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Antibioticresistance in the Pediatric Population: Acomprehensive Review of Current Trends and Stewardship Strategies

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ABSTRACT: Antibiotic resistance (AR) has emerged as a major global health concern, particularly within the paediatric population, where infectious disease burden and antibiotic exposure are high. Children frequently receive antibiotics for viral or self-limiting infections, often due to diagnostic uncertainty and parental pressure. Such inappropriate use has driven the rise of resistant pathogens, including Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, and Streptococcus pneumoniae. These organisms exhibit multidrug resistance that contributes to prolonged illness, treatment failure, and increased healthcare costs. This review discusses the epidemiology and drivers of paediatric antibiotic resistance, focusing on global and regional trends and the urgent need for effective antimicrobial stewardship (AMS) programs. Key factors such as over-the-counter antibiotic availability, lack of paediatric-specific guidelines, and inadequate microbiological surveillance are highlighted as major contributors. Implementation of paediatric AMS frameworks that promote evidence-based prescribing, dose optimization, and narrow-spectrum use has demonstrated improved clinical outcomes. Addressing this escalating issue requires coordinated efforts across healthcare, public health, and policy sectors. Strengthened stewardship practices, public education, and vaccination strategies are essential to curb resistance and preserve antibiotic efficacy for future generations.

KEYWORDS: Antibiotic resistance, Paediatrics, Antimicrobial stewardship, Global health, Multidrug resistance

I. INTRODUCTION

Antibiotic resistance represents one of the most significant public health challenges of the 21st century[1].In children, antibiotic resistance poses a particularly severe threat as paediatric infections are common, and empiric antibiotic therapy is frequently used[2]. Despite major advances in antimicrobial development, the misuse and overuse of antibiotics in children continue to drive resistance[3].The global burden of antimicrobial resistance continues to escalate, with paediatric populations bearing a significant share of the impact. Recent analyses estimate that antimicrobial-resistant infections account for hundreds of thousands of deaths among children annually, especially in low- and middle-income countries where diagnostic support and access to effective antibiotics are limited[9] . The clinical consequences include prolonged hospitalization, delayed recovery, and increased healthcare costs due to the need for second-line or combination therapies. Neonatal and paediatric sepsis caused by multidrug-resistant organisms has become a major contributor to mortality in hospital settings[16] . Furthermore, resistant pathogens such as Klebsiella pneumoniae and Streptococcus pneumoniae are now being detected increasingly in community-acquired infections, demonstrating the shift of resistance from hospital to community levels. Strengthening surveillance systems, promoting rational antibiotic use, and enforcing paediatric stewardship interventions are therefore critical to prevent the global spread of resistant infections and safeguard antibiotic efficacy for future generations.

EPIDEMIOLOGY AND GLOBAL TRENDS

Globally, antibiotic-resistant infections are increasing among pediatric populations[4] . In low- and middle-income countries, including India, the burden is particularly high due to limited diagnostic capacity, over-the-counter antibiotic availability, and suboptimal infection control[5] . Data from the Indian Council of Medical Research (ICMR) indicate alarming rates of multidrug resistance among pediatric isolates, with pathogens such as

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Escherichia coli, Klebsiella pneumoniae, and Staphylococcus aureus being particularly concerning[6] . Studies have shown that up to 40–60% of bacterial isolates from pediatric bloodstream and respiratory infections exhibit resistance to commonly used first-line antibiotics[7] . Globally, Streptococcus pneumoniae resistance to macrolides and Haemophilus influenzae resistance to ampicillin have been increasing, complicating empirical treatment in children[8] . In Africa and South Asia, neonatal sepsis caused by extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae is now a major cause of preventable deaths[9] . The World Health Organization's Global Antimicrobial Resistance and Use Surveillance System (GLASS) continues to highlight a rapid rise in multidrug-resistant infections in pediatric age groups, underscoring the urgent need for targeted stewardship and surveillance.

FACTORS CONTRIBUTING TO PEDIATRIC ANTIBIOTIC RESISTANCE

The drivers of pediatric antibiotic resistance include inappropriate prescribing, self-medication, incomplete treatment courses, and the use of broad-spectrum antibiotics[9] . Diagnostic uncertainty often leads physicians to initiate empirical therapy even for viral infections, which accelerates resistance development[10] . In many hospitals, the absence of pediatric-specific antibiotic guidelines and limited microbiological testing contribute to irrational antibiotic selection[11]. Overcrowded healthcare settings, inadequate infection-control measures, and the unregulated use of antibiotics in neonatal and pediatric intensive-care units further amplify resistance spread[12].

Beyond hospital factors, environmental and social contributors play a critical role. Over-the-counter availability of antibioticsencourages self-medication, while parental expectations frequently pressure clinicians to prescribe antibiotics unnecessarily[13]. In several developing regions, antibiotic residues have been detected in food, animal feed, and water sources due to extensive agricultural use[14] . Poor sanitation, contaminated drinking water, and substandard pharmaceutical formulations expose children to resistant organisms even before illness develops[15] . Collectively, these factors form a complex cycle of resistance transmission between humans, animals, and the environment, highlighting the need for a unified One-Health approach to mitigate pediatric antimicrobial resistance[16] .

CLINICAL CONSEQUENCES

Children infected with resistant pathogens experience longer hospital stays, higher morbidity, and mortality[12]. Neonates, in particular, are vulnerable to resistant sepsis, which contributes significantly to neonatal deaths in developing countries[14] . The economic burden is also substantial, driven by prolonged therapy and costly second-line drugs[15] .

ANTIBIOTIC STEWARDSHIP IN PAEDIATRICS

Antibiotic stewardship in pediatric practice is an essential strategy to combat the growing threat of antimicrobial resistance[27] . The goal of stewardship programs is to ensure the right antibiotic, at the right dose, for the right duration, and only when necessary. Children often receive antibiotics for upper respiratory and ear infections, where viral etiologies predominate, leading to unnecessary exposure. Implementing evidence-based clinical guidelines and improving diagnostic accuracy can significantly reduce inappropriate prescriptions. Hospital-based pediatric ASPs, incorporating multidisciplinary teams of pediatricians, pharmacists, and microbiologists, have demonstrated marked reductions in antibiotic consumption and resistance trends[28] . Such programs also include auditing prescriptions, reviewing empiric therapy, and encouraging the use of narrow-spectrum agents whenever possible.

Education and feedback are key elements of sustainable stewardship initiatives. Training healthcare workers in antibiotic selection and resistance mechanisms has shown measurable success in reducing misuse. In low- and middle-income countries, including India, national action plans have supported pediatric-specific ASP frameworks under ICMR and WHO guidance[29] . Integration of stewardship into infection prevention programs, supported by digital prescribing surveillance tools, can further enhance compliance and clinical outcomes. Continuous monitoring, parental awareness campaigns, and community engagement are essential to achieving long-term success in preserving antibiotic efficacy for future pediatric populations[29] .

EMERGING THREAT OF ANTIBIOTIC RESISTANCE IN CHILDREN

The emergence of multidrug-resistant organisms (MDROs) among children represents a growing global health emergency[33]. Recent epidemiological evidence highlights an alarming rise in pathogens such as extended-spectrum beta-

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lactamase (ESBL)-producing Enterobacteriaceae, carbapenem-resistant Klebsiella pneumoniae, methicillin-resistant Staphylococcus aureus (MRSA), and macrolide-resistant Mycoplasma pneumoniae. These organisms are now increasingly detected in both hospital and community settings, affecting neonates, infants, and immunocompromised children[35]. In neonatal units, outbreaks of multidrug-resistant Klebsiella and Acinetobacter species have been reported with mortality rates exceeding 30%, underscoring the severe clinical implications[36].

Globally, the spread of resistance genes through plasmids and mobile genetic elements accelerates the dissemination of resistance across bacterial species[37]. Poor infection control practices, prolonged hospitalizations, and extensive antibiotic exposure in neonatal intensive care units further intensify the problem. The COVID-19 pandemic has also indirectly aggravated antibiotic resistance due to widespread empiric antibiotic use and disrupted stewardship efforts[38]. In resource-limited regions, surveillance gaps, unregulated antibiotic distribution, and limited access to diagnostic tools make early detection difficult. If not addressed urgently, pediatric antibiotic resistance threatens to reverse decades of progress in infectious disease management and jeopardize child survival globally[39].

PATTERNS, DRIVERS, AND PREVENTION STRATEGIES

Patterns of pediatric antibiotic resistance differ significantly between regions, reflecting variations in antibiotic availability, prescribing behaviors, and infection control infrastructure[40]. In developed countries, resistance is often associated with hospital-acquired infections, whereas in low- and middle-income nations, community-acquired resistance is a growing concern due to widespread empirical use and unregulated antibiotic sales[41]. The most common resistance patterns in pediatric populations involve β-lactam and macrolide resistance, followed by increasing carbapenem resistance among gram-negative bacteria[42]. Major drivers include diagnostic uncertainty, lack of pediatric-specific antibiotic policies, and economic pressures that lead to the overuse of broad-spectrum agents[43]. Social and cultural factors—such as parental expectations for quick recovery, antibiotic sharing, and poor public knowledge—further exacerbate the problem[44].

Effective prevention strategies require a holistic, multisectoral approach based on the One Health framework. Strengthening national surveillance systems and implementing antimicrobial stewardship programs tailored for pediatric care are essential[45]. Promoting immunization programs reduces the incidence of bacterial infections and indirectly lowers antibiotic demand. Infection prevention and control measures—including hand hygiene, aseptic delivery practices, and safehospital environments—play a vital role[46]. In community settings, awareness campaigns can reduce unnecessary antibiotic use, while ensuring access to clean water and sanitation can minimize infection risk. Regulation of non-therapeutic antibiotic use in livestock and agriculture should be enforced globally to prevent environmental dissemination of resistance[47]. Capacity building for healthcare providers, development of rapid diagnostic tests, and integration of antibiotic education in school curricula can further strengthen preventive efforts[48].

TYPES OF ANTIBIOTIC RESISTANCE IN PEDIATRIC INFECTIONS

Antibiotic resistance in pediatric infections encompasses a diverse range of bacterial species and mechanisms that compromise treatment efficacy. The most common resistant organisms encountered in pediatric populations include Staphylococcus aureus (MRSA and MSSA), Escherichia coli and Klebsiella pneumoniae (ESBL and CRE producers), Acinetobacter baumannii (CRAB), Enterococcus faecium (VRE), and Pseudomonas aeruginosa. These pathogens are responsible for bloodstream, respiratory, skin, and soft tissue infections that often exhibit limited therapeutic options.

Methicillin-resistant and Methicillin-susceptible Staphylococcus aureus (MRSA and MSSA): MRSA remains one of the most clinically significant resistant pathogens in pediatrics. It arises from the acquisition of the mecA gene encoding penicillin-binding protein 2a (PBP2a), which reduces affinity for β-lactam antibiotics[50]. Pediatric MRSA infections, both hospital- and community-acquired, present as skin and soft tissue infections, pneumonia, and sepsis, particularly in neonates and immunocompromised children. MSSA infections, although sensitive to β-lactams, have shown emerging resistance to macrolides and fluoroquinolones, complicating empiric therapy. The rise of community-associated MRSA strains, such as USA300, further underscores the importance of surveillance and early detection in pediatric wards[49].

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Extended-Spectrum Beta-Lactamase (ESBL) Producing Enterobacteriaceae: ESBL-producing E. coli and K. pneumoniae are major causes of neonatal and pediatric sepsis, urinary tract infections, and pneumonia. These strains possess plasmid-mediated enzymes like TEM, SHV, and CTX-M that hydrolyze third-generation cephalosporins and monobactams[51]. The dissemination of ESBL genes through horizontal gene transfer has contributed to outbreaks in neonatal intensive care units (NICUs). Clinically, ESBL infections necessitate the use of carbapenems or combination therapy, but increasing carbapenem exposure has facilitated further resistance development[52].

Carbapenem-Resistant Enterobacteriaceae (CRE): CRE pathogens, especially Klebsiella pneumoniae and Enterobacter cloacae, represent a critical pediatric concern due to limited treatment options. Mechanisms include the production of carbapenemases such as KPC, NDM, and OXA-48, as well as efflux pumps and porin loss[53]. Infections often result in high mortality rates among neonates. Colistin, tigecycline, and newer β-lactam/β-lactamase inhibitor combinations (e.g., ceftazidime-avibactam) are sometimes used as last-resort therapies, though pediatric safety data remain limited[54].

Carbapenem-Resistant Acinetobacter baumannii (CRAB): A. baumannii is increasingly recognized in pediatric ICUs as a cause of ventilator-associated pneumonia and bloodstream infections. CRAB strains typically harbor OXA-type carbapenemases and demonstrate multidrug resistance through biofilm formation and outer membrane impermeability. The persistence of CRAB in hospital environments leads to recurrent outbreaks and cross-transmission, emphasizing the importance of strict infection control measures[55].

Vancomycin-Resistant Enterococci (VRE): VRE infections, primarily due to E. faecium, have emerged among immunocompromised and critically ill children. Resistance is mediated by the vanA and vanB genes, which alter the D-Ala-D-Ala target site to D-Ala-D-Lac, reducing vancomycin binding affinity. Clinical management often requires the use of linezolid or daptomycin, with dosing considerations for pediatric pharmacokinetics[56].

Multidrug-Resistant Pseudomonas aeruginosa: P. aeruginosa poses a challenge in cystic fibrosis, burn wound, and hospital-acquired infections. Mechanisms of resistance include efflux pumps, AmpC β-lactamases, and porinloss. Pediatric cases often involve persistent colonization, complicating long-term care. Combinationtherapy withantipseudomonal agents (e.g., ceftolozane-tazobactam or amikacin) may be required, though stewardship is vital to delay further resistance[57].

Clinical and Public Health Implications: The coexistence of these resistant organisms in pediatric settings has significant implications for empiric antibiotic choices and infection control practices. Early identification using rapid molecular diagnostics and adherence to stewardship principles are essential. Integrating surveillance data from pediatric units into national AMR monitoring systems, such as WHO GLASS, can facilitate timely interventions. Vaccination strategies, including pneumococcal and S. aureus vaccine development, may further reduce antibiotic pressure. The rising burden of multidrug-resistant infections among children underscores the need for continuous education, prudent antibiotic use, and international collaboration to mitigate resistance spread[58].

II. CONCLUSION

Antibiotic resistance in pediatric populations represents an urgent and complex global health challenge that undermines decades of medical progress[34] . Despite extensive research, surveillance, and awareness initiatives, the pace at which resistant organisms are emerging continues to outstrip the development of new antibiotics. The issue is particularly critical among children, where immature immune systems, limited drug options, and dosing challenges compound the risk of treatment failure[30] . Data from both developed and developing regions demonstrate that pediatric antibiotic resistance contributes to prolonged hospitalization, higher medical costs, and increased mortality rates[31].

Global initiatives by the World Health Organization (WHO), the Indian Council of Medical Research (ICMR), and the Centers for Disease Control and Prevention (CDC) have emphasized the importance of integrating antibiotic stewardship with strong infection control and preventive health systems[5] ,[4 5] . Achieving the **global targets for antimicrobial resistance** will require coordinated action across sectors—including healthcare, veterinary practice, agriculture, and environmental management[34] . The One Health framework provides a unifying strategy, recognizing that human, animal, and environmental health are interconnected and must be addressed together[15] .

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Sustained efforts must focus on strengthening diagnostic capacity, promoting rational antibiotic prescribing, and expanding pediatric antimicrobial stewardship programs[27] ,[29] . Investment in novel antimicrobials, alternative therapies such as bacteriophages, and rapid point-of-care diagnostics are essential to counter resistance[37] . Preventive strategies remain the cornerstone of mitigation: widespread immunization, improved sanitation, infection-control protocols, and public education can dramatically curb unnecessary antibiotic use[46–48]. Strengthening global surveillance systems such as WHO-GLASS will enable real-time monitoring of resistance trends and guide policy decisions[1].

Ultimately, combating pediatric antibiotic resistance requires long-term political commitment, adequate funding, and active participation from clinicians, policymakers, educators, and communities alike[34] . Through a concerted global response grounded in stewardship, prevention, and innovation, we can preserve the efficacy of existing antibiotics and safeguard the health of future generations.

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