International Journal of Basic & Clinical Pharmacology
Thalakkottor CG et al. Int J Basic Clin Pharmacol. 2025 Mar;14(2):263-268
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20250487

Original Research Article

Antibacterial prescription pattern and adverse drug reactions in childhood pneumonia

Christy George Thalakkottor[1]*, Prabitha Panattil[2], Suresh S. Vadakkedom[3]

[1]Department of Pharmacology, GMC Kottayam, Kerala, India
[2]Department of Pharmacology, GMC Ernakulam, Kerala, India
[3]Department of Pediatrics, GMC Kottayam, Kerala, India

Received: 03 January 2025
Accepted: 05 February 2025

***Correspondence:**
Dr. Christy George Thalakkottor,
Email: christygeorget94@gmail.com

ABSTRACT

Background: Antibacterial drugs play an important role in the treatment of Pneumonia-a leading cause of death globally among children. To determine the class, dosing schedule, Adverse Drug Reactions (ADRs), selection criteria and World Health Organisation (WHO) prescribing indicators of antibacterials used for pneumonia.
Methods: Following the Institutional Review Board (IRB) clearance, 18 months long descriptive study was conducted among 432 paediatric patients admitted with Pneumonia in a tertiary care center. Details on antibacterial prescription with selection criteria and associated ADRs were collected. Causality, preventability and severity of ADRs were assessed. WHO prescribing indicators were calculated. Data analysed using SPSS software.
Results: Aminopenicillins (61.2%) were the major antibacterial class prescribed and the major antibacterial was Ampicillin (34.6%) with dosage regimen 32-66 mg/kg Intravenously four times daily (34.4%) with mean treatment duration 3.6±1.26 days. Major route of administration was intravenous (57%) and 99% patients received empirical treatment. The ADRs reported were Gentamicin & Ampicillin induced Hypersensitivity reactions and Vancomycin induced Redman Syndrome. WHO prescribing indicators: Average number of antibacterials per encounter 2.42, Antibacterials prescribed by generic name 96.56%, Encounters with injection 98.37%, Antibacterials from Essential Medicines List (EML) 90.9%.
Conclusions: Aminopenicillins were the major antibacterial class, Ampicillin was the major antibacterial, Inj. Ampicillin 32-66 mg/kg intravenously four times daily with mean duration 3.6±1.26 days was the commonest dosage regimen prescribed. Most antibacterials were from EML, prescribed in generic name, selected empirically and administered intravenously. Three ADRs were reported. Prescribing indicators were calculated.

Keywords: Antibacterial drugs, Childhood pneumonia, Prescription pattern

INTRODUCTION

Pneumonia is the leading infectious cause of death globally among children <5 years, accounting for 740180 deaths in 2019 (WHO), which constitutes 14% of under 5 deaths and 22% of deaths in children aged 1-5 years.[1] India is among the top 15 countries with high disease burden, with morbidity rates of 0.2-0.5 episodes per child-year and 10-20% being severe.[2] Revised guidelines of WHO classifies pneumonia into "Pneumonia" (fast breathing and/or chest indrawing; requires home therapy with oral amoxicillin) and "Severe pneumonia" (with any danger sign; requires referral and injectable therapy), Danger signs being fast breathing, difficulty in breathing, chest wall indrawing, stridor.[3,4] Respiratory rate ≥50 breaths/min (age 2-12 months), ≥40 breaths/min (12-59 months) implies fast-breathing.[5] Beta-lactam antibacterials (benzyl penicillin, ampicillin, amoxicillin and ceftriaxone) interfering the bacterial cell wall

cross-linking, aminoglycosides (gentamicin)- interfering the bacterial-protein synthesis and cotrimoxazole-blocking the bacterial-folate metabolism (used in immunocompromised patients) are the WHO recommended antibacterials for childhood pneumonia.[3,6-8] This study describes the antibacterial prescription pattern for childhood pneumonia, ADRs, selection criteria and WHO prescribing indicators.

METHODS

Study type

This descriptive study was conducted among the in-patients diagnosed with pneumonia (revised WHO criteria).

Study place

The study was conducted in the Department of Paediatrics, in a tertiary care centre in Kerala.

Study duration

The study was conducted during July 2021 to December 2022 following IRB approval.

Calculated sample size was 762.[9] Children aged between 2 months-12 years (Department admissions include age group <12 years) were recruited. The study was conducted in 432 in-patients. Written informed consent/ informed assent was obtained from the child and legally accepted guardian. Using the proforma and case-records, demographic details and antibacterial prescription were collected. Antibacterial selection criteria were also determined.

Details of ADR were obtained by direct conversation with patient, entered into CDSCO (Central Drugs Standard Control Organisation) suspected ADR reporting form and informed to nearest ADR monitoring centre (AMC). Causality, Preventability and Severity of ADR were assessed using WHO-UMC (Uppsala Monitoring Centre) scale, Schumock-Thornton scale and Modified Hartwig-Seigel scale respectively. WHO prescribing indicators were calculated.

Data entered in Microsoft Excel and analysed using Statistical Package of Social Science (SPSS) software version-16. All qualitative variables were expressed as frequency and percentages; all quantitative variables were expressed as mean±standard deviation.

RESULTS

The mean age of the sample was 2.16±2.27 years with 288 (66.7%) aged 2 months -2 years. Male:female ratio was 3:2. Among 432 cases, 401 (93%) were 'Pneumonia' and 31 (7%) were 'Severe Pneumonia'. The mean hospitalisation duration for Severe Pneumonia was 9.68±6.12 days (minimum-4 days, maximum-30 days), for 'Pneumonia' 5.12±3 days (minimum 2 days, maximum 26 days). Among the 1048 antibacterials from 10 different classes prescribed, 875 (83.5%) were β-lactams. Most commonly prescribed antibacterials were aminopenicillins, cephalosporins and aminoglycosides respectively (Table 1).

Among the 19 different antibacterials prescribed to 432 patients, the major antibacterial was ampicillin (Table 2). The most common dosage regimen was ampicillin 32-66 mg/kg QID in 360 (34.4%), amoxicillin 30-42 mg/kg BD in 245 (23.4%), cefpodoxime 4.7-13 mg/kg BD in 75 (7.2%) and Gentamicin 4-10mg/kg OD in 57 (5.4%). Crystalline Penicillin 1 (0.1%) was the least prescribed one. Fixed dose combinations (FDC) included Amoxicillin+Clavulanic acid 10 (1%) and Piperacillin+Tazobactam 9 (0.9%). For those 31 patients with severe pneumonia, 102 antibacterials were prescribed; the major one was Ampicillin 21 (20.6%), followed by Cefpodoxime 13 (12.7%), Ceftriaxone 11 (10.8%) and Amoxicillin 11 (10.8%).

Among the patients with 'Severe Pneumonia', 3 antibacterials (17 (54.8%)) were used most commonly for treatment; intravenous Ampicillin+Gentamicin followed by oral Amoxicillin being most common. Among the patients graded with 'Pneumonia', 2 antibacterials (282 (70.3%)) were used most commonly, intravenous ampicillin followed by oral amoxicillin was most common. Intravenous antibiotics accounted for 597 (57%) of 1048 antibacterials, while oral antibiotics accounted for 451 (43%).

Ampicillin, 357 (34.06%) was the major intravenous antibacterial and amoxicillin, 268 (25.6%) was the major oral antibacterial. Generic prescriptions comprised of 1012 (97%). The mean treatment duration was as follows-ampicillin 3.6±1.26 days, amoxicillin: 6.5±0.8 days, cefpodoxime 5.8±0.9 days and gentamicin: 4.36±1.5 days. The longest treatment duration was 25 days-by clindamycin followed by meropenam-15 days; prescribed for severe pneumonia. the mean treatment duration (days) of individual drug used in: pneumonia- 5.01±1.8 and severe pneumonia. 89±3.06 respectively. Among the 1048 antibacterials, 953 (91%) were included in the EML.[10] Among the 432 patients, Culture and Sensitivity (C&S) was done for 43 patients (10%), specimen being blood. Among the 43 culture reports, majority-35 (81.3%) were 'Sterile' and 6 (13.9%) were positive cultures.

Methicillin resistant *Staphylococcus aureus* (MRSA) was the most common organism cultured, 3 (6.9%). Vancomycin and Linezolid were sensitive to all the cultured species. Among the 432 patients, 426 (99%) were treated empirically and 6 (1%) were treated according to C&S reports. All the patients (100%) were symptomatically better during discharge. Three adverse drug reactions (ADR) reported. Gentamicin and ampicillin induced hypersensitivity reactions, in the first case, the

suspected drug was discontinued and in the second case, the drug was discontinued and substituted with Cefotaxime. Redman syndrome occurred with vancomycin, in which the reaction subsided with decreased dose. Causality was 'probable' and preventability was 'preventable' in 3 cases, severity was 'mild' in 1st and 2nd, 'moderate' in third case.

WHO prescribing indicators: As this study involves antibacterial prescription pattern, in prescribing indicators the word 'drug' is replaced by 'antibacterials'.

Table 1: Class of anti-bacterial.

Class of antibacterials	Frequency	%
Aminoglycoside	84	8.0
Aminopenicillins	641	61.2
Carbapenams	17	1.6
Cephalosporins	207	19.8
Glycopeptide	14	1.3
Lincosamide	16	1.5
Macrolides	45	4.3
Oxazolidinones	14	1.3
Penicillins	1	0.1
Ureidopenicillins	9	0.9
Total	1048	100.0

Table 2: Anti-bacterial prescribed.

Antibacterials prescribed	Frequency	%
Amikacin	10	1.0
Amoxicillin	268	25.6
Amoxicillin+clavulanic acid	10	1.0
Ampicillin	363	34.6
Azithromycin	45	4.3
Cefixime	8	.8
Cefotaxime	49	4.7
Cefpodoxime	78	7.4
Ceftriaxone	56	5.3
Cefuroxime	14	1.3
Cephalexin	2	.2
Clindamycin	16	1.5
Crystalline penicillin	1	.1
Faropenam	7	.7
Gentamicin	74	7.1
Linezolid	14	1.3
Meropenam	10	1.0
Piperacillin+tazobactam	9	.9
Vancomycin	14	1.3
Total	1048	100.0

Table 3: WHO prescribing indicators.

Average no. of antibacterials per encounter	**Total no. of different antibacterials prescribed÷ No. of encounters surveyed**	**1048/432=2.42**
Percentage of antibacterials prescribed by generic name	(No. of antibacterials prescribed by generic name÷ No. of antibacterials prescribed) ×100	1012x100/1048 =96.56%
Percentage encounters with injection prescribed	No. of patient encounters with injection÷No. of encounters surveyed)x100	425x100/432=98.37%
Percentage of antibacterials prescribed from EML	(No. of antibacterials prescribed from EML÷Total no. of antibacterials prescribed) ×100	953x100/1048=90.9%

DISCUSSION

In this study, the most common age group affected was 2 months– 2 years, similar to previous studies, this might be due to the lower immunity level.[11–13] Children below 2 months were excluded due to their variable prescribing pattern. Majority were males; similar to previous studies.[11–16] The patients were classified into pneumonia and severe pneumonia based on WHO criteria.[3] Among the total patients, 93% had 'Pneumonia'(admitted due to the presence of vulnerable risk factors which may progress to severe pneumonia or inconvenience for the follow-up, majority treated on out-patient basis were not included in this study) and 7% had 'Severe Pneumonia', similar to other studies.[15] Variability may be present with other guidelines.[15] No cases of mortality were reported in our study. In this study, major age group with 'severe pneumonia' was 8months while that with 'pneumonia' was 1 year. Lack of immunization, passive smoking, low maternal education, undernutrition, low socioeconomic status and non-exclusive breast feeding are associated with severe pneumonia.[15,17] Patients with 'severe-pneumonia' had longer hospital stay; which included Intensive Care Unit (ICU) admission.[11,15,18]

In the present study, 1048 antibacterials from 10 different classes were prescribed to 432 patients, 83.5% being β-lactams. Gram positive organisms mainly *Streptococcus pneumoniae* the major etiological factor in childhood pneumonia, shows effective response towards β-lactams.[6,19] Aminopenicillins, a beta lactam drug, shows better response towards certain gram negative organisms too such as H influenzae- another major etiological factor in childhood Pneumonia.[6,20] In this study, aminopenicillins comprised 61.2% of the total antibacterials, similar to another study where Aminopenicillins (46.25%) were the most frequently prescribed antibacterial; followed by Macrolides (42%); 16 while in another study, macrolide

monotherapy was the most commonly used regimen (43.2%) which is in contrast with our study.[14]

In our study, 1048 prescribed antibacterials were categorised as 19 different antibacterials; Ampicillin was the major antibacterial, followed by Amoxicillin (Table 2). Ampicillin, an extended-spectrum Penicillin, covers the gram-negative organisms such as H influenzae in addition to the gram-positive organisms; also have more action against Listeria i.e., effective against a wide etiological spectrum causing childhood Pneumonia.[21] In this study, ampicillin in 'pneumonia' cases was promptly switched to oral amoxicillin (WHO recommendation).[3]

The most common dosage regimen of these antibacterials were more or less similar to previous studies.[16] Amoxicillin+Clavulanic acid and Piperacillin+Tazobactam were the FDCs prescribed similar to previous studies.[15,16] In a randomised controlled trial done by Vilas-Boas et al, oral amoxicillin BD dose was found to be as efficacious as TID dose.[22] In the present study,102 antibacterials were prescribed for 'severe pneumonia', the major one being ampicillin, followed by cefpodoxime, ceftriaxone and amoxicillin respectively. In the study conducted by Albuhairi et a., Ceftriaxone (55%) was the major antibacterial prescribed for 'severe pneumonia' followed by azithromycin (42.5%).[15]

Crystalline penicillin was the least prescribed antibacterial in this study, in contrast to Baby et al, where it was Cefpodoxime (8.3%).[13] Another study conducted by Khaja et al, showed Penicillin (0.9%) as the least prescribed antibacterial, similar to our study, along with gentamicin, vancomycin and piperacillin+tazobactam (0.9% each).[11]

In the present study, among the patients with 'Severe Pneumonia', treatment with 3 antibacterials was most commonly used, in which intravenous Ampicillin+Gentamicin (WHO recommendation) followed by oral Amoxicillin was most common. Among the patients with 'pneumonia', majority received atleast two drugs, intravenous ampicillin followed by oral amoxicillin was the commonest regimen. In a study done by Caballero et al, the combination antibacterial therapy was found to be superior to monotherapy, might be due to the extended coverage of typical-atypical etiological pathogens and due to the synergistic action.[23] This also prevents antimicrobial resistance.[24]

Macrolide+a narrow/broad spectrum antibacterial was the major combination therapy according to Lipsett et al.[14] Di Pietro et al, found Macrolide and Aminopenicillins+enzyme inhibitor (80.4%) as the commonest combination therapy.[16] According to Khaja et al, majority of the pneumonia patients (73%) were treated with single antibacterials and the major combination used was cephalosporin-derivatives with amikacin.[11]

In our study, majority of antibacterials were administered by intravenous route while the remaining by oral route-Ampicillin was the major intravenous drug; Amoxicillin was the major oral drug. In the study conducted by Di Pietro et al, 66.6% of antibacterials were oral and 33%were parenteral; Macrolides (62.31%) was the commonest oral antibacterial; Ampicillin±Sulbactam was the major parenteral antibacterial (74.24%).[16]

Adherence to generic drug prescriptions supports cost-effective and WHO-rational drug use criteria. Generic prescriptions accounted for 96.56% in this study, significantly higher than the 16.7% in Spain and comparable to over 60% in UK and Denmark.[25]

In this study, majority of the antibacterials were included in the EML. According to WHO, the essential drugs depend on the health requirements and health service structure of each country; should be available locally at reasonable cost and periodically updated according to the advice of experts in the respective field.[26] In our sample, 10% of patients underwent C&S. MRSA was the common organism cultured, vancomycin and linezolid were the sensitive antibacterials. Even though cloxacillin is effective against staphylococcus, the positive cultures didn't show sensitivity towards the drug; the drug was not being prescribed among the patients. In a study conducted by Albuhairi et al, blood cultures were frequently obtained, 78%.[15]

In another study by Khaja et al, blood cultures were send for 33.33% patients out of which 25.7% were positive, Ceftriaxone (77.8%) being the most sensitive drug, *Streptococcus pneumoniae* being the major pathogen.[11] Empirical treatment was given to 99% patients in our study, higher than the 91.43% reported by Khaja et al.[11] Despite limited culture testing, all patients were improved symptomatically suggesting effective institutional empirical antibacterial therapy. The institutional empirical therapy protocol covers the gram positive and certain gram-negative bacteria- the major etiological agents causing childhood Pneumonia.

Three ADRs were reported in our study. Similar cases were reported by Schrufer et al, Connolly et al and Khurana et al.[27–29] This study revealed that the hospital antimicrobial policy was in adherence with WHO recommendations.[3]

This is a single-centre study. Multi-centre studies are needed to establish standardized protocols. The sample size couldn't achieved due reduced hospital admissions during initial half of the study period due to the COVID pandemic.

CONCLUSION

Aminopenicillins were the major antibacterial class, Ampicillin was the major antibacterial, Inj. Ampicillin 32-66 mg/kg intravenously four times daily with mean duration 3.6±1.26 days was the commonest dosage regimen prescribed. Most antibacterials were from EML, prescribed in generic name, selected empirically and

administered intravenously. Three ADRs were reported. Prescribing indicators were calculated.

ACKNOWLEDGEMENTS

The author like to thank Dr. Dhanya S.P. who helped in data analysis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Pneumonia. 2022. Available at: https://www.who.int/newsroom/fact. Accessed on 12 September 2024.
2. Ghimire M, Bhattacharya SK, Narain JP. Pneumonia in South-East Asia Region: Public health perspective. Indian J Med Res. 2012;135(4):459–68.
3. World Health Organization. Revised WHO classification and treatment of pneumonia in children at health facilities: evidence summaries. Available at: https://www.ncbi.nlm.nih.gov. Accessed on 22 September 2024.
4. Ndu IK, Ekwochi U, Osuorah CDI, Onah KS, Obuoha E, Odetunde OI, et al. Danger signs of childhood pneumonia: caregiver awareness and care seeking behavior in a developing country. Int J Pediatr. 2015;2:167261.
5. Smith DK, Kuckel DP, Recidoro AM. Community-Acquired Pneumonia in Children: Rapid Evidence Review. 2021;104(6):618–25.
6. Pandey N, Cascella M. Beta-lactam antibiotics. InStatPearls. 2023 Jun 4. StatPearls Publishing.
7. Krause KM, Serio AW, Kane TR, Connolly LE. Aminoglycosides: An Overview. Cold Spring Harb Perspect Med. 2016;6(6):27029.
8. Batra P, Deo V, Mathur P, Gupta AK. Cotrimoxazole, a wonder drug in the era of multiresistance: Case report and review of literature. J Lab Physicians. 2017;9(3):210–3.
9. Nguyen PT, Tran HT, Truong HT, Nguyen VT, Graham SM, Marais BJ. Paediatric use of antibiotics in children with community acquired pneumonia: A survey from Da Nang, Vietnam. J Paediatr Child Health. 2019;55(11):1329–34.
10. Notification and Report on National List of Essential Medicines. 2022. Available at: https://main.mohfw.gov. Accessed on 12 September 2024.
11. Moinuddin K, Altaf MA. Study of prescribing pattern of antibiotic in pediatric patients with pneumonia. J Appl Pharm. 2012;4(3):67.
12. Kafle D. Prescribing pattern of antibiotics in respiratory tract infections in the pediatric indoor patients at Manipal teaching hospital. Nepal J Med Sci. 2022;7(2):46-51.
13. Baby B, Das S, Haque I, Sherief H. A Study on Prescribing Pattern of Antibiotics for Respiratory Tract Infection in Pediatric Outpatient in A Tertiary Care Hospital: A Prospective Observational Study. Int J of Pharm Sci Review and Res. 2019;21;59:30–3.
14. Lipsett SC, Hall M, Ambroggio L, Hersh AL, Shah SS, Brogan TV, et al. Antibiotic Choice and Clinical Outcomes in Ambulatory Children with Community-Acquired Pneumonia. J Pediatr. 2021;229:207-15.
15. Karuniawati HI, Yulianti T, Aini DK, Nurwienda FI. Impact of antimicrobial stewardship program on the use of antibiotics in pneumonia patients at teaching hospital in surakarta Indonesia. Int J Appl Pharm. 2021;13(1):20-3.
16. Di Pietro P, Della Casa Alberighi O, Silvestri M, Tosca MA, Ruocco A, Conforti G, et al. Monitoring adherence to guidelines of antibiotic use in pediatric pneumonia: the MAREA study. Ital J Pediatr. 2017;22;43:113.
17. Dean P, Florin TA. Factors Associated With Pneumonia Severity in Children: A Systematic Review. J Pediatric Infect Dis Soc. 2018;7(4):323–34.
18. Kafle D. Prescribing pattern of antibiotics in respiratory tract infections in the pediatric indoor patients at manipal teaching hospital. Nep J Med Sci. 2022;7(2):46–51.
19. Cutts FT, Zaman SMA, Enwere G, Jaffar S, Levine OS, Okoko JB, et al. Efficacy of nine-valent pneumococcal conjugate vaccine against pneumonia and invasive pneumococcal disease in The Gambia: randomised, double-blind, placebo-controlled trial. Lancet. 2005;26(9465):1139–46.
20. Gessner BD, Sutanto A, Linehan M, Djelantik IGG, Fletcher T, Gerudug IK, et al. Incidences of vaccine-preventable Haemophilus influenzae type b pneumonia and meningitis in Indonesian children: hamlet-randomised vaccine-probe trial. Lancet. 2005;365(9453):43–52.
21. Katzung BG, editor. Basic & clinical pharmacology. Fourteenth edition. New York Chicago San Francisco Athens London Madrid Mexico City Milan New Delhi Singapore Sydney Toronto: McGraw-Hill Education. 2018: 1250.
22. Vilas-Boas AL, Fontoura MS, Xavier-Souza G, Araújo-Neto CA, Andrade SC, Brim RV, et al. PNEUMOPAC-efficacy study group. Comparison of oral amoxicillin given thrice or twice daily to children between 2 and 59 months old with non-severe pneumonia: a randomized controlled trial. J Antimicrobial Chemoth. 2014;69(7):1954-9.
23. Caballero J, Rello J. Combination antibiotic therapy for community-acquired pneumonia. Ann Intensive Care. 2011;23:48.
24. Ahmed A, Azim A, Gurjar M, Baronia AK. Current concepts in combination antibiotic therapy for critically ill patients. Indian J Crit Care Med. 2014;18(5):310–4.
25. Rodríguez-Calvillo JA, Lana A, Cueto A, Markham WA, López ML. Psychosocial factors associated with

the prescription of generic drugs. Health Policy. 2011;101(2):178–84.
26. WHO Expert Committee on the Use of Essential Drugs - 1998 - The use of essential drugs eight. Available at: https://apps.who.int/iris/bitstream. Accessed on 21 August 2024.
27. Schrüfer P, Brockow K, Stoevesandt J, Trautmann A. Predominant patterns of β-lactam hypersensitivity in a single German Allergy Center: exanthem induced by aminopenicillins, anaphylaxis by cephalosporins. Allergy Asthma Clin Immunol. 2020;17;16:102.
28. Connolly M, McAdoo J, Bourke JF. Gentamicin-induced anaphylaxis. Ir J Med Sci. 2007;176(4):317–8.
29. Khurana C, de Belder MA. Red-man syndrome after vancomycin: potential crossreactivity with teicoplanin. Postgrad Med J. 1999;75(879):41–3.

Cite this article as: Thalakkottor CG, Panattil P, Vadakkedom SS. Antibacterial prescription pattern and adverse drug reactions in childhood pneumonia. Int J Basic Clin Pharmacol 2025;14:263-8.