



A STEP TOWARDS ANTIMICROBIAL STEWARDSHIP

Pediatrics

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ABSTRACT

INTRODUCTION : Antimicrobial resistance continue to increase and development of new antimicrobials is limited, making antimicrobial resistance a global concern. Antibiotic stewardship programs are being implemented worldwide to optimize antibiotic therapy. Despite increased awareness about the need of these programs, few ASPs exist and fewer comprehensive studies evaluate their effects.

AIM : To study the rationale of use of antibiotics in admitted pediatric patients in a tertiary care hospital.

MATERIALS AND METHODS : Retrospective analytical study done over a period of 6 months. Data was collected from case report files and analyzed. We analyzed the rationale of the choice of antibiotics, their dose, duration and route of administration in respect to the final diagnosis.

RESULTS : Out of 431 patients admitted during study period, 354(82.1%) patients were classified under diseases involving following major systems:

I. GIT

II. CNS

III. Respiratory system

I. GIT : Out of 144 patients, antibiotics were used in 53(36.8%). Antibiotic use could not be justified in 2.8% of GI diseases including Enteric fever(6.7%), Infective Hepatitis(9.9%), Bacillary Dysentery(12.5%), Gastritis(20%).

II. CNS : Out of 98 patients, antibiotics were used in 25(25.5%). Antibiotic use was not justified in 7.15%, comprising Febrile Seizures(8.8%), Epilepsy(2.8%), others(18.2%).

III. Respiratory system : Out of 89 patients, antibiotics were given in 55(61.8%) patients. Antibiotic use was not justified in 22.4%, comprising Pneumonia(41.6%), Bronchiolitis and WALRI(19.1%), others(9.4%).

IV. 12 patients with malaria and 5 patients with dengue were admitted. None received any antibiotics.

CONCLUSION :

GIT, CNS and Respiratory cases comprise 76.8% of the burden of admission. Out of total 431 patients, 151(35%) patients have received antibiotics, which was maximum in Respiratory illnesses and simultaneously maximum irrational antibiotic use is also seen in Respiratory illnesses.

KEYWORDS

Antibiotics, Rationale

INTRODUCTION :

Most of hospitalised patients receive antibiotics. These antibiotics are empirically started broad spectrum antibiotics without prior culture sampling. Rampant and irrational use of antibiotics leads to Antimicrobial resistance (AMR).

Nathwani and Sneddon[1] have described a rule of 30% on antibiotic prescription; which states that 30% of all hospitalized inpatients at any given time receive antimicrobials; over 30% of antibiotics are prescribed inappropriately in the community; up to 30% of surgical prophylaxis is inappropriate; 30% of hospital pharmacy costs are due to antimicrobial use.

Sale of antibiotics in India is on the rise with 40-60% increase over last five years.²

Indiscriminate use of antibiotics, over-the counter availability of antibiotics; laxity of regulatory bodies in approval of antibiotics; lack of public awareness about antibiotic resistance; injudicious use in veterinary practice; overburdened health infrastructure and inequity in healthcare contribute to increasing antimicrobial resistance.

WHO declared "Antimicrobial Resistance" as the theme for World Health Day, 2011. World Antibiotic Awareness week is held every year in November since 2015.

AMR leads to treatment failure, resulting increased morbidity and mortality, increased treatment costs and prolonged hospital stay, emergence of multidrug-resistant microbes, which are virtually non-treatable, thereby creating a 'post-antibiotic era' scenario; e.g. MDR-TB, XDR-TB, TDR-TB.

Antimicrobial stewardship program (ASP) was defined in 2007 by the Infectious Diseases society of America as "a cluster of interventions targeted towards the improvement and monitoring of appropriate antimicrobial use by selecting the most optimal drug regimen including the type of drug used, the dose, the duration of therapy and the route of administration".³

The main goals include :

- Improving patient outcome
- Improving patient safety
- Reducing resistance
- Reducing healthcare costs

WHAT NEEDS TO BE DONE?

- Appropriate empirical antimicrobial therapy, pending definitive diagnostic and culture reports
- Early and accurate identification of the pathogen and susceptibility
- Combination or monotherapy chosen on the basis of the pathogen identified
- De-escalation of initial broad spectrum therapy after definitive diagnosis.

Aims & Objectives :

The current study aims to study :

- Proportion of hospitalised patients prescribed antibiotics
- Specific antibiotics used in respect to specific diagnosis categorized systemically
- Percentage of irrational antibiotic use

in hospitalized patients over the period of 6 months.

MATERIALS AND METHODS :

- **Retrospective analytical study** method is used for the study.
- Data is collected from case report files. The final diagnoses are categorised systemically and the use of antibiotics is studied in respect to the final diagnosis.
- **Inclusion criteria** : Patients admitted in the pediatric ward of a tertiary care hospital over a period of 6 months from February 2017 to July 2017.

RESULTS :

Out of 431 patients admitted during study period, 151 (35%) received antibiotics. These 431 patients were studied under following groups :

Table 1 : Systemic distribution of patients

System	Number	%
GIT	144	33
CNS	98	23
Respiratory	89	21
Others	100	23
Total	431	100

A total of 431 admitted patients during study period, were categorized systemically according to their final diagnoses for study. 144 (33%) patients were of Gastrointestinal system, followed by 98 (23%) of Central Nervous system and 89 (21%) of Respiratory system.

Table 2 : Antibiotic use

System	Number	Antibiotic use	%
GIT	144	53	36.8
CNS	98	25	25.5
Respiratory	89	55	61.8
Others	100	18	18
Total	431	151	35

As shown in table 2, 151 out of 431 patients received antibiotics i.e. 35%. Of these 151 patients, 55 (39%) had respiratory illnesses followed by 53(37.6%) with Gastrointestinal illnesses and 25(16.5%) with Neurological illnesses.

Table 3 : GIT

Diagnosis	Antibiotics given	Total patients	%
ADD	8	49	16.32
Food poisoning	0	31	0
Cholera	21	21	100
Enteric fever	15	15	100
Infective hepatitis	3	11	27.27
Bacillary Dysentery	8	8	100
Gastritis	1	5	20
Surgical causes	4	4	100
Total	53	144	36.8

Out of 144 patients diagnosed with gastrointestinal illnesses, 53 (36.8%) received antibiotics. All 15 patients with Enteric fever received antibiotics. 8 out of 49 i.e 16.3% patients with Acute diarrheal disorder received antibiotics. 21 patients were diagnosed with Cholera and 8 with Bacillary dysentery; they all received antibiotics (100%). 3 (27.2%) out of 11 patients with Infective hepatitis, 1 (20%) out of 5 patients with Gastritis are given antibiotics. 31 patients are admitted with food poisoning, none of which received antibiotics.

Table 4 : CNS

Diagnosis	Total patients	Antibiotics given	%
CNS Infections	7	7	100.0
Febrile seizures	45	9	20.0
Epilepsy	35	4	11.4
Others	11	5	45.5
Total	98	25	25.5

25 out of 98 patients admitted with Neurological illnesses received antibiotics i.e 25.5%. 9 (20%) out of 45 patients admitted with Febrile seizures are given antibiotics. Whereas, of 35 patients admitted with diagnosis of Epilepsy, 4 (11.4%) received antibiotics. 6 (85.7%) patients with CNS infection received antibiotics out of 7.

Table 5 : Respiratory System

Diagnosis	Total patients	Antibiotics given	%
Pneumonia	36	36	100.0
Bronchiolitis	16	2	12.5
URTI	8	8	100.0

Measles	6	2	33.3
WALRI	5	2	40.0
HRAD	5	0	0.0
ARDS	4	4	100.0
Kerosene poisoning	4	1	25.0
Pertussis	2	2	100.0
Diphtheria	1	1	100.0
Near drowning	1	1	100.0
Hemoptysis	1	0	0.0
Total	89	59	66.3

59 (66.3%) out of 89 patients admitted with Respiratory illnesses received antibiotics, which includes all 36 (100%) patients with Pneumonia, 8 (100%) patients with URTI, 4 (100%) patients with ARDS, 2 (100%) patients with Pertussis, 1 (100%) with Diphtheria and 1 (100%) near drowning. 2 (40%) out 5 patients with WALRI, 2 (33.3%) out of 6 patients with measles, 1 (25%) out of 4 patients with Kerosene poisoning, 2 (12.5%) out of 16 patients with Bronchiolitis received antibiotics. None of the patients with HRAD and Hemoptysis are given antibiotics.

Table 6 : Other illnesses

Diagnosis	Total patients	Antibiotic use	%
Malaria	12	0	0
Dengue	5	0	0
Viral illnesses	83	18	21.68

18 out of 83 (21.68%) patients with a diagnosis of viral illnesses are given antibiotics. 12 patients with malaria and 5 with dengue illnesses did not receive antibiotics.

DISCUSSION :

Currently, antimicrobials are the most common category of drugs in the world. In 2004, the World Health Organization reported the figure for unwarranted antibiotics prescriptions standing at roughly 50%.⁸

Research has demonstrated a correlation between antibiotic use and resistance development. Drug use may be influenced by patient, prescriber and health care system related factors. Developing countries have high infectious disease burden, limited access to quality healthcare, lax regulations on manufacturing and marketing policies, lack of public awareness, easy over the counter availability of drugs leading to irrational antibiotic use and increasing antimicrobial resistance.⁹

Out of total 431 patients admitted during our study period, 151 (35%) received antibiotics, compared to 82% in Teaching hospital and 79% in Non-Teaching hospital in Ujjain in a study by Sharma et al.¹⁰

Out of these 431 patients, positive culture feedback was available in only 12 (2.8%) patients. The irrational use of antibiotics was seen maximally in patients admitted with respiratory illnesses 22%, followed by CNS conditions 7% and least in patients with Gastrointestinal illnesses 3%.

Global Scenario :

Contrary to expectations, antibiotic misuse and overuse is common not only in developing countries but also in the developed world.⁸

A European study presented in May 2004 reported 36% use of antibiotics within 2 weeks of symptoms in children , most frequently for acute respiratory infections (ARI) and diarrhoea-like syndromes.⁸

A large study in USA found 51% prevalence of antibiotic use for cold and URTI and over 20% of all antibiotic prescriptions were clinically useless. It was also found that only 20-25% of antibiotic use in USA was supported by results of culture and sensitivity tests.¹¹

A WHO study of antibiotic use in 13 low-, middle- and high income countries from 1992 to 1996 revealed that antibiotics were wrongly prescribed for approximately 30% of cases of URTI.¹²

In Australia, less than 50% of antibiotic use was as per antibiotic guidelines in a teaching hospital in Melbourne.⁸

A WHO-World Bank supported study found an antibiotic overuse of 43% in Indonesia.75-86% of patients received antibiotics for upper respiratory tract infection.¹³

In Pakistan, antibiotics accounted for 76% of prescribed drugs and almost 75% of antibiotics were given parenterally.¹⁴

In Nepal, 50.2% of the prescriptions contained an antimicrobial and 84.5% of the antimicrobials use was not supported by any evidence of infection. The prescription frequency of combination antimicrobials was 14.6%, of which 84.5% of combination prescriptions were for ampicillin + cloxacillin.⁸

In our study, 31 (7.2%) patients out of 431 received combination antibiotics. Antibiotics used are categorized systemically and analysed for rationale in respect to the final diagnosis.

1. GIT :

53 (36.8%) out of 144 patients admitted with diseases involving the Gastrointestinal system were given antibiotics.

1) Enteric fever :

Out of 15 patients admitted with enteric fever, 8 were culture proven and 7 patients were clinically suggestive of enteric. Third generation cephalosporins were started. Out of these, only 1 patient did not respond after 3rd generation cephalosporin, which was omitted after 8-10 days, and oral Azithromycin was started, defervescence was seen after 3 days and patient was discharged on Syp Azithromycin.

2) ADD :

Out of 49 patients admitted with acute diarrheal disease, antibiotics-3rd generation cephalosporin was started in 8 patients. Out of these 8 patients,

- 5 patients had underlying Severe Acute Malnutrition
- 3 patients were young infants with mismanaged feeding. Antibiotics were started and once sepsis was ruled out, they were discontinued.

3) Infective Hepatitis :

Out of 11 patients admitted with hepatitis, antibiotics were started in 3 patients. 2 out of these 3 patients presented with hepatic encephalopathy. In 1 patient, IV Ampicillin was given for 3 days, which cannot be justified.

4) Others :

- 31 patients admitted with food poisoning did not receive any antibiotics.
- Out of 5 patients admitted with gastritis, 4 did not receive any antibiotics. In 1 patient with chloride responsive alkalosis due to emesis, IV 3rd generation Cephalosporin was given for 6 days, which cannot be justified.
- 21 patients admitted with cholera, diagnosed by stool microscopy were rationally treated with single dose of oral Doxycycline.
- 8 patients were admitted with bacillary dysentery, of which 6 received oral cefixime. 2 patients were started on parenteral 3rd generation cephalosporin which was shifted to oral within 1 day. 1 patient had associated comorbidity in form of SAM. In 1 patient, the use of parenteral 3rd generation cephalosporin could not be explained.
- In 4 patients with surgical and other causes also, the use of antibiotics was rational.

2. CNS

25 out of 98 patients admitted with diseases involving the Nervous system received antibiotics.

1) Febrile seizures :

Out of a total 45 patients admitted with Febrile seizures, antibiotics were started in 9 patients in the form of IV 3rd generation Cephalosporins.

Out of these 9 patients,

- 4 patients were admitted in PICU
- GCS score less than 8 in 1 patient
- There was no expiry
- Mean duration of antibiotics was 4 days

Though antibiotics were started in these patients as they were admitted in PICU, but were discontinued within 3-4 days.

2) Epilepsy :

Out of a total of 35 patients admitted with epilepsy, antibiotics-IV 3rd

generation Cephalosporins were started in 4 patients.

Out of these 4 patients,

- 2 patients were admitted in PICU
- GCS score was less than 8 in 1 patient
- There was no expiry
- Mean duration of antibiotics was 3 days

Most common reasons to start antibiotics in these patients was admission in PICU and low GCS scores. Though antibiotics were started in these patients, they were stopped within 2-3 days.

3) CNS Infections :

Out of 7 patients admitted with CNS infections, 5 patients had viral meningoencephalitis, 1 patient had bacterial meningitis, 1 patient had cerebral malaria. In 5 patients with viral meningoencephalitis, antibiotics – IV 3rd generation Cephalosporin was started due to PICU admission and low GCS scores, but were discontinued within 3-4 days. In 1 patient with Pyogenic meningitis with hydrocephalus with EVD, IV 3rd generation Cephalosporin and Vancomycin were continued for 21 days. In 1 patient with Cerebral malaria, no antibiotics were given.

Thus, in CNS infections, antibiotic selection and use was rational in all patients.

4) Others :

In other 11 cases of trauma, transverse myelitis, hypocalcemic seizures, infantile tremor syndrome, hysteria, the use of antibiotics was rational.

3. Respiratory System :

55 (61.8%) out of 89 patients admitted with Respiratory illnesses received antibiotics.

1) Pneumonia :

Total 36 pneumonia patients were admitted, of which

- 15 were uncomplicated cases of lobar consolidation who received IV 3rd generation cephalosporin for a mean duration of 3 days and then shifted to oral cephalosporin with total treatment duration of 7-10 days.
- 21 patients presented with complicated pneumonias. Most common associated conditions in these patients were comorbidities like SAM, measles and complications like pleural effusion, empyema and other infections like meningitis.
- 5 of these complicated pneumonia patients were treated with only 3rd generation cephalosporins.

- In other 14 patients, other antibiotics were used such as
- IV Piperacillin- Tazobactam
- IV Vancomycin
- IV Clindamycin
- IV Ampicillin-Sulbactam
- IV Cefotaxim-Amikacin.

2) Bronchiolitis :

Out of 16 patients admitted with Bronchiolitis 2 patients received antibiotics. One patient was 1.5 month young infant with severe bronchiolitis on ventilatory support and received IV 3rd generation Cephalosporin and Aminoglycoside which were stopped after 4 days. Another patient was 7 month old with severe bronchiolitis who was started on IV 3rd generation Cephalosporin which was omitted within 2 days.

3) Others :

- 5 patients were admitted with **WALRI**, of which 2 received 3rd generation cephalosporin with a mean duration of 3-4 days, which cannot be justified.
- 2 patients were admitted with **Pertussis**, of which one received 10 days IV Piptaz and Vancomycin and 5 days of oral Azithromycin, while other patient was started on oral azithromycin.
- 6 patients with measles were admitted of which 2 patients with **measles with pneumonia** were admitted of which one received antibiotic IV Ceftriaxone and Vancomycin which was GCA child with FTT and multisystemic affection.
- 4 patients with **ARDS and cardiorespiratory failure**, parenteral 3rd generation cephalosporins with IV Vancomycin, Piperacillin-Tazobactam, Ampicillin-Sulbactam were used. These were critical patients admitted in PICU, requiring assisted ventilation and

- ultimately leading to expiry.
- 5 patients with **HRAD** were not given any antibiotics.
- 8 **URTI** patients were treated with oral amoxiclav, as combination was only available in hospital supply.
- In **Diphtheria**, IV 3rd generation Cephalosporin and Clindamycin were given.
- Of 4 patients with **Kerosene poisoning**, in 1 patient IV Ceftriaxone was started which was omitted within 2 days.
- In **near drowning**, the choice of antibiotics was rational.
- 1 patient with **Hemoptysis** was not given any antibiotic.

4. 12 patients with **Malaria** and 5 patients with **Dengue illnesses** were admitted. None received any antibiotics.

5. 83 patients were discharged with diagnosis of **Viral fever**, of which 18 had received empirical antibiotic – parenteral 3rd generation Cephalosporin on admission, which was discontinued within 3-4 days.

CONCLUSIONS

Maximum irrational use is seen in Respiratory illnesses 22% followed by 7% in Neurological illnesses and 3% in Gastrointestinal illnesses.

- Use** of antibiotics could not be justified in **7.2%**
- Choice** of antibiotics could not be justified in **11.1%**
- Route** of antibiotics could not be justified in **6.7%**
- Overall** antibiotics could not be justified in **11.4%**
- Duration of antibiotics was according to standard protocols.

Antibiotics used :

- IV 3rd generation Cephalosporins
- IV Ampicillin
- IV Piperacillin-Tazobactam
- IV Vancomycin
- IV Aminoglycoside
- IV Clindamycin
- IV Ampicillin-Sulbactam
- Oral 3rd generation Cephalosporins
- Oral Macrolides
- Oral Amoxiclav
- Oral Doxycycline

Dose : According to standard treatment guidelines

Duration : According to standard treatment protocols

Route : Antibiotics were started intravenously in most of the cases as most patients who were admitted were sick, as the stable patients were treated on OPD basis and hence not included in study. These antibiotics were then deescalated to oral as soon as the general condition of patient improved.

Limitations of Study :

The present study does not include

- Cost of treatment, and
- Duration of hospital stay.

Recommendations :

- Sensitization and regular updation of medical and paramedical personnel for the rational use of antibiotics should be carried out from time to time.
- Availability of reliable and early culture feedback will allow more specific use and choice of antibiotics.
- In uncomplicated CAPs, oral Amoxycillin instead of 3rd generation Cephalosporins could have been used as 1st line therapy.
- Stewardship programmes should be started and continued.

REFERENCES

- Nathwani D, Sneddon J. Practical guide to antimicrobial stewardship in hospitals. Available from: <http://bsac.org.uk/wp-content/uploads/2013/07/Stewardship-Booklet-Practical-Guide-to-Antimicrobial-Stewardship-in-Hospitals.pdf>. Accessed June 25, 2015
- Lawrence R, Jeyakumar E. Antimicrobial resistance: A cause for global concern. BMC Proc. 2013;7 (Suppl 3):S1.
- Yewale VN. IAP-ICMR Call to Action to tackle the antimicrobial resistance. Indian Pediatr. 2014;51:437-9.
- Antimicrobial Stewardship in Pediatrics: An Indian Perspective #NIDHI BEDI AND PIYUSH GUPTA
- Infectious diseases Society of America (IDSA). Promoting Antimicrobial Stewardship in Human Medicine. Available from: http://www.idsociety.org/stewardship_policy/. Accessed July 1, 2015.
- R.M.Klieman, Staneton ,N.F.Scor , J.W.Stgeme III, R.E. Beherman: Nelson Textbook of pediatrics 20th (1st south asia) edition
- O.P. Ghai, Vinod K. Paul, Arvind Bagga: Ghai essential pediatrics 8th edition

- Gaash, B. Irrational Use of Antibiotics. Available from : <http://www.indmedica.com/journals.php?journalid=3&issueid=124&articleid=1656&action=article>
- Ahiabu MA, Tersbøl BP, Biritwum R, Bygbjerg IC, Magnussen P. A retrospective audit of antibiotic prescriptions in primary health-care facilities in Eastern Region, Ghana. Health Policy Plan. 2016;31(2):250-258. doi:10.1093/heapol/czv048
- Sharma, M., Eriksson, B., Marrone, G. et al. Antibiotic prescribing in two private sector hospitals; one teaching and one non-teaching: A cross-sectional study in Ujjain, India. BMC Infect Dis 12, 155 (2012). <https://doi.org/10.1186/1471-2334-12-155>
- Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. J Am Med Assoc. 1997;278(11):901-4.
- Swindell, P.J., Reeves, D.S., Bullock, D.W., Davies, A.J. and Spence, C.E. Audit of antibiotic prescribing in a Bristol hospital. British Medical Journal. 1983; 286:118-122.
- Arustiyono. Promoting rational use of drugs at the community health centres in Indonesia, 1999, WHO World Bank Health Project IV. (http://dcc2.bumc.bu.edu/prdu/Other_Documents/ARUS_INDONESIA_PRDU.htm)
- Memon K. Use of drugs in Sind Province Pakistan primary health care facilities. (http://dcc2.bumc.bu.edu/prdu/Other_Documents/Khalil_Concentration_Paper.htm).