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Original Research Article

A cross sectional observational study to evaluate utilization of antimicrobials in paediatric department of a tertiary care teaching hospital

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ABSTRACT

Background: Antimicrobials play cardinal role in management of infectious disease. Paediatric age group forms significant part of developing countries and have high chances of acquiring infectious. Misuse and overuse of these antimicrobials are leading culprits in causing antimicrobials resistance. The purpose of this study was to analyse utilization of antimicrobials among paediatric department of a tertiary care teaching hospital.
Methods: A cross sectional observation study was conducted for three months in paediatric department of a tertiary care teaching hospital. The demographics and antimicrobials use details were observed daily from patients admitted to paediatric outpatient department, wards and intensive care unit to assess according to The World Health Organization-International Network of Rational Use of Drugs drug prescribing indicators and WHO antibiotics AWaRe (Access, Watch, Reserve) classification.
Results: In our study we found that mean antimicrobial use in OPD, wards and ICU was1.15±0.35, 1.12±0.33 and 2.25±1.01 respectively. Cephalosporins were most commonly prescribed in OPD (34.62%) and wards (65.26%) while piperacillin-tazobactam (29.93%) in ICU. Percent encounter with an antibiotic in OPD, Wards and ICU was 8.41%, 30.71% and 33.58% respectively. 56.69%, 81.35% and 55.80% antibiotics prescribed in OPD, Wards and ICU respectively were of Watch group. 5.66% Reserve group antibiotics were prescribed in the ICU.
Conclusions: Prescribing trends of antimicrobials is near to WHO standard but according to AWaRe classification, watch group antibiotics were prescribed more than Access group.

Keywords: Antimicrobials, AWaRe classification, Paediatrics, WHO/INRUD drug prescribing indicators

INTRODUCTION

Antimicrobials play a cardinal role in the management of infectious diseases and are routinely prescribed drugs in paediatric population.[1] Despite of medical advancement, infectious disease treatment is challenging due to emergence of resistance to these antimicrobials.[2] The first antimicrobial resistance was known in 1948. Misuse and overuse of these antimicrobials are leading culprits in causing every known pathogen in the present 21st century resistant to one or more antimicrobials, hence making antimicrobials resistance (AMR), a global health and development threat.[3]Additionally, it also prolongs hospital stay, increases mortality and morbidity, raises treatment cost and eventually places a greater burden on patients as well as on existing hospital resources.[4] Paediatric age group forms a significant part of the population of developing countries like India and are more prone to infections. Antimicrobials use amongst them should receive special attention as they are prone to increased risk of exposure to resistant strains in the later stages of their life.[5]

Currently there is global increase in AMR and considerable shortfalls in the development and availability of new antimicrobials. Therefore, implementing measures to maintain the usefulness of existing antimicrobial agents has become a top public health concern.[6,7] The World Health Organization in collaboration with the International Network of Rational Use of Drugs (WHO/INRUD) has developed prescribing indicators to measure the rational usage of drugs, to assess the prescribing pattern of antimicrobials and to detect barriers to Antimicrobial Stewardship (AMS) programme.[8] When understanding the pattern of antimicrobials utilization for the establishment of an AMS programme for paediatric population at institution, regional and national level; access to the data on paediatric antimicrobial prescriptions is essential.[9] In March 2017, the WHO classified antibiotics in the Essential Medicine List for Children (EMLc) into three groups: Access (A), Watch (Wa), and Reserve (Re). The Access group includes generally narrow-spectrum antibiotics recommended as first and second choice for most common clinical infection syndromes while generally broader spectrum antibiotic classes corresponding to the highest priority agents on the list of critically important antimicrobial drugs for human medicine belongs to Watch group and last-resort antibiotics for targeted use in multidrug-resistant infections belongs to the Reserve group. These groups are collectively called as the AWaRe classification.[10]

While a large number of antimicrobials utilization studies are available for adults all over the world, a very few studies provide information on utilization of antimicrobials in paediatrics. The nature and pattern of antimicrobials prescription changes with time. Thus, with this background we conducted this study in paediatric department of our hospital to gather information on the current trend of antimicrobials utilization. The primary aim of this study was to analyse utilization of antimicrobials among paediatric patients of outpatient department (OPD), wards, and intensive care unit (ICU) of a tertiary care teaching hospital with objective to use WHO-INRUD core prescribing indicators and WHO antibiotics AWaRe classification.

METHODS

This cross-sectional observational study was conducted over three months duration (January to March, 2022) in the department of paediatrics at a tertiary care teaching and general hospital located in Ahmedabad, Gujarat, India after getting approval from institutional review board (IRB). Written informed consent from patient's legally authorised representative (LAR) along with patient's age-appropriate assent were taken. Patients ≤ 18 years of age, irrespective of their gender in paediatric outpatient department (OPD), wards and intensive care unit (ICU) were included in the study while those patients who were discharge/left against medical advice, expired during study period and/or transferred for further treatment to other department or other hospital were excluded from the study.

The data collected included patient's demographic details such as age, gender and weight; indication of treatment; antimicrobials prescribed with its name (generic/trade), fixed dose combinations (FDCs) prescribed, dosage form, dose, frequency, route of administration, duration of treatment and duration of hospital stay (for inpatients). The operational definition of antimicrobial agent for this study included synthetic as well as naturally obtained drugs that act against microorganisms thereby covering all antibacterial, antifungal, antiviral and antiprotozoal agents. WHO-INRUD core prescribing indicators were used for analysis. Additionally, prescribed antibiotics in OPD, wards and ICU were classified into Access, Watch and Reserve group according to AWaRe criteria. Data collected over the stipulated time was entered into Microsoft Excel 2019 and appropriate statistical tests were applied to analyse the data using Statistical package for social sciences (SPSS) version 20.0.

RESULTS

In our study 544 (287 males and 257 females), 324 (174 males and 150 females) and 183 (96 males and 87 females) paediatric patients from OPD, Wards and ICU were enrolled respectively. During our study period, age group of 2-6 years made up majority of patient pool in OPD (196, 36.03%) and Wards (99, 30.56%) while neonates (123, 67.21%) formed majority of ICU patient pool. Distribution of enrolled patients based on their age is shown in (Figure 1).

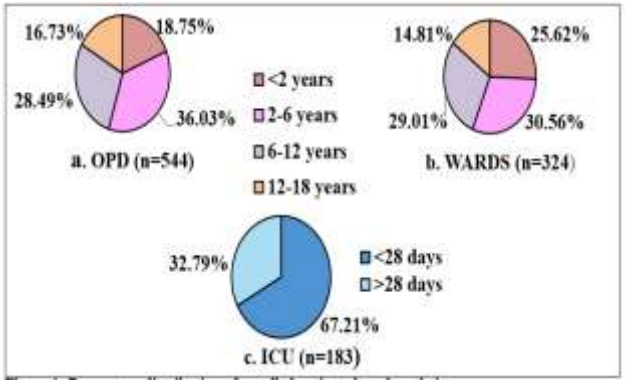

Figure 1: Percentage distribution of enrolled patients based on their age.

Dose of the antimicrobials prescribed to paediatric patients were based on their body weight, thus making weight an important demographic indicator. A total of 101 (18.57%) OPD patients, 82 (25.31%) wards patients and 49 (26.78%) ICU patients presented with lower weight for their age according to 'Indian Academy of Paediatrics (IAP) growth charts for 0-18 years'. The total number of antimicrobials prescribed to 544 OPD patients, 324 wards patients and 183 ICU patients was 624, 363 and 411 respectively. The (Figure 2) shows antimicrobials prescription pattern for OPD patients. cephalosporins were the most commonly prescribed group of antimicrobials in OPD (216, 34.62%). Additionally, (Figure 3) depicts the

antimicrobial prescription patterns amongst wards which showed Cephalosporins as the most commonly prescribed group of antimicrobials in patients admitted in the wards (237, 65.28%).

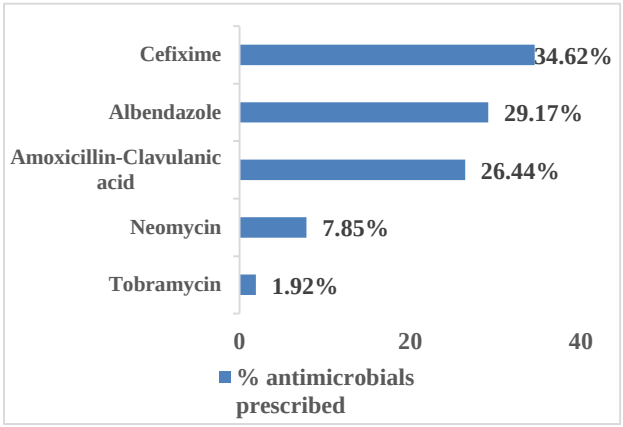

Figure 2: Prescription pattern of antimicrobials among OPD patients (n=624).

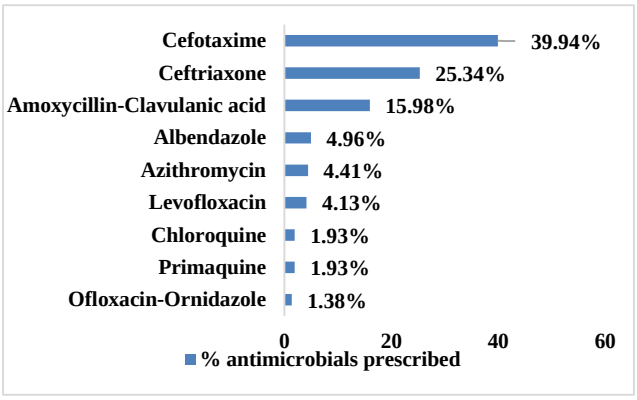

Figure 3: Prescription pattern of antimicrobials among WARDS patients (n=363).

Among the antimicrobials prescribed to patients admitted in the ICU, piperacillin-tazobactam (123, 29.93%) followed by amikacin (111, 27%) of Aminoglycosides group were the most frequently prescribed drugs. We further observed the use of meropenem (7.3%), colistin (5.11%) and tigecycline (1.46%) in ICU as depicted by (Figure 4). A single Acyclovir prescription was prescribed in ICU for the prophylaxis of chickenpox.

Among the out patients, the use of fixed dose combinations was very limited. FDC of amoxycillin-clavulanic acid was observed in 165 (26.44%) OPD prescriptions. FDCs of amoxycillin-clavulanic acid and ofloxacin-ornidazole were observed in 58 (15.98%) and 5 (1.38%) ward prescriptions respectively while FDCs of piperacillin-tazobactam, amoxycillin-clavulanic acid and cefoperazone-sulbactam were prescribed in 123 (29.93%), 17 (4.14%) and 15 (3.65%) ICU patients respectively (Figure 2-4).

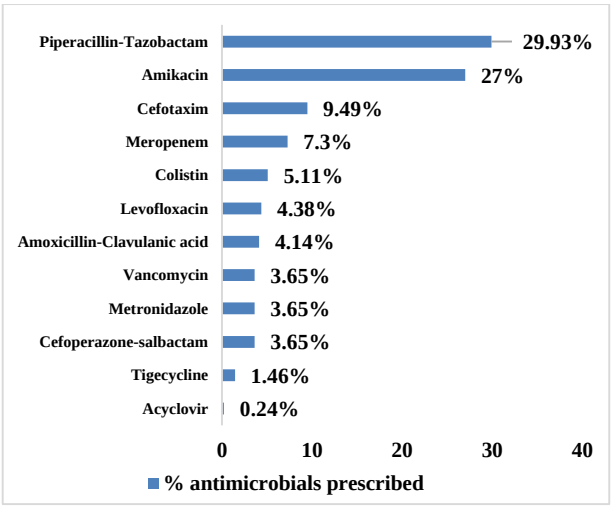

Figure 4: Prescription pattern of antimicrobials among ICU patients (n=411).

The percentage of prescriptions containing single antimicrobial was maximum in wards (87.96%) followed by OPD (85.29%) and ICU (12.04%). The percentage of prescriptions containing two antimicrobials were seen maximum in ICU (55.74%) followed by OPD (14.71%) and least in wards (19.44%). Only ICU prescriptions (24.59%) contained more than 2 antimicrobials. While assessing the disease pattern for antimicrobial prescribing among paediatric patients, it was found that 318 (58.46%) OPD patients and 112 (34.57%) wards patients received antimicrobials mainly for gastrointestinal illness while 62 (33.88%) ICU patients received mainly for respiratory illness. The (Table 1) provides information on the system wise disease pattern for prescribing antimicrobials in paediatric patients. Other indications for antimicrobials prescription were umbilical infection (49, 9.01%) and eye infection (12, 2.20%) amongst OPD patients. While amongst ward patients' other indications included viral fever (91, 20.09%) and *P. vivax* malaria (7, 2.16%) and among ICU patients' antimicrobials were prescribed for sepsis (23, 12.57%), preterm with low birth weight (22, 12.02%), intrauterine growth retardation (12, 6.56%), viral fever (9, 4.92%) and for a single case with history of mother suffering from chicken pox.

The mean number of antibiotics prescribed per patient in OPD (0.81±0.39), wards (1±0.20) and ICU (2.16±0.87) showed statistical significance ($p<0.01$) revealing that there is significant difference in the number of antibiotics prescribed per patient among OPD, wards and ICU. Furthermore, a statistically significant difference ($p<0.01$) was observed in the mean antimicrobials prescribed among OPD, wards, and ICU patients, with ICU patients receiving the highest number of antimicrobials (2.25±1.01). There was also a statistically significant difference ($p<0.01$) observed in the duration of antimicrobials treatment amongst OPD (4.39±1.71), wards (4.69±1.55) and ICU (6.61±3.77) patients (Table 2).

Table 1: System wise disease pattern for prescribing antimicrobials in paediatric patients.

System involved	OPD (n=544) Frequency (%)	WARDS (n=324) Frequency (%)	ICU (n=183) Frequency (%)
Central nervous	-	27(8.33)	12 (6.56)
Respiratory	165 (30.33)	66(20.37)	62 (33.88)
Gastrointestinal	318 (58.46)	112(34.57)	36 (19.67)
Genitourinary	-	21(6.48)	6 (3.28)
Others	61 (11.21)	98(30.25)	67 (36.61)

Table 2: Antimicrobials utilization in paediatric department.

Variable	OPD Mean±SD (Range)	Wards Mean±SD (Range)	ICU Mean±SD (Range)	P value
Antibiotics prescribed/patient	0.81±0.39	1±0.20	2.16±0.87	<0.01[#]
Antimicrobial prescribed/patient	1.15±0.35	1.12±0.33	2.25±1.01	<0.01[#]
Duration of antimicrobials treatment (days)	4.39±1.71 (1-7)	4.69±1.55 (3-14)	6.61±3.77 (3-22)	<0.01[#]

[#]one-way analysis of variance (ANOVA) test, p value <0.05 significant.

Table 3: WHO/INRUD core prescribing indicators.

Indicators	Optimal	OPD	Wards	ICU
Percent medicines prescribed by generic name	100	90.99	100	100
Percent encounters with an antibiotic prescribed	20.0-26.8	8.41	30.71	33.58
Percent encounters with an injection prescribed	13.4-24.1	0	90.74	97.81
Percent medicines prescribed from WHO essential medicines list for children 2021	100	90.99	98.46	88.52

According to the core prescribing indicators provided by WHO/INRUD, comparison between the utilization of antimicrobials in OPD, wards and ICU patients is presented in (Table 3).

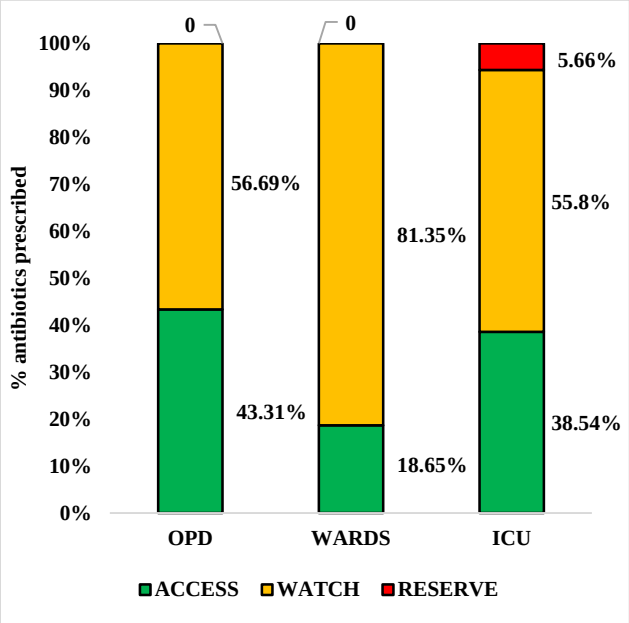

Figure 5: % antibiotics prescribed according to AWaRe classification.

Our study showed percent medicines prescribed by generic name in OPD (90.99%), wards (100%), and ICU (100%). The present study reveals the percentage of encounters with an antibiotic prescribed in OPD (8.41%), wards (30.71%) and ICU (33.58%). The use of injectable antimicrobials was much higher in wards (90.74%) and in ICU (97.81%). Further it also showed the percentage of antimicrobials prescribed by pediatrician from the WHO essential medicines list for children 2023 in OPD (90.99%), Wards (98.46%), and ICU (88.52%). Neomycin powder in the OPD, FDC of ofloxacin-ornidazole in the wards, and tigecycline, cefoperazone-sulbactam in the ICU were among the antimicrobials that were prescribed though they were not on the WHO's list of essential medications for children in 2023.

There were 422, 331, 410 antibiotic prescriptions in the OPD, Wards and ICU respectively. Neomycin powder and tobramycin eye drops were prescribed in 61 of the 422 OPD antibiotic prescriptions, levofloxacin and ofloxacin-ornidazole were prescribed in 20 of the 331 ward prescriptions, and levofloxacin, cefoperazone-sulbactam, and tigecycline were prescribed in 39 of the 410 ICU prescriptions, all of these antibiotics are not included in the AWaRe classification. Therefore, the 381 OPD antibiotic prescriptions, 311 wards antibiotic prescriptions, and 371 ICU antibiotic prescriptions were taken into consideration for analysis in accordance with AWaRe classification. Antibiotics prescribed in OPD, Wards, and ICU were from

Access group in 165 (43.31%), 58 (18.65%), and 143 (38.54%) cases, while they belonged to Watch group in 216 (56.69%), 253 (81.35%), and 207 (55.80%) cases, respectively. Reserve group of antibiotics were in 21 (5.66%) antibiotic prescriptions of the ICU. Classification of the prescribed antibiotics in OPD, wards and ICU is presented in (Figure 5).

DISCUSSION

Drug use evaluations (DUEs) are a low-cost, simple and important part of pharmaco-epidemiological studies. DUE of antimicrobials in paediatrics is important because it would reveal temporal trends and extent of its use in them. Majority number of OPD and wards patients belonged to 2-6 years age group which may be due to their low level of immunity.[11,12] In our study, neonates formed majority of ICU patient pool as they are highly susceptible to invasive bacterial infections, and suspected infection is one of the most common reasons for admission in ICU.[13] The pattern of antimicrobials use in the hospital varies depending on the diseases encountered during the study period and the specific region in which the institute is located. In our study, cephalosporins followed by aminopenicillins group were leading class of antibiotics prescribed in OPD and wards and this could attribute to its broad spectrum of activity, clinical efficacy, and tolerance across all age groups.[14] These findings were consistent with the maximum number of patients in OPD and wards who were suffering from gastrointestinal and respiratory illness. Piperacillin-tazobactam has a broad spectrum action against Gram-positive, Gram-negative (including *Pseudomonas aeruginosa*), and anaerobic bacteria while amikacin is effective in paediatric infections and is well tolerated by them.[15,16] In our study piperacillin-tazobactam and amikacin were most commonly prescribed in ICU while other studies shows cephalosporins as most frequently prescribed antimicrobial in paediatric ICU.[5,17] In our study, the use of tigecycline and colistin was less, indicating that higher antimicrobials were being added only in resistant cases while the use of meropenem was indicated as an add on to initial treatment. Mean antimicrobials prescribed per patient in other Indian studies in paediatric OPD from Uttar Pradesh was 2.78±0.63 while studies in paediatric wards from Andhra Pradesh and Kolkata was found to be 3.53 and 21.2±7 respectively.[11,18,19] While in our study mean antimicrobials prescribed per patient in OPD (1.15±0.35) and wards (1.12±0.33) were less than 2 as suggested by WHO. Values above the standard is suggestive of polypharmacy which may increase chances of the adverse drug reaction, non-adherence to antimicrobials and AMR.[20] While mean antimicrobials prescribed per patient observed in our ICU (2.25±1.01) was above standard but is similar to other study done in Mumbai (2.38±1.48).[5] Studies done by Sharma et al and Matthew et al showed percent medicines prescribed by generic name as 30% and 25.76% respectively.[20,14] While in our OPD (90.99 %), wards (100%), and ICU (100%), it was found to be in correspondence to WHO standard. A higher percentage of medications supplied under their generic names aids in reducing the cost of treatment. Because the antimicrobials in the EML are easily available in hospital pharmacy, the percentage of antimicrobials prescribed by pediatrician from the WHO essential medicines list for children 2023 in our OPD, wards, and ICU are close to the WHO standard. Injectable antimicrobials were majorly prescribed in wards which may be due limited availability of oral formulations in paediatrics. The present study revealed the percent encounters with antibiotics in wards (30.71%) and ICU (33.58%), which was higher than the WHO standard. Studies done in paediatric settings revealed the percent encounters with antibiotics in other developing countries like Iran (81.42%) and Gambia (54.1%) and similar Indian studies done in Andhra Pradesh (50.05%), Puducherry (60%), Kolkata (79.82%) and Mumbai (97%).[1,5,18,19,21,22] These contrasting results may be attributed to variation in disease pattern, socio-economic and cultural backgrounds, antimicrobials resistance trends and paediatrician's knowledge and experience.

An alarming observation was made that watch group of antibiotics were prescribed over access group of antibiotics in whole paediatric department of our hospital. Cefixime was the watch group antibiotic (56.69%) prescribed in OPD whereas FDC of amoxicillin-clavulanic acid belonged to the access group antibiotic (43.31). Watch group antibiotics prescribed in wards (81.35) were cefotaxime, ceftriaxone and azithromycin and FDC of amoxicillin-clavulanic acid formed the prescription of access group antibiotic (18.65%). ICU utilisation of watch group antibiotics (55.8%) was formed by piperacillin-tazobactam, cefotaxime, meropenem and vancomycin, whereas amikacin and FDC of amoxicillin-clavulanic acid formed access group antibiotics (38.54%). Colistin (5.66%) of reserve group was prescribed in ICU. Since watch group antibiotics have more potential of developing resistance than the access group antibiotics, the watch group antibiotics are considered as the target for stewardship monitoring.[10]

Limitations

Since this is a single centre study within a limited time period, the results can't be extrapolated to a larger population. The justification of the prescribed drug with regard to laboratory evaluation was not considered.

CONCLUSION

Antimicrobial resistance depends upon the extent and pattern of antimicrobials use. In our study, we found that prescribing trends of antimicrobials is near to WHO standard but according to AWaRe classification of antibiotics, antibiotics from watch group were more prescribed than from access group. The findings of this study would further be helpful in implementation of paediatric stewardship programme in our institution.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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