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Antimicrobial Resistance in Pediatric Populations: Trends, Drivers, and Stewardship Strategies

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Abstract

General Background Antimicrobial resistance poses a systemic threat to global health security by compromising established infectious disease treatment paradigms. **Specific Background** Pediatric populations exhibit unique vulnerability to resistant pathogens due to developing immune systems, frequent acute infections, and substantial antibiotic exposure. **Knowledge Gap** Despite recognized burdens, comprehensive child-specific surveillance data, diagnostic resources, and implementation research remain severely deficient, particularly within low- and middle-income countries. **Aims** This review investigates the current disease patterns, underlying medical causes, and management strategies associated with resistant infections in children. **Results** The analysis identifies incorrect empirical prescribing in the absence of microbiological diagnosis as the predominant cause of therapeutic failure. Furthermore, significant pharmacokinetic variations and diagnostic uncertainties disproportionately affect vulnerable subgroups, notably neonates and chronically ill infants, leading to prolonged hospitalizations and elevated treatment costs. Utilizing targeted tools, such as the World Health Organization AWaRe classification, offers promising mitigation pathways for healthcare providers. **Novelty** This study synthesizes the complex interplay between child physiological individuality, psychosocial prescribing pressures, and post-pandemic epidemiological shifts to contextualize the unique trajectory of childhood pathogen evolution. **Implications** Preserving therapeutic efficacy requires an immediate transition toward precision care, emphasizing age-stratified pharmacokinetic research, formalized prescribing guidelines, and targeted investments in centralized surveillance infrastructures globally.

Highlights:

- Incorrect empirical prescribing without microbiological diagnosis significantly accelerates pathogen survival mechanisms in children.

- Neonates and chronically ill infants face disproportionate vulnerabilities, resulting in prolonged hospitalizations and elevated healthcare costs.
- Utilizing the AWARe classification system and age-stratified pharmacokinetic research provides promising pathways for optimizing medication usage.

Keywords: Empirical Prescribing, Pathogen Survival, Neonatal Vulnerability, Healthcare Costs, Pharmacokinetic Research

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I. Introduction

There is evidence that antimicrobial resistance (AMR) poses one of the greatest threats to modern medicine due to an evolution in the survival mechanisms of microorganisms (including bacteria, viruses, fungi, and parasites) with respect to the use of pharmaceutical agents intended to eradicate these pathogens [1] which causes current treatment methods to be rendered ineffective, causing long term infections and increased rates of disease transmission. Due to the systemic nature of the threat posed by AMR to global health security, the International Pediatric Association and other major health organizations have referred to it as a "hidden pandemic", requiring immediate and unified international response to preclude a post antibiotic era [2].

In addition to posing risks to the individual clinical outcome for patients suffering from AMR, the crisis also has the potential to destabilize healthcare systems globally. Resistant infections can result in prolonged hospital stays, additional use of toxic "last resort" medications and an increase in healthcare costs [3]. The impact of AMR on the effectiveness of routine medical procedures that utilize prophylactic antibiotics (i.e., surgery, chemotherapy, neonatal intensive care) presents a significant challenge to advances made in the last hundred years of medical science; therefore, it is necessary for there to be a global shift in the management of infectious diseases [2], [4].

Pediatric populations demonstrate a unique level of vulnerability that sets their risk profile apart from that of adults. Children experience a disproportionate number of episodes of acute infectious disease during their development and maturation of their immune systems [4]; therefore, they have a greater number of healthcare contacts than do adults. This reality creates a unique window within the pediatric population for the selection and dissemination of resistant organisms; consequently, children represent both the largest proportion of victims of AMR and the largest reservoir of resistant strains [5].

Ampicillin, trimethoprim, and erythromycin are some of the most frequently detected drugs in the urine of children and among the most frequently used appropriate drugs in pediatric care. However, a large proportion of pediatric antibiotic prescriptions are unnecessary and do not provide a sufficient clinical benefit.

AMR develops easily in children due to the unnecessary exposure to antibiotics that eliminates a large number of microorganisms, facilitating the emergence of resistant bacteria in the presence of selection pressure [2]. AB treatment poses a significant risk of creating a resistant, more virulent strain of a given pathogen, after which the risk of secondary infections increases [4]. AB treatment negatively impacts the composition of a child's microbiome, which increases the likelihood that future infections will be more difficult to treat [5].

Children are at higher risk of complications from infections and of being reinfected [6]. Multiple studies have shown that even a single course of antibiotics can have lasting effects on the microbial flora of children. Even a single course of AB treatment of children can have lasting effects on the microorganisms, creating a microbiome that is difficult to treat in the future [3].

A troubling increase is noted in geographical areas low on AMR surveillance which can be due to a lack of sufficient AMR surveillance in many of these areas [5]. Even in some universal healthcare settings, pediatric prescriptions of antibiotics are consistently and significantly higher than those provided to adults, with some reports indicating that pediatric-specific antibiotic prescription rates can exceed more than 10% of the total pharmaceutical expenditures for a specified age group [7].

II. Methodology

The present article on antimicrobial resistance (AMR) in pediatrics, including epidemiological trends, clinical and social drivers, and stewardship initiatives, is examined in this paper using a thorough literature review technique. The paper might be structured as a systematic review with well-defined search procedures and eligibility criteria, or as a narrative review that permits examination of general trends and themes across studies, depending on the focus and target audience. The current paper uses PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar databases to perform a systematic search of pertinent peer-reviewed literature.

III. Result and Discussion

Epidemiology and Trends of AMR in Children:

This section contains the following aspects:

1. Global and Regional Prevalence Patterns

There is significant geographic variation in antimicrobial resistance in pediatric populations, and surveillance data shows concerning resistance rates among important bacterial infections. Globally, extensive monitoring programs offer vital information about the changing epidemiology of childhood resistance.

Escherichia coli continues to be the most common bacterium in pediatric infections, especially those of the urinary system,

and alarming resistance patterns have been observed on several continents. Third-generation cephalosporin resistance rates for *E. coli* were 43.7%–50.0%, according to national surveillance in China that examined 2,575,040 bacterial isolates from children ages 0–14 years (2018–2022). Carbapenem resistance was comparatively low, ranging from 1.2%–2.0% for imipenem and meropenem [8]. Between 2016 and 2020, 288,377 isolates were gathered from 11 tertiary children's hospitals in China as part of the ISPED multicenter initiative [9]. There are clear regional differences: a research conducted at a hospital in Chengdu found that 40% of pediatric respiratory isolates had extended-spectrum beta-lactamase (ESBL)-producing *E. coli* [10], whereas European surveillance from Norway revealed significantly lower ESBL rates of 2.4% among pediatric *E. coli* isolates [11]. Resistance to ampicillin/sulbactam and trimethoprim/sulfamethoxazole averaged 24% and 30%, respectively, between 2010 and 2020, according to North American data from three US tertiary centers that analyzed 17,747 positive pediatric urine cultures. Resistance to levofloxacin and third/fourth-generation cephalosporins started to rise significantly around 2015–2016 [12].

In juvenile populations, *Klebsiella pneumoniae* has an even more alarming resistance profile, especially with relation to carbapenem resistance. Third-generation cephalosporin resistance ranged from 31.8% to 42.7%, whereas carbapenem resistance rates among pediatric *K. pneumoniae* isolates were 7.3%–10.1% for imipenem and 8.2%–12.2% for meropenem, according to Chinese national surveillance [8]. The prevalence of carbapenem-resistant *K. pneumoniae* (CRKP) was 19.7%, according to the ISPED multicenter surveillance [9]. Particular clinical contexts revealed more concerning rates: an East China study revealed rising resistance to fourth-generation cephalosporins (24.0% to 42.9%) and carbapenems (7.8% to 17.6%) between 2015–2016 and 2017–2018 [14], while Beijing pediatric bloodstream infection surveillance (2015–2019) reported 50.8% carbapenem resistance among *K. pneumoniae* isolates [13]. Imipenem-resistant *K. pneumoniae* rates increased dramatically from 3.0% in 2005 to 25% in 2018, with newborn patients exhibiting especially high rates of 15.3%, according to the CHINET surveillance system [8].

Resistance patterns to *Streptococcus pneumoniae* differ significantly depending on the type of specimen and the location. In contrast to invasive isolates from Norway that showed 11.9% penicillin nonsusceptibility [11], Chinese national surveillance indicated comparatively low non-cerebrospinal fluid penicillin resistance of 0.7%–1.6% [8]. Beijing data revealed 4.1% penicillin resistance and 41.0% intermediate resistance [13], whereas a multicenter bloodstream monitoring study in China reported 28.3% penicillin resistance among juvenile *S. pneumoniae* isolates [9]. Penicillin-resistant *S. pneumoniae* prevalence in nasopharyngeal samples ranged from 0.40 to 14.6%, according to community carriage studies conducted in the Asia-Pacific area [10].

2. COVID-19 Pandemic Impact on Resistance Trends

Through several causes, such as decreased healthcare utilization, decreased antibiotic prescribing, and changes in infection control practices, the COVID-19 pandemic significantly changed the epidemiology of pediatric infectious diseases and patterns of antimicrobial resistance.

The most immediate impact was a dramatic reduction in respiratory specimen collection and corresponding decreases in respiratory pathogen isolation. By the end of March, collection of respiratory samples and isolation of respiratory pathogens had rapidly decreased. In the ISPED surveillance program, the proportion of respiratory tract samples decreased from 56.9% in 2019 to 44.0% in 2020, with decreases also observed for *S. pneumoniae*, *Haemophilus influenzae* and *Streptococcus pyogenes* [9]. This decline has been attributed to fewer respiratory infections as a result of non-pharmaceutical interventions and a decrease in healthcare-seeking behavior during lockdowns [10].

Trends over the years of the pandemic were heterogeneous, but from 2015 to 2020, the ISPED program reported lower rates of carbapenem resistance for *K. pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* [9]. The nationwide monitoring study from 2018 to 2022 revealed that the prevalence of methicillin-resistant *Staphylococcus aureus* and some carbapenem-resistant Enterobacterales decreased, but the distribution of pathogens did not considerably differ over time [8]. In the Shandong province, penicillin-resistant *S. pneumoniae* and carbapenem-resistant *E. coli* were found to be decreasing over time, while carbapenem-resistant *K. pneumoniae* seemed to be increasing over the same period [11].

Pediatric antibiotic prescribing decreased considerably during the pandemic, which may have affected antimicrobial resistance. A study comparing antimicrobial resistance of pediatric urinary pathogens pre-pandemic, during the pandemic, and post-pandemic found considerably decreased antibiotic prescribing but could not draw any conclusions about resistance trends themselves [12]. This interplay between reduced antibiotic pressure, infection epidemiology, and disruption of the healthcare system makes it difficult to attribute resistance to specific interventions.

3. Setting-Specific Surveillance and Resistance Patterns

Antimicrobial resistance burden varies significantly across clinical settings, with pediatric intensive care units representing particularly high-risk environments for multidrug-resistant organisms.

Pediatric Intensive Care Units consistently demonstrate the highest concentrations of resistant pathogens. A Saudi Arabian tertiary pediatric center found multidrug-resistant organisms (MDROs) in 54.3% of positive bacterial cultures from critically ill patients, with *K. pneumoniae* representing 39.5% of MDR cultures and mortality markedly higher among MDRO-infected patients (32.4% vs. 3.9%) [13]. MDR infection rate was 17.3 per 1000 patient-days in an Indian pediatric neurointensive care research, with the most common MDRs being *K. pneumoniae* (38.7%), *P. aeruginosa* (22.5%), and *E. coli* (12.9%) [14]. Multidrug-resistant Gram-negative bacteria rates ranged from 18.2% to 63.7%, with a mean of 47%, according to a comprehensive analysis of pediatric sepsis in PICUs [15]. All examined pathogens had 100% resistance to third-generation

cephalosporins, according to Ethiopian PICU surveillance [16]. 10.67% of patients colonized with carbapenem-resistant Enterobacteriaceae had 100% meropenem resistance, according to a study conducted in a PICU in India [17]. These findings highlight PICUs as key hubs for pediatric antibiotic resistance, which is fueled by invasive operations, high antibiotic exposure, and susceptible patient groups.

Although thorough surveillance data is still few, resistance profiles in emergency departments and outpatient settings are different. Though there are alarming growing tendencies, the research currently available points to reduced resistance rates when compared to intensive care settings. In a secondary care hospital in Nepal, community-acquired bloodstream infections revealed that 29.6% of *S. aureus* isolates were methicillin-resistant, and 96.5% of non-neonatal infections were community-acquired [18]. Recent antibiotic use (OR 2.65), daycare attendance (OR 1.49), and younger age were found to be risk factors for the carriage of resistant organisms in a meta-analysis of children living in the Asia-Pacific region [10]. The frequency of sentinel drug-resistant species, such as macrolide-resistant *S. pneumoniae*, was found to be correlated with the volume of primary care antibiotic prescriptions, according to European ecological studies [19].

Because of their high resistance rates and particular fragility, neonatal units require extra care. In Chinese surveillance, rates of neonatal carbapenem-resistant *K. pneumoniae* colonization/infection were 15.3%, which is much higher than rates in older pediatric groups [8]. Limited setting-stratified resistance data from emergency rooms and outpatient clinics in the majority of locations is one of the current surveillance gaps. Systematic gathering of setting-specific resistance data should be a top priority for future surveillance initiatives, especially in ambulatory care settings where the majority of pediatric antibiotic prescriptions take place.

Pathogens and Resistance Mechanisms in Pediatrics:

Antimicrobial resistance in pediatric populations represents a critical public health challenge. Recent genomic and molecular epidemiological studies from 2021 to 2026 have elucidated the specific pathogens, resistance genes, and molecular mechanisms underlying this growing threat in children.

Gram-Negative Pathogens

The two main pediatric Gram-negative bacteria that possess carbapenem resistance genes and extended-spectrum β -lactamase (ESBL) are *Escherichia coli* and *Klebsiella pneumoniae* [20], [21], and [22].

The β -lactamases of the CTX-M, TEM, and SHV families are the most common among organisms that produce ESBL. In addition to carbapenemase genes, a hypervirulent strain of *K. pneumoniae* ST11-KL64 that was isolated from children's blood carried blaCTX-M-65, blaTEM-1B, and blaSHV-12 [20]. BlaCTX-M-15 is commonly found on IncFIB plasmids in ESBL-producing *E. coli* clones [23].

The carbapenemase families KPC, NDM, OXA, and IMP are principally responsible for carbapenem resistance. blaKPC-2 was shown to be the predominant carbapenemase gene (88.2%) in a study of carbapenem-resistant *K. pneumoniae* (CRKP) from a pediatric hospital in China. Other genes detected were blaNDM-1 (4.7%), blaNDM-5 (4.7%), blaIMP-8 (2.3%), and blaOXA-181 (1.2%) [22]. 20% of the CRKP isolates in a pediatric hospital in Iran have blaNDM [21].

It is especially worrisome when extensively drug-resistant (XDR) phenotypes appear. The co-occurrence of blaNDM-5, blaCTX-M-65, blaOXA-10, blaTEM-1, and mcr-1.1 genes in *E. coli* ST156 was originally reported in a strain of the bacteria from Chinese children that was resistant to carbapenemase and colistin [24]. Twelve antibiotic resistance genes were present in an extensively drug-resistant *E. coli* isolate from a one-year-old child, and plasmids containing ARGs came from a variety of Enterobacteriaceae species [25].

Gram-Positive Pathogens

In pediatric, the most clinically significant resistant Gram-positive bacteria include *Staphylococcus aureus* and *Streptococcus pneumoniae*.

The main cause of penicillin resistance in *S. pneumoniae* is changes in penicillin-binding proteins (PBPs), particularly PBP1a, PBP2b, and PBP2x. According to a seminal study, β -lactam resistance in Japanese children spread throughout the country due to horizontal transmission of a particular PBP1a allele (pbp1a-13) with a 370SSMK mutation between pneumococcal clones [26]. Four loci, pbp1a, pbp2b, pbp2x, and murM, must undergo orderly horizontal gene transfer in order to acquire clinically significant amoxicillin resistance [27].

Target-site alteration by the erm(B) gene and active efflux mediated by mef class genes are the mechanisms by which macrolide resistance functions. Mef(E) was found in 50% of resistant isolates in an Ethiopian pediatric cohort [25].

The mecA gene, which codes for PBP2a and is carried on the movable staphylococcal cassette chromosome mec (SCCmec), confers methicillin resistance in *S. aureus*. Different SCCmec types (III, IV, and V) have been linked to MRSA in pediatric investigations [28]. ST239 MRSA with SCCmec type III showed the highest resistance rates in pediatric patients from Myanmar [28].

Clinical Drivers of AMR in Children

Medical practices, psychological dynamics, and biological diversity unique to each kid make up the complicated problem of antimicrobial resistance (AMR) in pediatric populations. Addressing these drivers is necessary to maintain the efficacy of currently available antibiotics and ensure the safety of patients in primary and emergency care settings.

1. Inappropriate and Excessive Prescribing Practices

The improper or excessive use of antibiotics, especially the reliance on empirical therapy without microbiological evidence, is a major clinical driver of antimicrobial resistance (AMR). Because of the perceived necessity for prompt management, empirical prescribing is still the standard practice for many acute presentations in pediatric emergency and outpatient departments [29]. A considerable number of these prescriptions are unneeded or use broad-spectrum drugs when narrow-spectrum alternatives would be enough, according to studies released in 2024 and 2025 [30].

Lack of culture confirmation frequently results in "antibiotic overkill," where doctors use strong antibiotics to treat bacterial infections or viral illnesses that resolve on their own. By applying selective pressure on the pediatric microbiome, this technique promotes the emergence of resistant bacteria. Though their application varies throughout healthcare levels, recent data indicates that stewardship interventions—such as audit-and-feedback and decision-support tools—are essential to lowering this empirical dependency [29], [33].

2. Diagnostic Uncertainty and Clinician-Caregiver Pressures

Since the symptoms of bacterial and viral infections often overlap, diagnostic ambiguity is a defining feature of pediatric medicine. Clinicians frequently resort to "defensive prescribing" because they are unable to quickly and conclusively differentiate between various etiologies [31]. When making bedside judgments, pediatricians note that the long-term concerns of AMR are frequently outweighed by the fear of missing a rare but serious bacterial infection, such as sepsis or meningitis [34].

Psychosocial stresses add to this ambiguity. Caregiver expectations are crucial in primary care and emergency situations; parents frequently believe that antibiotics are the sole effective treatment for their child's illness and may put pressure on doctors to write a prescription [29], [31]. In turn, clinicians may prescribe antibiotics to keep patients satisfied or because they believe they are pressed for time and cannot provide comprehensive advice on managing viral illnesses. High-risk prescribing practices are institutionalized in areas with limited resources because empirical therapy is required due to the absence of sophisticated diagnostic infrastructure [32], [34].

3. Pharmacokinetic and Pharmacodynamic Considerations in Pediatric Dosing

AMR is directly impacted by the substantial pharmacokinetic (PK) and pharmacodynamic (PD) complications brought forth by children's physiological individuality. Children, in contrast to adults, need weight- and age-adapted dosage, which is by its very nature variable and prone to error. Sub-inhibitory concentrations of antibiotics can remain when suboptimal dosing—whether it be an inadequate dose or an improper duration—fails to meet the required therapeutic targets. The selection of resistant mutants is facilitated by this environment [29], [33].

The best PK/PD targets for a variety of pediatric illnesses are also not widely agreed upon. It is difficult to maintain constant medication exposure in children due to factors such as the quick changes in renal clearance and volume of distribution as they develop [33]. Although recent studies employing machine learning and causal inference have started to more precisely map these unique dose needs, many physicians continue to use conventional, frequently out-of-date dosing guidelines [32]. It is becoming more widely acknowledged that using data from electronic health records and including clinical pharmacists are crucial tactics for navigating these challenges and reducing the risk of resistance [34].

Risk Factors and Vulnerable Subgroups

The pediatric population does not bear an equal share of the burden of resistance to antibiotics. The combination of biological, clinical, and socioeconomic factors make certain subgroups considerably more susceptible to infection with multidrug-resistant organisms (MDROs). In order to individualize antimicrobial stewardship and infection control methods, it is imperative to identify these susceptible groups.

1. Neonates and Infants

One of the most vulnerable subgroups for AMR is newborns, especially those born prematurely or with extremely low birth weights. They heavily rely on empirical antimicrobial therapy since their immune systems are still developing and lack the strong cellular and humoral defenses needed to effectively eradicate infections [35]. Additionally, early-life exposure to antibiotics, either directly or through maternal therapy, might disrupt this fragile ecology and select for a "resistome" rich in antibiotic resistance genes (ARGs) because the newborn gut microbiome is in a state of fast change [36].

This group's clinical manifestations frequently include early- and late-onset neonatal sepsis, which is increasingly brought on by resistant organisms including *Klebsiella pneumoniae* and *Escherichia coli* that produce extended-spectrum beta-lactamase (ESBL) [37]. Healthcare-associated infections (HAIs) are spread by risk factors include the use of invasive equipment (such as umbilical catheters), extended hospital stays, and mechanical ventilation. According to recent research, MDROs can be found in more than 80% of cases of neonatal sepsis in specific tertiary settings, and prognoses are especially

bad when carbapenem-resistant *K. pneumoniae* (CRKP) is present [35], [37].

2. Children with Chronic Conditions

Due to their frequent and extended interactions with healthcare institutions, children with chronic conditions like cancer, cystic fibrosis, and post-surgical patients are more vulnerable to AMR. Invasive infections are made more likely in pediatric oncology by the immunocompromised state brought on by chemotherapy and the need for continuous central venous access [39]. Due to the frequent cycles of broad-spectrum antibiotics used to treat febrile neutropenia, these patients' microbiome is continuously under selection pressure.

With some institutions reporting rates as high as 72% for certain illnesses, the prevalence of MDR Gram-negative bacterial infections in hospitalized immunocompromised children has increased significantly [39]. Similar to this, juvenile patients recovering from surgery, particularly those having complicated surgeries or organ transplants, are more likely to become colonized by carbapenem-resistant Gram-negative bacteria (CRGNB) and thereafter become infected [42]. Prior colonization with the same organism and extended exposure to drugs such as cefepime are the best indicators of obtaining these resistant strains [39], [40].

3. Hospitalized and ICU Pediatric Populations

Because of the high number of critically sick patients, the widespread use of broad-spectrum antibiotics, and the pervasiveness of invasive equipment, the pediatric intensive care unit (PICU) is a focus site for antimicrobial resistance (AMR). Through environmental pollution and healthcare worker-mediated transmission, hospitalized children in these settings are often exposed to multidrug-resistant bacteria [41].

In the PICU setting, resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and other carbapenem-resistant Gram-negative bacilli are prevalent. Natural barriers are broken by invasive operations such endotracheal intubation and the insertion of arterial or central lines, which give these resistant microbes entrance locations [37], [38]. Nearly 10% of critically ill or immunocompromised children are colonized with carbapenem-resistant bacteria before admission, according to recent surveillance data [42]. This underscores the significance of screening and stringent infection control measures in preventing outbreaks in high-risk wards.

Consequences of AMR in Pediatric Populations

The emergence of antimicrobial resistance (AMR) in pediatric patients presents a severe threat to global child health, leading to diminished clinical efficacy and significant strain on healthcare infrastructures. The consequences of AMR in children are multifaceted, encompassing adverse clinical outcomes, heightened economic burdens, and increased utilization of specialized medical resources.

1. Clinical Outcomes and Morbidity

The ineffectiveness of conventional empirical therapy, which raises morbidity and death, is the most direct effect of AMR in children. A clear disparity in the results between resistant and susceptible diseases is highlighted by recent data from 2024 to 2026. A multicenter cohort study conducted in Kenya, for example, found that children with antibiotic-resistant infections had a mortality rate of 26%, but children with susceptible infections had a mortality rate of just 9%, indicating a nearly threefold increase in risk [43]. The impact is even more noticeable in specialist populations, such pediatric oncology, where historical evidence indicates that fatality rates for bloodstream infections (BSI) caused by carbapenem-resistant Enterobacteriaceae (CRE) can exceed 30% [44].

AMR considerably lengthens hospital stays and illness duration in addition to mortality. Once confounding variables are taken into account, resistant infections are linked to a 60% increase in length of hospital stay (LOS) [43]. Children with infections caused by multidrug-resistant organisms (MDROs) typically need to be admitted to pediatric intensive care units (PICUs) and are more likely to suffer from consequences such multi-organ failure and septic shock. Concurrent meningitis and necrotizing enterocolitis are independent predictors of mortality for neonatal infections with carbapenem-resistant *Klebsiella pneumoniae* (CRKP), which are especially deadly [45]. Children experience delayed effective therapy and a higher risk of long-term consequences, such as kidney scarring, even for non-critical infections such urinary tract infections (UTIs) brought on by microorganisms that produce extended-spectrum beta-lactamases (ESBLs) [46].

2. Economic and Health System Impacts

Lengthier hospital stays, the requirement for more costly treatment drugs, and more diagnostic surveillance are the main causes of the significant financial burden of AMR in pediatric settings. Treatment costs for resistant infections have been estimated to be around 33% higher than those for susceptible cases [43]. The need for higher-tier antibiotics, including ceftazidime-avibactam for CRKP, and the use of combination treatments, which are frequently given for long periods of time—median 17 days for CRE-BSIs in some areas—are primarily to blame for this increase [47].

Additionally, the use of resources in the health system must be significantly increased in order to combat AMR. More regular microbiological cultures, specialized imaging, and consultation with infectious disease and pharmacology experts are necessary for patients with resistant infections [48]. Although antimicrobial stewardship programs (ASPs) are successful in lowering mortality and length of stay (LOS), their implementation also necessitates specialized human and financial

resources. A stewardship intervention in Peru, for instance, was demonstrated to lower absolute mortality by 4.2% and length of stay by a median of 3 days; nevertheless, such initiatives require continuous funding to remain effective [49]. Pediatric facilities are disproportionately burdened by the combined effect of these issues, especially in low- and middle-income nations where resources are already limited.

High-Acuity Environment Pressures

Intensive care's high acuity fosters a culture of "erring on the side of caution." Because sepsis treatment delays can be lethal, clinicians are frequently under tremendous pressure to start empirical broad-spectrum antibiotics very early. Slow culture turnaround times or the concern of missing a masked illness often postpone de-escalation once therapy has begun [51]. Building this culture requires a lot of work and institutional support, but trust and communication within the interdisciplinary team are crucial to overcoming these socio-behavioral barriers [50], [56].

1. System-Level Constraints and LMIC Challenges

In LMICs, the barriers to effective AMS are magnified by severe infrastructure and resource limitations that institutionalize suboptimal prescribing patterns.

Resource Limitations and Laboratory Capacity

In environments with limited resources, the main obstacles to stewardship are a lack of personnel and excessive workloads. To conduct prospective audit-and-feedback programs, many hospitals lack the specialized clinical pharmacists or infectious disease specialists needed [50], [54]. Additionally, laboratory infrastructure is frequently insufficient; clinicians are forced to rely almost entirely on empirical therapy due to limited access to trustworthy microbiology, particularly blood culture systems and susceptibility testing, which frequently uses higher-tier agents to cover for potentially resistant pathogens like organisms that produce extended-spectrum beta-lactamases (ESBLs) [53], [54].

Data Gaps and Surveillance Challenges

Accurate, up-to-date information on local resistance trends and antibiotic use is necessary for effective stewardship. But there are serious surveillance gaps in many LMICs. Clinicians find it challenging to choose suitable narrow-spectrum empirical treatments in some areas due to the lack of a centralized database to monitor the frequency of multidrug-resistant organisms (MDROs) [50]. The absence of automated prescription analytics and electronic health records (EHRs) makes it difficult and frequently impossible to measure the effectiveness of AMS interventions, even at the facility level [54], [55].

Socio-Behavioral and Implementation Research Gaps

Implementation is further hampered by socio-behavioral issues, such as opposition to change and a dearth of local stewardship "champions." Although POC testing is theoretically advantageous, systematic reviews have shown that there is little implementation research in low-income settings to identify which interventions are both scalable and successful [54]. In addition to financial investment, bridging this "implementation gap" calls for an emphasis on local capacity building and behavioral change.

Policy, Guidelines, and Global Initiatives

The special needs of pediatric and newborn populations are becoming more widely acknowledged in the global response to antimicrobial resistance (AMR). Evidence-based policies and standardized classification systems are guiding the alignment of national action plans, international frameworks, and local stewardship programs to maximize the use of antibiotics in children.

All world health organization (WHO) and global strategies, the role of AWARE in pediatrics, global political commitments, national action plans and regional initiatives, regional examples of nap implementation and local stewardship guidelines, and policy elements are all regulate a special regulation to protect children from the disease that could face.

IV. Conclusion and Recommendations

A paradigm change from adult-centric models to precision pediatric stewardship is required due to the growing threat of antimicrobial resistance (AMR) in pediatric populations to the health of children worldwide. The increasing frequency of multidrug-resistant organisms, especially Enterobacterales that produce ESBL and carbapenem-resistant infections, has been described in this review. These organisms now disproportionately impact neonates and critically ill children. Significant changes in resistance patterns were brought about by the COVID-19 pandemic, but the fundamental causes are still unclear diagnosis, improper empirical prescribing, and the intricate pharmacokinetic needs of developing children.

To curb the trajectory of pediatric AMR, the following multi-level recommendations are proposed:

1. Clinical Practice: To maximize the timing and interpretation of microbiological testing, clinicians should embrace a "diagnostic stewardship" mentality, going beyond the basic selection of antibiotics. To protect top-tier agents, adherence to

the WHO AWaRe (Access, Watch, Reserve) classification needs to be formalized. Additionally, in order to control caregiver expectations in primary and emergency care settings without sacrificing patient safety, "safety-netting" and delayed-prescribing techniques must be put into practice.

2. Research: The creation of solid, age-specific pharmacokinetic and pharmacodynamic (PK/PD) data is necessary to close the "evidence gap" in pediatric medicine. Individualized dosage support tools should replace population-based models in research. Large-scale, longterm studies are also needed to assess the effectiveness of new alternatives like bacteriophage therapy and host-response molecular markers, as well as the long-term clinical and economic effects of stewardship measures.

3. Policy: Clear, quantifiable goals for pediatric and neonatal populations must be included in national and international action plans. Funding for integrated surveillance systems and laboratory facilities that can deliver age-stratified, real-time AMR data should be a top priority for policymakers. Harmonizing indicators, such Days of Therapy (DOT) for pediatric settings, will enable meaningful benchmarking and the sharing of effective stewardship models across a range of resource situations on a worldwide scale. The medical community can advance toward a future in which the effectiveness of life-saving antibiotics is maintained for the following generation by combining these strategies.

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