Research Article

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Journal of Infectious Diseases and Treatment
ISSN 2472-1093

2021
Vol.7 No.1:1

Antibiotic Surveillance in Pediatric Intensive Care Unit of a Secondary Referral Healthcare Setting in South India

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Received date: March05, 2021; **Accepted date:** March19, 2021**; Published date:** March 26, 2021

Citation: Rathinavelu M (2021) Antibiotic Surveillance in Pediatric Intensive Care Unit of a Secondary Referral Healthcare Setting in South India. J Infec Dis Treat Vol.7 No.1:1.

Abstract

Background: Due to their maturing immune system and close proximity to one another, children are more liable to acquire and transmit infections than are adults. Despite frequent antibiotic use in children, the primaryfocus of antibiotic drug utilization research to datehas been the adult population. This study aims to evaluate the antibiotic utilization in a 5 bedded pediatric intensive care unit of a secondary referral hospital in south India.

Materials and methods: The cross-sectional observational study approved by institutional ethics committee and institutional review board of six months duration was performed in patients of both genders admitted to the PICU of age 1 month to 18 years, with at least one antibiotic administration.

Results: In a total of 84 PICU admissions, 96.43% were treated empirically. A total of 583 medications were prescribed, out of which 28.3% were antibiotics. In our study, amoxiclav, ceftriaxone and linezolid were observed to have a normal PDD: DDD ratio within limits. 95.24% was the survivor rate during the study.

Conclusion: The outcome of PICU antibiotic surveillance was found rational in relation to 95.24% survival rate, but WHO DUS metrics calculation of PDD:DDD ratio forecast there is more under-utilization, as dose calculation in pediatrics is weight based. In this regard, extensive research in exploring the new modalities like point prevalence survey, proportions of days covered, days of therapy; and antibiotic acquaintance by limiting of wasted drug weight in pediatric patients is highly recommended to ensure optimized and rational antibiotic use.

Keywords: Antibiotics; Drug utilization; Pediatric intensive care unit; Prescribing pattern

Introduction

The field of paediatric intensive care is rapidly growing in India. The number of intensive care units providing care to infants and children is also progressing at a rapid pace. Due to their maturing immune system and close proximity to one another, children are more liable to acquire and transmit infections than are adults [1]. Few children require intensive care during a hospital admission due to heterogenous mix of conditions including admissions for acute illness such as asthma or due to external causes such as injury as well as relatively rare problems such as metabolic diseases and complex congenital malformations.Antibiotics are among the most commonly used drugs in a Paediatric Intensive Care Unit (PICU),but the impact of potentially unnecessary antibiotic prescribing in this context is unclear. Without evidence to the contrary, many providers in the paediatric intensive care unit implement a “more-is-better” philosophy regarding antibiotics for critically ill patients, leading to overuse of antibiotics for infections without the identification of specific pathogen aetiology; and increased incidence of antibiotic-resistant organisms, which in turn represents a source of substantial morbidity and mortality. Antibiotic surveillance is mandatory to optimise antibiotic therapy and to prevent antimicrobial-resistance [2]. Despite frequent antibiotic use in children, the primary focus of antibiotic drug utilization research to date has been the adult population.Comprehensive and comparable country-specific paediatric antibiotic use data have only been published for a limited number of countries.However, availability of such data in Indian paediatric intensive care units are limited. There is thus a need to build pharmacoepidemiological research capacity and support in the areas of antibiotic utilization, safety and effectiveness. The objective of this cross sectional, observational study is to evaluate the antibiotic utilization in a paediatric intensive care unit of a secondary referral hospital in south India as per WHO-DUS metrics; which would help in developing strategies to minimize antibiotic misuse, and improving the patient clinical and humanistic outcomes with economic expenditures [3].

Materials and Methods

Study design and ethical approval

The current cross-sectional observational study of six months duration (May-October, 2019) approved by Institutional Ethics Committee (IEC) of the hospital and Institutional Review Board (IRB) of the institution was performed in a 5 bedded paediatric intensive care unit; to evaluate the antibiotic utilization [4].

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Study criteria

Consecutive patients of both genders admitted to the PICU of age 1 month to 18 years, with at least one antibiotic administration, regardless of previous admission history were enrolled in the study with day 1 of admission into PICU being considered as the first day of the study and were followed up to transfer, discharge or death [5].

Obtaining consent from study participants

The merits of the research study were clearly explained to the study participants and the attender (parents) to the best of understanding, and data were collected only from study participants who showed their willingness towards study and documented as informed consent [6].

Baseline data collection

Patient's medical records were scrutinized daily. Demographic facts, clinical diagnosis, details of antibiotic use, total number of drugs prescribed, culture and sensitivity data, length of stay, and cost of antibiotic therapy were recorded in data collection [7].

Data analysis

The collected data was further analysed as per the WHO-INRUD drug use indicators,which involved classification of prescribed antibiotics according to the Anatomical Therapeutic Chemical (ATC) – Defined Daily Dose (DDD) classification; and further calculating the Prescribed Daily Dose (PDD), and later the PDD to DDD ratio.

Results

Characteristics of studied patients

84 prescriptions were included in the analysis, out of which 58.3% were male and 41.7% were female respectively. The patients age distribution was groupedand the relative distribution is shown in **(Table 1).**

Age distribution	**Gender distribution**		**Total**
	Male	Female	
Neonates	0	0	0
(0-30 days)			
Infant	31	20	51
(1 month-2 years)			
Young child	12	7	19
(2-6 years)			
Child	6	6	12
(6-12 years)			
Adolescent	0	2	2
(12-18 years)			
Total	49	35	84
Mean + SD	9.8 + 12.85	7 + 7.81	16.8 + 20.66

Table 1: Characteristics of studied participant (N = 84).

Evaluation of prescription patterns according to various WHO/INRUD Drug Use Indicators

The 84 prescriptions contained 583 drugs. Out of these, 165 were antibiotics (28.30%), 81 (96.42%) patients were treated empirically and 3 (3.57%) patients received definitive antibiotic therapy after culture sensitivity report [8]. All the antibiotics were prescribed by generic name, out of which 130 (78.78%) were prescribed and administered by IV route, and 31 (18.78%) out of 165 were prescribed and administered as FDCs. All the 84 prescriptions evaluated according to WHO/INRUD indicators, is shown in **(Table 2).**

Prescribing indicators	
Average number of drugs prescribed per patient	6.94
Average number of antibiotics prescribed per patient	1.96
Average length of antibiotic therapy	4.3
Average length of empirical use of antibiotics	0.96
Percentage of antibiotics prescribed	28.3
Percentage of antibiotics prescribed by generic name	100
Percentage of antibiotics prescribed by intravenous route	78.78
Percentage of antibiotics prescribed as fixed dose combinations	18.78
Percentage of patients who received an antibiotic	45.2
Percentage of antibiotics available in hospital pharmacy	100
Patient indicators	
Average length of PICU stay	4.3
Percentage of mortality during PICU stay	4.76
Supplement indicators	
Percentage of patients who received antibiotic therapy as per sensitivity pattern	3.57
Patient who received empirical therapy	96.43
Patient who received definitive therapy	3.57

Table 2: Assessment of prescription patterns according to WHO/INRUD indicators.

Antibiotic utilization in pediatric intensive care unit

Ceftriaxone was the antibiotic highly used in the pediatric intensive care unit 30.6%; a detailed units of individual antibiotic utilization is shown in **(Table 3).**

Antibiotics	Units administered	Percentage of utilization
Meropenem	80	7.8
Amoxiclav	181	17.6
Azithromycin	96	9.3
Ampicillin	16	1.56
Ceftriaxone	314	30.6
Amikacin	68	6.64
Vancomycin	70	6.83
Piperacillintazobactam	45	4.39
Ciprofloxacin	64	6.24
Doxycycline	6	0.58
Cefotaxime	36	3.51
Linezolid	33	3.22
Clindamycin	9	0.8
Cefixime	4	0.39
Mupirocin	2	0.19

Table 3: Antibiotic utilization in PICU.

Pattern of antibiotics utilization as per the WHO ATC/DDD classification

DDDs mentioned in the table are for the oral route as obtained from the WHO ATC/DDD website 2012.Detailed quantitative and qualitative knowledge of antibiotic use is essential to implement approaches for limiting deviations and threats in utilization of antibiotics [9]. Antibiotic use in hospitals can be quantified using several methods. The Defined Daily Dose (DDD) as assigned by the World Health Organization (WHO) has been the most commonly used unit of measurement to quantify (e.g. as the number of DDDs used per 100 hospital days) in various settings and is particularly recommended to compare drug use between (international) settings, and has it shown its value for this purpose.Pattern of antibiotic utilization in the pediatric intensive care unit as per the WHO ATC/DDD classification is shown in **(Table 4).**

Antibiotics	DDD per 100 days	WHO DDD	PDD	PDD: DDD
Meropenem	**0.6**	**3**	**1.5**	**0.5**
Amoxiclav	1.67	3	1.9	0.63
Azithromycin	0.53	0.5	0.13	0.26
Ampicillin	0.22	6	0.96	0.16
Ceftriaxone	4.36	2	2	1
Amikacin	0.28	1	0.19	0.19
Vancomycin	0.48	2	0.7	0.35
Piperacillint azobactam	0.26	14	0.9	0.06
Ciprofloxacin	1.06	0.8	0.2	0.25
Doxycycline	0.08	0.1	0.04	0.4
Cefotaxime	0.37	4	1.56	0.39
Linezolid	0.22	1.2	0.9	0.75
Clindamycin	0.02	1.8	0.48	0.2
Cefixime	0.02	0.4	0.32	0.08

Table 4: Pattern of antibiotic utilization in PICU as per the WHO ATC/DDD classification.

Discussion

Profile of study participants

From the 84 subjects included in the study male subjects 58.33% were dominant than female 41.67%, many studies have reported a similar finding [10].The age group of infant and young child accounted for the majority of PICU admissions, has been seen in other studies.

Prescription pattern analysis as per the WHO/INRUD drug use indicators

The average number of antibiotics per prescription was 1.96, which was lower than that found in similar studies, where it ranged from 2.13 to 2.38 drugs per prescription,In our study, all the antibiotics were prescribed as generics, which helped in decreasing the overall cost of therapy; which was the highest in comparison to other studies.Antibiotics are commonly administered IntraVenous (IV) medications and is advantageous in the intensive care unit, in our study 78.78% of antibiotics were administered by IV route, relatively less and also higherin comparison to other studies [11]. The percentage of patients who received an antibiotic in our study was 45.2% may be due to lesser infectious paediatric intensive care unit admissions, similar findings were reported in European studies;while the study conducted in US,China,and Indiafound higher percentages of patients exposed to antibiotics [12].

All the antibiotics prescribed in our study were available in hospital pharmacy (100%), and were prescribed by generic name; and only 18.78% were FDCs, which was similar in comparison to other studies.The average length of PICU stay and length of antibiotic therapy in our study was 4.13 days, indicating an antibiotic was prescribed on each day of admission; similar to findings of other studies.

Percentage of mortality during PICU stay in our study was 4.76% found very lesser, with wide differences a mong other

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studies ranging from 2.1% to 7.1%,and 7.6%in some other studies a much higher mortality rate was observed [13].

In our study, percentage of patients who received antibiotic therapy as per sensitivity pattern was (3.57%) lower than other studies,and also observed empirical antibiotic therapy prescription showed clinical improvement.

Antibiotic utilization in paediatric intensive care unit

Ceftriaxone (30.6%) was the most commonly prescribed antibiotic in our study, findings of which is similar to other Asian studies. Our study has observed a substantial discrepancy in antibiotic prescription based on its severity and mortality. Rational use of antibiotics in the long run, therefore, demands continuous survey on how drugs are being prescribed and used; which could be facilitated by drug utilization studies.

ATC/DDD classification and DUS metrics

When there is a substantial discrepancy in prescription and utilization of antibiotics, it is important to take the differences into consideration in evaluating and comparing drug utilisation figures as ratios of PDD towards DDD. In our study, amoxiclav (0.63), ceftriaxone (1) and linezolid (0.75) were observed to have a normal PDD: DDD ratio within limits. However, the prescribed daily dose may show variation based on patient and disease factors. Differences between PDD and DDD in antibiotics have been reported in adults. Based on the narrow range of body weights in the pediatric population, the outcome of antibiotic assessment and utilization as per WHO DDD methodology in children (aged >1 month) is very limited and not recommended [14].

This has led to the successful development of (Point Prevalence Surveys) PPS's as a standardized web-based tool. Point prevalence survey determines the proportion of children on antibiotics, and provides information on the type of antibiotic used, indication and dosing; but the evidences in WHO SEAR countries in assessing antibiotic utilization in pediatric intensive care unit is very limited [15].

Conclusion

Antibiotics are among the most commonly used drugs in Indian settings of Paediatric Intensive Care Unit (PICU). Extensive research in exploring the new modalities like Point Prevalence Survey (PPS), Proportions of Days Covered (PDC) for both rationality and adherence, and Days Of Therapy (DOT); and antibiotic acquaintance by limiting of wasted drug weight in pediatric patients is highly recommended to ensure optimized and rational antibiotic use.

Acknowledgements

The authors would like to thank all medical and paramedical staffs of pediatric intensive care unit and management of Rural Development Trust (RDT) hospital, Bathalapalli for their constant support and continuous guidance.

Financial or other competing interests

None

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