



A STUDY ON ANTIBIOTIC USAGE PATTERN AND CULTURE SENSITIVITY ANALYSIS IN PEDIATRIC PATIENTS

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Abstract

The study aims to analyse prescription pattern of antibiotics in pediatric patients, to determine the antibiotic sensitivity, and resistance pattern, and to assess the prescription on comparison with WHO prescribing indicators in a tertiary care hospital, Dakshina Kannada district, Karnataka. A Prospective observational study carried out for a period of 8 months in the pediatric inpatient department. The prescribing pattern of the antibiotics was analyzed using the drug therapy details. Data were analyzed using descriptive statistics. The sensitivity and resistance pattern of organisms to antibiotics were also determined. A total of 200 patients were enrolled in the study. Male patients (57.5%) outnumbered the female patients (42.5%). The most common clinical condition treated was lower respiratory tract infection (22.5%). Penicillin (34.28%) was the most commonly prescribed class of antibiotic, in particular Amoxicillin clavulanate (47.5%). 45% of the antibiotics were prescribed by generic name. All the antibiotics were prescribed from WHO model list of essential medicines for children 2017. Majority of the antibiotics were administered by parenteral route (91.5%). Culture test was done only in 55 patients, out of which 16 showed positive results. *E.coli* was the most isolated organism, which shows maximum sensitivity toward nitrofurantoin, piperacillin-tazobactam and was found to be resistant towards gentamycin, ciprofloxacin, ampicillin, amoxicillin. The average cost of antibiotic per prescription was 624.8 INR. The present study gives an overview of the antibiotic prescription pattern in the pediatric patients. The findings of the study will aid in developing antibiotic policy and will contribute the antibiotic stewardship.

Key Words: Antibiotics, Prescription pattern, Pediatrics

Introduction

“Pediatrics is the specialty of medical science concerned with the physical, mental and social health of children from birth to young adult hood” (Pediatrician Workforce Statement, 2005). We live in an environment, which is heavily populated by microorganisms (Mishra *et al.*, 2014). In this environment the pediatric populations are most vulnerable to contract illness (Feleke *et al.*, 2013). Several host and microbial factors contribute to relatively high incidence of infectious disease in pediatric patients. A deficiency of both cellular and humoral immunity is seen in the immediate newborn period and in the first several years of life (Steinberg, 2009). The usage

of antibiotics has become a usual practice for the treatment of pediatric illness. Antibiotics are the most frequently prescribed drugs among pediatric patients (Feleke *et al.*, 2013). Most physicians follow a systematic approach for the selection of an antimicrobial regimen. Problems arise when the systematic approach has been replaced by the broad spectrum antibiotics so as to cover as many organisms possible. An “empiric” antimicrobial regimen is started before the organism is identified and sometimes before the documentation of the presence of infection and later “definitive” regimen is instituted when the organism is identified (Lee & Burgess, 2014). The indiscriminate usage of antibiotics will increase the risk of bacterial drug resistance (Alakhali & Mohammad,

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2014). Antimicrobial resistance refers to the unresponsiveness of a microorganism towards an antimicrobial agent. There are two types of antimicrobial resistance; Natural and acquired resistance. Some microorganisms are always resistant to certain antimicrobial agents due to the lack of metabolic process or the target site which is affected by particular drug, which is natural resistance. Acquired resistance is developed due to the use of an antimicrobial agent over a period of time (Tipathi, 2013). The antimicrobial resistance is an issue of global concern and is considered as a threat to the modern therapy due to the risk of ineffective treatment regimens and increased health care costs (Bytyqi *et al.*, 2017). Antimicrobial stewardship refers to a set of coordinated strategies, to improve use of antimicrobial medication with the goal of optimizing patient health outcomes, reducing the antimicrobial resistance and decreasing the unnecessary costs (Antimicrobial Stewardship, Internet). Prescription pattern monitoring studies are used with focus on prescribing, dispensing and administering of drugs. Prescribing skill reflects prescriber's knowledge, attitude and practice towards diagnosis and management of diseases (Mishra *et al.*, 2014). The present study focus to assess the prescription pattern of antibiotics in pediatric patients and the information obtained may aid in the improvement of prescription pattern. It may also help in framing antibiotic policy which will contribute to the antimicrobial stewardship programme.

Materials and Methods

A prospective observational study of 8 months duration was carried out in the pediatrics department of a tertiary care hospital. The ethical committee approval was obtained before starting the study. The study includes all the pediatric inpatients of age less than 16 years, diagnosed with an infectious disease and received at least one antibiotic. The patients admitted to ICU and those who haven't received the antibiotics were excluded from the study. The patient data collection form was designed as per the need of the study. The hospitalized patients of the pediatrics department who received antibiotics were reviewed on a daily basis and their case sheets were evaluated to obtain the necessary data. The patient demographic details like age, gender, height, weight, complaints on admission and final diagnosis was recorded. Details of drug therapy such as name of drug, dosage form, frequency, route of administration, duration of treatment, length of hospital stay, and number of drugs per prescription were recorded. The details of the culture sensitivity test were obtained from the laboratory investigation data of the patients. The cost of antibiotics

prescribed during the hospital stay was determined using the price list provided by the hospital pharmacy. The prescriptions were analyzed on comparison with WHO prescribing indicators which include i) Average number of drugs per patient encounter ii) percentage of antibiotics prescribed by generic name iii) percentage of antibiotics prescribed from essential drug list iv) percentage of antibiotics administered by parenteral route. Descriptive statistics was applied for analyzing the collected data. Data analysis was carried out using Statistical Package for Social Science (SPSS) 16.0 for windows.

Results

Demographic details of the pediatric patients

A total number of 200 patients were included in the study. The male patients 115 (57.5%) outnumbered the female patients 85 (42.5%). Fig. 1 illustrates the gender wise distribution of the study population.

Majority of the patients belongs to the age group of less than 2 years (45.5%), followed by the age group 2-6 years (37.5%). The age wise distribution of the paediatric patients are summarized in table 1.

Length of hospital stay

The mean length of hospital stay was found to be 4.66 ± 1.41 days. Majority of the patients were hospitalized for 4-6 days. The details are illustrated in table 2.

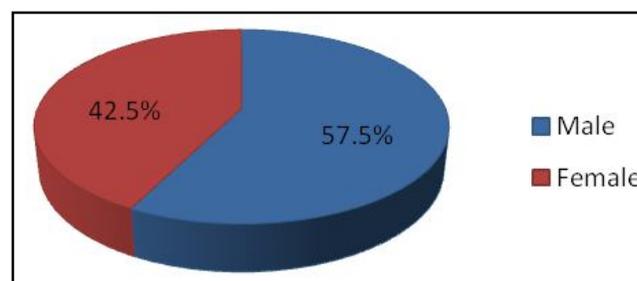


Fig. 1: Gender wise distribution of the patients.

Table 1: Age wise distribution of the patients.

Age in years	Male (n=115)	Female (n=85)	Frequency (n=200)	Percentage (%)
<2	56	35	91	45.5
2-6	39	36	75	37.5
7-11	8	8	16	8
12-16	12	6	18	9

Table 2: Length of hospital stay.

Sl. No.	Length of hospital stay (days)	Frequency (n=200)	Percentage (%)
1	1-3	41	20.5
2	4-6	138	69.0
3	6-10	21	10.5
Mean \pm SD: 4.66 ± 1.41			

Indications for which the antibiotic is used

During the study period, the most common clinical condition treated with the antibiotic was lower respiratory tract infection (41%) followed by upper respiratory tract infection (19.5%), subsequently other indications. The details of the indications treated with antibiotics are summarized in Fig. 2.

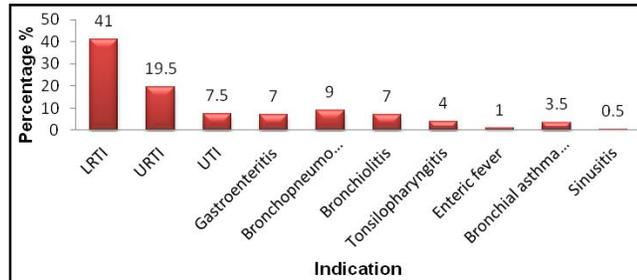


Fig. 2: Indication for which antibiotic is used.

Prescription pattern of antibiotics

A total of 280 antibiotics were prescribed among 200 patients. The most commonly prescribed class of antibiotics among the study population were penicillin (53%), followed by Cephalosporins (43%). Fig. 3 illustrates various class of antibiotics prescribed among pediatric patients.

Number of antibiotics per prescription

The average number of antibiotics per prescription was found to be 1.45±0.53. Mono antibiotic therapy was received by 61% of the patients, while the 36.5% and 2.5% of the patients received double and triple therapy respectively. The details are summarized in table 4.

Duration of Antibiotic therapy

Table 3: Prescription pattern of antibiotics.

Sl. No.	Class	Antibiotics	No. of patients (n=200)	Percentage (%)
1	Penicillin	Amoxicillin/Clavulanate (P)	86	43
		Amoxicillin/Clavulanate(O)	9	4.5
		Ampicillin(P)	2	1
		Piperacillin/Tazobactam (P)	9	4.5
2	Cephalosporin	Cefotaxime (P)	44	22
		Ceftriaxone (P)	41	20.5
		Cefixime (O)	1	0.5
3	Aminoglycoside	Amikacin (P)	58	29
		Gentamycin (P)	14	7
4	Macrolide	Erythromycin (O)	4	2
		Azithromycin (O)	5	2.5
		Clarithromycin (O)	2	1
5	Sulphonamide	Sulphamethoxazole/Trimethoprim (O)	4	2
6	Nitrofurantoin (O)	1	0.5	

P - Parenteral, O - Oral

Table 4: Number of Antibiotics per prescription.

Sl. No.	Number of Antibiotics	Percentage (%)
1	1	61
2	2	36.5
3	3	2.5

Table 5: Duration of antibiotic therapy.

Sl. No.	Number of days of Antibiotic therapy	No. of patients (n=200)	Percentage (%)
1	3	65	32.5
2	4	51	25.5
3	5	57	28.5
4	6	17	8.5
5	7	7	3.5
6	8	3	1.5

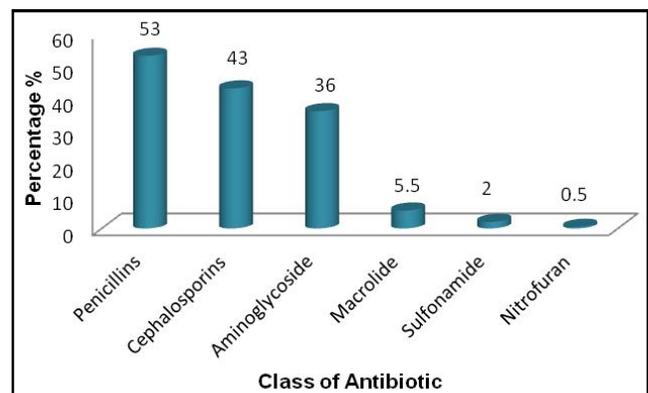


Fig. 3: Class of antibiotics prescribed in the study population.

The average duration of antibiotic therapy was found to be 4.28±1.18 days. Majority of the patients (32.5%) received antibiotic therapy for a duration of 3 days. 28.5% of the patients have received antibiotics for a duration of 5 days. The details of duration of antibiotic therapy among the study subjects are summarized in table 5.

Frequency of distribution of antibiotics for specific diagnosis

Among all patients treated with antibiotics, LRTI was the most common diagnosis. Cephalosporins (20) and Aminoglycosides (27) were prescribed in highest number for LRTI. Ceftriaxone and Cefotaxime were prescribed for almost all infections. Penicillin class of antibiotics were widely used in the management of respiratory tract infections table 6.

Distribution of co-administered medications

Among the study population, Bronchodilators (76%) were found to be the most commonly co-administered class of

Table 6: Frequency of distribution of antibiotics for specific diagnosis.

Diagnosis	CRO	CTX	CFM	AMK	GEN	ERY	AZM	AMP	AMC	TZP	SXT
LRTI	8	11	1	19	8	3	1	0	18	5	0
WALRI	7	2	0	6	0	0	4	0	22	0	2
URTI	6	6	0	5	1	0	0	2	22	1	2
UTI	3	9	0	6	2	0	0	0	1	1	0
Gastroenteritis	4	9	0	3	0	0	0	0	0	1	0
Bronchopneumonia	7	3	0	12	1	0	0	0	8	1	0
Bronchiolitis	2	3	0	3	0	1	0	0	9	0	0
Sinusitis	0	0	0	1	0	0	0	0	1	0	0
Enteric fever	2	0	0	0	1	0	0	0	0	0	0
Tonsilitis	0	1	0	1	0	0	0	0	4	0	0
Bronchial asthma with secondary infection	2	0	0	1	1	0	0	0	5	0	0
Pharyngitis	0	0	0	0	0	0	0	0	3	0	0

Drugs: CRO: Ceftriaxone, CTX: Cefotaxime, CFM: Cefexime, AMK: Amikacin, GEN: Gentamycin, ERY: Erythromycin, AZM: Azithromycin, AMP: Ampicillin, AMC: Amoxicillin-Clavulanic acid, TZP: Piperacillin-Tazobactam, SXT: Trimethoprim-sulphamethoxazole

Diseases: LRTI: lower respiratory tract infection, URTI: Upper respiratory tract infection, WALRI: Wheeze associated lower respiration illness, UTI: urinary tract infection.

medication which includes salbutamol, levo-salbutamol etc. Analgesics and antipyretics (69.5%) were also frequently prescribed. Paracetamol was found to be the commonly prescribed antipyretic. The details of the co-prescribed medications among the pediatric patients are illustrated in Fig. 4.

Assessment of WHO prescribing indicators

A total of 853 medicines were prescribed among 200 patients, out of which 280 were antibiotics. 45% of the antibiotics were prescribed by generic name and 91.5% were administered by parenteral route, table 7.

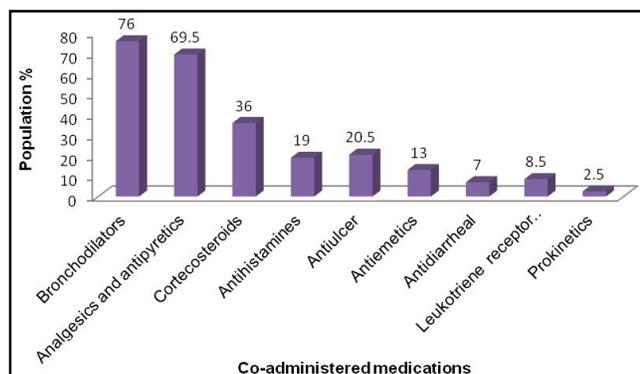


Fig. 4: Distribution of co-administered medications.

Table 7: Assessment of WHO prescribing indicators.

Sl. No.	WHO prescribing indicator	Result
1	Average number of drugs per prescription	4.25
2	Percentage of antibiotics prescribed by generic name.	45%
3	Percentage of antibiotics from WHO model list of essential medicines for children 2017	100%
4	Percentage of encounters with injectable antibiotics	91.5%

Most isolated organism

Among 200 patients studied, culture test was done in 55 patients. Out of which 16 showed positive test results and the remaining 39 were presented with negative results. *E. coli* was reported as the most isolated organism from 7 study subjects (3.5%) followed by *Staphylococcus aureus*. The details of the isolated organisms are summarized in Fig. 5.

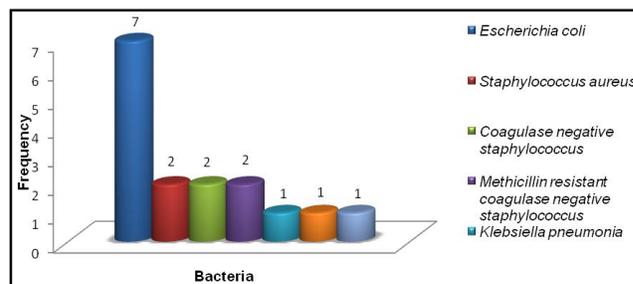


Fig. 5: Organisms isolated from the study subjects.

Antibiotic sensitivity pattern

E. coli, the most isolated organism showed maximum sensitivity towards nitrofurantoin, piperacillin-tazobactam and fosfomycin. Almost all the organisms were found to be sensitive towards ciprofloxacin and Trimethoprim-sulphamethoxazole.

Antibiotic Resistance pattern

E. coli, the most isolated organism showed maximum resistance towards gentamycin, ciprofloxacin, ampicillin, amoxicillin and cefixime. *Staphylococcus aureus* showed resistance towards benzyl penicillin, oxacillin

and erythromycin. Majority of the organisms were found to be resistant towards Gentamycin.

Average cost of antibiotics per prescription

Antibiotics accounted for a total cost of 1,24,857 INR. The average cost of antibiotic per prescription was found to be 624.28 INR. The costs incurred on different group of antibiotics are depicted in Fig. 6.

Discussion

In the present study majority of pediatric patients belongs to the age less than 2 years (45.5%), which can be attributed to the low level of immunity and susceptibility to infections of patients belonging to this age group. Similar results were seen in the studies carried out by Mishra *et al.*, (2014) and Woldu *et al.*, (2013), in which infections were mostly found in pediatric patients of age less than 2 years. (40.7% and 22.2% respectively).

There was a preponderance of male patients (57.5 %) when compared to the female patients (42.5%) which may be the reflection of general pattern of sex distribution in the population of the vicinity of study site. The studies conducted by Mishra *et al.*, (2014) and Shivaleela *et al.*, (2013), shows similar results. The mean of hospital stay was found to be 4.66 days. The results were similar to that reported by Prabahaar *et al.*, (2017), which was 5

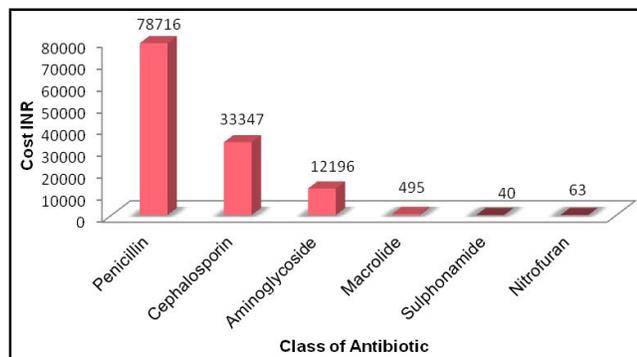


Fig. 6: Cost incurred by various class of antibiotics.

Table 8: Causative organism along with diagnosis.

Sl. No.	Causative organism	Diagnosis	No. of patients n=200
1	<i>Escherichia coli</i>	UTI	7
2	<i>Staphylococcus aureus</i>	URTI	2
3	<i>Coagulase negative staphylococcus</i>	LRTI	2
4	<i>Methicillin resistant coagulase negative staphylococcus</i>	LRTI	2
5	<i>Klebsiella pneumonia</i>	URTI	1
6	<i>Salmonella typhi</i>	Enteric fever	1
7	<i>Enterococcus species</i>	URTI	1

days and contradicts to the findings by Kanish *et al.*, (2014), (10.8 days). The shorter duration of the hospital stay indicates the better treatment facilities and techniques in the hospital. The mean duration of antibiotic therapy was 4.28 days which was less than the study conducted by Choudhury D.K. *et al.*, (2013), (6.05 days).

In the present study the most common indication for antibiotic use was respiratory tract infection (60.5%), in particular lower respiratory tract infections, which accounted for 41%. Similar results were reported by Mishra *et al.*, (2014), in which 61.4% of patients were diagnosed with respiratory tract infections. The results were contradictory to the findings seen in the study conducted by Narayan *et al.*, (2015) and Shivaleela *et al.*, (2013), in which gastroenteritis (31.5% and 20% respectively) was the most common indication for antibiotic use.

The average number of antibiotics per prescription was found to be 1.41 ± 0.53 and majority of the patients (61%) received single antibiotic therapy which was similar to the findings of Choudhury *et al.*, (2013), in which the average number of antibiotics per prescription was 1.41 ± 0.67 and 71% of the patients received single antibiotic therapy.

The most frequently prescribed class of antibiotic was found to be penicillins (53%) which was similar to the study conducted by Palikhe *et al.*, (2004), in which penicillins were prescribed for 64.1% of the patients, whereas the studies conducted by Kanish *et al.*, (2014), and Prabahaar *et al.*, (2017), reported the preponderance of cephalosporins (72.77% and 70% respectively). The combination of Amoxicillin- Clavulanic acid (43%) has been commonly prescribed among pediatric patients which was similar to the findings of Choudhury *et al.*, (2013), in which 35% of the patients have received amoxicillin-clavulanic acid.

Third generation Cephalosporins, ceftriaxone (22%) and Cefotaxime (20.5%) were the commonly prescribed ones among Cephalosporins. This was similar to the results of Kanish *et al.*, (2014), in which ceftriaxone and Cefotaxime accounted for 27% and 15% respectively. The increased rate of prescription of third generation antibiotics may be because, the patient could have already administered with lower generations of Cephalosporins and probably would have developed resistance towards it.

Bronchodilators (76%) were the frequently prescribed class of co-administered medication followed by analgesics and antipyretics (69.5%), which were similar to the findings of Feleke *et al.*, (2013), and

Shamshy *et al.*, (2011), in which bronchodilators were administered by 32% and 19.5% of the patients respectively. Antipyretics may be widely used due to the reason that, fever was chief complaint for admission in majority of patients. Increased use of bronchodilators can be attributed to the greater prevalence of respiratory tract infections among the study population.

Average number of drugs per prescription was found to be 4.25. This was greater when compared to the WHO standard (<2). The higher rates may be due to the reason that study is carried out in the in-patient setting. WHO indicators are more relevant among out-patient. But the values were similar with the findings of Narayan *et al.*, (2016), in which average number drugs per prescription was 4.23. Higher value indicates polypharmacy which can lead to increased risk of drug interactions, non-compliance to the therapy and increased cost of therapy.

In the present study only 45% percentage of the antibiotics were prescribed in the generic name which was considerably less than the WHO optimal value *i.e.* 100%. The results are higher than the values found in similar study conducted by Sharma *et al.*, (2016), in which only 30% of the antibiotics were prescribed in generic name. This shows the better performance of our hospital in this regard. The prescription by generic name is recommended which may reduce the cost to the patients.

In this study 100% of antibiotics were prescribed from WHO model list of essential medicines for children 2017, which was found to be exact with the WHO standard value *i.e.* 100%. In a similar study conducted by Akhtar *et al.*, (2012), 90% of the drugs were prescribed from the essential drug list. Prescribing medicines from the Essential list will reduce the irrationalities, by the appropriate selection of medicines and by minimizing the cost of therapy.

For majority of patients, antibiotics were administered by parenteral route (91%) which was considerably greater than the WHO optimal value which is less than 20%. (World Health Organization, Internet). This may be due to the reason that majority of the patients were admitted to the hospital in the advanced disease state which require parenteral administration of medicines. Also ceftriaxone and gentamycin which is frequently prescribed in the patients are available in parenteral form only. The results were similar to the findings of Narayan *et al.*, (2016), and Feleke *et al.*, (2013), in which 96% and 83% of the antibiotics were administered by parenteral route respectively.

Out of 55 patients in whom culture test was done, only 16 showed positive test results. The reduced number

of culture test being performed among the patients can be attributed to the reason that, treatment is based on the hospital antibiotic policy. Obtaining the cultures before initiating the therapy plays an important role in the patient care. In a similar study conducted by Palikhe *et al.*, (2004), culture was done only in 24 patients, out of which only 13 specimens showed positive results.

The most isolated organism was *E. coli* which accounted for 3.5 % which was similar to the results of Sriram *et al.*, (2008), in which *E.coli* were isolated from 2.5% of the patients. The antibiotic sensitivity and resistance pattern may aid in the selection of appropriate antibiotic and thereby ensuring the optimization of the therapeutic outcomes.

The average cost of antibiotics per prescription was found to be 624.28 INR. This was found to be less when compared to the findings of Kanish *et al.*, (2014), in which the average cost of antibiotics per prescription was found to be 3338 INR. Penicillin group of antibiotics accounted for the highest cost *i.e.* 63 % of the total cost which was similar to the findings of Kanish *et al.*, (2014), in which Beta lactams contributed mainly to the cost. Most of the patients will reach the tertiary care hospital in the advanced stage of disease or with prior exposure of antibiotics. So it becomes a necessity to prescribe higher generation of antibiotics which will increase the cost of therapy. The increase in cost of therapy may also lead to the non-adherence to the medications.

Conclusion

The present study gives an overview of the antibiotic prescription pattern in the pediatric patients. The most common clinical condition treated was lower respiratory tract infections (22.5%). Penicillin group of antibiotics (53%) were frequently used in the management of the infectious disease. Fixed drug combinations Amoxicillin-clavulanic acid (62%) was used commonly. As the resistance to the antibiotics are increasing day by day, prior culture test is preferred before initiating the therapy in possible cases and the antibiotics has to be selected based on the sensitivity and resistance pattern. *E.coli* was the most isolated organism and showed maximum resistance towards gentamycin, ciprofloxacin and ampicillin. 45% of the drugs were prescribed in generic name. The practice of prescribing drugs by generic names has to be promoted to reduce the dispensing errors and cost of therapy. The study concluded that the monitoring of the prescription is important in the pediatric population, to ensure the appropriate use of antibiotics and minimize the incidence of antibiotic resistance. The findings of the study will aid in developing antibiotic policy and will

contribute the antibiotic stewardship.

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