Antibiotic prescription practices in pediatric in-patient department of a Tertiary Care Hospital

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ABSTRACT

Objective: To assess the antibiotic prescription practice in pediatric in – patient department for common childhood illnesses.
Study Design: A Retrospective analytical study
Place and Duration: At Department of Pediatric Medicine Nishtar Medical University Multan, over a period of one year from 1st January to 31st December 2016.
Methodology: The clinical charts of admitted children 1 month – 15 years of age were analyzed. Children who received at least one antibiotic were included in the study. Along with demographic data, indication (diagnosis), name and duration of antibiotic, duration of hospital stay and the outcome were assessed. Number of antibiotics per prescription, days of antibiotics therapy/100 admission days, percentage of broad-spectrum antibiotic used and frequency of polypharmacy (≥ 2 antibiotics) were calculated to assess rational use of antibiotics.
Results: At least one antibiotic was prescribed to 85% of admitted children. Most common indications for antibiotic were pneumonia (35.13%) followed by meningitis (20.05%). Acute gastroenteritis (5.8%) and bronchiolitis (3.6%) were the two indications where antibiotic use was probably inappropriate. Mean number of antibiotics per patient was 2.0 (± 0.56) with mean duration of antibiotic therapy 8.4 (± 7.4) days. Most common antibiotic class used was cephalosporins (80%) and most common antibiotic prescribed was Ceftriaxone (64.12%). Two antibiotics were prescribed to 76% of the children. A significant proportion of the children received Vancomycin (36%) and carbapenem (19%).
Conclusion: The study indicated over – prescription of cephalosporins, vancomycin and carbapenem and irrational use of antibiotics in gastroenteritis and bronchiolitis.
Keywords: Pediatrics, Childhood illness, Inpatient, Prescribing pattern, Antibiotics, Rational use

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INTRODUCTION

Children are more susceptible to the infectious diseases due to their special environment like day care and schools facilitating the transmission of infectious agents[1]. Antimicrobials are the most common therapeutic agents prescribed to pediatric patients. It has been described that antibiotics prescribed to children in cases of self-limiting ailments like upper respiratory tract infection including otitis media, common cold as well as in bronchiolitis and acute gastroenteritis are inappropriate[2,3]. The reasons include high risk of serious bacterial infections, lack of disease management guidelines at local level, inability to differentiate viral etiology from bacterial owing to costly or non – existing definitive laboratory tests, parental pressure to prescribe antibiotics and lack of following good prescription guidelines[4]. Inappropriate use of antibiotics is not only futile and adds to economic burden but also contributes to the development of antimicrobial resistance by mechanism of selective pressure. Increasing antimicrobial resistance parallels the high antibiotic use across the globe[5, 6].

A study from Iran showed that 66% of the pediatric patients were on antibiotics at one point in time[7]. A Nigerian study found that 83.5% of children were prescribed with at least one antibiotic[8]. Similarly a study from India revealed that 60% of the children received either oral or parenteral antibiotic[9]. In a West African study, it was reported that 98.5% of the children

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encounters received at least one antibiotic. Of the children with cough and cold 54.5% and the children with diarrhea and dehydration 44.8% were prescribed antibiotics[10]. Chaw et al retrospectively reviewed the antibiotic use in admitted pediatric patients in Gambia in 2018. It was found that 54.1% of the patients received at least on antibiotic and most common antibiotics used were ampicillin (19.5%), Gentamicin (14.5%) and Ceftriaxone (12.5%). The most common disease diagnosis getting the antibiotics were pneumonia (37.1%) and sepsis (14.1%)[11].

Antibiotic resistance in both the community – onset and hospital – acquired infections has increased over the past two decades. The resistant pathogens include methicillin-resistant Staphylococcus aureus, vancomycin-resistant enterococci, and gram-negative bacteria producing extended-spectrum β-lactamases and carbapenemases[12]. This resistance has grown to the level that for some infections patients and physicians are confronted with a situation where none of the available antibiotics work. For these patients we have slipped back in time to pre-antibiotic area[13]. Global initiatives toward controlling the antibiotic misuse and thus antibiotic resistance include improvement in health – care infrastructure, health insurance, implementation of standard infection control practices, policies for prudent antibiotic use, and antibiotic stewardship programs in health care facilities coupled with continuous surveillance[14].

To tackle with the problem of increasing antibiotic resistance; antibiotic stewardship programs have been established in developed countries to foster the prudent use of antibiotics. But the impact of such programs requires prior knowledge of antibiotic prescription pattern in in-patient department of pediatrics as children represent an important target population for antibiotic use. We conducted this retrospective study to determine the antibiotic prescription practice for common childhood illnesses in pediatric in – patient department of a tertiary care teaching hospital that will support the need and would contribute evidence, for the establishment of national and regional guidelines and policies to promote rational antibiotic use. The current study is conducted with an objective to assess the antibiotic prescription practice in pediatric in – patient department for common childhood illnesses.

METHODOLOGY

This retrospective analytical study was conducted during 1st January to 31st December 2016 at Pediatric Medical Unit of Nishtar Hospital, Multan. All consecutive charts of children between age 1 month to 15 years who received at least one antibiotic during their hospital stay were included**.** Children who were taking only diuretics for cardiac failure, antihypertensive, anti-epileptic, anti-malarial and anti – tuberculosis drugs were excluded from the study. The 'Core drug use indicators' tool developed by WHO[15] for the evaluation of prescribing and dispensing practices were used which has been validated and extensively reviewed. The study was approved from institutional Ethics and Research Committee.

A master database spreadsheet was created in Excel 2016. An initial data on total number of admissions, age, gender and diagnosis of the patients during study period was obtained from admission/discharge register. For additional information the clinical charts were obtained from the Medical Records and Statistical Department of the hospital. Antibiotics used (name, class and number) and duration of each antibiotic used was noted for each patient from these charts. All the data entry was supervised and double checked to minimize the bias.

Data Analysis: The collected data from Excel spread sheet were imported into and analyzed using the Statistical Package for Social Sciences (SPSS Version 20 software). The mean ±, standard deviation for age and duration of antibiotic therapy (median and interquartile range (IQR) where applicable) and frequency and percentages for qualitative variables were calculated.

RESULTS

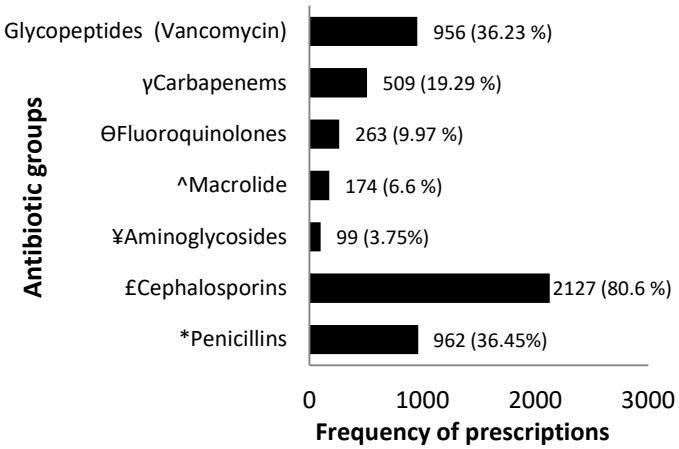
A total of 3107 children were admitted during the study period. Fifteen percent (n=468) did not receive any antibiotic. Females constituted 62% (n=1639) of the study population. Median age was 9 months. Mean number of antibiotics prescribed / patient were 2.0 (± 0.56) with mean duration of antibiotic therapy 8.4 (± 7.4) days.

Seventy six percent (n=2009) of the children were prescribed two antibiotics. Most common of the single antibiotic prescribed was Ceftriaxone (n=257, 75.8%), most common of the two – drug combination was Ceftriaxone + Vancomycin (n=457, 22.75%) followed by Ampicillin + Ceftriaxone (n=384, 19.11%) and most common of the three antibiotic combination was Ceftriaxone + Vancomycin + Meropenem (n=19, 8.12%) (Table-I).

Table-I: Combination of antibiotics prescribed in pediatric in-patients (N=2639)

Single antibiotic (n=339)	Ceftriaxone Cefoperazone Meropenem	257 (75.80%) 17 (05.01%) 14 (04.13%)
Two antibiotics (n=2009)	Ceftriaxone + Vancomycin Ampicillin + Ceftriaxone Meropenem + Vancomycin Benzylpenicillin + Ceftriaxone	457 (22.75%) 384 (19.11%) 276 (13.74%) 110 (05.48%)
Three antibiotics (n=234)	Ampicillin + Ceftriaxone + Vancomycin Ceftriaxone + Vancomycin + Meropenem Ceftriaxone + Vancomycin + Clarithromycin	17 (07.26%) 19 (08.12%) 12 (05.13%)

Cephalosporins were prescribed to 80% (n=2127) of the children and Penicillins were the second most common (n=962, 36.45%) antibiotics prescribed followed by Vancomycin (n=956, 36.23%) and carbapenems (n=509, 19.29%) (Fig-1).



*****Ampicillin, Benzylpenicillin, Co-amoxiclav, Piperacillin – tazobactam
¥ Amikacin
£Ceftriaxone, Cefotaxime, Cefoperazone/ sulbactam, Cefuroxime, Ceftazidime
^Azithromycin, Clarithromycin
Θ Ciprofloxacin, Levofloxacin, Moxifloxacin
ɣ Imipenem, Meropenem

Fig-1: Groups of antibiotics prescribed to pediatric in – patients (N=2639)

Antimicrobial days/100 admissions were highest for Ceftriaxone 271 days / 100 admissions followed by Vancomycin 186 days/100 admissions and Meropenem 88 days / 100 admissions (Table-II).

Most common reasons for antibiotic prescription were pneumonia (n=927, 35.13%) followed by meningitis (n=529, 20.05%), sepsis (n=249, 9.4%), acute gastroenteritis (n=154, 5.8%), bronchiolitis (n=94, 3.6%) and enteric fever (n=91, 3.45%) (Table-III).

Pneumonia in 23% (n=213) of the cases was treated with combination of Ampicillin and Ceftriaxone followed by Ceftriaxone and Vancomycin in 15.32% (n=142) of the cases.

Table-II: Most commonly prescribed antibiotics to pediatric in-patients (N=2639)

Antibiotic	Frequency, (%)	*Antimicrobial days/100 admissions
Ampicillin	726 (27.51%)	86
Amikacin	99 (3.75%)	-
Benzylpenicillin	132 (5.00%)	-
Ceftriaxone	1692 (64.12%)	271
Cefoperazone	276 (10.46%)	39
Cefotaxime	149 (5.65%)	-
Ciprofloxacin	261 (9.89%)	38
Clarithromycin	165 (6.25%)	-
Co-amoxiclav	97 (3.68%)	-
Meropenem	491 (18.61%)	88
Metronidazole	186 (7.05%)	-
Vancomycin	956 (36.23%)	186

Most common antibiotic used for treatment of meningitis was combination of Ceftriaxone and Vancomycin 36.29% (n =192) and the second most common antibiotic combination was Meropenem and Vancomycin in 17.77% (n=94). Sepsis was treated with Meropenem and Vancomycin in 32.13% (n=80), gastroenteritis with Ceftriaxone and Ciprofloxacin in 17.53% (n=27) of the cases. Enteric fever was managed using Ceftriaxone only in 43.96% (n=40) and Ceftriaxone combined with Ciprofloxacin in 37.36% (n=34) of the cases. Ampicillin combined with Ceftriaxone were used in treating 39.36% (n=37) cases of bronchiolitis (Table-III).

Table-III: Antibiotics used for six most common diagnoses in pediatric in-patients (N=2044)

Antibiotics / Diagnosis	Pneumonia (n=927)	Meningitis (n=529)	Sepsis (n=249)	Gastroenteritis (n=154)	Enteric fever (n=91)	Bronchiolitis (n=94)
Ceftriaxone	57 (06.15)	25 (4.73)	13 (5.22)	12 (7.79)	40 (43.96)	13 (13.83)
Ciprofloxacin	-	-	-	06 (3.90)	09 (9.89)	-
Meropenem	-	11 (02.08)	-	-	08 (8.79)	-
Ampicillin + Ceftriaxone	213 (22.98)	74 (14.00)	17 (6.83)	-	-	37 (39.36)
Ampicillin + Cefotaxime	43 (04.64)	08 (01.51)	24 (9.64)	17 (11.04)	-	04 (4.26)
Amikacin + Ceftriaxone	35 (03.78)	-	03 (1.20)	02 (1.30)	-	02 (2.13)
Ampicillin + Cefoperazone	33 (03.60)	-	15 (6.02)	-	-	10 (10.64)
Ampicillin + Meropenem	22 (02.37)	03 (0.57)	08 (3.21)	-	-	-
Ceftriaxone + Vancomycin	142 (15.32)	192 (36.29)	35(14.06)	11 (7.14)	-	08 (8.51)
Ceftriaxone + Ciprofloxacin	06 (0.65)	-	11 (4.42)	27 (17.53)	34 (37.36)	-
Ceftriaxone + Clarithromycin	57 (06.15)	-	-	-	-	05 (5.32)
Ceftriaxone + Metronidazole	-	-	-	14 (9.09)	-	-
Ceftriaxone + Co-amoxiclav	27 (02.91)	-	-	-	-	01 (1.06)
Benzylpenicillin + Ceftriaxone	-	74 (14.00)	-	-	-	-
Meropenem + Vancomycin	86 (09.28)	94 (17.77)	80 (32.13)	06 (3.90)	-	-
Ciprofloxacin +Metronidazole	-	-	05 (2.00)	33 (21.43)	-	-

DISCUSSION

We found a high frequency (85%) of antibiotics prescription to pediatric in – patients in our study. It was higher as compared to study by Choudhury et al (66%)[16] but comparable to a study from Southern Ethiopia (79.8%)[17]. One reason for high antibiotic prescription is that our hospital is a tertiary care hospital covering a wide area from where complicated cases are referred for management. Children below 5 years of age constituted 80.4% (58% were ≤ 12 months age) of the patients receiving at least one antibiotic. In a study from India 61% of the children receiving antibiotics were < 5 years of age[18]. It is plausible with the fact that increasing age leads to maturity of immune system, improved hygiene practices and decreased prevalence of infectious diseases. In our study, female pediatric patients 1639 (62%) out-numbered the male pediatric patients 1000 (37.9%). This is contrary to the studies from India (56%) and Ethiopia (65.7%) where male patients were dominant[9,17]. However, a combined antibiotic use prevalence study of five European databases stratified on age and gender indicated higher female: male ratio (1.19 – 1.57 : 1) in 0 – 9 year age group[19].

In our study, mean number of antibiotics prescribed per patient was 2.0 (± 0.56) and mean duration of antibiotics prescribed was 8.4 days (± 7.4). Compared to study by Akande *et al* mean number of antibiotic per patient was higher in our study (2.0 vs. 1.0) while mean duration of antibiotic therapy was lower (8.4 vs. 10.59 days)[8]. Antimicrobial days per 100 admission was highest (271 days per 100 admissions) for Ceftriaxone followed by vancomycin (186 per 100 admissions).

Seventy six percent of the children received combination of two antibiotics and most common of these was Ceftriaxone-Vancomycin. Single antibiotic was prescribed to 13% of the children and most common single antibiotic was ceftriaxone. Combination of three antibiotics was used in 9% of the children with Ceftriaxone-Vancomycin-Meropenem being the most common combination.

Pneumonia was the most common diagnosis for which antibiotics were prescribed in our study. It concurs with the studies by Choudhury et al[16] where pneumonia was most common reason for antibiotics prescription. In a study by Leo *et al* 14.5% of antibiotics were prescribed to patients with pneumonia[20]. Higher frequency of pneumonia indicates increased pneumonia incidence in our country[21]. Most common antibiotic prescribed for the treatment of pneumonia was combination of Ampicillin and Ceftriaxone. This was followed by Ceftriaxone–Vancomycin and Meropenem–Vancomycin. Antibiotic use for pneumonia in our study is in contrast to the guidelines advocating use of amoxicillin, ampicillin and gentamicin[22]. A study from Ethiopia also found combination of antibiotics (Gentamicin-Ceftriaxone, Crystalline penicillin-Gentamicin, Ampicillin-Gentamicin)[23]. The possible reason for such pattern of antibiotic prescription could be severity of pneumonia leading to hospital admission, underlying medical condition (cystic fibrosis, congenital heart disease), failed response to first line antibiotics or complication like empyema thoracis or para-pneumonic effusion.

In children, antibiotics are not indicated for acute gastroenteritis unless complicated by dysentery as per WHO guidelines[24]. We found inappropriate use of antibiotics in gastroenteritis. Common antibiotics prescribed were combination of ciprofloxacin-metronidazole (21%), ceftriaxone-ciprofloxacin (17.5%) and ampicillin-Cefotaxime (11%). Stool culture facility is not available at our facility that could help differentiate bacterial versus viral cause of gastroenteritis in children. Similarly, antibiotic use in bronchiolitis was not rational as its viral disease and self-limiting. However, superimposed bacterial infection in bronchiolitis warrants antibiotic use.

Children suffering from enteric fever were treated with ceftriaxone (44%), combination of ceftriaxone–ciprofloxacin (37%) and ciprofloxacin (9.89%). However, use of meropenem (8.79%) for treating enteric fever is quite high. A study from Karachi showed that > 96% of the S. typhi isolates are sensitive to cephalosporins and 90 – 94% were sensitive to quinolones[25].

Bacterial meningitis is caused by different pathogens depending on the age of patient, isolating bacteria from cerebrospinal fluid is tedious and meningitis has got high morbidity and mortality if antibiotic therapy is delayed. Most common antibiotics prescribed for meningitis were ceftriaxone-vancomycin (36%), Benzylpenicillin-Ceftriaxone (14%), Ampicillin-Ceftriaxone (14%) and Meropenem-Vancomycin (17.77%).

In our study, highest proportion of the antibiotic prescribed was from Cephalosporins (80%) and ceftriaxone was the most common antibiotic from this class and overall as well (64%). Second most common antibiotic class utilized was penicillins and Ampicillin was most common drug used from this class. Following Cephalosporins and penicillins, highest proportion of the children was prescribed vancomycin (36%) and Carbapenems (19%). Use of Ceftriaxone and Vancomycin was much higher compared to study by Prajapati et al where cephalosporins were prescribed to only 25.5% and Vancomycin to 4.71%[26]. The high use of Carbapenems and glycopeptides at our setup is probably due to lack of microbiological evidence of infectious agents and free of cost availability of these antibiotics.

CONCLUSION

The study indicated over – prescription of cephalosporins, vancomycin and carbapenem and irrational use of antibiotics in gastroenteritis and bronchiolitis.

CONTRIBUTION OF AUTHORS

Khalid M: Conceived idea, Designed methodology, Literature search, Data analysis and interpretation, Manuscript writing, Critical revision of manuscript

Rasheed J: Data collection and compilation, Data interpretation, Manuscript writing

Wakeel N: Data collection and compilation

Aleem T: Data collection and compilation

Zafar F: Final critical review of manuscript and approval

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