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Review Article

# Cephalosporins in pediatrics: Navigating antimicrobial resistance impact and adverse effects – A comprehensive review

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ABSTRACT

**Background and Objective:** Antibiotic overuse and abuse are the primary causes of microbial resistance and the rise in healthcare costs, and human factors such as abuse, and misuse have accelerated the spread of AMR. Cephalosporin drugs are the most commonly administered drugs to pediatric populations due to their high efficacy and low side effect profile. This study aims to assess which class of antibiotic is mostly used the prevalence of third-generation cephalosporin use in pediatric patients and its impact on the development of resistance.

**Materials and Methods:** A PubMed database and reference lists of pertinent research on antibiotic usage, antimicrobial resistance, and prescription use of cephalosporin medicines were used to search the English-language literature. The publications linked here were retrospective, prospective studies using empiric antibiotic therapy for paediatric patients.

**Key Content and Findings:** A review of relevant literature confirms that Cephalosporins are more prioritized than Penicillins due to their low toxicity and high safety effect, and their higher stability to beta-lactamases. Third-generation cephalosporins are more commonly used in the pediatric population, leading to resistance development and adverse effects such as pseudolithiasis and reversible cholelithiasis. Ceftriaxone has the potential to precipitate ceftriaxone-calcium salts complex in the lungs and kidneys and can cause allergic reactions (Skin Manifestations), gastrointestinal problems, haematological abnormalities, and gallbladder resolution deficit. Ceftriaxone-induced urticaria, rash, exanthema, and pruritus are the most common adverse effects.

**Conclusion:** According to studies, the usage of third-generation cephalosporins in pediatric patients is increasing dramatically, which may play a role in the development of resistance and increased risk of production of unwanted reactions such as dermal allergies and other side effects. To reduce the dangers associated with cephalosporin usage, it is critical to follow proper prescription guidelines and prevent inappropriate or extended use of antibiotics. This can be reduced by utilizing narrower-spectrum antibiotics where necessary.



## 1. Introduction

Antimicrobials can be lifesaving in the treatment of bacterial infections and are the most usually administered drugs to pediatric populations.[1] When compared to adults, children are more susceptible to a broader range of ailments. This can be due to a variety of circumstances, including inadequate immune system development, but most significantly, unlike adults, kids are both uninformed of threats and unable to make decisions to safeguard their health.[2] And, also due to

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the variations in pharmacodynamic and pharmacokinetic properties, infants and children make up a considerable part of the population in underdeveloped nations.[1] Recurrent infections of the respiratory tract and gastrointestinal system are common in children.[3] Viral infections are estimated to account for 60% to 85% of all instances of acute infectious diarrhoea, including pathogens for which antibiotics may be prescribed (e.g., Campylobacter spp., Shigella spp., Escherichia coli, etc).[4] According to WHO standards, only 13.4-24.1% of antibiotics should be provided, yet studies show that parenteral antibiotic administration is far more common (83-85%) than oral antibiotic treatment (15%) in the paediatric population.[5] Antibiotic overuse and abuse are the primary causes of the development of microbial resistance and the rise in healthcare costs.[4] Excessive antimicrobial usage results in needless drug-related side effects as well as increased healthcare expenses.[6] Despite the fact that antimicrobial resistance is a natural result of genetic alterations, irrational human antibiotic use both encourages and accelerates the process. Some of the human factors that have accelerated the spread of AMR include antibiotic abuse and misuse, incorrect diagnosis and improper antibiotic prescribing, self-medication, insufficient healthcare settings, poor personal hygiene, and broad agricultural use. Antibiotic use has been demonstrated to alter the makeup of both adult and neonatal microbiomes, with a short course of antibiotics having a 6-month effect on microbiota composition.[7] WHO statistics indicates that infections with bacteria resistant to drugs result approximately 700,000 deaths worldwide, with about 200,000 of those deaths occurring in neonates. If such resistance did not exist, up to 40% of mortality in patients with a HAI-MRO or 12% of all HAI deaths may be prevented.an estimated 2.39 billion dollars were spent on treating MDR infections in the USA alone, a financial burden that had a considerable influence on healthcare systems.[8–10] Antibiotic resistance has become a widespread among the most commonly used antibiotics (ampicillin and gentamicin). And ceftriaxone, a second-line antibiotic, is one of the most frequently used antibiotics, having a greater utilisation density than ampicillin, a first-line medicine.[2] Ceftriaxone are the most commonly used antibiotics from the same group; however, cefotaxime and amikacin were from two separate groups. Beta-Lactam antibiotics were the most commonly administered and favoured antibiotics for combination treatment in paediatric patients.[3] It is a burden on our society that must be limited. For these compelling reasons, we have conducted a review on the pediatric use of cephalosporin, its resistance, emerging threats, and potential strategies to overcome it.

## 2. Materials and Methods

### 2.1. Search strategy and selection criteria

An extensive analysis of published publications from 2015 to 2023 was carried out. Using PubMed, Scopus, and Web of Science, the systematic review was carried out in accordance with the PRISMA checklist. PRISMA criteria, which guarantee transparency, correctness, and comprehensive reporting of systematic reviews, were followed in conducting the review.[11] The main focus was on the prospective and observational studies, and relevant reference lists about antibiotic usage, antimicrobial resistance, and prescription cephalosporin medicine use were searched. This article covered cephalosporin medications' relative risks, problems, harmful effects on children, and extensive usage in the paediatric population.

### 2.2. Inclusion criteria

1. English-language literature was selected.
2. Inclusion prioritized literature elucidating antibiotic use, antimicrobial resistance, and cephalosporin drug prescriptions.
3. The study's core focus was on pediatrics.
4. Only articles published from 2015 onward were included to capture the latest insights.

### 2.3. Exclusion criteria

1. Non-English literatures were excluded.
2. The study intentionally sidestepped content centred on adults to maintain a pediatric focus.
3. Articles predating 2015 were deliberately omitted to ensure contemporary and relevant findings.

### 2.4. Data extraction and management

The open-access, web-based technology was used to filter the search results. Each author separately extracted the data, and any differences were addressed and settled. Full-text screening was available for articles that referenced occupational safety, health and safety evaluation hazards, risk assessment techniques, or risk reduction in their title or abstract. Disagreements were settled through conversation after full texts were reviewed by all writers for inclusion.

### 2.5. Cephalosporin

Cephalosporins are beta-lactam antimicrobials that are used to treat gram-positive and gram-negative bacterial infections. Cephalosporin prevents bacteria from synthesising their cell walls. The five generations of cephalosporins are useful against various infectious diseases like skin infection, resistant bacteria, meningitis, and other infections.[12] More than 50% of in-patient pediatrics were on antibiotics, especially on third-

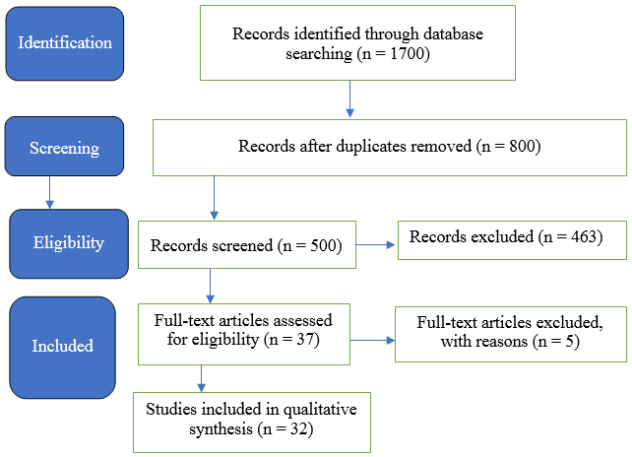


**Figure 1:** PRISMA 2022 flow diagram from:Trifu A, Smîdu E, Badea DO, Bulboacă E, Haralambie V. Applying the PRISMA method for obtaining systematic reviews of occupational safety issues in literature search. In MATEC Web of Conferences 2022 (Vol. 354). EDP Sciences. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

generation antibiotics without diagnosis or provisional diagnosis.[13] Cephalosporins are more prioritized than Penicillins and cephalosporins were proven more beneficial in bacteriology because of their low toxicity and high safety effect.[13,14] Another reason for the Cephalosporin priority over penicillin is the increased report of allergic reactions with penicillin, as some patients are hypersensitive to penicillin.[13] In that the number of prescriptions for third generation cephalosporins increased from 2010 to 2014 most remarkably; simultaneously there was a marked decrease in the use of first and second-generation cephalosporins in pediatric patients.[15] The third generation cephalosporins are active against both gram-negative and positive bacteria but more active against gram-negative bacteria and useful for the organisms which are resistant to the first and second-generation cephalosporins. The third-generation cephalosporin antibiotic shows more stability to beta-lactamases than first or second generations cephalosporin, especially with those infections which occur due to bacteria like Klebsiella, Haemophilus influenzae, Escherichia coli and Pseudomonas aeruginosa.[16] However, bacteria that belong to the cephalosporin antibiotic family, such as Listeria monocytogenes, show intrinsic resistance, which is a type of natural resistance.[17] The most common bacterial mechanisms behind intrinsic resistance are the natural activity of efflux pumps and decreased permeability of the outer membrane, particularly in relation to the lipopolysaccharide, or LPS, present in gram-negative bacteria.[18]

Prospective and observational study:

Current evidence based on different studies indicates that the third-generation cephalosporin is a more commonly used antibiotic in the pediatric population.

According to the preceding remark, there is a sharper increase in the usage of third generation cephalosporins in the pediatric population, which may be the cause of resistance development. The widespread use of third-generation cephalosporins contributes to the emergence and dissemination of ESBL-producing bacterial infections.[15] Non-constrained usage of third-generation cephalosporins may enhance Escherichia coli and Klebsiella pneumonia resistance.[13] In the pediatric population with the risk factor of rapid decline in enteral nutrition, long-term hunger, and weight loss, the use of third-generation cephalosporin might produce adverse effects such as pseudolithiasis and reversible cholelithiasis. Pseudolithiasis and reversible cholelithiasis are conditions that develop after the complex formation between ceftriaxone with calcium which gets precipitated in the gallbladder, resulting in abnormalities in the gallbladder on ultrasonography. Nephrolithiasis is an uncommon consequence of ceftriaxone medication. Nephrolithiasis can be caused by inorganic salt precipitation as well as genetic/metabolic abnormalities that promote stone modulator malfunction. These ceftriaxone-related problems, biliary pseudolithiasis, and nephrolithiasis are frequently asymptomatic and transitory after ceftriaxone medication. The chance of developing biliary sludge or stone development is increased in older children.

Abnormal gallbladder sonograms with biliary sludge or lithiasis were found in 20.9% of the ceftriaxone group and 5.9% of the cefotaxime group. The prevalence of nephrolithiasis was 1.2% in the ceftriaxone group and 1.5% in the cefotaxime group.[25] As we know from the above statement that ceftriaxone has the danger of precipitating ceftriaxone-calcium salts complex in the lungs and kidneys, the WHO and FDA have advised to not give ceftriaxone and calcium-containing fluids to new-borns at the same time.[5]

Ceftriaxone also causes allergic responses (like, rash, eosinophilia, fever, anaphylactic shock) gastrointestinal problems (rise transaminase enzyme temporarily), hematological abnormalities (granulocytopenia, thrombocytopenia, haemolytic anemia), and gallbladder resolution deficit. Because ceftriaxone is heavily linked to plasma proteins (97%), it can displace bilirubin from its protein binding sites in newborns, exacerbating physiological jaundice.[5]

## 3. Case Study

Bartkowska-Śniatkowska A et. al., 2 July 2015 has reported that ceftriaxone can cause transient reversible biliary pseudolithiasis infrequently but rarely causes nephrolithiasis or ceftriaxone–calcium precipitates in the lungs and kidneys. The incidence of this phenomenon in the paediatric population has been reported to range from 3% to 50%, particularly in older children receiving higher doses of ceftriaxone (>2 g/kg/day) as long-term therapy (5-

**Table 1:** The generation of cephalosporins and their antibacterial activity.

| Generation | Example | Active against |
|---|---|---|
| first-generation cephalosporins | Adroxil, cefazolin, and cephalexin [19] | solely active against gram-positive organisms [14] |
| second-generation | cefaclor, cefotetan, cefamandole, and loracarbef [20] | improved activity against gram-negative and some anaerobes, although there is less activity against gram-positive microbes [14] |
| The third-generation class of cephalosporins (most commonly prescribed group) | ceftriaxone, cefdinir, cefixime, cefixime, cefditoren, cefpodoxime, ceftazidime, cefoperazone, ceftizoxime, ceftibuten, and others [16] | Activity against both gram-negative and gram-positive organisms. They are more effective against gram-negative bacteria and species that are resistant to first and second-generation cephalosporins. Active against pseudomonas aeruginosa show more stability Klebsiella, Haemophilus influenzae, and Escherichia coli [14] |
| The fourth-generation cephalosporins | Cefepime [21] | active on many gram-positive and gram-negative strains ICU pneumonia, gastrointestinal infections, sepsis, and meningitis are all examples of severe infections [14] |
| The novel fifth-generation cephalosporins | Ceftaroline [22] | active against methicillin-resistant Staphylococcus aureus (MRSA), penicillin-resistant streptococci, ampicillin-susceptible, beta-lactamase-producing Enterococcus faecalis [14] |

**Table 2:** Various observational and prospective study findings.

| Study name | Number of participants and study duration | Results |
|---|---|---|
| A Prospective Study on Cephalosporin Utilization by Pattern in Pediatric Patients | Enrolled 3736 patients and 6 months duration | 67.57% ceftriaxone, 29.62% Cefotaxime Sodium, 1.94%, Ceftazidime and 0.92 % Cefixime were used among 2863 pediatric patients who were on antibiotics [13] |
| A study of antimicrobial use in children admitted to pediatric medicine ward of a tertiary care hospital | Enrolled 265 children and 12 months duration | Total number of antibiotics were 535 and the highest prescribed antibiotic ceftriaxone 84.71%. whereas cephalexin 0.2% and ceftazidime 0.2% and Ceftazidime, cefotaxime plus gentamicin, cefepime, and ampicillin plus gentamicin were prescribed only to 13.5% of participants diagnosed as very severe pneumonia [23] |
| Increased use of third-generation cephalosporin antibiotics in the outpatient setting in Korean children and adolescents. | Enrolled 1,039, 756 pediatric patients and 4 years duration | the use of cefpodoxime increased by 96.0% while the use of cefuroxime decreased in pediatric population for serious infections such as meningitis, lower respiratory, tract complicated urinary tract infection, skin, bone and joint infections and bacteraemia [15] |
| A study of antimicrobial use in children admitted to pediatric medicine ward of a tertiary care hospital. | enrolled 80 children and one year duration | Cefuroxime was mostly prescribed and the use of other drugs like Ceftazidime, cefotaxime plus gentamicin, cefepime, and ampicillin plus gentamicin were prescribed only to 13.5% participants diagnosed as very severe pneumonia who was having the symptoms like, breathlessness, cold, and crying [24] |

6 days), with symptoms spontaneously disappearing within 1-2 weeks of drug discontinuation. [26]

Taormina G et. al., 3 April 2021 has reported that the presence of fluoroquinolone resistance in this isolate is concerning because ciprofloxacin is commonly used for chemoprophylaxis of close contacts and it is often more convenient to prescribe and administer than other options. Fluoroquinolone resistance in N. meningitidis in the United States is uncommon, but several cases were reported in Minnesota and North Dakota in 2007–2008. As a result, the CDC recommended avoiding ciprofloxacin as chemoprophylaxis for contacts of further meningococcal disease cases in this area. More frequent susceptibility testing of N. meningitidis isolates may be useful to assess resistance and inform prophylaxis decisions. [27]

Toczyłowski K et. al., 10 July 2022 has reported that the Various reports have documented that the hyperinflammatory responses are seen in children after the first wave of COVID. SARS- CoV-2 exposure triggers cytokine storm (exaggerated innate and adaptive immune response) and causes Multisystem inflammatory syndrome in children (MIS-C). Therapy essentially consists of anti-inflammatory and immunomodulatory medications, but according to the report (90%) children diagnosed with MIS-C were administered at least one antibiotic and in that (14%) children received antibiotics from at least three different classes. (81%) children were treated with third generation antibiotics. All infants with MIS-C were on antibiotics due to the increased procalcitonin level and same symptoms as lower respiratory tract infection antibiotic treatment should

be terminated as soon as the MIS-C diagnosis is established or when negative results of the microbiological examination are obtained 64% of children were on broad-spectrum antibiotics and from total children 84% were diagnosed with MIS-C. It is difficult to avoid antibiotic use in the initial phase of treatment because of the disease pattern and the similarity of symptoms to serious bacterial infections. The bacterial infections in patients with MIS-C are rare so emphasis the early withdrawal of antibiotics after the diagnosis of MIS-C.[28]

In a rare case, Vivek S. Guleriaet.al. (Apr-Jun 2014) reported Ceftriaxone-induced DRESS syndrome. The patient initially received ceftriaxone (1 g, IV, every 24 h) for pneumonia. On the 7th day, transaminase elevation occurred, and by the 11th day, there was a recurrence of high-grade fever, maculopapular rash over the trunk and extremities, and swelling of wrists and ankles. A diagnosis of ceftriaxone-induced DRESS was confirmed using RegiSCAR criteria. Ceftriaxone was halted, and the patient was treated with dexamethasone (4 mg, thrice daily for 2 days) followed by oral prednisolone (60 mg/day tapered over 6 weeks). Remarkably, symptomatic improvement began within 48 hours of initiating steroid therapy.[29]

VageeshwariDevuni. et. al., April-June 2019 has reported that Common side effects of ceftriaxone include urticaria, rash, exanthema, and pruritus; these are often caused by IgE antibodies binding to mast cells after drug exposure. The patient presented with a rash and red raised skin lesions over the face, trunk, and upper limbs, along with intense itching; a cutaneous examination revealed a diffuse erythematous, blanchable, maculopapular rash over the cheeks and abdomen; the patient's medical history included prior medication with Tab. Monocef 1gm BD and Inj. Depo-Medrol 80 mg; a confirmed diagnosis of ceftriaxone-induced skin rash led to the initiation of treatment with Inj. Decadron 1CC IV BD and Inj. Avil 1CC IV, which address the inflammatory mediators released during the antibody reaction on the surfaces of mast cells.[30]

## 4. Discussion

Our review found that Cephalosporins have been the drug of choice for the treatment of various infections since they have a better widespread over an array of organisms i.e., they have a good susceptibility over gram-negative and gram-positive bacteria. Cephalosporins are also preferred over other antimicrobials because they have a better efficacy and low toxicity along with lower incidence of allergic reactions over penicillin and other antibiotics. There are 5 generations of Cephalosporin drugs, but the third generation is preferred since it works on gram-positive and negative bacteria and has more stability than the prior two generations.

Cephalosporins have been the most prescribed antibiotics in the current scenario especially in the paediatric population since they are more susceptible to infections and a long-term use of antibiotics can lead to AMR (antimicrobial resistance).[14]

The diverse and highly beneficial class of beta-lactam antibiotics known as cephalosporins works through a mode of action that depends on bacterial replication to be effective. The main ways that bacteria build up tolerance to Cephalosporins include drug inactivation by beta-lactamases or mutations of the antibacterial target (PBPs).[31]

As many infectious diseases become resistant to antimicrobials, it is a serious cause for concern that antimicrobial resistance might become a significant issue and cause future problems for the child or patient.[13] Antibiotic off-label usage, in which many antibiotic prescriptions are written for the same patient, is the main source of concern. The majority of off-label medicines these days are written for neonates. Among the 15 antibacterial medications prescribed in paediatrics most frequently, only six had supporting data. There should be a specialised approach to managing off-label medication as the risk of antibiotic resistance is rising globally.[32]

Additionally, The use of third-generation cephalosporins is sharply increasing in the paediatric population, which, in light of the statement above, maybe the root of the emergence of resistance. Third-generation cephalosporin usage is ubiquitous, which aids in the development and spread of bacterial infections that produce ESBL. Third-generation cephalosporin usage without restriction may increase resistance to Klebsiella pneumonia and Escherichia coli. The usage of third-generation cephalosporin may result in negative side effects such as pseudolithiasis and reversible cholelithiasis in the paediatric population with the risk factor of rapid fall in the overall development of the child.[13]

Patients who are sensitive to cephalosporins or who have experienced anaphylactic shock from penicillin or another beta-lactam antibiotic are among those who should not take it. Due to claims that ceftriaxone displaces bilirubin from albumin, raising free bilirubin concentrations and raising the risk of jaundice in newborns, ceftriaxone is contraindicated in infants with hyperbilirubinemia. It's crucial to keep an eye out for allergic reactions like hives, itching, and swelling as well as potential anaphylactic response symptoms. Additionally, doctors and pharmacists must routinely check renal function as it may possibly necessitate adjusting the cephalosporin dose and/or frequency (except for ceftriaxone).[14]

Following the complicated synthesis of ceftriaxone and calcium that precipitates in the gallbladder and causes anomalies in the gallbladder on ultrasonography, pseudolithiasis and reversible cholelithiasis are diseases that emerge. A rare side effect of ceftriaxone therapy is nephrolithiasis. Inorganic salt precipitation and

genetic/metabolic disorders that encourage stone modulator dysfunction can both contribute to nephrolithiasis. After taking ceftriaxone, these issues, biliary pseudolithiasis, and nephrolithiasis, are typically asymptomatic and transient. Children who are older have a higher risk of getting biliary sludge or stones.[25]

Additionally, ceftriaxone might result in gastrointestinal issues (temporarily raising transaminase enzyme), allergic reactions (such as rash, eosinophilia, fever, and anaphylactic shock), haematological abnormalities (such as granulocytopenia, thrombocytopenia, and haemolytic anaemia), and gallbladder resolution insufficiency. Because ceftriaxone is heavily associated with plasma proteins (97%), it can displace bilirubin from its protein binding sites in newborns and worsen physiological jaundice.[26]

In the context of multidrug resistance, new medications have been licenced to treat organisms that exhibit resistance to several drugs. These include siderophore cephalosporins (cefiderocol), new aminoglycosides (plazomicin), tetracycline derivatives (eravacycline), fourth-generation fluoroquinolones (delafloxacin), novel combinations of one β-lactam and one β-lactamase inhibitor (meropenem and vaborbactam), and agents under development to treat drug-resistant tuberculosis (pretomanid).[33]

Our review article presented a comprehensive examination of the safety, effectiveness, and possible consequences for antimicrobial resistance of cephalosporins in paediatric healthcare, making our systematic review the first to do so. Study insights guide future research and practical applications in this vital field of pediatric healthcare.

The main key findings highlight the significance of using cephalosporins sparingly in paediatric healthcare, weighing their advantages against the possible hazards of side effects and antibiotic resistance. Healthcare procedures are guided by this knowledge to protect paediatric patients' health and safety in the face of changing infectious disease control obstacles.

## 5. Limitations

Limitations of this study include potential biases arising from the retrospective and observational nature of the analyzed literature, introducing selection bias. The focus on English-language publications might limit global representation. Variability in prescription practices across regions may affect generalizability. Additionally, data extraction and management processes, while carefully conducted, could have inherent subjectivity. Despite these limitations, the study provides valuable insights into pediatric cephalosporin use, resistance, and associated challenges, contributing to the ongoing discourse on prudent antibiotic practices.

## 6. Conclusion

Our review underscores the pivotal role of Cephalosporins which are the most often given antibiotics in children due to their widespread use, effectiveness, low toxicity, and low frequency of adverse reactions. Because of its higher effectiveness and lower toxicity, the third generation is chosen. However, the escalating off-label use, particularly in neonates, and the rising prevalence in the usage of third generation cephalosporins in paediatric patients is increasing dramatically, which may be a role in the development of resistance. Non-restricted use of these antibiotics can result in the formation and spread of bacterial infections producing extended-spectrum beta-lactamases (ESBLs). Antimicrobial resistance is a big issue, and the usage of third generation cephalosporins in the paediatric population is growing, which may be the source of resistance.

Unrestricted use of third generation cephalosporins may result in increased resistance to Klebsiella pneumonia and Escherichia coli, as well as undesirable side effects such as pseudolithiasis and reversible cholelithiasis in the paediatric population. Ceftriaxone is contraindicated in hyperbilirubinemia neonates due to reports that it displaces bilirubin from albumin, elevating free bilirubin concentrations and increasing the risk of neonatal jaundice. It is critical to monitor renal function and look for allergic responses and probable anaphylactic response signs. Cephalosporin antibiotics have been shown to produce dermatological side effects such as Red Mann Syndrome and other skin manifestations.

To reduce the dangers associated with cephalosporin usage, it is critical to follow proper prescription guidelines and prevent inappropriate or extended use of antibiotics. This can be reduced by utilising narrower-spectrum antibiotics where necessary, employing susceptibility testing to guide treatment decisions, and taking into account the potential side effects and dangers associated with each antibiotic. Future research should focus on refining prescribing guidelines, exploring innovative alternatives, and addressing emerging challenges in pediatric antimicrobial therapy.

## 7. Source of Funding

None.

## 8. Conflict of Interest

None.

## References

1. Patel NN, Patel DJ, Desai HA. Antimicrobial utilization pattern among pediatric inpatients of a tertiary care hospital in Central Gujarat. *Natl J Physiol Pharm Pharmacol*. 2019;9(11):1152–5.
2. Chaw PS, Schlinkmann K, Raupach-Rosin H, Karch A, Pletz MW, Huebner J, et al. Antibiotic use on paediatric inpatients in a teaching

hospital in the Gambia, a retrospective study. *Antimicrob Resist Infect Control*. 2018;7:82. doi:10.1186/s13756-018-0380-7.
3. Thapaliya K, Shrestha S, Bhattarai S, Basnet D, Chaudhary RK. Prescribing pattern of antibiotics in pediatric hospital in chitwan district in Nepal. *World J Pharm Pharm Sci*. 2015;4(11):1631–41.
4. Okubo Y, Miyairi I, Michihata N, Morisaki N, Kinoshita N, Urayama KY, et al. Recent Prescription Patterns for Children With Acute Infectious Diarrhea. *J Pediatr Gastroenterol Nutr*. 2019;68(1):13–6.
5. Bartkowska-Śniatkowska A, Jończyk-Potoczna K, Zielińska M, Rosada-Kurasińska J. Adverse reaction to ceftriaxone in a 28-day-old infant undergoing urgent craniotomy due to epidural hematoma: review of neonatal biliary pseudolithiasis. *Ther Clin Risk Manag*. 2015;11:1035–41.
6. Paul T, Hamid MR, Alam MS, Nishuty NL, Hossain M, Sarker T, et al. 6.Prescription pattern and use of antibiotics among pediatric outpatients in Rajshahi city of Bangladesh . *Int J Pharm Sci Res*. 2018;9(9):1964–70.
7. Amin MT, Aty MAE, Ahmed SM, Elsedfy GO, Hassanin ES, El-Gazzar AF, et al. Over prescription of antibiotics in children with acute upper respiratory tract infections: A study on the knowledge, attitude and practices of non-specialized physicians in Egypt. *PLoS One*. 2022;17(11):e0277308. doi:10.1371/journal.pone.0277308.
8. Romandini A, Pani A, Schenardi PA, Pattarino GAC, Giacomo CD, Scaglione F, et al. Antibiotic Resistance in Pediatric Infections: Global Emerging Threats, Predicting the Near Future. *Antibiotics (Basel)*. 2021;10(4)::393. doi:10.3390/antibiotics10040393.
9. Barrasa-Villar JI, Aibar-Remón C, Prieto-Andrés P, Mareca-Doñate R, Moliner-Lahoz J. Impact on Morbidity, Mortality, and Length of Stay of Hospital-Acquired Infections by Resistant Microorganisms. *Clin Infect Dis*. 2017;65(4):644–52.
10. Johnston KJ, Thorpe KE, Jacob JT, Murphy DJ. The incremental cost of infections associated with multidrug-resistant organisms in the inpatient hospital setting-A national estimate. *Health Serv Res*. 2019;54(4):782–92.
11. Page MJ, Mckenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Antibiotics (Basel)*. 2021;10(4):393. doi:10.3390/antibiotics10040393.
12. Magdaleno A, Saenz ME, Juarez AB, Moretton J. Effects of sixantibiotics and their binary mixtures on growth of Pseudokirchneriellasubcapitata. *Ecotoxicol Environ Saf*. 2015;113:72–8. doi:10.1016/j.ecoenv.2014.11.021.
13. Juno AA, Baig MT, Khan RA, Krishan, Musatafa B, Shahid U, et al. A Prospective Study on Cephalosporin Utilization by Pattern in Pediatric Patients. *J Hunan Univ (Nat Sci*. 2022;49(2):34–40. doi:10.55463/issn.1674-2974.49.2.3.
14. Bui T, Preuss CV. Cephalosporins. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
15. Song I, Park SJ, Byun SJ, Choe YJ, Shin JY. Increased use of third-generation cephalosporin antibiotics in the outpatient setting in Korean children and adolescents. *Pediatr Int*. 2018;60(9):803–10.
16. Arumugham VB, Gujarathi R, Cascella M. Third Generation Cephalosporins; 2022. [Updated 2022 Sep 19]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549881/.
17. Reygaert WC. An overview of the antimicrobial resistance mechanisms of bacteria. *AIMS Microbiol*. 2018;4(3):482–501.
18. Cox G, Wright GD. Intrinsic antibiotic resistance: mechanisms, origins, challenges and solutions. *Int J Med Microbiol*. 2013;303(6-7):287–92.
19. Hsieh WC, Ho SW. Evaluation of antibacterial activities of cephalosporin antibiotics: cefazolin, cephaloridine, cephalothin, and cephalexin. *Zhonghua Min Guo Wei Sheng Wu Xue Za Zhi*. 1975;8(1):287–92.
20. Rhyou H, Nam YH, Kim S, Doo G, Ha CY, Nam HJ, et al. Cefaclor-induced hypersensitivity: Differences in the incidence of anaphylaxis relative to other 2nd and 3rd generation cephalosporins. *PLoS One*. 2021;16(7):e0254898. doi:10.1371/journal.pone.0254898.
21. Feigin RD, Cherry JD, Kaplan SL. Feigin and Cherry's Textbook of Pediatric Infectious Diseases. 6th Edn.; 2009. doi:10.1016/B978-1-4160-4044-6.50004-2.
22. Duplessis C, Crum-Cianflone NF. Ceftaroline: A New Cephalosporin with Activity against Methicillin-Resistant Staphylococcus aureus (MRSA). *Clin Med Rev Ther*. 2011;3:a2466. doi:10.4137/CMRT.S1637.
23. Baidya S, Hazra A, Datta S, Das AK. A study of antimicrobial use in children admitted to pediatric medicine ward of a tertiary care hospital. *Indian J Pharmacol*. 2017;49(1):10–5.
24. Rashid MM, Chisti MJ, Akter D, Sarkar M, Chowdhury F. Antibiotic use for pneumonia among children under-five at a pediatric hospital in Dhaka city, Bangladesh. *Patient Prefer Adherence*. 2017;11:1335–42.
25. Ustyol L, Bulut MD, Agengin K, Bala KA, Yavuz A, Bora A, et al. Comparative evaluation of ceftriaxone- and cefotaxime-induced biliary pseudolithiasis or nephrolithiasis: A prospective study in 154 children. *Hum Exp Toxicol*. 2016;36(6):547–53.
26. Bartkowska-Śniatkowska A, Jończyk-Potoczna K, Zielińska M, Rosada-Kurasińska J. PMCID. 2015.
27. Taormina G, Campos J, Sweitzer J, Retchless AC, Lunquest K, Mcnamara LA, et al. Ciprofloxacin-Resistant Neisseria meningitidis Isolated From a 5-Month-Old Boy in the United States. *J Pediatric Infect Dis Soc*. 2021;10(3):379–81.
28. Toczyłowski K, zna JŁZ, Pałyga-Bysiecka I, Ludwikowska KM, Okarska-Napierała M, Dudek N, et al. Use of broad-spectrum antibiotics in children diagnosed with multisystem inflammatory syndrome temporarily associated with SARS-CoV-2 infection in Poland: the MOIS-CoR study. *Int J Infect Dis*. 2022;122:703–9. doi:10.1016/j.ijid.2022.07.021.
29. Guleria VS, Dhillon M, Gill S, Naithani N. Ceftriaxone induced drug rash with eosinophilia and systemic symptoms. *J Res Pharm Pract*. 2014;3(2):72–4. doi:10.4103/2279-042X.137077.
30. Devuni V. Ceftriaxone induced rash dermatitis: a case report. *Int J Sci Healthcare Res*. 2019;4(2):176–8.
31. Etebu E, Arikekpar I. Antibiotics: Classification and mechanisms of action with emphasis on molecular perspectives. *Int J Appl Microbiol Biotechnol Res*. 2016;4:90–101.
32. Tang L, Zhao K, Hou N. Off-label use of antimicrobials among hospitalized children: a retrospective study of 3,406 patients. *Front Microbiol*. 2023;14:1173042. doi:10.3389/fmicb.2023.1173042.
33. Terreni M, Taccani M, Pregnolato M. New Antibiotics for Multidrug-Resistant Bacterial Strains: Latest Research Developments and Future Perspectives. *Molecules*. 2021;26(9):2671. doi:10.3390/molecules26092671.

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