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ASSESSMENT OF DOSING AND ANTIBIOTIC USE PATTERN IN PAEDIATRIC PATIENTS IN SOUTH INDIA; A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Objective: The overprescription, misuse and irrational use of antibiotics is a worldwide problem causing antibiotic resistance, significant mortality, morbidity and increased healthcare cost. Hence this study has been carried out inorder to assess the antibiotic use pattern and it's dosing in pediatric population to reduce irrational usage of antibiotics in pediatrics. **Methods:** A prospective observational study was carried out assessing 200 patients/ prescriptions; including inpatients, outpatients and community pharmacy prescriptions. **Results:** A total of 273 antibiotics was found to be prescribed. And 54 patients (27%) required replacement from firstly prescribed antibiotic to produce the intended therapeutic effect; 18 different antibiotics was prescribed and most common individual antibiotic was amoxicillin/ clavulanic acid and cephalosporin were the most commonly used drug category. Clinical conditions encountered was 31, RTI (41.87%) being the most common. Generic name was prescribed for 13.92% of the drugs. The prevalence of antibiotic sensitivity test was 8.51% with 97.06 % total dose appropriateness. **Conclusion:** Out of total antibiotic prescription, 61% of cases followed standard guidelines. No unwanted effects was noticed or reported in the study population during the study period. These findings may help the healthcare workers to be aware of the trends followed and to promote necessary changes in the algorithms.

KEYWORDS antibiotics; dosing; pediatrics; prescription; sensitivity.

INTRODUCTION

Irrational use of antibiotics contributes to increased antibiotic resistance. To avoid overprescription of antibiotics it is important to check whether the drugs are prescribed according to WHO prescribing indicators and are from essential drug list.[1] For infections in infants and children, the antibiotic treatment depends on rapid diagnosis of the disease, identification of pathogens, and appropriate application of specialized pharmacokinetic and pharmacodynamic knowledge.[2-4] Studies show that medication errors causing harm were three times more likely in children than in the adults. Pediatric patients are at a higher risk of experiencing medication errors than adults because of the need of dose calculation based on patient's age, weight (mg/kg), BSA (mg/m2), and clinical condition.[2-4] Antimicrobial resistance (AMR) threatens the effective prevention and treatment of ever-increasing infections caused by bacteria, parasites, viruses and fungi. One method to help reduce AMR is to ensure appropriate prescription and administration of empiric antibiotics. WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately and that half of all patients fail to take them correctly.[5] Prescription pattern monitoring studies (PPMS) are drug utilization studies and a tool for assessing the prescribing, dispensing and distribution of medicines. They are designed to assess drug usage appropriateness and have the potential to make objective evaluation and analysis of health professional's work and provide them with feedback to stimulate thinking about their practice and looking for ways to improve their own performance.[6,7] The performance of antimicrobial sensitivity testing by the clinical microbiology lab is important to confirm sensitivity to chosen empirical antimicrobial agent or to detect resistance in individual bacterial isolates.[8] The overuse and misuse of antibiotics have been observed globally such that the antibiotics are prescribed for almost 50% of viral respiratory tract infections and viral gastroenteritis cases.[9] With the emergence of multidrug resistant microorganisms together with a decline in the development of new antibiotics, many researchers fear that the world is heading towards a 'post antibiotic era' where human beings may die of common infectious diseases that could have been effectively treated with easily available antibiotics. Conducting this study

contributes in understanding and improving the scenarios on paediatric antibiotic usage and it's dosing. The hypothesis generation helps to contribute in development of quality antibiotic prescribing and prevent unnecessary errors of medication usage.

MATERIALS AND METHODS

A prospective observational study was done over 200 subjects between 1 to 16 age group from November 2019 to April 2020 at a tertiary care hospital and community pharmacies in south India. The inclusion criteria was the pediatric inpatients with antibiotic prescription, pediatric outpatients with antibiotic prescription and pediatric prescriptions from community pharmacies. The exclusion criteria was casualty or emergency units. The study materials included case sheet of pediatric inpatients and outpatients, pediatric antibiotic prescriptions from community pharmacies, data collection forms, standard guidelines for antibiotic use in pediatrics and dose calculations (WHO indicators, National treatment guidelines for antimicrobial use), primary literature articles related to prescribing and dosing of antibiotics in pediatrics from authenticated data bases and journals such as: BMJ pediatrics, PubMed, Public Library of Science (PLOS), International Journal of Contemporary Pediatrics, International Journal of Basic & Clinical Pharmacology. Based on data extraction table, the dosing of antibiotics and prescription pattern of antibiotics were formatted.

RESULTS

1.0) Demographic characteristics of pediatric patients in study.

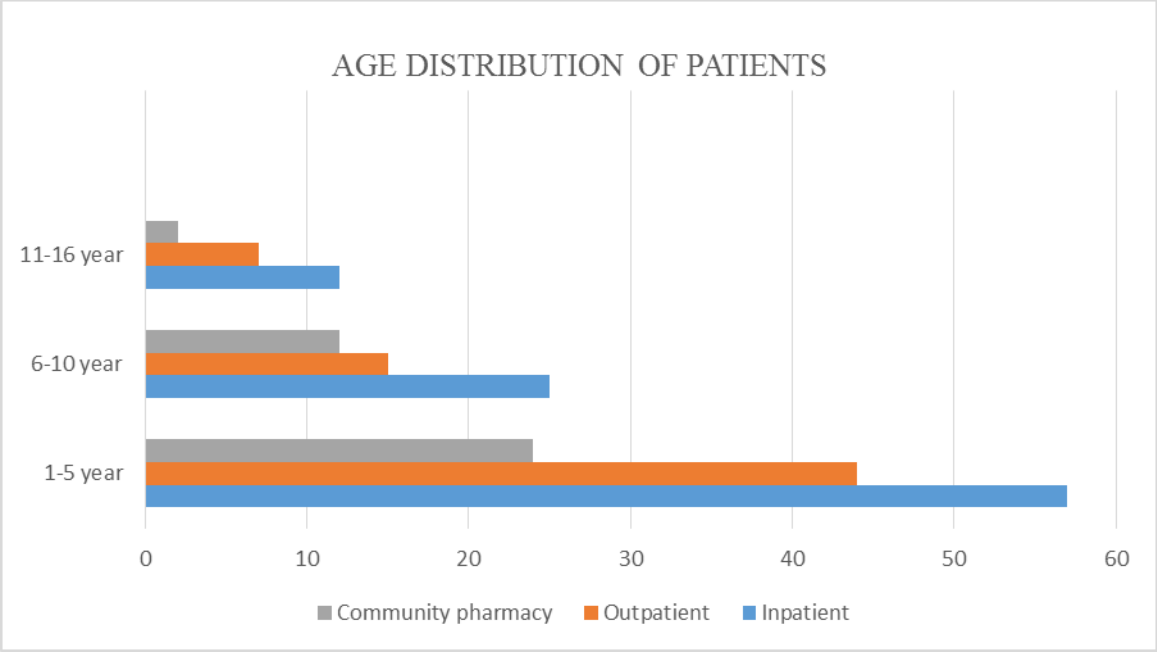
The subject population of study are the pediatric patients from a tertiary care hospital and community pharmacy prescriptions from Calicut, India. This includes pediatric cases of both inpatients and outpatients as well as prescriptions from community pharmacies. A total of 200 cases were collected and assessed. In it, 47% was inpatient cases (n=94), 33% outpatient cases (n=66) and 20% community pharmacy prescriptions (n=40).

Table 1.1. Gender distribution of pediatric patients

Gender	Male	Female	
IP	42	52	Male (n=96): 48%
OP	36	30	Female (n=104): 52%
CP	18	22	

IP, inpatient; OP, outpatient; CP, community pharmacy

The age group of patients was classified into 1-5 years, 6-10 years and 11-16 years. The distribution of IP, OP and CP subjects are depicted in fig.1. The mean age of pediatric patients enrolled in study was found to be 5.5 years with a standard deviation of 0.62.



The patients enrolled in this study had stayed up in the hospital from a minimum of 1 day to a maximum of 12 days. The mean of hospital stay was found to be 3.81 i.e., 4 DAYS with a calculated 0.89 standard deviation.

Table 1.2. Duration of hospital stay of subjects

Days	Number of patients	Percentage
01-03	59	62.76
04-06	17	18.01
07-09	14	14.89
10-12	04	04.25

2.0) Antibiotic usage patterns.

The subjects had followed either a single antibiotic course throughout the admission or had been prescribed more than one antibiotic one after the other depending on their response and alleviation of signs and symptoms. The average number of antibiotics per encounter was found equal to 1.37 with a calculated standard deviation of about 0.23 (Table 2.1).

Table 2.1. Number of antibiotics prescribed.

No of antibiotics	No of patients			Total	Percentage
	IP	OP	CP		
Single	47	60	39	146	73
More than one					
2	31	6	1	38	19
3	13	0	0	13	6.5
4	3	0	0	3	1.5

IP, inpatient; OP, outpatient; CP, community pharmacy

Various routes of administration encountered in this study includes oral, intravenous, intraocular, auricular etc. The pattern is shown in Table 2.2. The antibiotic as tablet- 73 antibiotics (26.73%). Syrups- 96 antibiotics (35.16%). Injections- 87 antibiotics (31.86%). Suspensions 8 antibiotics (2.93%). Capsules- 5 antibiotics (1.83%). Eye drops- 2 antibiotics (0.73%). Eardrops- 2(0.73%); detailed in Table 2.3a, 2.3b, 2.3c and fig 2.1.

Table 2.2. Route of administration of prescribed antibiotics.

Routes	No of antibiotics			Total	Percentage
	IP	OP	CP		
Oral	75	69	38	182	66.66
Intravenous (IV)	84	3	0	87	31.86
Intraoccular	1	0	1	2	0.73
Auricular	0	0	2	2	0.73

IP, inpatient; OP, outpatient; CP, community pharmacy

Table 2.3a. Various antibiotics encountered in the study.

Antibiotics as prescribed	Generic name	Number of prescriptions			Total	%
		IP	OP	CP		
Injections						
Supacef	Cefuroxime	21	0	0	21	7.69
Monocef	Ceftriaxone	13	0	0	13	4.76
Augmentin	Amoxicillin/ clavulanate	12	0	0	12	4.39
Amikacin	-	8	0	0	8	2.93
Taxim O	Cefotaxime	7	0	0	7	2.56
Gentamycin	-	5	0	0	5	1.83
Moxclav	Amoxicillin/ clavulanate	3	0	0	3	1.09
Pipzo	Piperacillin/tazobactam	3	0	0	3	1.09
Metrogyl	Metronidazole	2	0	0	2	0.73
Ampoxin	Ampicillin/cloxacillin	2	0	0	2	0.73
Fortum	Ceftazidime	2	2	0	2	1.46
Ceftriaxone	-	1	0	0	1	0.36
CP	Vancomycin	1	0	0	1	0.36
Ceftriaxone+ sulbactum	-	1	0	0	1	0.36
Opox	Cefpodoxime	1	1	0	2	0.73
Keftragard	Ceftriaxone/sulbactam	1	0	0	1	0.36
Uniroxim	Cefuroxime	1	0	0	1	0.36

IP, inpatient; OP, outpatient; CP, community pharmacy

Table 2.3b. Various antibiotics encountered in the study.						
Antibiotics as prescribed	**Generic name**	**Number of prescriptions**			**Total**	**%**
		IP	**OP**	**CP**		
Tablets						
Azitromycin	-	11	2	5	18	6.59
Taxim O	Cefotaxime	10	4	1	15	5.49
Moxclav	Amoxicillin/ clavulanate	1	8	1	10	3.66
Covatil	Cefuroxime	7	0	0	7	2.56
Erox	Amoxicillin	0	4	0	4	1.46
Zedocef	Cefpodoxime	0	2	1	3	1.09
Cefixime	-	0	2	1	3	1.09
Cefpod	Cefpodoxime	2	0	0	2	0.73
Cefpodoxime	-	0	1	1	2	0.73
Cefakind	Cefuroxime	0	1	0	1	0.36
Doxy	Doxycycline	3	0	0	3	1.09
Augmentin	Amoxicillin/ clavulanate	0	1	0	1	0.36
Moxikind	Amoxicillin/ clavulanate	1	0	1	2	0.73
Monocef	Ceftriaxone	0	1	0	1	0.36
Ciprobid	Ciprofloxacin	0	1	0	1	0.36
Capsules						
Ampoxin	Ampicillin/cloxacillin	4	0	0	4	1.46
Supacef	Cefuroxime	0	0	1	1	0.36

IP, inpatient; OP, outpatient; CP, community pharmacy

Table 2.3c. Various antibiotics encountered in the study.						
Antibiotics as prescribed	**Generic name**	**Number of prescriptions**			**Total**	**%**
		IP	**OP**	**CP**		
Syrups						
Moxclav	Amoxicillin/ clavulanate	9	17	5	31	11.35
Taxim O	Cefotaxime	16	5	3	24	8.79
Erox	Amoxicillin	0	9	1	10	3.66
Augmentin	Amoxicillin/ clavulanate	4	2	3	9	3.29
Altacef	Cefuroxime	3	0	0	3	1.09
Azithral	Azithromycin	2	0	6	8	2.93
Orelox xt	Cefpodoxime	0	1	0	1	0.36
Mega cv	Amoxicillin/ clavulanate	0	1	2	3	1.09
Doxycycline	-	0	1	0	1	0.36
Bicef	Cefadroxil	0	0	5	5	1.83
Cefixime	-	0	0	1	1	0.36
Suspensions						
Augmentin duo	Amoxicillin/ clavulanate	2	3	0	5	1.83
Zedocef	Cefpodoxime	0	2	0	2	0.73
Opox	Cefpodoxime	0	1	0	1	0.36
Eye drops						
Ciplox	Ciprofloxacin	1	0	1	2	0.73
Eardrops						
Ciplox	Ciprofloxacin	0	0	2	2	0.73

IP, inpatient; OP, outpatient; CP, community pharmacy

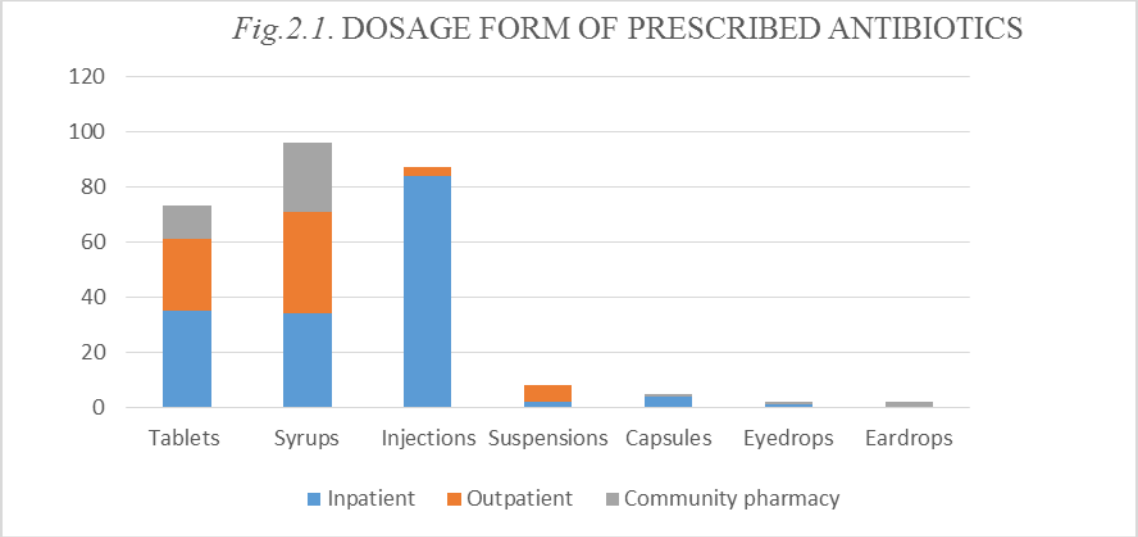
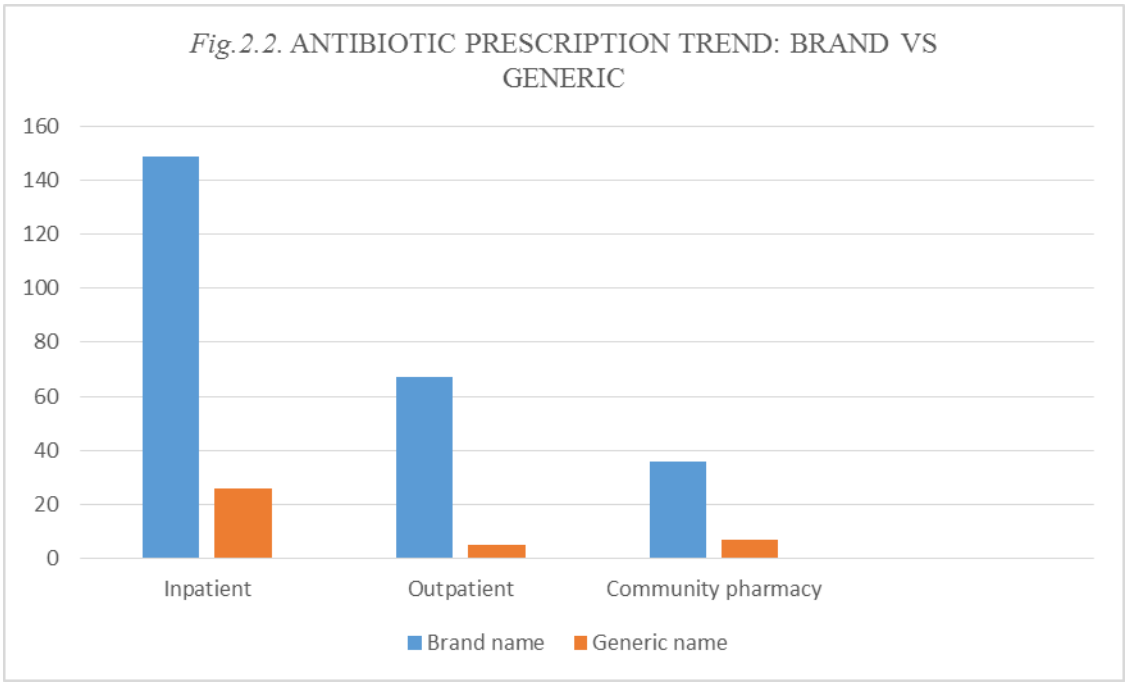


Fig 2.2 shows the different types of antibiotics prescribed in the patients with both their brand name and generic name. It includes the same antibiotics with different brand names varying between the physicians. Of all the 290 antibiotics (as of prescribing numbers), only 38 of them were prescribed in their generic name.



Three major indicators namely; the average number of antibiotics per encounter, percentage of drugs prescribed by generic name, and the percentage of encounters with an injection prescribed are depicted in Table 2.4.

Table 2.4. WHO prescribing indicators	
Prescribing indicators	Outcome
1) Average number of antibiotics per encounter	1.37
2) Percentage of drugs prescribed by generic name	13.92%
3) Percentage of encounters with an injection prescribed	31.86 %

There was 94 inpatient cases involving 160 antibiotics, 66 outpatients involving 72 antibiotics. Of this, 97 cases analysed followed the treatment guidelines i.e. 61 % while 63 had slight variations from the same in terms of initial doses and first line therapy i.e. 39 %. The antibiotic sensitivity test related findings were as follows.

Total inpatient cases- 94

No of sensitivity tests – 8

Prevalence of sensitivity test in inpatient = 8.51%

3.0) Clinical conditions and dose appropriateness.

About a number of clinical conditions in both inpatients and outpatients was encountered; which included upper respiratory tract infection, lower respiratory tract infection, urinary tract infection, bronchopneumonia, adenoid hypertrophy, febrile seizure, acute diarrheal disease, gastroenteritis, fever adenotonsilitis, laryngotracheobronchitis, pancreatitis, peritonitis, appendicitis, inguial hernia, meningism, hand foot mouth disease, peptic ulcer disease, constipation, emphysema, bronchitis, bronchiolitis, spinal muscular atrophy, cervical lymphadenitis, WALRI, consolidation upper lobe, consolidation (R) lower lobe, anemia, ovarian cyst, follicular tonsilitis, diarrhea. The antibiotics prescribed in the patients may vary depending on the national guideline/ empirical therapy followed. After assessment of drugs prescribed, a small deviation from rightful dosing have been noticed which is detailed in Table 3.

Table 3. Dose appropriateness of antibiotics prescribed.

Dosing of drug	No of antibiotics			Total	Percentage
	IP	OP	CP		
Appropriate	154	70	41	265	97.06
Inappropriate	6	2	0	8	2.93

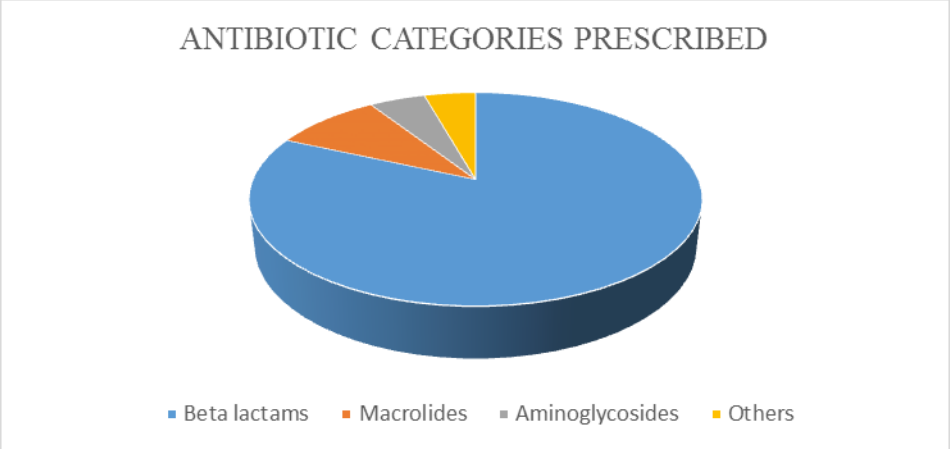
IP, inpatient; OP, outpatient; CP, community pharmacy

4.0) Antibiotic indications.

The combination therapy of antibiotics incorporates utilizing at least two medications together to re-establish or expand the viability of the two medications against the bacterial microorganism that is impervious to the conventional antibiotics. Table 4.0 consists of the common antibiotic combinations came across in the study. The different antibiotic classes involved beta lactams, tetracyclines, fluoroquinolones, glycopeptide antibiotics and nitroimidazoles (fig 4). The beta lactam antibiotics included penicillins and cephalosporins. Various generations of cephalosporin were prescribed; the first generation cephalosporin prescribed included cefadroxil (5 i.e. 4%), second generation were cefuroxime (34 i.e. 27.2%). Third generation involved cefotaxime (48), ceftriaxone (17), cefpodoxime (13), cefixime (4), ceftazidime (4); altogether making upto 68.8 %.

Table 4. Combination of antibiotics prescribed

Sl. No.	Combination antibiotics	No of Antibiotics	Percentage
1.	Amoxicillin + clavulanic acid	76	27.83
2.	Piperacillin + tazobactam	3	1.09
3.	Ampicillin + cloxacillin	6	2.19
4.	Ceftriaxone + sulbactam	2	0.73
	Total	87	31.86



DISCUSSION

A prospective observational study was carried out in 200 subjects. It included 94 inpatient cases (47%), 66 outpatient cases (33%) and 40 community pharmacy prescriptions (20%). The inpatients constitute for 42 males and 52 females, the outpatients being 36 male and 30 females and the community prescription assessment marked for 18 males and 22 females. This makes a total of 96 male subjects (48%) and 104 female subjects (52%).The 62.5 % patients fall into 1-5 years of age, 26 % and 11.5 % falls to 6-10 years and 11-16 years respectively. The mean age of patients enrolled in study was found to be 5.5 years with a standard deviation of 0.62. The hospital admission duration was 1-12 days. The mean of hospital stay was found to be 3.81 i.e., 4 days, with a calculated 0.89 standard deviation. The subjects had followed either a single antibiotic course throughout the admission or had been prescribed more

than one antibiotic one after the other depending on their response and alleviation of signs and symptoms. The subjects have undergone monotherapy as well as combination therapy depending upon the severity of their clinical presentation. It was also found that 73% of analysed cases followed only one or the same antibiotic. 47 inpatient cases, 60 outpatient cases and 39 community pharmacy prescriptions, making a total of 146 cases. And in 27% cases, two to four antibiotics (one after the other) have been used to achieve the appropriate therapeutic effect. Two antibiotics followed in 31 inpatient cases, 6 outpatient cases and 1 community pharmacy prescription. Three antibiotic was followed in 13 inpatient case only and 4 antibiotics was followed in 3 inpatient cases. In terms of percentage, it was about 19% cases involving 2 antibiotics, 6.5 % involved 3 antibiotics and 1.5% involved 4 antibiotics. The average number of antibiotics per encounter was found equal to 1.37 with a calculated standard deviation of about 0.23. The antibiotic in tablet form was prescribed in 35 inpatient, 26 outpatient and 12 community pharmacy prescriptions making a total of 73 antibiotics (26.73%). Syrups in 34 inpatients, 37 outpatients and 25 community pharmacy prescriptions to be total of 96 antibiotics (35.16%). Injections in 84 inpatients and 3 outpatients making a total of 87 antibiotics (31.86%). Suspensions in 2 inpatients and 6 outpatients with a total of 8 antibiotics (2.93%). Capsules in 4 inpatients and 1 community pharmacy prescription being a total of 5 antibiotics (1.83%). Eye drops in 1 inpatient, and 1 community pharmacy prescription being a total of 2 antibiotics (0.73%). Eardrops in 2 community pharmacy prescriptions (0.73%). The drug administration pattern was found to be 66.66% orally, 31.86 % intravenously, 0.73% intraocular and 0.73 % auricular. Oral administration (182) took place in 75 inpatients, 69 outpatients and 38 community pharmacy cases. IV administration (87) in 84 inpatients and 3 outpatients. Intraocular route in 1 inpatient and 1 community pharmacy case. Auricular route in 2 community pharmacy subjects. Also, IV administration of drugs were carried out only by properly trained healthcare workers. About 31 clinical conditions were entered by physicians. And the frequent ones were lower respiratory tract infections constituting for 35 cases (21.87%) and the second most frequent was upper respiratory tract infections diagnosed in about 31 subjects (19.38%) followed by urinary tract infections in about 20 subjects (12.50%). The least encountered diagnosis involved meningism, hand foot mouth disease, peptic ulcer disease, bronchitis, bronchiolitis, spinal muscular atrophy etc. other conditions include febrile seizure, fever, adenoid hypertrophy, constipation, diarrhea etc. Of all the antibiotics prescribed, which constitute for 290 antibiotics, only 38 of them were prescribed in their generic name which makes up to 13.92 % and 252 (86.08%) of them were prescribed in their brand names. The antibiotics prescribed in the patients for same therapeutic indication may vary between physicians (depending on the national guideline/ empirical therapy followed). After assessment of drugs prescribed, a small deviation from rightful dosing have been noticed. Of the antibiotics prescribed, 31.86% was combination therapy. And four major combination of drugs used were amoxicillin/ clavulanic acid (27.83%), Piperacillin/ tazobactam (1.09%), Ampicillin/ cloxacillin (2.19%) and Ceftriaxone/ sulbactam (0.73%). The drug classes involved beta lactam antibiotics, aminoglycosides, macrolides and other antibiotics (tetracyclines, fluoroquinolones, glycopeptide antibiotics and nitroimidazoles). The beta lactam antibiotics includes penicillins and cephalosporins; of which the cephalosporins were the most commonly prescribed ones. Prevalence in antibiotic sensitivity testing is the proportion of a particular population found to be tested by any AST methods at a specific time. The average number of antibiotics per encounter was 1.37, percentage of drugs prescribed in generic name was 13.92 % and the percentage of encounters with an injection prescribed was 31.86%. The prescribing of antibiotics in inpatients and outpatients accounting for a total of 160 cases were assessed with the "National treatment guidelines for antimicrobial use". Of this, 97 cases analysed followed the treatment guidelines i.e. 61 %.

CONCLUSION

A total of 200 cases was collected of which 94 inpatient, 66 outpatient files and 40 community prescriptions were involved. Female subjects were more compared to male subjects constituting about 52%. For 146 patients (73%), the same antibiotic was able to cure the indication while 54 patients (27%) required replacement from firstly prescribed antibiotic to produce the therapeutic effect. The increased brand name prescription of drugs may often misguide the patient bystanders to follow the same brand of medicine prescribed by the physician to produce the intended effect and may further contribute to increased cost of treatment. Antibiotic sensitivity tests were only carried out in selected inpatients. The prevalence being 8.51%. It should be carried out in all the inpatients who are undergoing antibiotic therapy inorder to optimize and achieve the appropriate therapeutic goal in the individual. 265 of them were prescribed in the pediatric dose range constituting 97.06 % dose appropriateness. And the assessment of antibiotic prescription as per the national treatment guidelines did not meet upto its mark. Though no unwanted effects in the studied population was noticed or reported during the study period. These results have aided in identifying the trends of prescription pattern in pediatric patients and their appropriateness in dosing. Also these findings may help the healthcare workers to be aware of the trends followed and if to promote necessary changes in the algorithms.

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