Research Article

Investigation of prescription pattern for antimicrobials in pediatric population at district general hospital

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Abstract

Background: Rational use of antibiotics is very essential for improving patient safety on long term use to avoid antibiotic resistance in pediatrics. **Objective:** The main objective of our research was to know the prescription pattern of antimicrobial agents in pediatric population. **Material and Methods:** A prospective observational study was conducted in the department of general medicine in district general hospital, Amravati for the period of 6 months. All patients of either sex aged <16 years receiving any category of antimicrobial agents were included and the prescribing and tapering pattern of antibiotics were reviewed. **Results:** Prescribing pattern was observed and analysed in 120 participants during the study period. The majority of the 120 children who received antimicrobials was males (61%) and hailed from rural and low socioeconomic background. Gentamicin, cefotaxime, ceftriaxone, amikacin, and amoxicillin were predominantly used which indicates that aminoglycoside and 3rd generation cephalosporins uses most frequently in the pediatric age group. The most common indications for these drugs were used for lower respiratory tract infection (LRTI), upper respiratory tract infection (URTI) and acute febrile illness (AFI). Two antimicrobial related ADR's were observed in the pediatric age group. **Conclusion:** Not much variation was found in the pattern of prescription amongst the healthcare professionals. Hence, the present study concludes that the prescribing pattern of antimicrobials in the pediatric patient of the hospital is found to be rational according to the guidelines.

Keywords: Pediatric, antimicrobials, prescription pattern, adverse drug reactions

Introduction

Pediatric care encompasses a broad spectrum of health services ranging from preventive health care to the diagnosis and treatment of acute and chronic diseases. The pediatric population comprises of 20-25 percent of the total world population, and numerous acute and chronic diseases can affect this sub population. Premature neonates have poorly developed organ functions and are at highest risk of eliciting unexpected toxicity or poor clinical response from sub optimal dosage regimens of drug usage. This alters the pharmacokinetics or dosage requirements in this population. Pediatricians and other medical personnel who provide health care for infants and children in developing countries are faced with numerous challenges due to the shortage of appropriate drugs, costs and lack of infrastructure, lack of data available on pharmacokinetic and pharmacodynamics of the pediatric population. Infectious diseases represent a major cause of morbidity and mortality in India and are responsible for a large proportion of hospital admissions, particularly in children. Antibiotics and other antimicrobials, therefore, constitute an important category of drugs, both in the community and in hospitals. The rising incidence of bacterial resistance to commonly used antibiotics, particularly the emergence of multi-drug resistant organisms has made it mandatory that antibiotics are used in pediatrics practice (Newland et al., 2012). The use of antimicrobial agents has become a routine practice for the treatment of pediatric illnesses and antibiotics are among the most commonly prescribed drugs in pediatrics. They are commonly prescribed for children with conditions for which they provide no benefit, including viral respiratory infections such

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as the common cold. Broad-spectrum antibiotic use is increasing which adds unnecessary cost and promotes the development of antibiotic resistance (Resi et al., 2003). Several professional societies have issued guidelines designed to reduce the use of antibiotics worldwide by means of various control strategies. Detailed knowledge of antibiotic prescription pattern is important before policies and measures can be implemented. Most of the drugs prescribed for children have not been tested in the pediatric population.

In pediatrics, the continuously increase use of antibiotics contributes to the emergence of antibiotic resistance. A study showed, from 511270 antimicrobial prescriptions 219257 children were identified (Resi et al., 2003). In addition adverse drug reactions and increase cost of therapy are also contributed features. Along with that the inappropriate use of antibiotics also is a key reason of bacterial resistance. Antimicrobial resistance of Streptococcus pneumoniae and Haemophilus influenzae presents a challenge to clinical case management, particularly in programs for acute respiratory tract infection)ARI(, including pneumonia, in developing countries (Mastro et al., 1993). According to the WHO, the rational medicine use included the appropriate use of medicine, in the proper dose, for an adequate period of time, and at the lowest cost to the individuals and their community. Globally, irrational drug use is a serious problem with WHO estimating that more than half of all medicines are being inappropriately prescribed, dispensed or sold (Versporten et al., 2013). The prevalence rates of inappropriate antimicrobial use of 37, 47, and 8% in India, Turkey and Israel respectively have been reported. Further studies in Africa including from Nigeria and Ethiopia have also reported high magnitude of inappropriate use of medicines (Abula and Desta, 1999). We face huge challenges in rational use of antimicrobials starting with general lack of awareness and unsatisfactory levels of personal hygiene and environmental sanitation to lack of surveillance mechanisms for monitoring antimicrobial use and resistance, mostly empirical use of antibiotics due to dearth of microbiology laboratory support, absence of or ineffective antibiotic use policies in most healthcare settings and nonhuman use of antimicrobials. With widespread use of antibiotics, the prevalence of resistance also increases. The association of resistance with the use of antimicrobials agents has been documented in both in- and out-patient settings. The occurrence of adverse drug reactions)ADRs(is another problem with antimicrobial use. ADRs in pediatric population may have relatively more severe effect than adults leading to significant morbidity among children (Prajapati and Bhatt, 2012). The various diseases in which antimicrobials are used most frequently in treatment of Upper respiratory tract infection (URTI), Pneumonia, Bronchiolitis, Asthma, Diarrhoea, Bacterial meningitis, Septicaemia, Typhoid fever, AGE)Acute gastroenteritis(, AFI)Acute febrile illness(. Rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, and the lowest cost to them and their community. Some of researchers reported studied for pattern of parenteral antimicrobial prescription among pediatric patients and prescribing pattern of antimicrobials in pediatric hospital for the children below one year or infants are at a special risk for receiving multiple courses of antibiotics. The rising prevalence of penicillin-resistant pneumococci worldwide mandates selective susceptibility testing and epidemiological investigations during outbreaks (Appelbaum, 1992). It have therefore become very important to monitor and evaluate the prescribing patterns of antibiotics in children. Considering the prevalence of use of antibiotics and severity of the problem of pediatric patient's setup the present research was planned to know 'pattern' of antimicrobials use in pediatric population.

Materials and methods

This is a qualitative study using prospective observational which conducted for six months to gather details about how patients perceive any category of antimicrobial therapy. Institutional ethics committee approval was taken (REC/17/GCOPA/4) at government district general hospital and Pharm. D pharmacy practice centre of Government College of Pharmacy Amravati for the study. The individuals briefed about the study and informed consent was taken prior to their participation in the study. Patients of either sex aged between 1month-16 years, if in-house prescription contained antimicrobial agents admitted to the department of pediatrics, medicine wards and intensive care unit (ICU).Patients of either sex aged >16 years of age, patient not willing to sign consent, unconscious patients were excluded.

Sample size was 120 populations of various departments over a period of 6 months from October 2017 to March 2018 in district general hospital, Amravati. The data was collected on a prevalidated case record proforma. Patient data relevant to the study has been collected from treatment charts/case sheets, laboratory reports and patient or patient's caregiver's interview by using patient data collection form. It includes the patient demographics data (name, age, gender, area) and occupation, the dosage regimen, duration of therapy, duration of hospitalization, laboratory data, adverse drug reaction, drug therapy and other relevant information. The result about various parameters was screened gender wise and age wise distribution, pediatric population use antimicrobials use,

rationality, concomitant and comorbid diseases etc. The filled-in patient proforma sheet entered and analyzed using Microsoft excel. The data generated in this study were analyzed for ADR, documentation and reporting of ADRs, appropriateness of drug, dose, frequency and duration. The data have been summarized by routine descriptive statistics, namely mean correlation from numerical variables, counts and percentages for categorical variables.

Results

During the study period of October 2017 to March 2018, one hundred and twenty in-patient's prescription was screened from district general hospital, Amravati. Among which all the 120 prescriptions were having the use of antimicrobial agents which was collected among the pediatric population. From 120 pediatric IPD population 47 children were found to be female (39%) and 73 children were found to be male (61%). The detailed demographic data is demonstrated in table 1. This can be attributed to the out-dwelling lifestyle and occupational outdoor stay of males. The data of 120 patients was distributed according to the area wise as slum, rural, urban among which 67 patients belong to the slum area, 62 patients belong to rural area and 31 patients belong to urban area. This data indicates that the children from slum area (67) are more prone to diseases that occur in pediatric population and children from urban area (31) are less prone to diseases. Slum patients are usually seen more in government hospitals due to the better cost effectiveness and affordable cost of the treatment.

The age groups were classified as per USFDA guidelines as neonates which include patients with age group from birth to 1 month of age, infants which includes the patients with age group from 1 month to 2 years of age, 3rd classification includes the children which consists of age group from 2 years to 12 years of age, and the last class includes the patients of group 12 years to <16 years of age, called as adolescents. Frequency of occurrence of diseases was seen to be more in the age group of 2 years to 12 years of age. Only 1 patient from the adolescent age group was found. 40 patients among 120 patients belong to the infant age group i.e, age of 2 years to 12 years.From 120 pediatric IPD population 47 children were found to be female (39%) and 73 children were found to be male (61%). Among the study of 120 patients, antimicrobials agents were used 340 times. Figure 1 is depicted commonly prescribed antimicrobial agents in pediatric population. In the present study, the most frequently antimicrobial agents used gentamycin, ampicillin, amoxicillin, cefotaxim, pipzo, ciprofloxacin, metronidazole, amikacin, artesunate, cotrimoxazole, doxycycline, tazobactam, piperacillin, framycetin, amoxclav, furazolidoneetc.Gentamycin is used in the frequency of 59, Cefotaxime 57, Ceftriaxone 43, Amoxicillin 34, Amikacin32, these were the most commonly used antimicrobials in the pediatric, and this indicates that gentamycin being a broad spectrum antibiotic was used more frequently among the pediatric population. Cefotaxim and ceftriaxone are mostly prescribed antibiotic in children as they have certain advantages that have made them a popular choice among pediatrician in the world. Moreover, Amoxicillin and amikacin are also among most frequently used drugs with frequency of 34 and 32

Table1. Basic demographic data *(n=120)*

Gender	Number of Patients	Number of Patients (%)
Male	73	61
Female	47	39
Area wise		
Slum	67	55.8
Rural	62	51.6
Urban	31	25.8
Age in years		
1 month	20	16.6
1 month - 2 yrs	19	15.8
2-12 yrs	80	66.6
>12 yrs	1	0.8

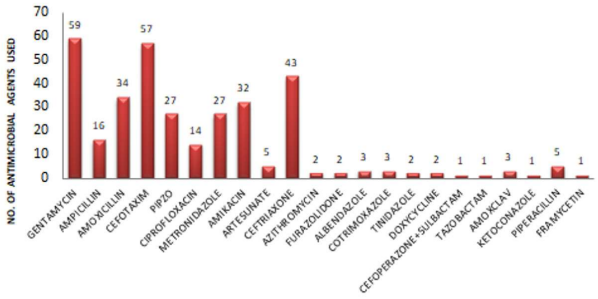

Figure 1. Commonly prescribed antimicrobial agents in pediatric population

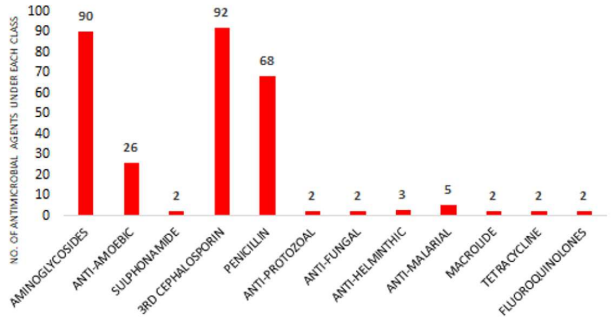

Figure2. Classification wise distribution of data

Table 2. Rationality of antimicrobial agents

Indications	Antimicrobial agents			
	Cefotaxim	Ceftriaxone	Amoxicillin	Amikacin
AFI	Yes	Yes	Yes	Yes
AGE	Yes	No	No	-
Blood infection	-	Yes	Yes	Yes
Enteric fever	Yes	Yes	No	No
Fracture	Yes	-	No	-
LRTI	Yes	Yes	Yes	Yes
URTI	No	No	Yes	-
Poisoning	Yes	-	Yes	-
CNS	Yes	Yes	-	Yes
Skin infection	-	No	No	-
UTI	Yes	Yes	Yes	-
Other	No	No	Yes	Yes
Eye infections	No	-	No	-

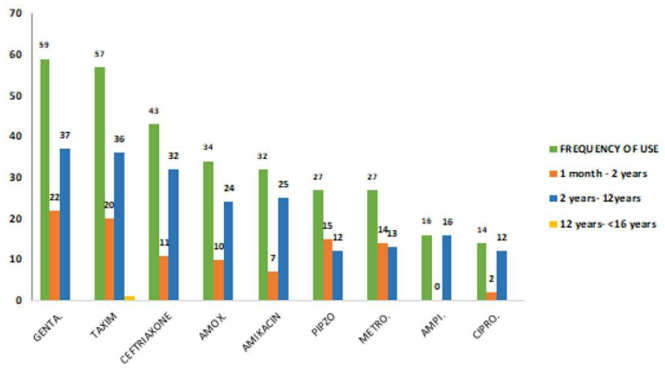

Figure3. Distribution of antimicrobial agents in age groups

respectively. Framycetin (1), ketoconazole (1), tazobactam (1), albendazole (3), cotrimoxazole(3), doxycycline (2), azithromycin (2) etc were the least frequent antimicrobial agents used in the prescription, of pediatric population.

Cefotaxim and ceftriaxone are mostly prescribed antibiotic in children as they have certain advantages that have made them a popular choice among pediatrician in the world (Figure 2). These include a broad range of antimicrobial activity, concentration dependent bactericidal activity, and excellent tolerance in pediatric patients with almost no dose-related toxicity. Amino glycosides antibiotics are less slightly used as compared to 3rd generation cephalosporin. Aminoglycoside antibiotics include Gentamicin and amikacin. Penicillin (68) and antiamoebic (26) are also used commonly. Less frequently used antimicrobial agents are sulphonamides, antiprotozoal, santifungal, antihelminthic, macrolide, tetracyclin, and fluoroquinolones. Figure 3 is depicted the data about the distribution of antimicrobial agents in various age groups such as infant, children and adolescents. Gentamicin (59) is most commonly used drug among

Table 3. Rationality of number of antimicrobials prescribed per prescription

Use of Antimicrobials	7 Antimicrobials	6 Antimicrobials	5 Antimicrobials	Rationality
No. of Days	4	4	4-11	
Enteric Fever	Yes	-	-	Irrational
Candidiasis with AFI	-	Yes	-	Irrational
Otitis Media Infection	-	-	Yes	Irrational
Malaria	-	-	Yes	Rational
AGE	-	-	Yes	Rational
AFI	-	-	Yes	Irrational
AFI with Anemia	-	-	Yes	Irrational

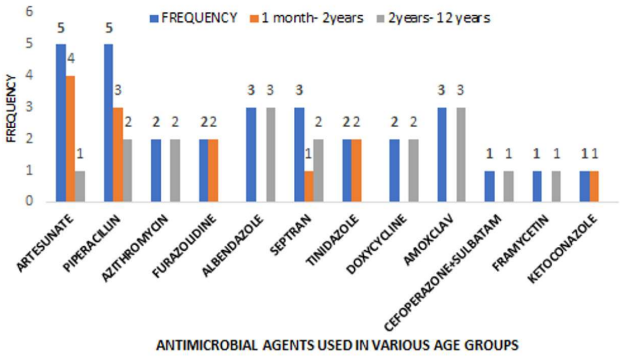

Figure 4. Distribution of less frequently used drugs

the age group of 2 years- 12 years and less in 1 month-2 years. Cefotaxim is used more in children and less in infants, and is the only drug used in adolescent in DGH, Amravati. In case, of Pipzo and Metronidazole are used less frequently in children i.e, 12 and 13 respectively and they are used more frequently in infant age group i.e, 15 and 14 respectively. Remaining drugs such as Amoxicillin, Amikacin, Ampicillin, ciprofloxacin are used more commonly in children age group rather than in infants.Rationality of antimicrobial agents is given in table 2. The rationality of various antimicrobial agents such Cefotaxim, Ceftriaxone, Amoxicillin, Amikacin which suggests that in AFI almost all the antimicrobials like taxim, amox, amikacin and ceftriaxone were used in acute febrile illness and none of these were used for treating eye infections. Cefotaxim was rationally used in AFI, AGE, enteric fever, fracture, LRTI, poisoning, CNS, UTI. Ceftriaxone was rationally used in AFI, Blood infections, enteric fever, LRTI, CNS, and UTI. Amoxicillin was rationally used in Blood infections, LRTI, URTI, poisoning, UTI and other related indications. Amikacin is seen to be rationally used in AFI, blood and CNS related infections, LRTI etc.

Among the less frequently used drugs such as artesunate, piperacillin, azithromycin, furazolidine, albendazole, septran, tinidazole, doxycycline, amoxclav, framycetin and ketoconazole, 2 drugs like artesunate and piperacillin are used most frequently in infant age group i.e 4 and 3 respectively. Albendazole, amoxclav are used almost equally in 2-12 years age group. Cefoperazone+sulbactam, framycetin and ketoconazole are very less commonly used (Figure 4). In the study population of 120 patients there were 41 prescriptions in which 2 antimicrobial agents were prescribed, 34 prescriptions in which 3 antimicrobial agents were prescribed, 26 prescriptions in which 4 antimicrobial agents were prescribed, 5 prescriptions were seen in which 5 antimicrobial agents were prescribed (Figure5). Equal distribution of 6 and 7 antimicrobial agents was seen in 1 prescription. Lastly the number of prescriptions containing single drug were found to be 12. The rationality of number of antimicrobial agents prescribed as per prescription in the population of 120 patients is given in table 3. Two cases of rationality were found in our studies which were used for the indication of malaria and acute gastroenteritis and 5 cases of irrationality were found for the indication of enteric fever, candidiasis with AFI, otitis media infection and AFI with anemia.

Figure 6 is represents the data distribution about the drug-drug interactions observed in the prescription studied among 120 pediatric populations. It was found from the study that among 120 prescriptions, interactions were found in 42 patients and there were no interactions seen in 78 prescriptions. Among 42 prescriptions 33 minor ADR's, 18 major ADR's which require significant monitoring and 4 serious ADR's were found. There were 34 prescriptions in which 1 interaction was found, 4 interactions in 1 prescription, 2 interactions in 4 prescriptions and 3 interactions in 3 prescriptions were found. 14 prescriptions were seen in which interaction was between 2 antimicrobial agents. Interaction of antimicrobial agent with other non-antimicrobial agent was seen in 28 prescriptions and 13 prescriptions shown interaction of non- antimicrobial agent with non-antimicrobial agent. Figure 7 is depicted the data about frequency of occurrence of diseases in pediatric population. There were 68 patients presenting with 1 disease or a single diseased state. 40 patients with 2 diseases i.e comorbidities were seen in 40 patients and 10 patients showed the condition of diseases occurring in same patient. 2 cases of patients presenting with 4 diseases were seen. 12 were assessed for concomitant diseases. Adverse drug

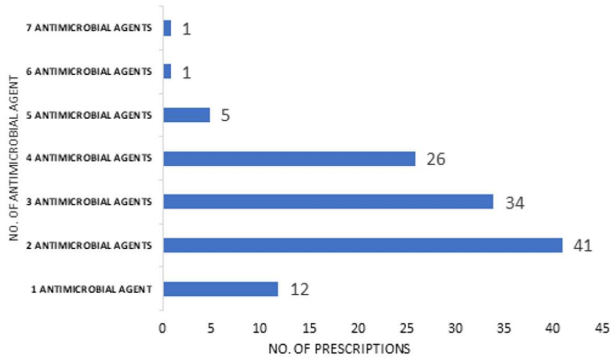

Figure5. Number of antimicrobial agents per prescription

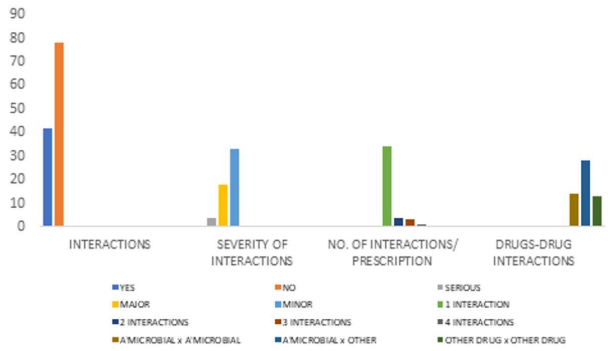

Figure 6. Data on drug- drug interaction found in prescriptions

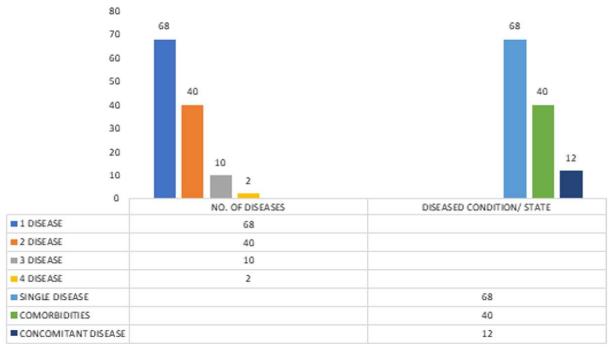

Figure7. Data on frequency of occurence of diseases

Table 4. Data on adverse drug reaction found in the study

Drug causing ADR	Classification	No. of ADR observed	Adverse reaction observed	Management
Amoxicillin	β-Lactam	1	Rashes	Withdraw of drug
Piperacillin	β-Lactam	1	Itching all over body	Withdraw of drug
Sodium Valproate	β-Lactam	2	Nausea and vomiting	Carbamazepine used as alternative

reactions are reason for concern if it occurring in the pediatric population. In our study we found three adverse drug reactions among which 2 were related to antimicrobial agents and 1 ADR is obtained from non- antimicrobial agent (Table 4). Piperacillin showed the ADR of itching all over the body which was given through IV route. Sodium valproate showed a less serious ADR of nausea and vomiting in children of age group 5 years, who was administering that drug since two years, which was then replaced with Carbamazepine.

Discussion

Antimicrobials are commonly used for the treatment of many infections which makes time to time reviewing of the prescription and rational prescribing of the drugs is essential to increase the therapeutic efficacy and decrease the adverse effects of the drugs in pediatrics. In addition, the study tried to describe the common diseases encountered and the commonly prescribed antimicrobial drugs. Considering the prevalence of use of antibiotics and its severity of the problem in patient, investigation of antimicrobials utilization pattern help to evaluate and analyze the reasons for increased and inappropriate use in population. The study will be use to improve the patient safety by observing the prescribing pattern as irrational use of antibiotics. From the observational data, the children from rural area (62) were prone to diseases as seen in slum area. The reason for such a large difference between both the population i.e, slum and urban may be socio-economic reason, lack of education, lack of awareness, not maintaining proper hygiene, living in open places, lack of knowledge regarding proper sanitation. Frequency of occurrence of diseases was seen to be more in the age group of 2 years to 12 years of age. Gentamycin is used in the most frequency as compared to other antimicrobials in the pediatric, and this indicates that gentamycin being a broad spectrum antibiotic was used more frequently among the pediatric population. Cefotaxim and ceftriaxone are mostly prescribed antibiotic in children as they have certain advantages that have made them a popular choice among pediatrician in the world. Moreover, Amoxicillin and amikacin are also among most frequently used drugs with frequency of 34 and 32 respectively. Even the data shows the use of 4 combination drugs those are Pipzo (piperacillin+tazobactam), Amoxclav (amoxicillin+clavulanic acid), cefoperazone and sulbactam, and cotrimoxazole (sulfamethoxazole+ trimethoprim). Cefotaxim is used more in children and less in infants, and is the only drug used in adolescent in district general hospital, Amravati. Cefotaxim was rationally used in AFI, AGE, enteric fever, fracture, LRTI, poisoning, CNS, UTI. Ceftriaxone was rationally used in AFI, Blood infections, enteric fever, LRTI, CNS, and UTI. Amoxicillin was rationally used in Blood infections, LRTI, URTI, poisoning, UTI and other related indications. Amikacin is seen to be rationally used in AFI, blood and CNS related infections, LRTI etc. The similar result was reported by Ashok Kumar Malpani et. al. (2016) for clinical guidelines for diagnosis and treatment manual for curative programmes in hospitals and dispensaries, guidance for prescribing to check the rationality of cefotaxime, ceftriaxone, amikacin and amoxicillin in the given indications (Malpani et al., 2016; Palikhe, 2004).

Two cases of rationality were found for the indication of malaria and acute gastroenteritis; and 5 cases of irrationality were found for the indication of enteric fever, candidiasis with AFI, otitis media infection and AFI with anemia.It was found from the study that among 120 prescriptions, interactions were found in 42 patients. Interaction of antimicrobial agent with other non-antimicrobial agent was observed in 28 and 13 prescriptions with non-antimicrobial agent. These findings as same as results obtained in the previous studies conducted by Rauniar et al., 2000; Kallariede et al., 2010. ADR due to Amoxicillin was found in ortho IPD, which was a certain ADR which causes rashes on the body of children. Piperacillin showed the ADR of itching all over the body which was given through IV route. Sodium valproate showed a less serious ADR of nausea and vomiting in children of age group 5 years, who was administering that drug since two years, which was then replaced with Carbamazepine. This finding is similar to findings of the study conducted by (Aagaard and Hansen, 2010). There was a lack of appropriate guidelines and drug interaction reporting is emerging scope of pharmacy should be considerable. Most of the drugs were prescribed for right indication to right patient, however some factors such as in appropriate drug history, improper mentioning of dose and frequency, wrong administration time, dose omission, improper dose tapering etc. were found to be deviating away from the rationality. The significance of the study is to improve the patient safety on long term use of antimicrobial therapy by observing the prescribing pattern as irrational use of antibiotics can increase the risk of adverse effects. Moreover, the lack of medical education from the health care professionals to the patients enforces the conduction of the study. It has therefore become very important to monitor and evaluate the prescribing patterns of antibiotics. A key strength of this study is supported by a recently published scoping review that found patients wanted sufficient information from pharmacists to allow them to make appropriate clinical decisions. Interestingly, overtime and perhaps with changing demographics and patients' expectations of healthcare professionals, researchers have found that an increasing proportion of patients prefer sharing decision roles with clinicians. Potential limitation

of this study was the limited sample due to short study period. The data were collected only from October 2017 to March 2018. Further studies using large and more complete data from various settings would be needed to solidify the findings in this study. Very few patients were available in dermatology department as most of the patient did not require hospital admission. Regional language barrier during communication with patients when supporting staff not available in the ward was another limitation.

Conclusion

In conclusion, the most commonly prescribed antimicrobial agents in the district general hospital includes gentamicin, cefotaxime, ceftriaxone, amikacin, and amoxicillin, which indicates that aminoglycoside and 3rd generation cephalosporins were used most frequently in the pediatric age group. The most common indications for these drugs were used for the treatment of LRTI, URTI, AFI and AGE. Antimicrobial agents are used most frequently in children age group, and the use of non-antimicrobial agents such as antipyretics, analgesics, IV fluids were used most commonly. Two antimicrobial related ADR's were observed in the pediatric age group. The drug-drug interactions were observed in many cases, but many of the drug use in the hospital for particular indications were found to be rational as compared to the irrational use. Hence, the present study concludes that the prescribing pattern of antimicrobials in the pediatric outpatient of the hospital is found to be rational according to the guidelines.

Author's Contribution

M.S: Participated in its design, coordination and helped to draft the manuscript, P.G: Collecting and recording data, participated in the design of the study, S.D: Data gathering and helped to draft the manuscript, R. T: Literature reviews, editing manuscript. All authors read and approved the final manuscript.

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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