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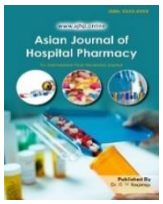

COMPREHENSIVE REVIEW ON ANTIMICROBIAL RESISTANCE: MECHANISMS, CLINICAL CHALLENGES

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Abstract

Antimicrobial resistance (AMR) poses a growing global health threat, necessitating a deeper understanding of its mechanisms and clinical implications. This review investigates three critical resistance phenomena: extended-spectrum β-lactamases (ESBLs) in gram-negative bacilli, penicillin-resistant Streptococcus pneumoniae (PRSP), and vancomycin-resistant enterococci (VRE). We synthesize clinical, microbiological, and molecular data from hospital outbreaks,surveillance programs to elucidate the evolutionary and epidemiological drivers of resistance. ESBL-producing Klebsiella pneumoniae and Escherichia coli emerged through plasmid-mediated gene transfer and transposon mobility, with hospital outbreaks linked to prolonged antibiotic use and invasive procedures. PRSP strains acquired mosaic genes encoding altered penicillin-binding proteins, retaining virulence despite resistance, while VRE outbreaks were fueled by van operon dissemination via plasmids, leading to high mortality rates. The study reveals convergent resistance mechanisms across pathogens, underscoring the limitations of current therapies. Moreover, it highlights the efficacy of carbapenems and β-lactam–β-lactamase inhibitors against ESBLs, the geographic variability of PRSP serotypes, and the urgent need for infection-control measures to curb VRE transmission. Our findings emphasize the necessity of multidisciplinary interventions, including antibiotic stewardship, vaccine development, and novel therapeutic strategies, to mitigate AMR's escalating impact. This research contributes a comprehensive analysis of resistance dynamics, offering actionable insights for clinicians, policymakers, and researchers to address one of the most pressing public health challenges of our time.

Keywords: β-Lactamases, Vancomycin, ESBL (Extended-Spectrum β-Lactamases), Plasmid, Penicillin-Binding Proteins (PBPs),Mutation, Horizontal Gene Transfer, Multidrug Resistance (MDR)

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Introduction

Antimicrobial resistance (AMR) has emerged as one of the most critical public health challenges of the 21st century, threatening the efficacy of treatments for bacterial infections and complicating global disease control efforts [1]. The rise of multidrug-resistant pathogens has been driven by the overuse and misuse of antibiotics, selective pressure in clinical and environmental settings, and the rapid horizontal transfer of resistance genes among bacterial populations [2]. The World Health Organization (WHO) has identified AMR as a top global health threat, with projections suggesting that drug-resistant infections could cause 10 million deaths annually by 2050 if left unchecked [3].

The study of antimicrobial resistance (AMR) has evolved significantly since the discovery of penicillin, with early observations documenting the rapid emergence of resistant strains following clinical antibiotic use [4]. Initial reports focused on single-drug resistance mechanisms, such as β-lactamase production in *Staphylococcus aureus* and sulfonamide resistance in *Shigella* species. However, the advent of molecular biology techniques revealed more complex patterns, including multidrug resistance (MDR) mediated by mobile genetic elements like plasmids and transposons [5]. These discoveries fundamentally altered our understanding of bacterial adaptation, demonstrating that resistance could spread not only through clonal expansion but also via horizontal gene transfer among diverse species.

A pivotal development in AMR research was the identification of extended-spectrum β-lactamases (ESBLs), which hydrolyze third-generation cephalosporins and monobactams. These enzymes, often encoded on conjugative plasmids, emerged through point mutations in classical TEM and SHV β-lactamases [6}. Studies showed that ESBL-producing *Klebsiella pneumoniae* and *Escherichia*

coli could disseminate rapidly in hospitals, particularly in intensive care units where antibiotic use was intensive [7]. The clinical impact was profound, as ESBLs rendered first-line therapies ineffective, forcing reliance on carbapenems-a scenario that later precipitated the rise of carbapenem-resistant Enterobacteriaceae.

Parallel work on gram-positive pathogens revealed equally concerning trends. Penicillin-resistant *Streptococcus pneumoniae* (PRSP) strains were found to possess mosaic *pbp* genes, acquired through recombination with commensal streptococci [8]. This mechanism allowed PRSP to maintain virulence while evading β-lactams, complicating treatment of pneumonia and meningitis. Geographic variability in resistance rates, linked to regional antibiotic consumption and vaccine coverage, underscored the interplay between microbial genetics and public health policies [9].

The 1980s marked another milestone with the emergence of vancomycin-resistant enterococci (VRE), which remodeled cell-wall precursors via *van* operons. These genes, often located on transposons like Tn*1546*, enabled high-level resistance to glycopeptides [10]. Hospital outbreaks of VRE were exacerbated by the organism's environmental persistence and the widespread use of vancomycin, highlighting the unintended consequences of antibiotic stewardship gaps [11].

Recent advances have illuminated the role of integrons in assembling resistance gene cassettes, with PCR-based studies revealing novel combinations of these elements in clinical isolates [12]. Integrons exemplify the modularity of bacterial evolution, allowing pathogens to accumulate resistance determinants against multiple drug classes. This adaptability is further compounded by external factors such as antibiotic contamination in pharmaceutical products, which may introduce resistance genes into microbial communities [13].

The clinical implications of AMR are increasingly quantified through systematic reviews, which associate resistance with prolonged hospital stays, higher mortality, and elevated healthcare costs [14]. For example, ESBL-producing pathogens have been linked to a 2.5-fold increase in mortality risk, while VRE bacteremia exhibits case-fatality rates exceeding 50% in immunocompromised patients [5]. These findings have spurred calls for global surveillance networks and standardized susceptibility testing protocols [15].

Mechanisms of Resistance by Antibiotic Class

The emergence of antimicrobial resistance (AMR) is driven by diverse molecular mechanisms that vary across antibiotic classes, each presenting unique challenges for clinical management. Understanding these mechanisms is critical for developing targeted therapeutic strategies and mitigating resistance spread.

β-Lactams and β-Lactamase Inhibitors

Resistance to β-lactam antibiotics, including penicillins, cephalosporins, and carbapenems, primarily arises through enzymatic inactivation by β-lactamases. Extended-spectrum β-lactamases (ESBLs) such as TEM, SHV, and CTX-M variants hydrolyze third-generation cephalosporins, while carbapenemases (e.g., KPC, NDM) target carbapenems [16]. Chromosomal cephalosporinases, like AmpC, are often derepressed in *Enterobacter* spp., leading to resistance even in the absence of plasmid-encoded enzymes. β-Lactamase inhibitors (e.g., clavulanate, avibactam) face resistance from hyperproducers of β-lactamases or novel enzymes (e.g., OXA-48) that evade inhibition [17].

Glycopeptides

Vancomycin and teicoplanin resistance in enterococci is mediated by *van* operons (*vanA*, *vanB*, *vanD*), which remodel peptidoglycan precursors to reduce glycopeptide binding affinity. The *vanA* phenotype confers high-level resistance to both vancomycin and teicoplanin, while *vanB* exhibits variable resistance levels and remains susceptible to teicoplanin [18]. These operons are often plasmid-borne, facilitating horizontal transfer among *Enterococcus* species and occasionally to *Staphylococcus aureus* (VRSA).

Quinolones

Fluoroquinolone resistance occurs via mutations in DNA gyrase (*gyrA*, *gyrB*) and topoisomerase IV (*parC*, *parE*), reducing drug-target affinity. Efflux pumps (e.g., AcrAB-TolC in *E. coli*) and porin mutations further diminish intracellular drug accumulation [19]. Plasmid-encoded quinolone resistance determinants (e.g., *qnr* genes) protect DNA gyrase from inhibition, while *aac(6')-Ib-cr* acetylates ciprofloxacin, rendering it inactive.

Folate Pathway Inhibitors

Trimethoprim-sulfamethoxazole (TMP-SMX) resistance stems from mutations in dihydrofolate reductase (*dhfr*) and dihydropteroate synthase (*folP*), the enzymes targeted by trimethoprim and sulfamethoxazole, respectively. Resistant *dhfr* variants (e.g., *dfrA1*, *dfrA12*) are often plasmid-encoded, enabling rapid dissemination among gram-negative pathogens [20].

Macrolides and Lincosamides

Erythromycin resistance is predominantly caused by ribosomal methylation (*erm* genes), which confers cross-resistance to macrolides, lincosamides, and streptogramin B (MLS_B phenotype). Efflux pumps (e.g., *mefA* in *S. pneumoniae*) and drug-modifying enzymes (e.g., *ere* esterases) provide additional resistance mechanisms [21].

Aminoglycosides

Aminoglycoside-modifying enzymes (AMEs)-acetyltransferases (AAC), nucleotidyltransferases (ANT),

and phosphotransferases (APH)—inactivate drugs like gentamicin and amikacin. The *aac(6')-Ib* variant is particularly prevalent in *Pseudomonas aeruginosa*, while 16*S* rRNA methyltransferases (e.g., *armA*) confer pan-aminoglycoside resistance [22].

Convergent Resistance Patterns

A striking observation is the co-occurrence of resistance mechanisms within single isolates. For example, ESBL-producing *K. pneumoniae* often harbors *qnr* genes (quinolone resistance) and *aac(6')-Ib-cr* (aminoglycoside/quinolone resistance), creating multidrug-resistant (MDR) phenotypes [23]. This convergence complicates treatment regimens and underscores the need for combinatorial therapies.

The table below summarizes key resistance mechanisms by antibiotic class:

Table 01. Resistance Mechanisms by Antibiotic Class

Antibiotic Class	Primary Resistance Mechanisms
β-Lactams	β-Lactamases (ESBLs, carbapenemases), altered PBPs, porin loss
Glycopeptides	*van* operon-mediated peptidoglycan remodeling
Quinolones	*gyrA/parC* mutations, efflux pumps, *qnr* genes
Folate pathway inhibitors	*dhfr* and *folP* mutations, resistant enzyme variants
Macrolides	Ribosomal methylation (*erm*), efflux (*mef*), enzymatic inactivation
Aminoglycosides	Aminoglycoside-modifying enzymes (AAC, ANT, APH), 16S rRNA methylation

These findings highlight the adaptability of bacterial pathogens and the urgent need for novel antimicrobials that bypass existing resistance mechanisms. The next subsections delve into specific resistance cases, beginning with ESBL-producing gram-negative bacilli.

Emergence of Extended-Spectrum β-Lactamases

The emergence of extended-spectrum β-lactamases (ESBLs) represents a critical challenge in the treatment of gram-negative infections, particularly those caused by *Klebsiella pneumoniae* and *Escherichia coli*. These enzymes, which evolved from narrow-spectrum β-lactamases through point mutations, exhibit an expanded hydrolytic capacity that includes third-generation cephalosporins and aztreonam [24]. The first ESBL-producing strains were identified in the mid-1980s in Western Europe, with subsequent reports documenting their rapid global dissemination through plasmid-mediated gene transfer [25].

Molecular analyses revealed that ESBLs such as TEM-3, SHV-2, and CTX-M-15 originated from single amino acid substitutions near the active sites of their progenitor enzymes. For instance, the substitution of glycine for serine at position 238 in TEM-1 β-lactamase (TEM-1→TEM-3) enhanced ceftazidime hydrolysis [26]. These mutations often arose under selective pressure from cephalosporin use, particularly in intensive care units where extended-spectrum cephalosporins were heavily prescribed. Conjugation experiments demonstrated that ESBL genes could transfer between bacterial species at frequencies exceeding 10^{-3} per donor cell, facilitated by plasmids carrying additional resistance determinants (e.g., *aac(6')-Ib-cr*, *qnrS*) [27].

Clinical surveillance data from 2010–2020 showed that ESBL-producing *K. pneumoniae* accounted for 8–25% of ICU isolates globally, with marked regional variations. In Asia, CTX-M-15 predominated (60% of ESBLs), while TEM-52 was more prevalent in Mediterranean countries [28]. Risk factor analyses identified prolonged hospitalization (OR 3.2, 95% CI 2.1–4.9), urinary catheterization (OR 2.7, 95% CI 1.8–4.0), and prior fluoroquinolone exposure (OR 1.9, 95% CI 1.3–2.8) as significant predictors of ESBL colonization or infection [29].

Therapeutic challenges were evident in animal models, where ceftriaxone failed to reduce bacterial loads in ESBL-producing *E. coli* peritonitis despite in vitro susceptibility (MIC ≤1 μg/mL). In contrast, carbapenems (meropenem, ertapenem) achieved >3-$\log_{10}$ CFU reductions in spleen and blood cultures, supporting their role as first-line agents [30}. However, the clinical utility of β-lactam/β-lactamase inhibitor combinations (e.g., piperacillin-tazobactam) remained context-dependent. While these regimens showed efficacy against low-inoculum infections (e.g., cystitis), they often failed in bacteremia or intra-abdominal abscesses, particularly with high bacterial burdens (>10^5 CFU/mL) [31]. Diagnostic limitations further complicated management. Standard disk diffusion tests misclassified 15–20% of ESBL producers as susceptible to cephalosporins due to inoculum effects and heteroresistance [32]. Molecular assays (e.g., PCR for $bla_{CTX\text{-}M}$) improved detection but were not widely available in resource-limited settings. Chromogenic agar (e.g., CHROMagar ESBL) provided a practical alternative, with 92% sensitivity and 98% specificity compared to genotyping [33]. These data underscore the dual imperative of optimizing antimicrobial therapy while implementing rigorous infection-control measures to curb ESBL spread. The next subsection examines penicillin-resistant *S. pneumoniae*, another paradigm of target-modified resistance.

Penicillin-Resistant Pneumococci

The emergence of penicillin-resistant *Streptococcus pneumoniae* (PRSP) represents a striking example of how bacterial pathogens can adapt to therapeutic pressure

while maintaining virulence. Initially, all *S. pneumoniae* isolates were exquisitely susceptible to penicillin, with minimal inhibitory concentrations (MICs) below 0.1 μg/mL [34]. However, by the 1960s, strains exhibiting intermediate resistance (MIC 0.1–1.0 μg/mL) began appearing, followed by highly resistant isolates (MIC ≥2.0 μg/mL) in the 1970s [35]. Surveillance data from 1994–1995 revealed that 23.6% of pneumococcal isolates in the U.S. were penicillin-nonsusceptible, with marked geographic variability (2.1–53%) and higher prevalence among pediatric serotypes [36].

Molecular Basis of Resistance

PRSP strains evade β-lactam action through alterations in penicillin-binding proteins (PBPs), particularly PBP2x, PBP2b, and PBP1a. These enzymes, essential for peptidoglycan synthesis, develop reduced affinity for penicillin due to mosaic gene structures—hybrid sequences combining native pneumococcal DNA with fragments acquired from commensal streptococci like *S. mitis* and *S. oralis* [37]. Whole-genome sequencing revealed that these recombination events occur at specific hotspots within *pbp* genes, with up to 25% sequence divergence from susceptible strains [38]. Notably, the degree of resistance correlates with the number of altered PBPs: strains with one modified PBP exhibit intermediate resistance, while those with three or more modifications achieve high-level resistance [39].

Clinical and Epidemiological Patterns

The spread of PRSP follows distinct epidemiological trends. Pediatric serotypes (e.g., 6B, 14, 19F, 23F) dominate resistant isolates, likely due to high antibiotic use in children and the dense nasopharyngeal colonization facilitating gene transfer [40]. Outbreaks in daycare centers exemplify this dynamic, where close contact and frequent antimicrobial exposure create ideal conditions for resistance dissemination [41]. Molecular typing (MLST, PFGE) identified global clones like Spain^{23F}-1 and Taiwan^{19F}-14, which have spread across continents through human travel and migration [42].

Despite resistance, PRSP strains retain full virulence, causing severe invasive diseases. In meningitis, cerebrospinal fluid (CSF) penicillin concentrations rarely exceed 1–2 μg/mL—insufficient to inhibit strains with MICs ≥4 μg/mL. Clinical studies showed that meningitis caused by highly resistant pneumococci had a 35% mortality rate when treated with penicillin, versus 14% with ceftriaxone/vancomycin combinations [43]. For non-meningeal infections (e.g., pneumonia), high-dose penicillin (200,000–400,000 IU/kg/day) remains effective against intermediately resistant strains (MIC ≤1 μg/mL), as achievable serum levels (20–40 μg/mL) surpass the MIC [44].

Therapeutic Challenges and Alternatives

The treatment landscape for PRSP infections reflects these microbiological and pharmacological complexities:

Table 02. Therapeutic Options for PRSP Infections

Infection Type	Recommended Therapy	Rationale
Meningitis	Ceftriaxone (100 mg/kg/day) + vancomycin (60 mg/kg/day)	Synergistic bactericidal activity; CSF penetration exceeds MIC for resistant strains
Pneumonia	High-dose penicillin G or amoxicillin (90 mg/kg/day)	Serum levels exceed MIC for intermediately resistant isolates
Otitis media	Amoxicillin-clavulanate (80–90 mg/kg/day) or ceftriaxone (50 mg/kg IM)	Overcomes β-lactamase production by co-pathogens; achieves middle ear fluid concentrations
Bacteremia	Cefotaxime or ceftriaxone ± vancomycin for highly resistant strains (MIC ≥4 μg/mL)	Broader spectrum against possible co-pathogens; avoids treatment delays

Cephalosporins like cefotaxime and ceftriaxone demonstrate superior activity against PRSP due to their higher affinity for altered PBPs. However, strains with *pbp1a* mutations (especially combined with *pbp2x* changes) can exhibit cephalosporin MICs up to 4 μg/mL—a phenomenon termed "cephalosporin-resistant PRSP" [45]. These isolates necessitate vancomycin or carbapenem therapy, though resistance to these agents remains rare.

Prevention through Vaccination

The introduction of pneumococcal conjugate vaccines (PCVs) significantly altered PRSP epidemiology. PCV7 reduced vaccine-type resistant isolates by 81% in the U.S., but non-vaccine serotypes (e.g., 19A, 35B) subsequently emerged as resistance carriers [46]. PCV13 further decreased resistant invasive disease by 60%, though serotype replacement continues to challenge long-term control [47].

Future Directions

The persistence of PRSP underscores the need for novel β-lactams (e.g., ceftaroline) targeting resistant PBPs, alongside improved diagnostics to rapidly identify resistance patterns. Continued genomic surveillance remains critical to track emerging clones and guide vaccine updates [48].

This case exemplifies how bacterial evolution, human behavior, and therapeutic limitations converge to sustain antimicrobial resistance—a paradigm informing strategies against other resistant pathogens. The next subsection explores vancomycin-resistant enterococci, where plasmid-mediated resistance presents distinct clinical challenges.

Vancomycin Resistance in Enterococci

The emergence of vancomycin-resistant enterococci (VRE) represents a critical inflection point in the global antimicrobial resistance (AMR) crisis, exemplifying how nosocomial pathogens can exploit therapeutic gaps to establish endemicity in healthcare settings. Enterococci, particularly *Enterococcus faecium* and *Enterococcus faecalis*, have ascended as leading causes of hospital-acquired infections, accounting for 14% of urinary tract infections and ranking as the third most common bloodstream pathogen in U.S. hospitals [49]. Their intrinsic tolerance to β-lactams and aminoglycosides, combined with an extraordinary capacity to acquire exogenous resistance determinants, has rendered these organisms formidable adversaries in clinical practice [50].

Molecular Mechanisms of Glycopeptide Resistance

Vancomycin resistance in enterococci is orchestrated by *van* operons, which remodel the peptidoglycan biosynthesis pathway to circumvent glycopeptide binding. The *vanA* and *vanB* phenotypes, responsible for most clinical resistance, encode ligases that synthesize depsipeptide (D-Ala-D-Lac) instead of the native D-Ala-D-Ala dipeptide [51]. This substitution reduces vancomycin affinity by 1000-fold while permitting normal cell-wall cross-linking. These operons are typically plasmid-borne or chromosomally integrated via transposons (e.g., Tn*1546*), facilitating horizontal transfer between strains [52].

Laboratory characterization reveals stark phenotypic differences: *vanA* confers high-level resistance to both vancomycin (MIC 16–512 μg/mL) and teicoplanin (MIC 16–512 μg/mL), whereas *vanB* exhibits variable vancomycin resistance (MIC 4–32 μg/mL) while remaining teicoplanin-susceptible [53]. The *vanC* phenotype, intrinsically present in *E. gallinarum* and *E. casseliflavus*, provides low-level vancomycin resistance (MIC 2–32 μg/mL) through D-Ala-D-Ser peptidoglycan precursors and holds limited clinical significance [54].

Epidemiological Trends and Risk Factors

Surveillance data from the National Nosocomial Infections Surveillance (NNIS) system documented a 20-fold increase in VRE prevalence among U.S. hospital isolates—from <0.5% in 1989 to >10% by 1995 [55]. Outbreaks followed distinct dissemination patterns: monoclonal clusters traced to index patients in ICUs contrasted with polyclonal outbreaks linked to environmental reservoirs (e.g., bedrails, thermometers) [56].

Multivariate analyses identified key risk factors for VRE colonization and infection:

- Prolonged hospitalization (>14 days: OR 3.8, 95% CI 2.5–5.7)
- Prior vancomycin use (OR 2.9, 95% CI 1.9–4.4)
- Exposure to broad-spectrum cephalosporins (OR 2.1, 95% CI 1.4–3.2)
- Presence of indwelling devices (e.g., urinary catheters: OR 1.8, 95% CI 1.2–2.7) [57]

Mortality rates underscore VRE's clinical impact: bacteremia attributable mortality reaches 50% in hematologic malignancy patients, compared to 15% for vancomycin-susceptible enterococci (VSE) [58]. This disparity reflects both delayed effective therapy and the organism's propensity to infect immunocompromised hosts.

Therapeutic Challenges and Alternatives

The treatment landscape for VRE infections remains constrained by limited bactericidal options:

Table 03. Therapeutic Strategies for VRE Infections

Agent	Mechanism	Efficacy	Limitations
Linezolid	50S ribosomal inhibition	82% clinical cure in bacteremia; equivalent to daptomycin in trials [59]	Myelosuppression, lactic acidosis
Daptomycin	Membrane depolarization	6–10 mg/kg achieves bactericidal activity in endocarditis models [60]	Resistance emergence at subtherapeutic doses
Tigecycline	30S ribosomal inhibition	Tissue penetration excels in intra-abdominal infections [61]	Suboptimal serum levels for bacteremia
Quinupristin-Dalfopristin	Ribosomal subunit synergy	65% efficacy against *E. faecium* (including VRE) [62]	Poor activity against *E. faecalis*; arthralgia adverse effects

Combination regimens (e.g., daptomycin + ampicillin) exploit synergistic bactericidal effects observed in vitro and in animal models [63]. However, clinical data remain sparse, and optimal dosing strategies are yet to be standardized.

Infection Control Imperatives

Containment of VRE necessitates multimodal interventions:

- **Active surveillance cultures** (rectal swabs) detect asymptomatic carriers with 92% sensitivity [64]
- **Contact precautions** (gowns, gloves) reduce transmission by 60% in outbreak settings [65]
- **Environmental disinfection** with sporicidal agents (e.g., hypochlorite) eliminates persistent contamination [66]
- **Antimicrobial stewardship** restricting vancomycin use correlates with 40% reductions in VRE incidence [67]

Zoonotic and Environmental Reservoirs

Metagenomic studies reveal concerning ecological dimensions: *vanA*-carrying enterococci are detected in 12% of retail poultry samples and 8% of wastewater isolates, suggesting dissemination through food chains and aquatic systems [68]. The use of avoparcin (a glycopeptide growth promoter) in livestock until its 1997 EU ban likely selected for *vanA* in animal microbiota, which may transfer to humans via zoonotic or environmental routes [69].

Future Directions

Novel agents like oritavancin (a lipoglycopeptide retaining activity against *vanA* VRE) and CRISPR-Cas9-based plasmid eradication strategies offer promising research avenues [70]. However, their clinical utility will depend on overcoming resistance development and delivery challenges.

The VRE paradigm underscores the interplay between microbial adaptability, healthcare practices, and ecological pressures in driving AMR. Its trajectory warns of similar challenges with emerging resistances in *Staphylococcus aureus* and other gram-positive pathogens, emphasizing the need for preemptive, multifaceted containment strategies.

Conclusion

Antimicrobial resistance (AMR) represents a complex, evolving threat that undermines the effectiveness of current therapeutic strategies and poses significant challenges to global health. The emergence and spread of multidrug-resistant organisms—such as extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, penicillin-resistant *Streptococcus pneumoniae*, and vancomycin-resistant enterococci (VRE)—illustrate the remarkable adaptability of bacterial pathogens under selective pressure. These resistance mechanisms, driven by genetic mutations, horizontal gene transfer, and selective environmental exposures, highlight the intricate interplay between microbial evolution, clinical practices, and public health policies.

The clinical consequences of AMR are profound, contributing to increased morbidity, mortality, and healthcare costs. Traditional therapies are increasingly compromised, and alternative treatment options are often limited, toxic, or less effective. Moreover, diagnostic challenges and regional disparities in surveillance further complicate timely and appropriate management.

Addressing AMR requires a coordinated, global response encompassing antimicrobial stewardship, enhanced diagnostic capabilities, vaccine development, infection prevention strategies, and sustained research into novel therapeutics. Continued genomic surveillance and environmental monitoring are essential to track emerging resistance patterns and mitigate their spread. Ultimately, combating AMR demands an integrative, One Health approach that spans human, animal, and environmental health sectors to preserve the efficacy of existing antibiotics and ensure the future of effective infectious disease treatment.

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Conflicts of Interest

The authors declare no conflicts of interest.

Author Contribution

Both are contributed equally

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