused by viruses (e.g., flu), is seen in some under-developed as well as developed countries [3, 4].

World Health Organization (WHO) has defined the rational use of antibiotics as "the use of antibiotics that is economical for the patients as well as which maximizes the beneficial effects, and decreases the chances of both the harmful effects and the development of AMR" [5, 6]. Approximately, 30−50% of all inpatients have been prescribed minimum one antibiotic, and 30% of the hospital budget is characterized by antibiotics [7]. According to another study, 20−50% of the antibiotic use is irrational [8]. The irrational use has a great impact onthe quality of provided healthcare services [9], medication therapy expenditures [10] as well as on the incidence of harmful effects [11]. With the decline in the development of newer antibiotics and the emergence of multi-drug-resistant microbes (MDRM), the investigators are dread of upcoming "post-antibiotic era". The consequence of this era may be the increase in mortality rate of individuals with treatable infections [3, 12].

Organizations such as WHO and International Network for the Rational Use of Drugs (INRUD) functioning for the rational use of antibiotics in order to minimize the development of AMR [13, 14]. Very first step to achieve this goal is to measure the prescribing trend because most authorities come to an agreement that effective surveillance of antibiotic practice is essential for controlling unnecessary and/or incorrect antibiotic prescribing to prevent AMR [12, 15-17]. Therefore, the objective of this study was to assess the prescribing trend of antibiotics among pediatrics in two tertiary-care hospitals in Lahore, Punjab, Pakistan.

Material and Methods

Study design and study settings

A descriptive, non-experimental and cross-sectional study was conducted in two tertiary care hospitals in Lahore, Punjab province of Pakistan.

Study population and sample size

Sampling population consisted of pediatric patients aged <18 years, suffering from any infectious disease. The minimum sample size was 322, as calculated using the Raosoft sample size calculator [18], with 95% confidence interval (CI) and 5% margin of error [Equation 1].

$$n = N\,x/((N-1)E2\ +\ x)$$ ……..Equation 1

Where N is the population size, x is the CI and E is the margin of error.

Data collection method

A performa was designed for the collection of data from selected hospitals during five months i.e. 1st December, 2016 to 30th April, 2017. Data was collected from the medical records of patients. Data includes patient demographics (i.e. age, weight, gender), current diagnosis for which patient visited the hospital and prescribing pattern of antibiotics (i.e., dose, frequency, route).

Data analysis

Statistical Package for Social Sciences (IBM Corp. Released 2012. IBM SPSS Statistics for Windows Version 21.0. Armonk, NY: IBM Corp.) and Microsoft Excel (MS Office 2013) were used for data analysis. *P*-value <0.05 was taken as the mark of significance for statistical tests. Descriptive statistics were used to present the results.

Ethics approval and consent to participate

Ethical approval was obtained from the Pharmacy Research Ethics Committee (PREC) at the Akhtar Saeed College of Pharmaceutical Sciences, ACPS (Reference: 10-2016/PREC, dated November 22, 2016). The permission to conduct this study was also obtained from the administrators of the tertiary care hospitals.

Results

Medical records of 322 patients were investigated. Most of the patients were male (n = 174, 54%), <1 year of age (n = 125, 38.8%), ≤10kg of weight (n = 204, 63.4%) and prescribed with 1 antibiotic (n = 190, 59%) (Table 1).

Table 1: Characteristics of the patients (n = 322)

Variable	N	%
Gender		
Male	174	54
Female	148	46
Age		
<1year	125	38.8
1-5years	115	35.7
6-10years	40	12.4
11-18years	42	13
Weight		
≤10kg	204	63.4
11-20kg	64	19.9
21-30kg	31	9.6
>30kg	23	7.1
Antibiotics prescribed per prescription		
1	190	59.0
2	119	37.0
3	12	3.7
4	1	0.3

The most frequently diagnosed infections were; gastrointestinal tract (GIT) infections (n = 136, 42.2%), fever (n = 117, 36.3%) and upper respiratory tract infections (URTIs) (n = 79, 24.5%). A detailed list of infections and prescribed antibiotics is presented in Table 2.

Table 2: List of infections and antibiotic agents prescribed for their treatment among study population

Infections	N (%)	Drugs	Dose	f	N (%)
Fever	117 (36.3)	Ceftriaxone	≤250 mg	OD	3 (2.4)
				BD	39 (31.2)
				TID	3 (2.4)
			251-500 mg	OD	4 (3.2)
				BD	25 (20)
				TID	1 (0.8)
			500-1000 mg	BD	9 (7.2)
			>1000 mg	BD	9 (7.2)
		Co-amoxiclav	≤250 mg	BD	3 (2.4)
				TID	7 (5.6)
			251-500 mg	BD	3 (2.4)
				TID	3 (2.4)
		Ciprofloxacin	≤250 mg	BD	15 (12)
			251-500 mg	BD	1 (0.8)

Pneumonia	55 (17.1)	Ceftriaxone	≤250 mg	OD	6 (5.1)
				BD	7 (5.9)
				TID	1 (0.8)
			251-500 mg	OD	18 (15.3)
				BD	9 (7.6)
				TID	1 (0.8)
			>500 mg	OD	3 (2.5)
		Amikacin	≤50 mg	BD	16 (13.6)
			>50 mg	BD	1 (0.8)
		Vancomycin	≤150 mg	TID	10 (8.5)
			>150 mg	TID	1 (0.8)
		Co-amoxiclav	≤150 mg	TID	14 (11.9)
			151-250 mg	TID	17 (14.4)
			251-500 mg	OD	1 (0.8)
				BD	1 (0.8)
				TID	5 (4.2)
			>500 mg	TID	1 (0.8)
		Clarithromycin	<100 ml	BD	3 (2.5)
				TID	3 (2.5)
URTIs (cough, pharyngitis, tonsillitis)	79 (24.5)	Ceftriaxone	≤250 mg	OD	4 (4.5)
				BD	24 (27.3)
				TID	4 (4.5)
			251-500 mg	BD	18 (20.5)
				TID	1 (1.1)
			500-1000 mg	BD	5 (5.7)
			>1000 mg	BD	10 (11.4)
		Co-amoxiclav	≤250 mg	BD	2 (2.3)
				TID	6 (6.8)
			251-500 mg	BD	2 (2.3)
				TID	4 (4.5)
		Amikacin	≤50 mg	BD	1 (1.1)
			>50 mg	BD	2 (2.3)
		Clarithromycin	.200 ml	TID	2 (2.3)
		Ciprofloxacin	≤250 mg	BD	3 (3.4)
Bronchitis	28 (8.7)	Ceftriaxone	≤250 mg	OD	4 (17.4)
				BD	8 (34.8)
				TID	1 (4.3)
			251-500 mg	OD	2 (8.7)
				BD	2 (8.7)
			500-1000 mg	BD	2 (8.7)
		Co-amoxiclav	≤250 mg	TID	3 (13)
		Amikacin	≤50 mg	BD	1 (4.3)
Tuberculosis	8 (2.5)	Co-amoxiclav	>500 mg	TID	1 (9.1)
		Ceftriaxone	≤250 mg	BD	2 (18.2)
			251-500 mg	BD	4 (36.4)
		Vancomycin	≤250 mg	TID	1 (9.1)
			251-500 mg	TID	2 (18.2)
		Meropenem	250 mg	TID	1 (9.1)
Typhoid fever	3 (0.9)	Ceftriaxone	≤250 mg	BD	2 (66.7)
			251-500 mg	BD	1 (33.3)
GIT infections	136 (42.2)	Ceftriaxone	≤250 mg	OD	5 (3.5)
				BD	17 (12.1)
			251-500 mg	OD	5 (3.5)

				BD	13 (9.2)
			>500 mg	BD	11 (7.8)
		Amikacin	≤50 mg	BD	8 (5.7)
			>50 mg	BD	2 (1.4)
		Vancomycin	≤150 mg	BD	1 (0.7)
				TID	4 (2.8)
			>150 mg	TID	1 (0.7)
		Co-amoxiclav	≤200 mg	TID	4 (2.8)
		Ciprofloxacin	≤250 mg	OD	2 (1.4)
				BD	58 (41.1)
			250-500 mg	OD	1 (0.7)
				BD	6 (4.3)
			>500 mg	BD	2 (1.4)
		Meropenem	≤150 mg	TID	1 (0.7)
Skin infections	4 (1.2)	Ciprofloxacin	≤150 mg	BD	4 (100)
Pyosepsis	15 (4.7)	Ceftriaxone	≤250 mg	BD	5 (25)
			251-500 mg	OD	1 (5)
			>500 mg	OD	2 (10)
		Amikacin	≤50 mg	BD	6 (30)
			>50 mg	BD	4 (20)
		Ciprofloxacin	≤250 mg	BD	2 (10)
Encephalitis	1 (0.3)	Ceftriaxone	600 mg	BD	1 (50)
		Vancomycin	240 mg	TID	1 (50)
Abscess	2 (0.6)	Ceftriaxone	Up to 300 mg	OD	1 (25)
			>1000 mg	OD	1 (25)
		Vancomycin	Up to 350 mg	TID	2 (50)
Myositis	2 (0.6)	Ciprofloxacin	250 mg	BD	2 (50)
		Meropenem	500 mg	BD	2 (50)
Malaria	3 (0.9)	Ceftriaxone	150 mg	BD	4 (36.4)
			>500 mg	BD	3 (27.3)
		Vancomycin	50 mg	TID	4 (36.4)
Measles	2 (0.6)	Ceftriaxone	600 mg	BD	2 (50)
		Vancomycin	240 mg	TID	2 (50)
Meningitis	4 (1.2)	Ceftriaxone	≤250 mg	BD	5 (50)
		Vancomycin	≤250 mg	TID	5 (50)

Cephalosporins (n = 235, 73%), penicillins (n = 80, 24.8%), and fluoroquinolones (n = 76, 23.6%) were most frequently prescribed antibiotic classes. Whereas, most frequently prescribed antibiotics agents were; ceftriaxone (n = 235, 73%), ciprofloxacin (n = 76, 23.6%) and co-amoxiclav (n = 71, 22%) (Table 3).

Table 3: Commonly prescribed antibiotic classes and agents among selected pediatrics

Class of antibiotics	ATC Codes	N (%)	Agents	ATC Codes	N (%)
Penicillins	J01C	80 (24.8)	Co-amoxiclav	J01CR02	71 (22)
			Meropenem	J01DH02	6 (1.9)
			Imipenem	J01DH51	3 (0.9)
Cephalosporins	J01D	235 (73)	Ceftriaxone	J01DD04	235 (73)
Aminoglycosides	J01G	42 (13)	Gentamicin	J01GB03	3 (0.9)
			Amikacin	J01GB06	39 (12.1)
Flouroquinolones	J01M	76 (23.6)	Ciprofloxacin	J01MA02	76 (23.6)
Macrolides	J01FA	8 (2.5)	Clarithromycin	J01FA09	8 (2.5)
Others	J01X	34 (10.6)	Vancomycin	J01XA01	34 (10.6)

The commonly prescribed antibiotic combinations among pediatrics were; co-amoxiclav+ceftriaxone (n = 42, 13%), ceftriaxone+vancomycin (n = 26, 8.1%) and ceftriaxone+ciprofloxacin (n = 12, 3.7%) (Table 4).

Table 4: Commonly prescribed antibiotic combinations among selected pediatrics

Combinations of antibiotics	N	%
Ciprofloxacin+ Ceftriaxone	12	3.7
Ceftriaxone+ Co-amoxiclav	42	13.0
Co-amoxiclav + Amikacin	9	2.8
Imipenem+ Gentamicin	2	0.6
Ceftriaxone+ Vancomycin	26	8.1
Vancomycin+ Clarithromycin	3	0.9
Ceftriaxone+ Amikacin	17	5.3
Vancomycin+ Co-amoxiclav +Amikacin	1	0.3
Meropenem+ Ciprofloxacin	2	0.6
Vancomycin+ Meropenem	2	0.6
Ceftriaxone+ Amikacin+ Clarithromycin	1	0.3
Ceftriaxone+ Co-amoxiclav + Clarithromycin	1	0.3
Ciprofloxacin+ Meropenem+ Amikacin	1	0.3
Ciprofloxacin+ Amikacin	1	0.3
Meropenem+ Gentamicin	1	0.3
Clarithromycin+ Co-amoxiclav	1	0.3
Ceftriaxone+ Co-amoxiclav +Amikacin	6	1.9
Ceftriaxone+ Co-amoxiclav + Vancomycin+ Clarithromycin	1	0.3
Ceftriaxone+ Clarithromycin	1	0.3
Ceftriaxone+ Co-amoxiclav + Vancomycin	2	0.6

Discussion

This study set out to determine the prescribing trends of antibiotics among pediatrics. The study population was suffering from 21 different types of infections and a total of 9 antibiotics were prescribed for their treatment. Most of the antibiotics were prescribed for GIT infections (n=136, 42.2%), fever (n=117, 36.3%), and URT infections (n=79, 24.5%).

GIT infections include abdominal pain, vomiting, diarrhea, dysentery and gastritis. These infections may be caused by viruses (rotavirus), bacteria (commonly *E. coli*, *Campylobacter*, *Salmonella*) [19]. Contaminated water can be a possible cause of GIT infections in immune-compromised patients, pediatrics and elders [20]. In our society, there is a greater risk for water to become contaminated because of poor sewerage system. Water can also be contaminated by certain chemicals such as arsenic, uranium; or by fertilizers or pesticides. Poor disposal system of waste products from manufacturing processes can also contaminate drinking water [20]. Usually rehydration therapy or symptomatic therapy is recommended for GIT infections. Antibiotics are only recommended in case where bacteria have been identified; otherwise these agents are not effective against viral infections [20]. In this study, antibiotics were recommended to every patient having GIT infection, whether it was minor or severe infection.

In most of the cases, URT infections in pediatrics are caused by several families of viruses so antibiotics should not be used for these infections [21]. The cause of prescribing antibiotics in URT infections is that the diagnosis is not done correctly; also the prescribers are pressurized by patients' caregivers to prescribe antibiotics [21]. According to one study, about 40-50% patients are prescribed with antibacterial agents for the treatment of viral respiratory tract infections [22]. In case of fever, it may be the symptom of any RTI, flu, UTI, etc. Instead of antibiotics, antipyretics should be used for fever [23]. Antibiotics are used only when bacteria is the cause. The misuse of antibiotics is the leading cause of development of antibiotic resistant microbes [24].

The most commonly prescribed antibiotic class in this study was cephalosporins (n=235, 73%), and ceftriaxone (n=235, 73%) was the most commonly used agent in pediatrics. Similarly, some other studies had also shown that the ceftriaxone and other broad spectrum cephalosporins are the most commonly prescribed antibiotics [25, 26]. Due to this extensive use of the third generation cephalosporins, extended β-lactamase (ESBL) producing microorganisms are rising; this inclination can be overturned by the use of combination of broad

spectrum penicillins along with the aminoglycosides rather than cephalosporins [27].

Ceftriaxone is the safe antibiotic for use in pediatrics but excessive use of ceftriaxone is harmful. In addition to the emerging antibiotic resistance, wide range of ADRs, including urolithiasis and hemolytic anemia, had been reported with the use of cephalosporins especially the ceftriaxone [28, 29]. A study conducted in Iran showed that ceftriaxone is reported as the cause of the highest number of deaths. This data was extracted from Iranian Pharmaco-vigilance Database [29]. Hence, it is recommended that the excessive use of ceftriaxone and other antibiotics should be avoided to prevent the occurrence of resistance against antibiotics.

In this study, mostly prescriptions contain only one antibiotic (n=190, 59%). We had also detected that more than one antibiotics were prescribed to individual patient i.e., up to 4 antibiotics were prescribed in single prescription. The use of larger number of medicines in single prescription had a greater risk of occurrence of non-adherence towards the treatment as well as there were more chances of drug interactions and severe harmful effects [30].

Most commonly used antibiotic combination was of ceftriaxone and co-amoxiclav (n=42, 13%) for the treatment of infectious diseases in pediatrics. Other prescribed combinations were; ceftriaxone + vancomycin (n=26, 8.1%) and ceftriaxone + ciprofloxacin (n=12, 3.7%). Due to emergence of multi-drug resistant bacteria or some other reasons such as to increase the effect of antibacterial action of antibiotics, the combination antibiotics are used for the treatment of infectious diseases [31]. However, the combination use of more than one antibiotics may cause serious undesirable effects including the development of resistance, risk of toxicity, hypersensitivity reactions, super-infections [32]. Our study also had seen 8 cases of hypersensitivity reactions in patients that were prescribed combination of ceftriaxone and ciprofloxacin. The broad spectrum antibiotic can be used instead of using combination of more than one antibiotic.

As all the pediatrics had infectious diseases so we had seen a considerable extensive use of antibiotics in all the selected patients. The parenteral route was used for most of the antibiotics in this study. A pilot study conducted in India had also reported the wide use of parenteral antibiotics therapy [27]. The extensive use of the injections causes various harmful effects such as blood borne contagious diseases [33, 34]. Nicolau Syndrome was reported due to parenteral administration of antibiotic [33, 35]. Nicolau Syndrome is basically a skin and soft tissue necrosis that is recognized as a severe complication but it is not common in all patients [36]. Generally, parenteral antibiotic treatment is recommended when the patient is unable to administer oral antibiotic or where the greater and urgent effect is desired [37]. The parenteral administration of drugs requires appropriate trained personnel. Improper parenteral administration can cause harmful effects such as allergic reactions, or infections or thrombus may be formed at the site of administration [38].

This study has some limitations. First, the study was conducted in one city of Pakistan so results cannot be generalizable to entire country. However, since the healthcare system is same in entire country so our findings are likely to be similar for entire country. Second, since it was a cross sectional study so outcomes associated with improper prescribing of medicines cannot be seen. Future longitudinal studies may address this aspect.

Conclusion

The most frequently diagnosed infections among the study population were gastrointestinal tract infections, fever and upper respiratory tract infections. Cephalosporins were the top most used class of antibiotics in this study followed by penicillin and fluoroquinolones. Among cephalosporins, ceftriaxone was most commonly used agent. The most frequently prescribed antibiotics combinations was co-amoxiclav+ceftriaxone followed by ceftriaxone+vancomycin and ceftriaxone+ciprofloxacin, respectively. The parenteral route was most commonly used for the administration of antibiotics.

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List of Abbreviations

AMR: Antimicrobial Resistance
WHO: World Health Organization
SPSS: Statistical packages for social sciences
URTIs: Upper respiratory tract infections
UTI: Urinary tract infection
GITIs: Gastro-intestinal tract infections

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