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PRESCRIBING PATTERN of ANTIBIOTICS in PEDIATRIC HOSPITAL in NEPAL

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INTRODUCTION

Paediatrics is the branch of medicine dealing with the development, diseases and disorders of children. Infancy and childhood is a period of rapid growth and development. The various organs, body system and enzymes that handles the drugs develops at different rates. The immune systems are not fully matured. So, infants and children are among the most vulnerable population groups to contract illnesses. [1]

We are living in a environment that is heavily polluted by micro-organisms and other pollutants which directly affects person's health. Numerous acute and chronic diseases can effect paediatric population. Lower respiratory tract infections are the leading cause of death in children below five years of age. Acute respiratory infection, acute watery diarrhoea, sepsis and viral fever are the common childhood illnesses [2]. The use of antimicrobial agents, especially antibiotics has become a routine practice for the treatment of paediatric illnesses. According to the National Ambulatory Medical Care Survey (NAMCS), antibiotics are the second leading drugs prescribed in paediatrics [3]. Therefore, a proper selection of antibiotics along with prescribing of appropriate dose, formulation, pharmacokinetics profiles, response, and Adverse Drug Reactions (ADRs) is important.

Paediatrics is the special group of children mostly ranges between 0-12 years having different physical, mental and social health [3].

Excessive and inappropriate use of antibiotics causes increase incidence of ADRs, emergence of resistant microorganisms and associated infections, morbidity and mortality, drug toxicity, long hospitalization period, increase of healthcare costs, polypharmacy and suboptimal pharmacy [4]. It is observed in many studies that 20 - 50% of all antibiotic use is inappropriate and sub-optimal. Prescribing inappropriate spectrum antibiotic, indication of an antibiotic for little/no sign of bacterial infection, prolonged courses for minor infections and overuse of parenteral preparations are the general errors observed in antibiotic usage [5].

The rising incidence of bacterial resistance to common antibiotics, particularly, multi- drug resistant pneumococci, has prompted the need to use antibiotics judiciously in paediatrics. So, rational use of antibiotic is extremely important. As per the World Health Organization, 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 at the lowest cost to them and their community [6].Antimicrobial agents are the most commonly used and misused of all the drugs. The inevitable consequence of the widespread use of antimicrobial agents has been the emergence of antibiotic-resistant pathogens. The fact that one of the most important causes of acquiring resistance is the lack of rational antibiotic [7].

In order to describe the drug utilization pattern in health facilities, WHO developed a set of standarized drug use indicators which can provide a basis for planning and implementation of rational medicine use strategies if any problems are identified. Specially, the prescribing indicators are useful in identifying problems in general prescribing. They includes : Average number of drug per encounter (measures degree of poly medication), Percentage of drug prescribed by generic name (which measures the cost effectiveness of health system to produce and use drugs), the percentage of encounters with antibiotic and injection prescribed (measures the level of use of two important, but commonly overused and costly forms of drug therapy) and percentage of drugs prescribed from National Essential Medicine list [8].

Appropriate drug utilization studies have been found to be crucial to evaluate whether drugs are properly used and utilized in terms of medical, social and economic aspects. Hence, it is essential that antibiotic prescribing pattern should be assessed periodically in pediatrics.

RESEARCH OBJECTIVE:

General objective

To study antibiotic utilization pattern in paediatrics of Ishan Children and Women's Hospital.

Specific objective

- To identify disease pattern among paediatrics.
- To study the prescription pattern of antibiotic for paediatrics.
- To find out ADR due to antibiotics.
- To find out the antibiotic sensitivity pattern among paediatrics.

METHODOLOGY

Study site and design

The study was a hospital based prospective and cross-sectional study conducted in Ishan Children and Women's Hospital, Basundhara, Kathmandu, Nepal for a period of three months from July 2019 to September 2019.

Study Population

The study was done in the Inpatient Department of Ishan and Women's Hospital. The data was collected from the paediatric inpatient aged be upto 12 years to whom at least one antibiotic was used.

Sampling Method

All the pediatric Inpatients upto 12 years who were on antibiotic prescription and were willing to give consent were included in the study. The ward was visited daily and necessary information as per the data collection form were noted. The purposive sampling technique was used.

Data was collected by using a data collection form (pro-forma) which contained information on patient demographics, disease diagnosed, physical examinations, patient's history, investigations, and antibiotics used.

Sample size

For cross-sectional type of study,

Using formula,

n =

where,

z= 5% type 1 error = 1.96 (from table)

p = Expected proportion of population =50%

d = Marginal error = 5%

So, on calculating,

n =

= 384

More than 384 samples (upto 12 years)

CRITERIA FOR SAMPLE SELECTION

A. Inclusion criteria:

- Patients admitted to ward of either sex and with age upto 12 years.
- Patient to whom at least one antibiotic was prescribed.
- Patient who are willing to give consent.

B. Exclusion criteria:

- Out-patient and emergency pediatric patient.
- Patients of either sex aged upto 12 years of age.
- Patients who are not willing to consent.
- Unconscious patients. (E.g. continuous coma state).

RESULTS

Demographic distribution of patients in the study (n= 390):

Age

During the study period total 390 prescriptions were collected and assessed. In the study, patients were divided into three groups based on different age. Among 390 patients, the highest number of patients were in age group < 1 year i.e .44.6 % and lowest number were in age group 5-12 years i.e 20.3 %

Age in years	Frequency	Percentage (%)
< 1	174	44.6
1-5	137	35.1
5-12	79	20.3
Total	390	100

Table 1: Age distribution of patients in year

Gender distribution

Out of 390 sample size, 269 patients were male and 121 were female. The percentage of male and female patients was 69 %and 31 % respectively.

Distribution of disease pattern in different age group of patients (n= 390)

The most prevalent disease among studied patients was Pneumonia 117 (30%) followed by Surgical cases 82 (21%), Sepsis 56 (14.35), CNS disorder 34 (8.7%) and others are outlined in Table 2.

Diagnosis	Age			Total n(%)
	< 1 year	1-5 years	5-12years	
Pneumonia	66	41	10	117 (30)
CNS disorders	13	19	2	34 (8.7)
Haematological disorders	0	1	0	1 (0.25)
GI disorders	15	7	3	25 (6.41)
Urinary Tract Infections (UTI)	2	6	2	10 (2.56)
Enteric fever	2	18	15	35 (8.98)
Surgical cases	27	21	34	82 (21)

Mosquito repellent	0	1	0	1 (0.25)
ingestion				
Combinations	8	13	8	29 (7.43)
Total	174	137	79	390 (100)

Table 2: Frequency distribution o f d iagnosis i n paediatric population

COMBINATIONS

Febrile seizure with LRTI, Bronchiolitis with secondary infection,

Tonsilopharyngitis with ulcer, Sepsis with meningitis, Pharyngitis with ulcer, Subacute bowel

obstruction with pancreatitis, Neonatal jaundice with sepsis, Sepsis with pneumonia

Respiratory Tract Infections (RTIs) Pneumonia,

Pharyngitis, Tonsilitis, Bronchiolitis,

Tonsilopharyngitis, otitis media.

Postsurgical cases

Acute appendicitis, Laprotomy, Peridural phimosis, Jejunal arteriosus, Cystitis, Rectovestibular fistula, Perineal ectopic anus, Cytoscopy, Urethroplasty, Proximal penile

hypospadias, Thoracotomy, Inguinal hernia, Thyroglossal cyst

CNS DISORDERS

Meningitis, Seizure, Convulsion, Meningitis

Route of administration of Antibiotics

In this study, 94.96% of antibiotics were administered by parenteral routes and 5.03% were administered by oral route.

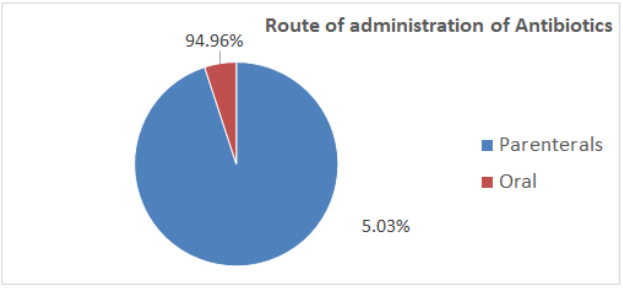

Figure 1: Routes of administration of antibiotics in the study

ANTIBIOTIC PRESCRIBED TO THE STUDY POPULATION (N=390)

In this study, the most commonly prescribed antibiotics was Beta-lactam antibiotics (51.94%) followed by Aminoglycosides (21%), Anti-anaerobics (11.32%), Fluoroquinolones (9.93%), Macrolides (5.51%). The least prescribed antibiotics were Sulphonamides (0.25%), Tetracycline (0.25%), and Colistin antibiotic (0.12%).

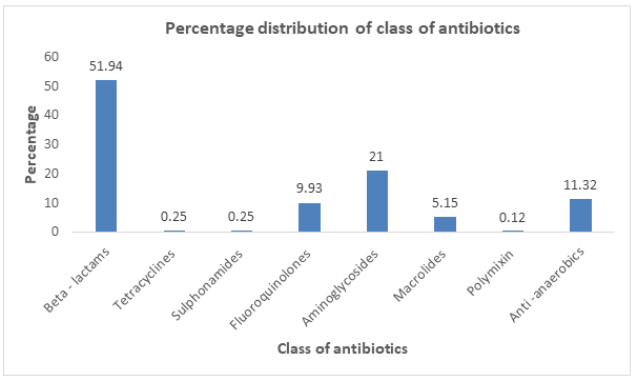

Figure 2: Antibiotics prescribed to study population

Distribution of Beta lactam antibiotics in the study

Among Beta-lactam antibiotics, Cephalosporin (40%) was found to be widely prescribed antibiotic followed by other cell wall inhibitors (7.16%) and Penicillin group (4.77 %).

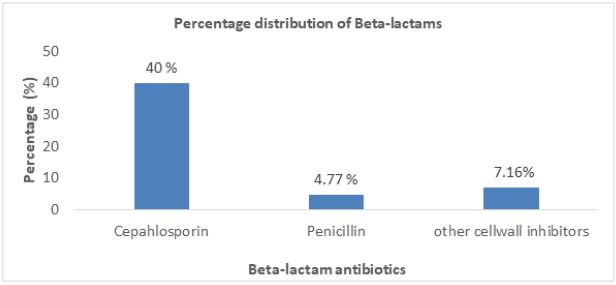

Figure 3: Percentage distribution of Beta lactam antibiotic

DISTRIBUTION OF CEPHALOSPORIN ANTIBIOTIC IN THE STUDY

It was found that among Cephalosporin, third generation Cefotaxime (48.74%) was leading antibiotic prescribed followed by Ceftriaxone + Tazobactam (31.76%), Ceftriaxone (9.43%) alone and other antibiotics.

Cephalosporin	Frequency	Percentage (%)
Cefotaxime	155	48.74
Ceftriaxone	30	9.43
Cefdinir	3	0.94
Cefixime	22	6.91
Cefipime	2	0.62

Ceftazidime	4	1.25
Ceftriaxone+ Tazobactam	101	31.76
Ceftriaxone + Sulbactam	1	0.31

Table 4: Percentage distribution of Cephalosporin

Penicillin and other Beta-lactam antibiotics prescribed in the study population

Other Beta-lactam antibiotics	Frequency	Percentage (%)
Ampicillin	16	4.4
Meropenem	14	3.84
Aztreonam	1	0.3
Vancomycin	15	3.88

Table 5: Penicillin and other Beta-lactams prescribed in patients

Commonly seen ADR (Adverse Drug Reaction) due to antibiotics

ADR was only recorded in patients receiving single antibiotics. The habit of recording adverse drug reaction must be encouraged at all level of health care institution. Fever was resulted due to Cefotaxime, diarrhea was mainly seen due to Cefotaxime and Tobramycin.

Drugs	Adverse Drug Reaction	Frequency
Cefotaxime	Fever	42
Cefotaxime	Diarrhea	6
Tobramycin	Diarrhea	4

Table 6: ADR seen in patients due to antibiotics

DISCUSSION

Most of the hospitalized pediatric patients belonged to age group of less than a year. This is indicative of susceptibility of infant below one year towards various infective diseases. The research study done by Thapaliya et al.; in 2015, Nepal [9] and Alemnew G et.al ; in 2015 ,Ethiopia also found that most of the study population were belonged to age group less than one year. This is because the immune system of babies less than one year are not fully developed and matured. For this reason, they are more prone to infections.

Similar findings were seen in other studies done by Palikhe N. in 2015 [27]. In an article by Maximilian and Philip, in 2014, mentioned that sex has a major impact on outcome from a range of infectious diseases starting from the beginning of life. They also quoted that morbidity and mortality rates are higher in males than in females throughout life which could be attributed to stronger humoral and cellular immune response to infection or antigenic stimulation in females than in males.[11]

Pneumonia was the leading cause of hospital admission among patients < 1 year of age.

Similar findings were seen in other studies done by Thapaliya K .et.al in 2015 [9] and Palikhe N in 2004 [27]. This shows uniformity in the diseases of the children irrespective of the different regions.

A report prepared by International Vaccine Access Centre (IVAC) in 2014 revealed that pneumonia in developing countries remain fairly stagnant despite of major reductions in these diseases globally. Pneumonia accounts for 15 % of deaths in children under 5 years old (WHO).

This may be due to lack of immunization against Pneumococcus, Hib (Haemophillus influenza type –B), Pertusis among paediatric population. Environmental factors such as air pollution, inappropriate hygiene habits and parenteral smoking may also increases child's susceptibility to Pneumonia and other RTIs.[1]

The second most common diagnosis was Surgical cases and it was done commonly in patients

aged from 5-12 years. Sepsis was more common in patients less than a year. CNS disorder

was most common in patients aged from 1-5 years. The percentage of injectable prescribed in the study was higher compared to the study done by Alemnew G et al in 2015 i.e (76%) [10] and Palikhe N. in 2004 i.e 75% [27] . The injectables were prescribed more because the study was only focused in In-patients.

The excessive use of injectable is common in many developing countries. Excessive use of parenteral can lead to pain and discomfort in pediatrics. It seems necessary for the pediatric patient to be treated by parenteral route of administration but especial consideration should be taken. Some infections like-CNS infections or patient groups like- neonates and infants requires parenteral use. As much as possible, parenteral usage should be minimized and should only be used in severe and emergency conditions for quick control of infections. It decreases administrative and family related costs of patients.

These results were in quite agreement with the research conducted by Alakhali et al. [18] and Kuber BR et.al [11] where Cephalosporin were the most commonly prescribed antibiotic 52% and 44.3% respectively. Higher prescription rate of Cephalosporin could be attributed to its broad spectrum of activity and tolerance across all age group. It has potent action on aerobic Gram negative as well as some Gram positive bacteria.

This may be due to Cefotaxime has received wide acceptance as a first line antibiotic for many infections in neonates, infants and children. It has favorable safety profile in infants. It exerts potent action on aerobic Gram positive and Gram negative organisms. Due to the broader spectrum of Cefotaxime compared to other antibiotics, it is often used as single agent and causes potentially lower toxicity. Due to better penetration

of Cefotaxime into the CSF, it is considered as standard therapy for treatment of meningitis.

However, Cefotaxime is not effective against anaerobes, particularly Staphylococcus aureus, Pseudomonas aeruginosa. So, caution must be exercised before using Cefotaxime as part of the standard empiric antibiotic strategy for infants. The widespread use of Cephalosporin is associated with the increase in development of resistance to Gram negative bacteria. In settings where broad-spectrum antibiotic use is common, Cephalosporin resistance are increasing.[25]

The antibiotics like Gentamycin, Amikacin, Azithromycin and Ceftriaxone was sensitive to all of the micro-organisms. The similar study done by Shamshy K et.al in 2011 [1] reported that commonly used antibiotic Amikacin was found to be resistant in five cases except in case of UTI. Three antimicrobial especially Penicillin, Gentamycin, Amoxicillin+ Cloxacillin were found resistant in almost all cases. The findings was different from this study.

Similar study done by Malpani AK et.al in India and Alemnew G et.al in Ethiopia also showed that Beta-lactams was the most commonly prescribed antibiotic i.e 67.43% and 60.6% respectively. This may be due to broad spectrum activity of Beta-lactam antibiotics. Also, compared to other classes of antibiotics, Beta-lactam agents are usually safe and well-tolerated among children.

In study done by Kuber RB et.al in India showed that Macrolide antibiotics- Azithromycin (26.2%) was the leading antibiotic prescribed followed by Cephalosporin's- Cefixime (24.3%) and the other antibiotics which was different from this study. The wider variation in common prescribed antibiotics might be due to empirical therapy in developing countries.

In this study, it was found that, in some cases, same pathogenic organism was isolated among different patients but, same antibiotic which was sensitive to one patients were resistant to others. This highlights that problem of antibiotic resistance is in growing condition. The bacteria which was supposed to be sensitive to particular antibiotic in all patients is now slowly developing resistance. This study suggests urgent national action plan to tackle antibiotic resistance. Awareness must be created among individuals that antibiotics should only be taken when prescribed by physicians. Also, physicians should prescribe antibiotics only when needed and avoid empirical therapy. The prescribing of antibiotics must be based on current treatment guideline and sensitivity pattern of organisms to avoid increase in bacterial resistance.

Also, this study highlights importance of Antimicrobial Susceptibility Testing. It gives physicians idea about resistance in organisms and choose the antibiotics which are susceptible to specific organism to treat infection.

CONCLUSION

In this study, Beta- Lactam was the most commonly used Antibiotics in pediatrics. Among them, Cefotaxime was the most frequently prescribed antibiotic among children under 1 year of age in Pneumonia. The results obtained in this study showed that the use of antibiotics per prescription was higher and generic prescribing was comparatively lower than WHO recommended value. Use of parenteral antibiotics was high. The most common ADR found due to Cefotaxime was fever. Only 165 samples were sent for culture test and among them, 13 were culture positive. The isolated organisms were Staphylococcus aureus, Streptococcus spp., Acinetobacter spp. and E.coli. Staphylococcus aureus. So, this study suggests that strategies and guideline for antibiotic prescription should be strictly implemented and empirical prescribing should be discouraged.

The information can be taken as a reference for the preparation of antibiotic treatment guidelines and related policies to reduce drug resistance. It can be used by policymakers to improve the prescribing and consumption of antibiotic properly.

LIMITATIONS

- The study was limited to Ishan Children and Women's Hospital only. Therefore, the study could not be generalized.
- This academic research was conducted within limitation of time and resources.
- The study was limited to small sample size.

REcOMMENDATIONS

- Empirical therapy and antibiotic overuse should be discouraged among physicians as they leads to development of bacterial resistance.
- Use of antibiotics should be guided by Culture and Antibiotic Sensitivity testing.
- Prescribers should follow Antibiotic Prescribing Guideline while prescribing for pediatrics.
- The habit of recording ADR must be encouraged among health care professionls. Pharmacovigilance programs must be mentioned in policies of hospital, heath institutions. Pharmacists must be in unique position to report ADR.
- The selection of antibiotic for prescription must be based on Hospital formulary and not on individual physician's preferences. For this Drug and Therapeutic Committee must be established in hospital.
- Physicians should follow the prescribing guidelines for pediatrics. Dose selection must be appropriate and calculations must be based on Body Surface Area.
- Physicians must consider various factors affecting drug profile in children before prescribing.
- Similar type of study should be conducted throughout the country to assess the pattern of antibiotic use.

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