ECRONICON OPEN ACCESS

EC MICROBIOLOGY
Editorial

The Global Threat of Multidrug-Resistant Pathogens: A Call for Action

Tamer A Addissouky[1,2,3,4]*

[1]*Medical Laboratories Techniques Department, College of Technology and Health Sciences, AL-Mustaqbal University, Hillah, Babylon, Iraq*

[2]*Department of Biochemistry, Science Faculty, Menoufia University, Menoufia, Egypt*

[3]*New Burg El-Arab Hospital, Ministry of Health, Alexandria, Egypt*

[4]*American Society for Clinical Pathology (ASCP), Chicago, USA*

***Corresponding Author:** Tamer A Addissouky, Medical Laboratories Techniques Department, College of Technology and Health Sciences, AL-Mustaqbal University, Hillah, Babylon, Iraq and Science Faculty, Menoufia University, Egypt and New Burg El-Arab Hospital, Ministry of Health, Alexandria, Egypt and MLS, ASCP, USA.

Received: October 25, 2024; **Published:** November 06, 2024

Abstract

Background: Antimicrobial resistance (AMR) has emerged as a critical global health challenge, with over 1.27 million deaths annually attributed directly to multidrug-resistant infections. The World Health Organization (WHO) and other international bodies have highlighted the escalating threat of AMR, which disproportionately affects low- and middle-income countries (LMICs). If left unaddressed, AMR could result in 10 million annual deaths by 2050 and cause significant economic losses, potentially up to $100 trillion globally.

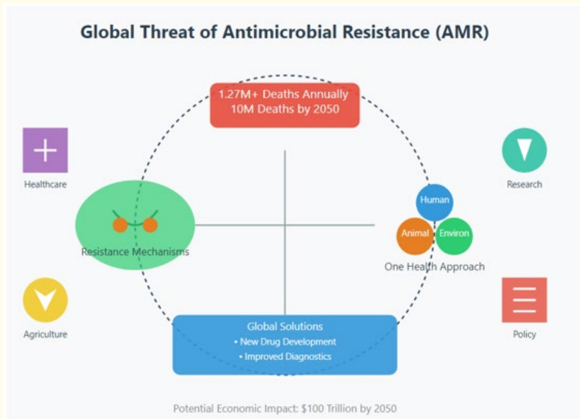
Purpose: The purpose of this article is to explore the biological mechanisms that drive AMR, the key factors contributing to its spread, and the global health implications. It also outlines current global responses and offers recommendations for addressing the crisis.

Main Body: AMR is driven by genetic mutations and the horizontal transfer of resistance genes, accelerated by the overuse and misuse of antibiotics in healthcare, agriculture, and environmental contamination. The global health implications are severe, with the rise of untreatable infections leading to prolonged hospital stays, higher mortality, and increased healthcare costs. Vulnerable populations, such as neonates and immunocompromised individuals, are disproportionately impacted. Efforts to combat AMR must adopt a One Health approach, integrating human, animal, and environmental health strategies. Key global responses include WHO's Global Action Plan and National Action Plans, which emphasize surveillance, antimicrobial stewardship, and research into new antibiotics and diagnostics.

Conclusion: Urgent global action is required to mitigate AMR's devastating effects on public health and economies. Future efforts must prioritize innovation in drug development, improved diagnostic tools, and robust AMR surveillance systems. Coordinated international collaboration, alongside national policy reforms, is essential for a sustainable solution to this global threat.

Keywords: *Antimicrobial Resistance; Multidrug-Resistant Pathogens; One Health Approach; Global Health Security; Antibiotic Stewardship*

Graphical Abstract



Figure

Abbreviations

AMR: Antimicrobial Resistance; WHO: World Health Organization; LMICs: Low- and Middle-Income Countries; SDGs: Sustainable Development Goals; HGT: Horizontal Gene Transfer; PPE: Personal Protective Equipment; FAO: Food and Agriculture Organization; OIE: World Organisation for Animal Health; EU-JAMRAI: European Union's Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections; NAPs: National Action Plans

Article Highlights

- AMR could cause 10 million annual deaths by 2050 without global intervention.
- Misuse of antibiotics in healthcare, agriculture, and the environment drives resistance.
- Coordinated global action is critical for developing new antibiotics and diagnostic tools.

Background

Current state of antimicrobial resistance (AMR)

Antimicrobial resistance (AMR) has emerged as an unparalleled global health threat. According to the latest global estimates (2023-2024), AMR is responsible for over 1.27 million direct deaths annually, with millions more affected by infections complicated by resistant organisms [1-3]. The World Health Organization (WHO) reports that drug-resistant infections are present in every region of the world, with low- and middle-income countries (LMICs) bearing the heaviest burden. In addition to its impact on human health, AMR exerts a significant economic burden. The World Bank projects that by 2050, AMR could cost the global economy up to $100 trillion in lost output if no action is taken. Healthcare systems are already feeling the strain, with prolonged hospital stays, higher medical expenses, and increased investments in infection control measures. The mortality burden is alarming, with projections indicating that AMR could lead to 10 million deaths annually by 2050 [4,5].

Significance of the crisis

The COVID-19 pandemic has heightened awareness of infectious disease threats, but AMR represents a slower, yet equally destructive, pandemic. In a post-pandemic world, the interconnectedness of global health security is more evident than ever. AMR not only threatens human health but also undermines progress towards several Sustainable Development Goals (SDGs). Goal 3, which focuses on good health and well-being, and Goal 2, which aims for zero hunger, are particularly vulnerable to the impacts of AMR, as resistant infections can compromise food security, maternal and child health, and the treatment of chronic diseases [6,7].

Evolution and mechanisms of resistance

Biological foundations

The development of resistance in pathogens is driven by specific genetic mechanisms. Bacteria acquire resistance through mutations in their DNA or by acquiring resistance genes from other bacteria. Horizontal gene transfer (HGT), which includes transformation, transduction, and conjugation, plays a pivotal role in spreading resistance genes across bacterial populations. Mobile genetic elements, such as plasmids, transposons, and integrons, facilitate the rapid dissemination of resistance traits, enabling bacteria to adapt quickly to antimicrobial pressures [8-12].

Drivers of resistance

Several human activities exacerbate the spread of resistance. The misuse of antibiotics in healthcare settings, such as inappropriate prescribing and overuse, accelerates the selection of resistant strains. In agriculture, antibiotics are often used to promote animal growth and prevent infections, contributing to the development of resistant bacteria that can transfer to humans through the food chain. Environmental contamination from pharmaceutical manufacturing and improper disposal of antimicrobial agents further propagates resistance genes in natural ecosystems. Global travel and interconnected trade networks also contribute to the rapid transmission of resistant strains across borders [13-17].

Global health implications

Clinical impact

Resistance to antibiotics leads to treatment failures, complicating the management of common infections like pneumonia, tuberculosis, and urinary tract infections. As infections become harder to treat, patients experience longer hospital stays, which in turn increases their risk of acquiring healthcare-associated infections. The financial implications are significant, with costs rising due to more intensive treatments and prolonged care. Vulnerable populations, such as neonates, the elderly, and immunocompromised individuals, are disproportionately affected by resistant infections, facing higher mortality rates [18,19].

Healthcare system challenges

The rise of AMR has severely limited therapeutic options, as many first-line antibiotics are no longer effective. This has led to the use of last-resort drugs, which are often more expensive, toxic, and less accessible. Additionally, diagnostic limitations hinder the ability to rapidly identify resistant strains and tailor treatments accordingly. Infection control measures, from hand hygiene to isolation protocols, are crucial but can be difficult to enforce consistently. Healthcare workers are also at increased risk of exposure to resistant pathogens, particularly in resource-limited settings where personal protective equipment (PPE) may be scarce [20,21].

One health approach

Human health considerations

The One Health approach, which recognizes the interconnectedness of human, animal, and environmental health, is critical to addressing AMR. In human healthcare, antimicrobial stewardship programs aim to optimize the use of antibiotics, ensuring they are prescribed only when necessary and with the correct dosage and duration. Prevention strategies, such as vaccination and infection control, reduce the spread of infections, thereby decreasing the need for antibiotics. Surveillance systems are essential for detecting and monitoring resistance patterns, allowing for timely interventions [22-26].

Animal health

In agriculture, the overuse of antibiotics in livestock is a major driver of resistance. Implementing best practices in veterinary medicine, such as using antibiotics only for therapeutic purposes and under veterinary supervision, is essential. Food safety measures, including proper handling and cooking of animal products, can prevent the transmission of resistant bacteria to humans [27,28].

Environmental factors

The environment acts as a reservoir for resistant organisms and resistance genes. Contaminated water systems, particularly in areas where human or animal waste is inadequately managed, can facilitate the spread of resistance. Soil contamination from agricultural runoff and the improper disposal of industrial waste further exacerbates the problem. Effective waste management and environmental monitoring are crucial components of the One Health approach [29].

Current global response

International organizations

Several international bodies are leading the fight against AMR. The WHO Global Action Plan outlines strategic objectives for reducing AMR, including improving awareness, strengthening surveillance, and promoting the development of new antibiotics. The Food and Agriculture Organization (FAO) and the World Organisation for Animal Health (OIE) have launched initiatives to combat antimicrobial misuse in agriculture and veterinary medicine. Regional cooperation frameworks, such as the European Union's Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), enhance collaboration and information sharing across borders [30,31].

National action plans

Many countries have developed National Action Plans (NAPs) to address AMR, focusing on surveillance, policy implementation, and healthcare system adaptation. These plans often include the establishment of national surveillance programs to track resistance trends and the development of guidelines for antibiotic use in both human healthcare and agriculture. Research funding has been prioritized in several countries to support the development of new antibiotics and diagnostic tools [32,33].

Innovation and research priorities

Drug development

The discovery of new antimicrobial agents is a top priority, as resistance continues to render existing drugs ineffective. Novel antimicrobial classes, which target previously untapped bacterial processes, are urgently needed. Alternative therapeutic approaches, such as bacteriophage therapy, antimicrobial peptides, and immunotherapies, offer promising avenues for combating resistant infections. However, significant barriers to development exist, including high research costs, regulatory hurdles, and limited market incentives [34-38].

Diagnostic advances

Rapid diagnostic tools are essential for identifying resistant infections and guiding appropriate treatment. Advances in point-of-care diagnostics, which provide results within minutes, can help reduce unnecessary antibiotic use. Resistance monitoring tools, such as whole-genome sequencing, allow for the early detection of resistance patterns and the tracking of outbreaks [39].

Preventive strategies

Vaccination is one of the most effective ways to prevent infections and reduce antibiotic use. The development of vaccines against resistant pathogens, such as *Staphylococcus aureus* and *Klebsiella pneumoniae*, is a critical area of research. Novel infection control approaches, including the use of antimicrobial coatings on medical devices, can also help prevent the spread of resistant infections. Behavioral interventions, such as public education campaigns, play a key role in promoting responsible antibiotic use [40,41].

Economic considerations

Healthcare costs

AMR significantly increases healthcare costs by prolonging hospital stays and requiring more expensive treatments. The indirect societal costs, such as lost productivity and the long-term care of patients with chronic resistant infections, further strain economies. Developing nations, in particular, are disproportionately affected, as they often lack the resources to implement effective AMR control measures [42].

Investment needs

To combat AMR, substantial investments are needed in research and development, infrastructure improvement, and capacity building. Funding is required to support the discovery of new antibiotics, develop advanced diagnostic tools, and implement comprehensive surveillance systems [43].

Economic models

Economic incentives, such as push and pull mechanisms, are crucial for stimulating innovation in antibiotic development. Push incentives, including grants and subsidies, reduce the financial risks associated with early-stage research. Pull mechanisms, such as market entry rewards, provide financial rewards for successfully bringing new antibiotics to market. Public-private partnerships can also play a pivotal role in driving research and ensuring equitable access to new treatments [44].

Policy recommendations

Global coordination

International agreements and data-sharing frameworks are essential for coordinating the global response to AMR. Clear resource allocation mechanisms and standardized reporting systems can enhance the effectiveness of global surveillance efforts [45].

National policies

At the national level, robust regulatory frameworks are needed to control the use of antibiotics in healthcare and agriculture. These policies must be backed by effective implementation strategies and ongoing monitoring and evaluation to ensure compliance [46].

Local actions

Local healthcare facilities play a crucial role in combating AMR through the implementation of infection control policies and antimicrobial stewardship programs. Community engagement and educational initiatives are also vital for raising awareness about the responsible use of antibiotics [47].

Future perspectives

Emerging threats

New resistance mechanisms, such as the production of metallo-beta-lactamases, continue to emerge, posing an ongoing challenge to treatment. Cross-border transmission of resistant pathogens, particularly in regions with limited healthcare infrastructure, exacerbates the global spread of AMR. Climate change is also expected to influence the emergence and dissemination of resistant organisms by altering global ecosystems and disease patterns [48].

Opportunities

Despite the challenges, there are significant opportunities for progress. Technological advances, such as artificial intelligence and machine learning, can accelerate the discovery of new antibiotics and improve resistance surveillance. International cooperation, through initiatives such as the Global Antimicrobial Resistance Research and Development Hub, can drive the development of sustainable solutions to AMR [49].

Conclusion

Immediate action is needed to address AMR, with priorities including the development of new antibiotics, the implementation of robust surveillance systems, and the promotion of responsible antibiotic use. Long-term strategies must focus on strengthening healthcare systems, improving agricultural practices, and safeguarding the environment. Measurable objectives, such as reducing the incidence of drug-resistant infections by a specified percentage within a set timeframe, are essential for tracking progress. A clear timeline for implementation, supported by ongoing monitoring and evaluation, will ensure that efforts to combat AMR are successful. Success indicators, such as the number of new antibiotics developed or the reduction in antibiotic misuse, will provide tangible evidence of progress in the fight against this global threat.

Ethical Approval and Consent to Participate

Not applicable.

Clinical Trial Number

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Materials

All data are available and sharing is available as well as publication.

Competing Interests

The author hereby that they have no competing interests.

Funding Support

Corresponding author supplied all study materials. There was no further funding for this study.

Authors' Contributions

The corresponding author completed the study protocol and was the primary organizer of data collection and the manuscript's draft and revision process. The corresponding author wrote the article and ensured its accuracy.

Acknowledgements

The author thanks all the researchers who have made great efforts in their studies. Moreover, we are grateful to this journal's editors, reviewers, and readers.

Bibliography

1. Ruiz-Pérez R., *et al*. "Emerging global trends in next-generation alternatives to classic antibiotics for combatting multidrug-resistant bacteria". *Journal of Cleaner Production* 478 (2024): 143895.
2. Coque TM., *et al.* "Antimicrobial resistance in the global health network: Known unknowns and challenges for efficient responses in the 21st century". *Microorganisms* 11.4 (2023): 1050.
3. Salam MA., *et al*. "Antimicrobial resistance: A growing serious threat for global public health". *Healthcare* 11.13 (2022): 1946.
4. Guevara YA., *et al*. "A historical, economic, and technical-scientific approach to the current crisis in the development of antibacterial drugs: Promising role of antibacterial peptides in this scenario". *Microbial Pathogenesis* 179 (2023): 106108.
5. Aslam B., *et al*. "AMR and sustainable development goals: at a crossroads". *Globalization and Health* 20 (2024): 73.
6. Esiovwa R., *et al*. "Bridging the gaps in the global governance of antimicrobial resistance: The UN sustainable development goals and global health security agenda". *Routledge Open Research* 1 (2023): 1-8.
7. Jawad A. "Commentary: Antibiotic resistance, sustainable development 2030 and poverty in developing countries". *Journal of Developing Country Studies* 8.1 (2024): 1-8.
8. Vanacker M., *et al*. "The fitness cost of horizontally transferred and mutational antimicrobial resistance in *Escherichia coli*". *Frontiers in Microbiology* 14 (2023): 1186920.
9. Blakely GW. "Mechanisms of horizontal gene transfer and DNA recombination". Molecular Medical Microbiology (Third Edition) (2023): 309-324.
10. Michaelis C and Grohmann E. "Horizontal gene transfer of antibiotic resistance genes in biofilms". *Antibiotics* 12.2 (2023): 328.
11. Addissouky TA., *et al*. "Oxidative stress and inflammation: elucidating mechanisms of smoking-attributable pathology for therapeutic targeting". *Bulletin of the National Research Centre* 48 (2024): 16.
12. Aysha L Sezmis., *et al*. "Horizontal gene transfer, fitness costs and mobility shape the spread of antibiotic resistance genes into experimental populations of *Acinetobacter baylyi*". *Molecular Biology and Evolution* 40.3 (2023): msad028.
13. Adil M and Tiwari P. "Occurrence, fate, detection, ecological impact and mitigation of antimicrobial resistance genes derived from animal waste". Occurrence and Behavior of Emerging Contaminants in Organic Wastes and Their Control Strategies (2023): 33-51.
14. Endale H., *et al*. "Potential causes of spread of antimicrobial resistance and preventive measures in one health perspective-a review". *Infection and Drug Resistance* 16 (2023): 7515-7545.
15. Addissouky TA., *et al*. "Revolutionary Innovations in Diabetes Research: From Biomarkers to Genomic Medicine". *Iranian Journal of Diabetes and Obesity* 15.4 (2023): 228-242.
16. Addissouky TA. "Precision medicine for personalized cholecystitis care: integrating molecular diagnostics and biotherapeutics". *Bulletin of the National Research Centre* 48.89 (2024): 1-17.
17. Manaia CM., *et al*. "The complex interplay between antibiotic resistance and pharmaceutical and personal care products in the environment". *Environmental Toxicology and Chemistry* 43.3 (2024): 637-652.
18. Baral B., *et al*. "Infectious diseases and its global epidemiology". Nanostructured Drug Delivery Systems in Infectious Disease Treatment (2023): 1-24.

19. Razonable RR. "Protecting the vulnerable: Addressing the COVID-19 care needs of people with compromised immunity". *Frontiers in Immunology* 15 (2024): 1397040.

20. Kouko DW. "Assessment of infection prevention and control knowledge, practices, implementation and barriers among healthcare workers and support staff at Pumwani Maternity Hospital, Nairobi Kenya". Uonbi.ac.ke (2023).

21. Sengupta M., *et al*. "One health approach to addressing fungal infection disparities". *Current Fungal Infection Reports* 18 (2024): 13-25.

22. Muteeb G., *et al*. "Origin of antibiotics and antibiotic resistance, and their impacts on drug development: a narrative review". *Pharmaceuticals* 16.11 (2023): 1615.

23. Addissouky TA., *et al*. "Recent advances in diagnosing and treating *Helicobacter pylori* through botanical extracts and advanced technologies". *Archives of Pharmacology and Therapeutics* 5.1 (2023): 53-66.

24. Addissouky TA., *et al*. "Recent trends in *Helicobacter pylori* management: harnessing the power of AI and other advanced approaches". *Beni-Suef University Journal of Basic and Applied Sciences* 12.80 (2023): 1-18.

25. Addissouky TA., *et al*. "Towards personalized care: Unraveling the genomic and molecular basis of sepsis-induced respiratory complications". *Archives of Clinical Toxicology* 6.1 (2024): 4-15.

26. Addissouky TA., *et al*. "Emerging biomarkers for precision diagnosis and personalized treatment of cystic fibrosis". *Journal of Rare Diseases* 3.28 (2024): 1-12.

27. Kariuki JW., *et al*. "Antibiotic use by poultry farmers in Kiambu County, Kenya: exploring practices and drivers of potential overuse". *Antimicrobial Resistance and Infection Control* 12.3 (2023).

28. Kisoo L., *et al*. "Practices and drivers for antibiotic use in cattle production systems in Kenya". *One Health* 17 (2023): 100646.

29. Verma A., *et al*. "Application of wastewater in agriculture: Benefits and detriments". In: Rai, P.K. (eds) River Conservation and Water Resource Management. Advances in Geographical and Environmental Sciences. Springer, Singapore (2023).

30. Garden H. "Collaborative Mechanisms for Sustainable Health Innovation". OECD science, technology and industry policy papers (2023).

31. Anderson M., *et al*. "Challenges and opportunities for incentivising antibiotic research and development in Europe". *The Lancet Regional Health - Europe* 33 (2023): 100705.

32. Avello P., *et al*. "National action plans on antimicrobial resistance in Latin America: An analysis via a governance framework". *Health Policy and Planning* 39.2 (2024): 188-197.

33. Paula Avello., *et al*. "National action plans on antimicrobial resistance in Latin America: an analysis via a governance framework". *Health Policy and Planning* 39.2 (2024): 188-197.

34. Keck JM., *et al*. "New agents are coming, and so is the resistance". *Antibiotics* 13.7 (2024): 648-648.

35. Addissouky TA., *et al*. "Transforming glomerulonephritis care through emerging diagnostics and therapeutics". *Journal of Biomedical Research* 5.1 (2024): 41-52.

36. Addissouky TA., *et al*. "Precision medicine and immunotherapy advances transforming colorectal cancer treatment". *Journal of Cancer Biology* 5.2 (2024): 38-43.

37. Addissouky TA., *et al*. "Harnessing innovation for the future of breast cancer management". *Clinical Research in Oncology* 1.1 (2024): 10-17.

38. Liu GY., *et al*. "Antimicrobial resistance crisis: could artificial intelligence be the solution?". *Military Medical Research* 11 (2024): 7.

39. Struelens MJ., *et al*. "Real-time genomic surveillance for enhanced control of infectious diseases and antimicrobial resistance". *Frontiers in Science* 2 (2024): 1298248.

40. Addissouky TA., *et al*. "Realizing the promise of artificial intelligence in hepatocellular carcinoma through opportunities and recommendations for responsible translation". *Jurnal Online Informatika* 9.1 (2024): 70-79.

41. Akay Seref and Anan Yaghmur. "Recent advances in antibacterial coatings to combat orthopedic implant-associated infections". *Molecules* 29.5 (2024): 1172.

42. Evans Otieku., *et al*. "Healthcare provider cost of antimicrobial resistance in two teaching hospitals in Ghana". *Health Policy and Planning* 39.2 (2024): 178-187.

43. Chen C., *et al*. "Characterising global antimicrobial resistance research explains why one health solutions are slow in development: An application of AI-based gap analysis". *Environment International* 187 (2024): 108680.

44. Matthey MA and Hollis A. "Pull me - push you? The disparate financing mechanisms of drug research in global health". *Global Health* 20.1 (2024): 14.

45. Ruckert A., *et al*. "One health governance principles for AMR surveillance: A scoping review and conceptual framework". *Research Directions One Health* 2 (2024).

46. Trinh LTN., *et al*. "A scoping review on best practices of antibiotic resistance control in the private health sector and a case study in Vietnam". *Discover Public Health* 21 (2024): 53.

47. Cassim J., *et al*. "Building an Antimicrobial Stewardship Model for a Public-Sector Hospital: A Pre-Implementation Study". *Journal of Medical Microbiology* 73.7 (2024).

48. Shanta Ayasha., *et al*. "Resistance and co-resistance of metallo-beta-lactamase genes in diarrheal and urinary-tract pathogens in Bangladesh". *Microorganisms* 12.8 (2024): 1589.

49. Abel K., *et al*. "System-wide approaches to antimicrobial therapy and antimicrobial resistance in the UK: The AMR-X framework". *The Lancet Microbe* 5.5 (2024): e500-e507.

Volume 20 Issue 11 November 2024