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**Original Research Article**

# Study of antimicrobial use in paediatric inpatients in a tertiary care hospital in Ahmedabad, India

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## ABSTRACT

**Background:** Inappropriate use and overuse of antibiotics are important factors leading to increased bacterial resistance apart from increased risk of adverse reactions. The aim of this study was to derive antibiotic use percentage, study its pattern and compare antibiotic prescribing indicators with standard indicators.
**Methods:** This prospective observational study was conducted from 1st August 2018 to 31st July 2019 on paediatric inpatients from 1 month to 14 years. All the relevant data was taken from the case records of patients at the time of discharge. The data included: age, sex, hospital stay, clinical diagnosis and details of antimicrobial treatment.
**Results:** From 989 patients, 85.9% were diagnosed with infectious illness, of which 60.1% had viral and 36.7% had bacterial infection. The use of antimicrobial drugs was 42.7% and antibiotics was 40.4%. The mean number of antibiotics received was 1.13±0.31. 90% patients received single antibiotic. 88.8% drugs were prescribed by generic name and 99% drugs were prescribed from essential drug formulary. 17 different antibiotics were used out of which ceftriaxone (62.5%) was the most commonly used. Groupwise, antibiotic use was cephalosporins (68.4%), penicillin (20.2%), aminoglycosides (4.31%), fluoroquinolones (0.9%) and macrolides (0.22%). The use of higher antibiotics like vancomycin (3.86%) and carbapenems (0.68%) was quite less.
**Conclusions:** The antibiotic use in our hospital was higher than the WHO standard but less as compared to majority of other studies. Use of cephalosporins was more and penicillin was less as compared to other studies. This suggests that there is a need of implementing antibiotic stewardship programs to enhance rational antibiotic prescribing.

**Keywords:** Antimicrobials, Antibiotics, Paediatric, Rational, Prescribing

## INTRODUCTION

Infectious diseases caused by antibiotic resistant organisms result in high morbidity and mortality globally.[1] Inappropriate use and overuse of antibiotics are the most important factors leading to increased bacterial resistance. This further leads to poor patient outcome and spread of infections due to multi drug resistant organisms.[2] In clinical practice, antibiotics can be overprescribed; for example, antibiotics can be prescribed for conditions in which antibiotics are not indicated such as respiratory viral illnesses.[3] Also, the inappropriate use of broad-spectrum agents when narrower spectrum agents are indicated is common.[4]

Antibiotic use among children should receive particular attention because the high frequency of community acquired infections, longer life expectancy and increased risk of exposure to antibiotic resistance strains in future.[5]Although rates of serious bacterial infections are low in children, the rates of antimicrobial use and resistance are comparable with adults. Antimicrobial stewardship programmes in paediatrics have unique characteristics and issues.[6]

India is a lower middle-income developing country and has high potential for overuse and misuse of antibiotics and have less public awareness of antimicrobial resistance.[7] The world health organization has developed prescribing indicators to measure the rational usage of drugs in primary care and to assess the prescribing pattern of antibiotics.[8]

The primary aim of this study was to derive antibiotic use percentage, study its pattern and compare antibiotic prescribing indicators with standard WHO indicators as well as with other regions and countries. Simultaneously we also studied common clinical and etiological diagnosis as well as identified common bacterial isolates.

## METHODS

This prospective observational study was conducted in the department of paediatrics at a tertiary care teaching and general hospital located in Ahmedabad, Gujarat state, India. The study was approved by institutional scientific and ethical committee. The study duration was of one year from 1st August 2018 to 31st July 2019.

All the patients from 1 month to 14 years hospitalized during the study duration were included in the study. Patients who took discharge against medical advice or were transferred to other centres were excluded. All the relevant data was taken from case records of patients at the time of discharge. The data included: age, sex, hospital stay, clinical diagnosis, antimicrobial treatment and microbiology workup (bacterial isolates on blood and urine cultures and their antibiotic sensitivity pattern). As per the clinical diagnosis the patients were grouped into viral, bacterial, protozoal or tuberculous illness. Our operational definition of antimicrobial agent included synthetic as well as naturally obtained drugs that attenuate microorganisms thereby covering all antibacterial, antifungal, antiviral and antiprotozoal agents. The details of antimicrobial treatment included prescription name (generic or trade name), number and duration of antimicrobial agent. All the relevant data was then entered in Microsoft excel sheet and data was analysed using MS excel 2007 and IBM SPSS statistics 20.

## RESULTS

From August 2018 to July 2019, 989 patients were admitted who fulfilled the inclusion criteria. Out of this 536 (54.2%) were male and 453 (45.8%) were female. Male to female ratio was 1.18:1. The age range was 1 month-1 year:249, 1-5 year:342, 5-10 year:218 and 10-14 year:180.

As per the final diagnosis given at discharge, 850 (85.9%) patients were diagnosed having infectious illness whereas the rest 139 (14.1%) patients were diagnosed with non-infectious illness. Out of the total 850 patients with final diagnosis suggesting infectious illness, 511 (60.1%) patients were diagnosed having viral infection, 312 (36.7%) with bacterial infection, 15 (1.7%) with both bacterial and protozoal infection, 9 with protozoal infection (1.05%) and 3 with tuberculosis (0.35%) (Table 1).

**Table 1: General characteristics of pediatric inpatients during the study period (n=989).**

| Variable | Categories | Frequency N (%) |
|---|---|---|
| **Sex** | Male | 536 (54.2) |
| | Female | 453 (45.8) |
| **Age (in year)** | 1 month-1 | 249 (24.4) |
| | 1-5 | 342 (34.6) |
| | 5-10 | 218 (22.04) |
| | 10-14 | 180 (18.2) |
| **Type of clinical diagnosis** | Non infectious disease diagnosis | 139 (14.1) |
| | Infectious disease diagnosis | 850 (85.9) |
| | Viral | 511 (60.1) |
| | Bacterial | 312 (36.7) |
| | Bacterial, protozoal | 15 (1.7) |
| | Protozoal | 9 (1.05) |
| | Tuberculosis | 3 (0.35) |
| **Length of hospital stay (days)** | Mean | 5.57±3.97 |
| | Range | 1-30 |
| **Outcome** | Discharge | 982 |
| | Death | 7 |

The six most common diagnosis from 511 patients with viral infections were, viral fever in 251 (49.1%), acute diarrheal disease in 93 (18.2%), viral wheeze in 48 (9.4%), bronchiolitis in 44 (8.6%), dengue in 40 (7.8%) and acute viral hepatitis in 24 (4.7%). The six most common diagnosis from 312 patients with bacterial infection were, enteric fever in 130 (41.6%), urinary tract infection in 62 (19.9%), pneumonia in 49 (15.7%), tonsillitis in 17 (5.4%), liver abscess in 17 (5.4%) and dysentery in 9 (2.9%). 9 patients were diagnosed with *P. vivax* malaria and 3 were diagnosed as tuberculosis. The mean duration of hospital stay was 5.57±3.97 days (range: 1-30 days, median: 4 days). Out of the total 989 patients, there were 7 deaths and remaining patients were discharged (Table 1).

Blood and urine cultures were sent in all the patients with suspected bacterial infection. Blood culture was positive in 74 patients. The most common organism was *Salmonella typhi* (59), followed by *Salmonella paratyphi* (8), methicillin resistant S*taphylococcus aureus* (MRSA) (2), *Brucella* species (2), Methicillin sensitive *Staphylococcus aureus* (MSSA) (1), *Salmonella* species (1) and *Klebsiella* (1) (Figure 1). Urine culture was positive in 55 patients. The most common organism found was *E. coli* (48), followed by *Proteus vulgaris* (5) and *Klebsiella* (2) (Figure 2).

Of the total 989 patients, 423 (42.7%) patients were given antimicrobials. 400 (40.4%) patients received antibiotics, 26 (2.6%) received antivirals, 24 (2.4%) received antiprotozoals, 3 (0.3%) received anti tuberculous drugs and 1 (0.1%) received anthelminthics.

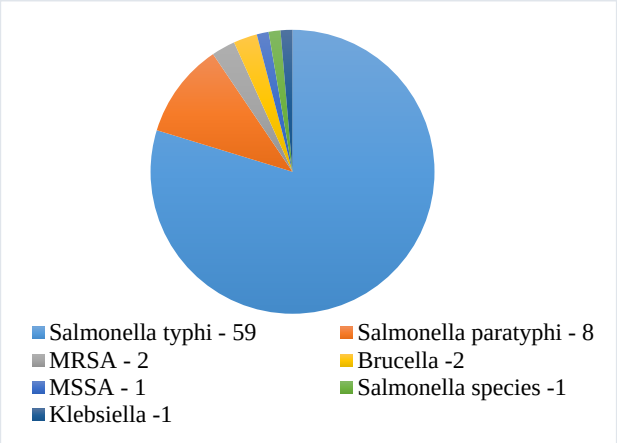


**Figure 1: Bacteria isolated on blood culture in patients with suspected bacterial infection.**

The mean number of antibiotics received was 1.13±0.31. 360 (90%) patients received single antibiotic, 39 (9.7%) patients received 2 antibiotics and 1 received 3 antibiotics. The median was 1 with range 1-3.

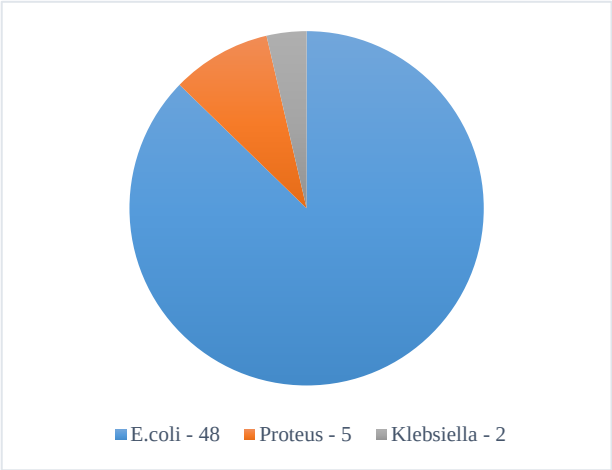


**Figure 2: Bacteria isolated on urine culture in patients with suspected bacterial infection.**

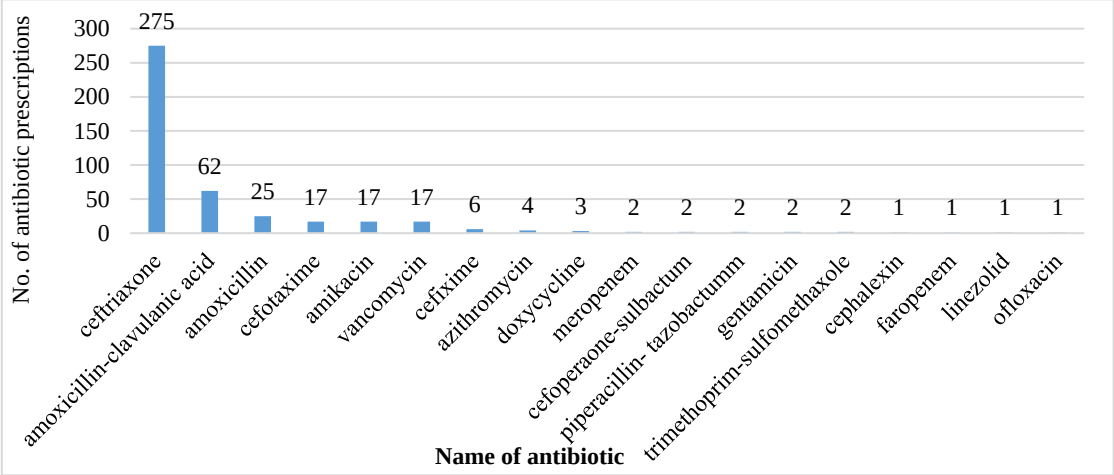


**Figure 3: Pattern of antibiotic used in children aged >28 days to 14 years during the study period.**

Out of total 440 antibiotic prescriptions in 400 patients, the most common antibiotic prescribed was ceftriaxone (275, 62.5%) followed by amoxicillin-clavulanic acid (62, 14.09%), amoxicillin (25, 5.68%), cefotaxime (17, 3.86%), amikacin in (17, 3.86%), vancomycin (17, 3.86%), cefixime (6, 1.36%), azithromycin (4, 0.9%), doxycycline in (3, 0.68%). There were 2 prescriptions each of piperacillin tazobactam, gentamicin, meropenem and trimethoprim sulfamethoxazole and 1 prescription each of cefoperazone sulbactam, cephalexin, faropenem and ofloxacin (Figure 3). The most common antiviral drug used was oseltamivir in 21 followed by acyclovir in 5 patients. The most common antiprotozoal drug was metronidazole in 15 followed by chloroquine in 8 and artemisinin in 1 patient.

## DISCUSSION

As per WHO recommendations, surveillance system is needed in every country to assess the antibiotic use by experts in clinical practice at local as well as national level. Antibiotic stewardship should be encouraged in each and every hospital. Monitoring antibiotic use as well as identification of prevalent common organisms is necessary in every hospital. This study was undertaken to study the antibiotic use in our hospital in terms of amount and type of antibiotic used. Simultaneously, we also studied the common bacterial isolates.

Our study included 989 patients which is a large study of this kind done in a tertiary care hospital in this region. Male to female ratio was 1.18:1 which shows male have

slightly more incidence of various illnesses in childhood and may be more susceptible for infectious illnesses particularly. Similar observation has been made by various studies.[9,10]

The greatest number of hospitalized paediatric patients belonged to the age group 1-5 years. Also, infants constituted the next most common group. This suggests that children below 5 years constitute the majority of paediatric hospital admissions. This observation is seen by various studies.[7-11] Also, there is higher susceptibility of infections at young age and hence there is a need for greater concern for the health of under five-year age of children.

In our study, 85% of children presented with infectious illnesses which suggests that still infectious diseases are the major reason for hospital admissions in developing countries like India. Children below 5 and particularly infants are more susceptible to various infections due to prevalence of malnutrition, anaemia and immaturity of immune system.

From the total children, 511 (60.1%) children had final diagnosis suggestive of viral illnesses like viral fever, acute diarrheal disease, viral wheeze, bronchiolitis, dengue fever, acute viral hepatitis etc. which suggests that viral infections are the most common cause of hospitalization in children and hence antibiotics are not required if the diagnosis is straightforward. In practice, in common clinical scenario like acute respiratory infection, acute diarrheal disease, acute febrile illness etc. due to similarity of the symptoms in bacterial and viral infection clinician depends on investigations to justify the use of antibiotics. So, there are chances for the use of more antibiotics if investigations and culture facilities are not available or not affordable or if standard guidelines are ignored. In our study, only 2.9% patients with viral infection as a diagnosis received antibiotics which were later on stopped after appropriate investigations and institutional practice of following standard guidelines. So, it can be said that by careful analysis, support of investigations and use of standard guidelines, antibiotic use can be restricted. In a study done in Poland before and after the implementation of the health care reforms, they have found 50 percent reduction in rate of antibiotic use.[12]

In our study, 312 (37.5%) patients had final diagnosis suggestive of bacterial infection. This suggests that in the current scenario, viral infections are more common cause of hospitalization as compared to bacterial infections. The most common bacterial diagnosis was enteric fever. 74 bacterial isolates were found on blood culture of which 68 isolates were of salmonella. This suggests high burden of enteric fever in our region. All the isolates of salmonella were sensitive to 3rd generation cephalosporins. As per standard guidelines, all these patients were treated with ceftriaxone and this is the reason of high use of 3rd generation cephalosporins in our study. The other isolates included MRSA (2), *Brucella* (2), MSSA (1) and *Klebsiella* (1). Out of 3 *Staphylococcus aureus* isolates 2 were methicillin resistant and 1 was methicillin sensitive. Both MRSA were community acquired and cultured from two patients, one with empyema and another with shock. *Brucella* which is very difficult to culture was isolated in two patients. 55 bacterial isolates were found on urine culture of which the most common were *E. coli* (48) followed by *Proteus* (5) and *Klebsiella* (2).

In the current scenario, antimicrobial resistance has reached to significant proportion globally. There are two main reasons for the development of resistance, prevalent of resistant genes among the microbes and misuse and overuse of antibiotics. The antimicrobial resistance is seen not only with bacteria but it is seen with all categories of microbes (viral, fungal, rickettsia, chlamydial and parasites). Increase in global trade and movement of people can lead to transfer of resistant organisms across the globe. Hence, documentation of resistant organisms and surveillance of antimicrobial use has to be done in all countries by health care experts.[10] In our study, we found good number of cultures sent so as to document the microorganisms and their resistance pattern.

**Table 2: WHO prescribing indicators estimated in paediatric department during the study period.[13]**

| WHO prescribing indicator | Average/ percentage (%) | WHO standard[13] (%) |
|---|---|---|
| **Average number of drugs per encounter** | 1.13±0.31 | 2 |
| **Percentage of encounter with one or more antibiotic** | 40.4 | 20-26.8 |
| **Percentage of drugs prescribed by generic name** | 88.8 | 100 |
| **Percentage of drugs from essential drug formulary list** | 99 | 100 |

The present study reveals that the percentage of encounters with one or more antibiotics was 40.4%, which was higher than the WHO standard (20-26.8%) (Table 2).[13] Similar studies done in different regions of India and worldwide in various countries are shown in the Table 3 and 4 respectively. In our study, the percentage of encounters with one or more antibiotic was less as compared to the studies done in institutions of Ghana (70.6%), Gambia (54.1%) and Iran (81.42%).[14-16] It was more as compared to studies done in Latvia (26-38%), Brazil (24.4%) and Spain (16.5%).[17-19] Study done in USA was a very large study which showed percentage of antibiotic use of 38-72% in different states of USA with mean use of 60%.[20] On comparing our study with similar Indian studies (from Andhra Pradesh, Puducherry

and Kolkata percentage of encounter with antibiotic was 50.05, 60 and 79.82% respectively), our antibiotic usage was quite less.[7,10,21]

Average number of drugs per encounter in our study was 1.13±0.31.90% patients in our study were prescribed single antibiotic. The WHO standard value for average number of drugs prescribed per patient encounter is 2. Values higher than the standard is suggestive of polypharmacy which may increase the adverse drug reaction, non-adherence and antibiotic resistance. Other Indian studies from Andhra Pradesh, Karnataka and Kolkata reported this parameter to be 3.53, 1.46 and 21.2±7 respectively.[7,9,21] Among 440 antibiotic prescriptions, 390 (88.8%) prescriptions were prescribed with generic names. The use of generic names in our study was less as per WHO criteria but more than some other studies.[7,13] About 99% drugs were prescribed from WHO model list of essential medicines which is also near to WHO standards.[22]

**Table 3: Comparison of various parameters derived in our study with various other Indian studies.**

| Name of the study | Kumar et al[7] Andhra Pradesh | Gopal et al[10] Puducherry | Pasha et al[9] Kalburgi, Karnataka | Baidya et al[21] Kolkata | Present study |
|---|---|---|---|---|---|
| **Number of subjects** | 845 | 959 | 209 | 332 | 989 |
| **Percentage of antibiotic use (%)** | 50.05 | 60 | - | 79.82 | 40.4 |
| **Average number of drugs per encounter** | 3.53 | - | 1.46 | 2±0.27 | 1.13±0.31 |
| **Type of antibiotic used (%)** | | | | | |
| **1. Cephalosporins** | 46.33 | 53.75 | 28.08 | 42.80 | 68.40 |
| **2. Penicillin** | 25.33 | 36 | 42.95 | 30.84 | 20.2 |
| **3. Aminoglycosides** | 9.7 | 4.3 | 16.11 | 10.70 | 4.31 |
| **4. Fluoroquinolones** | 10.63 | 2.8 | 2.89 | 2.80 | 0.9 |
| **5. Macrolides** | 12.7 | 20 | 0.48 | 2.62 | 0.22 |

**Table 4: Percentage of antibiotic use in studies conducted in different countries worldwide.**

| Name of study | No. of subjects | Percentage of antibiotic use (%) |
|---|---|---|
| **Labi et al[14] Ghana** | 716 | 70.6 |
| **Chaw et al[15] Gambia** | 917 | 54.1 |
| **Shiva et al[16] Iran** | 140 | 81.42 |
| **Al Ghazali et al[11] Yemen** | 148 | 64.18 |
| **Fernanda et al[18] Brazil** | 318 | 24.4 |
| **Sviestina et al[17] Latvia** | 320-424 | 26-38 |
| **Croche et al[19] Spain** | 630 | 16.5 |
| **Gerber et al[20] USA** | 556692 | 60 (38-72) |

The pattern of antibiotics use in the hospital depends upon the common infectious diseases in the particular region in which institute is located. In our hospital, cephalosporin group was most commonly used of which injection ceftriaxone was the commonest antibiotic. Other Indian studies also have documented cephalosporins as the most commonly used antibiotic, however our use is more. It is due to high burden of enteric fever in our region as previously mentioned.

The use of penicillin is less in our institute as compared to other studies which should be encouraged. The use of aminoglycosides is quite less in our institute which can be considered good, as nephrotoxicity and ototoxicity can lead to long term sequelae. Commonly aminoglycosides like amikacin and gentamicin are used as a 2nd antibiotic with penicillin and cephalosporins. But in our study, we found that a single sensitive antibiotic suffices in treatment and there is no need of using polytherapy except in certain conditions. The use of macrolides like azithromycin in our hospital is similar to other studies. Only one patient was given fluoroquinolone (ofloxacin) as the guidelines say that fluoroquinolones should not be used in children less than 12 years unless there is no other sensitive antibiotic. This was strictly followed at our institute.

There are clear guidelines and indications for use of broad-spectrum antibiotics in clinical practice and this should be followed. Using narrow spectrum antibiotics as per indications or after antibiotic sensitivity report will help to reserve broad spectrum antibiotics. Also, when empirical antibiotics are used initially but later on investigations do not identify bacterial aetiology and the child is not acutely ill, antibiotics can be withdrawn.

## CONCLUSION

The prevalence of antibiotic resistance depends upon volume and pattern of antibiotic use. Overuse of antibiotics and their inappropriate use is seen in both developing as well as developed countries. In order to overcome this problem, there is a need of developing antibiotic stewardship programs to enhance rational antibiotic prescribing. Every hospital should develop its own antibiotic prescribing guidelines to increase the rational use of antibiotics as per standard guidelines and local antibiotic sensitivity pattern.

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