

# Antimicrobial Utilization in a Rural Children's Hospital of South India

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## ABSTRACT

**Background:** The "more-is-better" antimicrobial prescribing philosophy besides resistance is a significant contributor to suffering and death in children. Only a few nations have given comprehensive and comparable statistics on pediatric antimicrobial usage. However, such pediatric research is scarce in India, which necessitates antimicrobial pharmaco-surveillance. **Materials and Methods:** The retrospective antimicrobial drug use study was conducted in a rural children's hospital of south India. The antimicrobial pediatric prescription was investigated using WHO/INRUD prescribing indicators and classified according to the WHO ATC index. The antimicrobial use was calculated by using DDD and its deviation if any to prescribed daily dose was determined. **Results:** Pneumonia was the most common illness and the main reason for hospitalization in 38% of infants and toddlers. A total of 79.66% antimicrobial agents were administered intravenously. Ceftriaxone ( $n=40$ , 33.9%) was the commonly used antimicrobial agent, with a PDD:DDD value of 0.84. **Conclusion:** The pediatric antimicrobial utilization was adequately studied which found no discrepancies, but on contrary it was observed that prescribing practices was not consistent with WHO core prescribing indicators. This necessitates the implementation of pediatric antimicrobial stewardship programs.

**Keywords:** Antimicrobials, ATC/DDD Index, Drug Utilization, Observational Studies.

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## INTRODUCTION

Infection with antimicrobial resistance results in life-threatening illnesses and protracted hospitalization, increased healthcare expenditures and cost of second-line drugs and therapy failures.<sup>1-3</sup> Pediatric prescription commonly comprises of antimicrobials.<sup>4-11</sup> Based on an assumption of linearity between the exposure and total body weight, pediatric antimicrobial dosage regimens were developed using adult pharmacokinetic data.<sup>12,13</sup> Despite being frequently employed in clinical practice, this approach lacks empirical support and may result in improper antimicrobial use in newborns and young children.<sup>14,15</sup> Additionally, the "more-is-better" antimicrobial prescribing philosophy besides resistance is a significant contributor to suffering and death in children.<sup>16</sup> Only a few countries' comprehensive and comparative pediatric antimicrobial utilization data have been published.<sup>17-19</sup> However, such pediatrics study is very few in India, which necessitates a regional level antimicrobial surveillance. In order to promote rational drug use, the World Health Organization

(WHO) facilitates the Anatomical Therapeutic Chemical (ATC) Classification/Defined Daily Dose (DDD) system as a standard tool for evaluating and comparing drug use studies.<sup>20</sup> Keeping this in mind, we conducted the current study in a rural children's hospital in south India to investigate pediatric antimicrobial utilization and its prescribing pattern.

## MATERIALS AND METHODS

The cross-sectional retrospective antimicrobial drug use study was performed in a 45 bedded pediatric department of a rural hospital in Andhra Pradesh state, after obtaining permission from concerned hospital authority [RDTHBTP/CERT/ETHICS/2021/018]. 100 prescriptions were assessed in accordance to the basic parameters of different types of drug use studies of WHO recommendations in conducting retrospective studies at a single health facility, from medical databases/registries.<sup>21</sup>

Prescriptions of pediatric patients of both genders, diagnosed with infections and started on at least one antimicrobial agent were included; and prescriptions with incomplete data were excluded. Patients' personal details, baseline conditions, laboratory investigations, antimicrobial agent name, dose, dosage, therapy days, route and rate of administration, prescribed as generic or



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brand and Fixed-Dose Combination (FDCs) and its availability in hospital pharmacy were recorded from the pediatric patient medical records (July-December 2021) made available in the medical record department. Antimicrobial use was investigated as per the WHO core prescribing indicators<sup>21</sup> and DUS metrics.<sup>22</sup> The ATC codes were assigned to each antimicrobial agent and the value of DDD/100 bed-days was computed. Following formulas were used to calculate the outcomes in term of the antimicrobial drug utilization: DDD/100 bed-days=No. of Units administered in a given period (mg)x100/DDD (mg)xNo. of Days x No. of Beds x Occupancy Index.

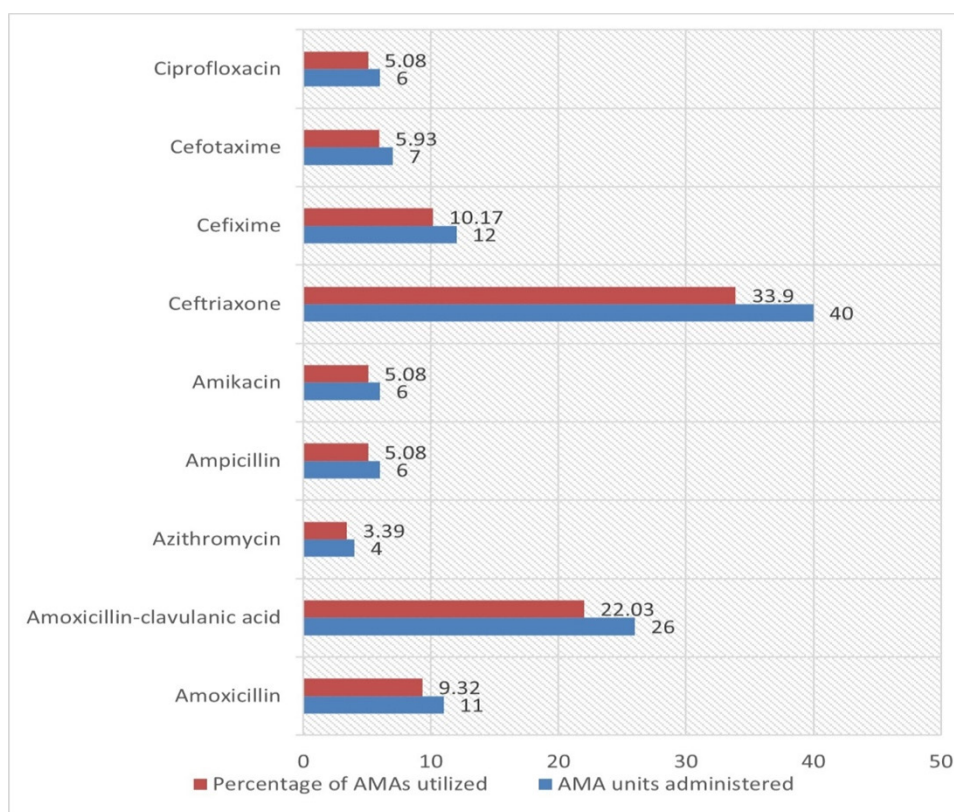
Occupancy Index=In patient days of care x100/No of bed days available

DDD=Number of issued items xAmount of drug per item/WHO recommended DDD of drug.

PDD=Total amount of drug/Duration of hospital stay.

## RESULTS

In the study, we evaluated 100 paediatric prescriptions. There was a total of 63% male and 37% female. Table 1 summarises the characteristics of the demography. In 100 paediatric prescriptions, a total of 575 drugs were identified, with an average of 5.75 drugs per encounter. The encounters prescribed with antimicrobials and the mean antimicrobial in each prescription are 118 (20.52%) and 1.18% respectively. Of the 100 pediatric prescriptions, 94 (79.66%) of antimicrobials were prescribed as injections and 83 (70.33%) by generic names and 100% are from hospital formulary containing essential drugs<sup>23</sup> responses are thoroughly analyzed



**Figure 1:** Antimicrobial agent's utilization in pediatric prescriptions.

**Table 1:** Demographic characteristics of the pediatric patients (n=100).

Age group	Gender distribution		Total
	Male	Female	
New born (0-27 Days).	0	0	0
Infants and Toddler (1-23 Months).	23	15	38
Preschool (2-6 Years).	17	11	28
School (6-12 Years).	13	8	21
Adolescent (12-18 Years).	10	3	13
Total	63	37	100

**Table 2: Pattern of antimicrobial agents use (WHO-INRUD) drug use prescribing indicators.**

WHO core prescribing indicators	n (%)	
Total number of prescriptions handled.	100	
Total number of drugs prescribed.	575	
Total number of antimicrobial agents used.	118	
Average number of drugs per encounter.	575:100	5.75
Percentage of encounters with antimicrobials.	118:100	1.18
Percentage of antimicrobial agents prescribed by generics.	83:118	70.33
Percentage of antimicrobial agents prescribed as an injection.	94:118	79.66
Percentage of antimicrobial agents used as FDCs.	30:118	25.42
Percentage of drugs prescribed from hospital formulary.	100	

**Table 3: Pattern of antimicrobial agent utilization as per the ATC/DDD classification.**

Antimicrobial agent	ATC Code	DDD/100 bed-days	WHO DDD	PDD	PDD:DDD
Amoxicillin	J01CA04	0.22	3	1	0.27
Amoxicillin-clavulanic acid	J01CR02	1.67	3	1.88	0.63
Azithromycin	J01FA10	0.18	0.3	0.5	0.08
Ampicillin	J01CA01	0.20	6	0.75	0.26
Amikacin	J01GB06	0.18	1	1	0.17
Ceftriaxone	J01DD04	2.84	2	1	0.84
Cefixime	J01DD08	0.21	0.4	0.5	0.03
Cefotaxime	J01DD01	0.14	4	0.8	0.57
Ciprofloxacin	J01MA02	0.12	0.8	1	0.13

and reported in Table 2. In addition, we observed that pediatric prescriptions with antimicrobial agents are in line with the WHO Medically Important Antimicrobial List.<sup>24</sup> Ceftriaxone ( $n=40$ , 33.9%) was most commonly observed in the majority of pediatric prescriptions, followed by Amoxicillin+clavulanate ( $n=26$ , 22.03%) and others,<sup>25</sup> results of which are reported in Figure 1. The pediatric antimicrobial use was assessed for any deviations of the PDD from the DDD, observation of which are presented in Table 3.

## DISCUSSION

Infection is the most common cause of acute illness in children<sup>26</sup> for which antimicrobials are the most common medicine used,<sup>6</sup> prevalent in hospitals and community.<sup>27</sup> However, improper antimicrobial use leads to development of resistance, that burden patients with increased healthcare expenditures, protracted hospitalization and higher risk of morbidity and mortality.<sup>28-32</sup> It is essential for healthcare professionals to prescribe antimicrobial in pediatric population appropriately.<sup>33</sup> Hence, the current study is designed to investigate the pediatric antimicrobial use in a rural children's hospital of south India.

In this study around 63% of the pediatric patient were male, similar to reports from Ethiopia<sup>34</sup> and Nepal<sup>35</sup> and other Indian studies;<sup>36-39</sup> and 38% of patients were between the ages of 1 and 23 months, which could be attributed to a higher sensitivity to infections, poor hygiene, food, vaccination and age. This demands a greater attention towards infant's health.

The rate of encounters with antimicrobial prescribed in this study was 20.52%, in comparison to Baidya *et al.*<sup>36</sup> (80%) was an important indicator for its appropriateness.<sup>21</sup> In our study, out of 100 pediatric prescriptions, we found more contrary observations regarding the average number of drugs per prescription (5.75) and percent encounters with injections (79.66%) in comparison to the WHO recommended value.<sup>21</sup>

The average number of antimicrobials in each pediatric prescription (1.18) was found to be in line with WHO core prescribing indicators<sup>21</sup> and good, in comparison to other Indian studies 2.38,<sup>37</sup> 1.917,<sup>38</sup> 1.97<sup>40</sup> and 3.00<sup>41</sup> respectively.

Across the globe, prescriptions with generic names will be rational and cost-effective, this ranges from 13.3% to 93%,<sup>42,43</sup> and in our study, we found 70.33% of prescriptions by generic name, which was more in comparison to observations of Dimri *et al.*<sup>44</sup> (5.8%);

and lower in Nsimba *et al.*<sup>42</sup> (87%), Baidya *et al.*<sup>36</sup> (98.69%), Prajapati and Bhatt.<sup>40</sup> (83.5%) and Mali *et al.*<sup>37</sup> (80.95%) studies. All pediatric prescription drugs (100%) were available in the hospital pharmacy of our study out of which 25.42% were FDCs compared to Mali *et al.*<sup>37</sup> (80.76%) and 7.69%. In our study, we found antimicrobials (79.66%) were given intravenously less in comparison to other studies (84.1%),<sup>36</sup> and (94.88%).<sup>37</sup> In intensive care units, antimicrobials are beneficial and often administered intravenously, but in general paediatric practice utmost care has to be taken for intravenous preparation and administration, if not it leads to more adversity and medication errors.<sup>45,46</sup> Excessive injection use causes discomfort and edema and also increases the expense of sterilization and nursing services. In India, it is estimated that three billion injections are given each year, with 1.89 billion of them being harmful. According to the evidence, the prescriber is a micro-level leader in minimizing injection misuse and making injections safer.<sup>47</sup>

Ceftriaxone, which has also been shown in other studies,<sup>48-50</sup> was the most commonly used individual antimicrobial in this study. Cephalosporins play a substantial role in the treatment of many types of infections. Ceftriaxone is widely used in all age groups of children to treat bacterial infections, which have more beneficial effects; many clinical trials support its use in pediatric.<sup>51-55</sup> Ceftriaxone due to its prolonged half-life, is advantageous in severe pediatric infections when administered as a 12-hr dosing regimen.<sup>56</sup> In this study, ceftriaxone dosing was 500 mg, bd, IV with 2.84 of DDD/100 patient bed days. In the pediatric practice of antimicrobial agents' utilization, we observed no discrepancies in PDD:DDD ratio, but the study revealed a higher application of antimicrobial drugs as intravenous delivery, which must be controlled. DDD is a widely used method for comparing and evaluating drug use<sup>57</sup> on a national and international scale. The number of DDD calculated in our study for antimicrobials in children can set a benchmark for future studies in evaluating the pediatric antimicrobial consumption.

## CONCLUSION

The pediatric antimicrobial utilization was adequately studied which found no discrepancies, but on contrary it was observed that prescribing practices was not consistent with WHO core prescribing indicators. This necessitates the implementation of pediatric antimicrobial stewardship programs.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**ATC:** Anatomical Therapeutic Chemical; **DDD:** Defined Daily Dose; **EDL:** Essential Drug List; **FDCs:** Fixed Dose Combinations; **IEC:** Institutional Ethics Committee; **INRUD:** International Network of Rational Use of Drugs; **PDD:** Prescribed Daily Dose; **WHO:** World Health Organization; **DUS:** Drug Use Studies.

## ETHICS APPROVAL

The cross-sectional retrospective antimicrobial drug use study was performed after obtaining Institutional Ethics Committee (IEC) approval from concerned hospital authority [RDTHBTP/CERT/ETHICS/2021/018].

## SUMMARY

Antimicrobials are commonly used medications in children because of their increased susceptibility to infections. However, the impact of prescribing in this context is unclear and the evidence on pediatric antimicrobial utilization is at scarce in India. In our study, the antimicrobial agents were investigated using WHO/INRUD prescribing indicators and classified according to the WHO ATC index. The antimicrobial use was calculated by using defined daily dose its deviation if any to prescribed daily dose was determined in pediatric prescriptions. The study observed no deviations in terms of antimicrobial utilization, but the prescribing practices was not consistent with WHO core prescribing indicators.

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