Journal of Pioneering Medical Sciences
Received: November 25, 2024 | Accepted: January 30, 2025 | Published: February 05, 2025
Volume 14, Issue 01, Pages 64-72

DOI https://doi.org/10.47310/jpms2025140109

A Liability to Health-Care System: Antibiotic Resistance Emerging Trends and Global Challenges

Habeeb Ali Baig[*1], Nawal Salama Gouda[2], Mallem Dinakar[3], Abdelrhman Elhaj[4], Vineet Madduru[5] and Tanvi Madduru[6]
[1,2]Department of Microbiology, Faculty of Medicine, Northern Border University, Arar, 91431, Saudi Arabia
[3]Department of Forensic Medicine and Toxicology, Viswabharathi Medical College, Kurnool, 518467, India
[4]Department of Medical laboratory technology, College of Applied Medical Sciences, Northern Border University, Arar, 91431, Saudi Arabia
[5]Dermatology of Forefront, 5750 Centre Avenue #500, Pittsburgh Pennsylvania, 15206, USA
[6]Lexington High School, 251 Waltham St Lexington, Massachusetts, 02421, USA

Author Designation: [1,2]Assistant Professor, [3]Professor, [4]Lecturer, [5]Medical Assistant, [6]Senior

*Corresponding author: Habeeb Ali Baig (e-mail: docbaig@yahoo.com).

Abstract Antibiotics are developed to kill those germs that infect the human body. When these germs develop resistance to the drugs, the treatment of the patients becomes highly complex. This study aimed to highlight the phenomenon of antibiotic resistance and new emerging diseases. The study found that the process of developing resistance among germs is a natural and evolving process. Bacteria use intrinsic resistance to various antibiotics (multi-drug resistant) by the changes in the channels and pumps in cell membrane, inhibiting the influx of drugs. Significant gaps remain in proportion to the global impact of investment, international collaboration and collective action on antibiotic resistance. When the germs, bacteria and fungi develop resistance, they also transmit this resistance to other bacteria. Research in antibiotics resistance is focused on two aspects. In the first aspect, researchers find out those bacteria that have become resistant. Some bacteria develop resistance to some antibiotics, in which case, the patients may be treated with other antibiotics. Antibiotic-resistant genes (ARG) are transferable by HGT (horizontal gene transfer) where genetic elements like plasmid, transposons and insertion sequences were transferred which is the second aspect of reserachers. The study tries to investigate the culpability of antimicrobial resistance to the healthcare system by reviewing various articles. As per WHO guidelines, healthcare professionals should develop surveillance programs in their facilities and report information regarding antibiotic-resistant pathogens. The methodology includes systematic literature review, clinical data analysis and microbial resistance profiling. Specific outcomes highlight rising antibiotic resistance patterns, impact on healthcare costs and effectiveness of alternative treatments in mitigating resistance trends.[47] The study also found that some bacteria develop resistance against all antibiotics. The interventions should focus on preventive measures because the new antibiotics are costly and the bacteria may also develop resistance against new antibiotics

Key Words Antibiotics, antibiotics resistance, resistant bacteria, resistant germs, public health issue, global health, antimicrobial stewardship

INTRODUCTION

Antibiotics are prescribed by the physicians for the cure and treatment of various infections and diseases. Antibiotic resistance in pathogens imposes serious health-care burden that is associated with increased morbidities, including exacerbation of the infection and mortality which is chiefly caused by self-medication and excessive use of broad-spectrum antibiotics [1]. Global initiatives against antibiotic resistance have made progress through surveillance and stewardship programs, yet challenges persist due to inadequate regulation, overuse and slow antibiotic development, necessitating stronger global coordination and innovation [2].

The most World Economic Forum Global Risks indicates antibiotic resistance a major threat to human health, globally [3]. Approximately, 25000 deaths are reported in Europe as a result of multi-drug resistance, annually, contributing to financial burden of €1.5 billion [4]. The spread of antibiotic resistance is alarming worldwide and remains a serious public health concern. Antibiotic-resistant infections are observed more susceptible to treatment failure, resulting in increased treatment time, mortality and health care costs [5]. ARB (Antibiotic Resistant Bacteria) has been reported to be ubiquitously present in the environment (including, soil, surface water, sediment, especially in places with anthropogenic pressure, like, antibiotic residues in wastewater effluents [6,7]. This is because standardized monitoring is limited. Existing antibiotic surveillance systems are primarily limited to isolates from clinical settings [7,8]. Antibiotic resistance exacerbates the emergence of enteric bacterial infections including, Shigella, Salmonella typhi, *Helicobacter pylori* that are prevalent in many low- and middle-income countries [9]. As with antibiotic resistance, there are several standardized systems for monitoring gut pathogens in high- and low-income countries. The WHO Global Foodborne Infections Network is a promising surveillance system investigating the isolation of antibiotic-resistant enteric pathogens thoughis found limited to selected pathogens [10]. The file emphasizes specific pathogens and regions due to their critical role in the spread of antibiotic resistance, healthcare burden and public health risks. Pathogens like *Shigella, Salmonella typhi, Helicobacter pylori* and *Pseudomonas aeruginosa* were selected due to their increasing resistance trends. The focus on low- and middle-income regions highlights disparities in surveillance, antibiotic misuse and healthcare infrastructure. These areas face significant challenges in combating resistance, making them key to global health strategies.

Antibiotic resistance is part of the Global Health Security Agenda, International Health Regulations, UN Sustainable Development Goals, strengthening healthcare systems and several international health issues such as primary care and health plan appear on the agenda [11,12]. The nature of antimicrobial resistance across the disease and industry is an obstacle to creating a strong and sustainable case for ultimately driving local impact. Significant gaps remain in proportion to the global impact of investment, international collaboration and collective action on antibiotic resistance [13,14]. Therefore, current review focused on the antibiotic resistance and emerging trends.

This study acknowledges this issue that the growing use of antibiotics may eventually make the medicines worthless and increase the prevalence of dangerous and life-threatening diseases. Public health professionals should raise awareness for promoting a balanced use of antibiotics. Physicians and doctors are also responsible for reviewing the history of the patients and prescribing medication based on the past usage of the drugs by the patient. If there is a history of high usage, the patient may be persuaded to follow a treatment that may take an extended time, but that will reduce the excessive usage of antibiotics. Socioeconomic factors significantly influence antibiotic resistance trends. Poverty, inadequate healthcare access and poor sanitation promote misuse of antibiotics. In contrast, high-income settings face overprescription and agricultural overuse. Global disparities in education and regulation exacerbate resistance, necessitating targeted policies for effective antibiotic stewardship [15].

The rationale of this study is based on the premise that despite the efforts of the medical experts and public health professionals, there is a gradual increase in antibiotics resistance [4]. Therefore, there is a need for identifying the causes and critical factors that lead to this phenomenon. Moreover, the healthcare professionals should also evaluate the dynamics of those new and emerging diseases that are diagnosed due to antimicrobial resistance. Recent research highlights antibiotic resistance challenges and potential mitigation strategies. Optical sensing advances improve tetracycline detection, aiding surveillance [16]. Lower respiratory infections contribute significantly to antimicrobial resistance burdens [17]. Vaccination plays a crucial role in reducing resistance, preventing infections and decreasing antibiotic dependence [18].

In light of this background, the current review follows; 1) To examine the phenomenon of antibiotic resistance, highlighting gaps in surveillance and public awareness. 2) To analyze healthcare professionals' efforts in reducing resistance and improving monitoring. 3) To describe emerging diseases linked to antimicrobial resistance. 4) To recommend effective responses, emphasizing education and surveillance improvements.

METHODS

The study was based on the review of academic literature concerning antibiotics resistance. The researcher reviewed the latest and current literature published in the last ten years related to antibiotics resistance. Online editions of newspapers and magazines were also reviewed to know the new and emerging diseases caused by antibiotics resistance. The inclusion criteria encompassed studies focusing on antibiotic resistance trends, contributing factors and healthcare system impacts. Exclusion criteria omitted non-peer-reviewed articles, outdated research, non-relevant pathogens and studies lacking empirical data. Only studies with robust methodologies and significant findings were considered.

The findings have been presented in the form of thematic analysis and these themes collectively highlight the criticality of the situation and the effective interventions in the contemporary context. Past studies have discussed extensively about antibiotics resistance and the current findings in this study further enrich this literature. To validate sources, triangulate data from peer-reviewed articles, government reports and expert interviews. Cross-reference findings on antibiotic resistance trends, treatment failures and public health impacts to ensure reliability. To ensure data reliability, non-peer-reviewed sources were carefully cross-referenced with peer-reviewed articles, government reports

Table 1: Some of the Samples that are studies

Reference	Topic	Key Findings	Scope
Frieri *et al.* [1]	Antibiotic Resistance	Increasing resistance due to misuse and overuse of antibiotics	Public health impact
Mboowa *et al.* [5]	Antimicrobial Resistance in Uganda	Rising antimicrobial resistance in surgical wards between 2014 and 2018	Hospital setting
Guo *et al.* [6]	Wastewater Treatment and Antibiotic Resistance	Identified hotspots for antibiotic resistance genes and mobile genetic elements	Environmental analysis
Cox and Wright [20]	Intrinsic Antibiotic Resistance	Detailed mechanisms and challenges in addressing intrinsic resistance	Molecular and biochemical insights
Poole *et al.* [23]	Efflux Operons in Resistance	Evidence for efflux operons' role in multidrug resistance in *Pseudomonas aeruginosa*	Microbial resistance research
Pagès *et al.* [28]	Efflux Pump Inhibitors	Exploration of inhibitors targeting bacterial efflux pumps	Therapeutic development
Langford *et al.* [34]	Bacterial Co-Infection and COVID-19	Meta-analysis showing bacterial co-infection rates in COVID-19 patients	Clinical setting

and reputable health organizations. Expert opinions were consulted and sources with known credibility were prioritized. Furthermore, trends and statistics were corroborated across multiple independent publications to verify consistency and accuracy [19] (Table 1).

Mechanism of Antibiotic Resistance

Intrinsic Resistance

Intrinsic resistance refers to the natural, inherent ability of certain bacteria to resist the effects of specific antibiotics. This resistance is not acquired through mutation or horizontal gene transfer but is due to the bacteria's genetic makeup, such as lacking the target site for the antibiotic or having protective cell wall structures [21].

Intrinsic resistance is characterized by structural and functional alteration in response of antibiotics. Bacterial species are resistant to antibiotics irrespective of their types and does not include genetic changes. Gram-positive bacteria can be multi-drug resistant by the changes in the channels and pumps in cell membrane, inhibiting the influx of drugs. This has also led to increase in gram-positive infection. Some studies have shown that these changes can be supported by the insertion of genetic loci. Together, these factors are known as intrinsic resistome [20]. It is also indicated that environmental factors such as water and hygiene, can also contribute to resistance [22].

Permeability of Outer Membrane

In bacteria, the CM (cytoplasmic membrane) is act as a barrier between the external environment and the cytoplasm. These biological membranes are flexible, self-adhesive membranes because they are composed of lipid bilayer components. The membrane's fluidity directly affects the degree of permeability, making it more permeable [23]. Though if the permeability is decreased and it will decrease the fluidity which have detrimental effect on the structure and activity of numerous membrane proteins present in this bilayer. To circumvent this limitation and as an act of self-preservation, some bacteria collect additional external structures that act as permeation barriers to trap potentially poisonous substances. A stout outer peptidoglycan layer, teichoic acid ornating along with covalent protein, is representative of gram-positive bacteria. It provides malleable solidity and neutralizes the osmotic pressure generated by the cytoplasm [24,25]. Peptidoglycans from Gram-positive bacteria have been calculated to have a high permeability threshold and be usable for molecules up to 30-57 kDa [26]. This is evidence for gram-positive organisms' comparable intrinsic sensitivity to myriad antibiotics [27]. However, Gram-negative bacteria are inherently insensitive to multiple antimicrobials due to a much thinner molecular sieve called the "outer membrane" (OM) surrounding a relatively thin layer of peptidoglycan. Biological membranes are primarily composed of glycerophospholipids [16]. However, gram-negative OMs have a distinctive arrangement of lipid molecules (i.e., lipid A) covalently linked to polysaccharide units. Saturated fatty acid chains are present in LPS, facilitating tight packing of hydrocarbon chains. Individual lipid molecules are linked with multiple fatty acid chains (6-7). Both contribute to a decrease in membrane fluidity and, thus, an increase in the permeability threshold.

Multi Drug Resistance (MDR) Efflux Pumps

Efflux pumps are membrane proteins that actively transport antibiotics and other harmful substances out of bacterial cells, contributing to antibiotic resistance. By reducing intracellular drug concentrations, these pumps allow bacteria to survive even in the presence of antibiotics, making infections harder to treat and posing a significant threat to healthcare systems [28].

Effluent pumps are widespread on the chromosomes of all organisms that do not produce antibiotics [29], suggesting that they evolved for other purposes than to avoid antibiotic use [30,31]. The foremost examples of antimicrobial resistance by efflux-mediation were documented for tetracycline in the 1970s [32-34]. Since then, Pore active efflux of various antimicrobials has been established in many gram-positive and gram-negative bacteria. Substrate-dependent diverter pumps may expel only one molecule or may have a broader spectrum and may export a structurally different class of molecules. The outcome of the broad substrate specificity exhibited by the pumps is that they transport one or more molecules and often release toxic molecules produced by the host. These observations provide evidence of a survival mechanism in their natural habitat, rather than a development to directly counter the selective pressure induced by the clinical use of antibiotics. Multi-drug resistance (MDR) efflux pumps are transport proteins that expel antibiotics from bacterial cells, reducing drug efficacy. Globally, MDR bacteria, driven by overuse of antibiotics and genetic adaptations, threaten public health. These pumps contribute to treatment failures, complicating infection control and necessitating new antimicrobial strategies to combat resistant pathogens [35].

These observations provide evidence of survival in their naturalistic habitat instead of directly countering the selective pressure induced by the clinical use of antibiotics. The molecular base for this intrinsic phenotype is associated with the original OM and diminished permeability. Later, it was shown that the inherent resistance of P. aeruginosa to various categories of antibiotics (tetracyclines, chloramphenicol and norfloxacin) was due to a chromosome-encoded efflux pump [36]. Indeed, removing the MexAB-OprM efflux pump in *P. aeruginosa* strains sensitized to various antimicrobial agents [37]. This is the first documented report of intrinsic bacterial antibiotic resistance due to active efflux. This seems to be a coincidence. In this initial observance, active efflux was the underlying cause of diminished susceptibility of various Gram-negative bacteria with intrinsic resistance to antibiotics such as linezolid (reported in *E. coli* and *P. aeruginosa*) [27,36]. Macrolide antibiotics (*E. coli* and *Haemophilus influenzae*) [38,39] and the recently released glycylcycline, tigecycline (*P. aeruginosa*) [40]. Environmental factors like antibiotic overuse, pollution and heavy metals drive multidrug resistance (MDR) by activating bacterial efflux pumps. These pumps expel antibiotics, reducing drug efficacy and promoting resistance. Stress conditions, biofilms and horizontal gene transfer further enhance MDR, accelerating resistance trends and complicating infection treatment in healthcare and environmental settings.

In prokaryotes, there are five main subclasses of efflux proteins in bacterial membranes: ABC (ATP binding cassette), MF (major mediator), MATE (multidrug and toxic compound efflux), SMR (low multidrug resistance) and cleavage. RND (Resistive Node Family) [35,41,42]. Antibiotic leakage is an "active" process, meaning energy is required to drive a compound "up" along a concentration gradient. Apart from the ABC family, which hydrolyzes ATP to provide energy for the export of molecules, the rest of the repulsive protein family uses proton motive power to provide energy for the export of substrates [45].

Chromosomal Mutations and Horizontal Gene Transfer

Antibiotic-resistant genes (ARG) are transferred through horizontal gene transfer (HGT) via genetic elements like plasmid, transposons and insertion sequences. Genetic mutations play a crucial role in antibiotic resistance by enabling bacteria to evolve and survive exposure to antibiotics. These mutations can occur spontaneously or through horizontal gene transfer, leading to resistant strains. As a result, previously treatable infections become harder to manage, posing significant challenges to healthcare systems [46]. A study by computed molecular mechanism of fusidic acid resistance and showed that resistance is facilitated by protein-protein interaction where FusB protein of the drug binds to domain IV and V of elongation factor G (EFG), that induces translocation of peptidyl t-RNA during protein synthesis, leading to conformational changes [45]. Some of the common genes associated with antibiotic resistance include 16S rRNA, intI1, sul1, qnrS and blaTEM [46]. It is crucial to consider the genetic mechanism of various resistances. Antibiotics are destroyed by bacterial enzymes such as β-lactamase. The enzymes destroy the active component of antibiotics. Antibiotics are also resisted by changing the structure where antibiotic is to be targeted. It is accomplished through the mutations in the bacterial DNA.7 Chromosomal mutations and horizontal gene transfer drive global antibiotic resistance, threatening public health worldwide. Mutations alter bacterial DNA, while gene transfer spreads resistance across species. Poor antibiotic stewardship, overuse in agriculture and inadequate healthcare policies accelerate resistance, making infections harder to treat and increasing mortality, particularly in low-resource settings [47].

Methicillin-resistant Staphylococcus aureus (MRSA) refers to a family of bacteria that have created a genetic distinction from other strains of Staphylococcus aureus [9]. Vancomycin-resistant Staphylococcus aureus (VRSA) has produced another strain of Staphylococcus aureus and they have developed resistance to glycopeptide antibiotic vancomycin [9]. Environmental factors, such as antibiotic overuse, pollution and agricultural practices, drive resistance trends by promoting chromosomal mutations and horizontal gene transfer. Stressors like antibiotics and heavy metals select for resistant strains, while gene transfer spreads resistance across bacterial populations, accelerating the emergence of multidrug-resistant pathogens and threatening public health (Figure 1).

Clinical Assessments, Lab Input and Surveillance

As per WHO guidelines, healthcare professionals should develop surveillance programs in their facilities and report information regarding antibiotic-resistant pathogens [23]. This team development and reporting mechanism can highlight patterns regarding the demographics, types of infection and types of resistant bacteria.

Penicillin was the first antibiotic that was introduced at the commercial level in 1928 [22]. The resistance of germs against penicillin was first found in 1942 and further resistant germs were also found in 1967 and 1976 [22]. Resistance was also discovered for other antibiotics such as Vancomycin, Azithromycin and Caspofungin [22]. The efforts of healthcare professionals are directed to identifying the germs that have developed resistance against antibiotics.

The defense strategies of bacteria can take a variety of forms [25]. In the first strategy, germs restrict the access of the effective ingredients of antibiotics to the human body. For example, Gram-negative bacteria develop an outer membrane and protect the entry of antibiotics through this membrane [25]. The second strategy employs methods for getting rid of antibiotics entirely. Bacteria make use of their cell walls where antibiotic drugs are removed through the use of pumps. For example, Pseudomonas aeruginosa create pumps exclusively for getting rid of antibiotics [25]. The third strategy is highly risky and poses a high risk to the health of the individuals. In this strategy, the antibiotics are destroyed and changed due to which they lose their significance. This is achieved by the enzymes and proteins of the bacteria that destroy and alter the composition of antibiotics. For example, Klebsiella pneumonia produces carbapenemases that destroys the antibiotics, which is most common against beta-lactam [25]. Bacteria also develop new cell processes that can lead to the bypass of antibiotic-mediated destruction. The last strategy employed by the antibiotics is affecting the targets of the antibiotics. The drugs are developed to target specific parts of the bacteria. If the target is affected and the drugs are made to deviate from their site-of-effect and the antibiotics lose their significance. For example, Escherichia coli bacteria carry a gene known as MCR-1 [25]. This gene is used by the bacteria to add a compound to the wall of the cell. When this composition is developed, the drugs cannot latch into bacteria (Figure 2).

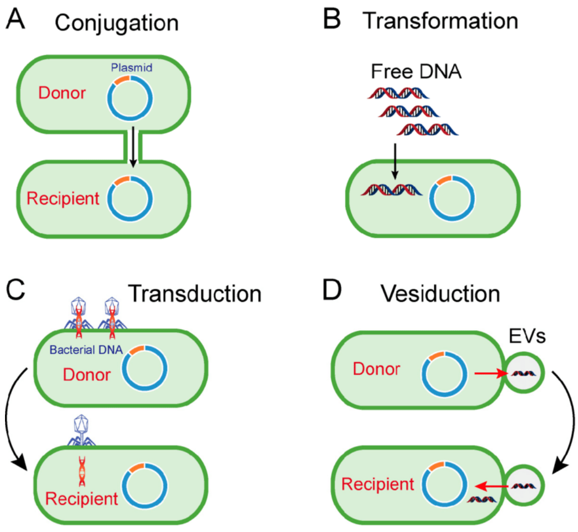

Figure 1: Chromosomal mutations and horizontal gene transfer

COVID19 and Antibiotic Resistance

It was observed that 8% patients with COVID19 are reported to be presented to concurrent bacterial infection, whereas, 72% of COVID19 patients are administered with antibiotic [48]. Furthermore, numbers of antibiotics are studied for the treatment of COVID19. Lack of knowledge regarding the infection and increased intake of over-the-counter antibiotics has also increased the exposure to antibiotics in these patients. Antibiotic resistance surged during COVID-19 due to increased misuse of antibiotics, prolonged hospital stays and overwhelmed healthcare systems. Disruptions in infection control, diagnostics and antimicrobial stewardship programs exacerbated resistance. The pandemic highlighted the urgent need for global surveillance, judicious antibiotic use and strengthened healthcare policies to combat emerging superbugs effectively (Figure 3) [48].

In community-acquired pneumonia, hospitalized COVID19 patients given antibiotics such as amoxicillin, clavulanate, macrolide, ceftriaxone, macrolide and levofloxacin (Figure 4) [49]. Another study showed that intake of antibiotics does not reduce the risk of mortality among these patients. These data can forecast upsurge in antibiotic resistance in the population [50]. This can also affect the treatment of a number of serious bacterial infections such as tuberculosis [36]. In a recent study, Mahmoudi [51] analyzed the prevalence of bacterial coinfection among

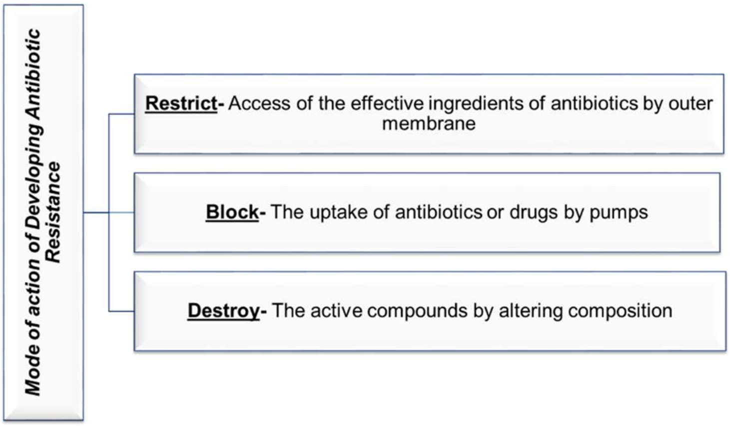

Figure 2: The mode of action bacteria to develop antibiotic resistance

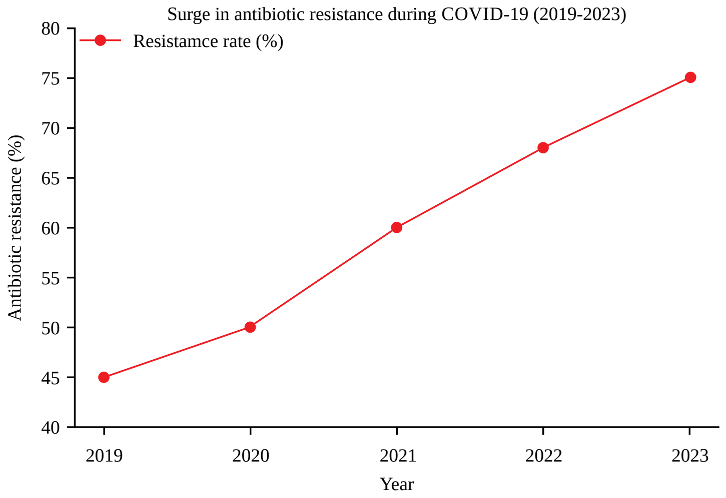

Figure 3: Graphical representation of antibiotic resistance for COVID 19

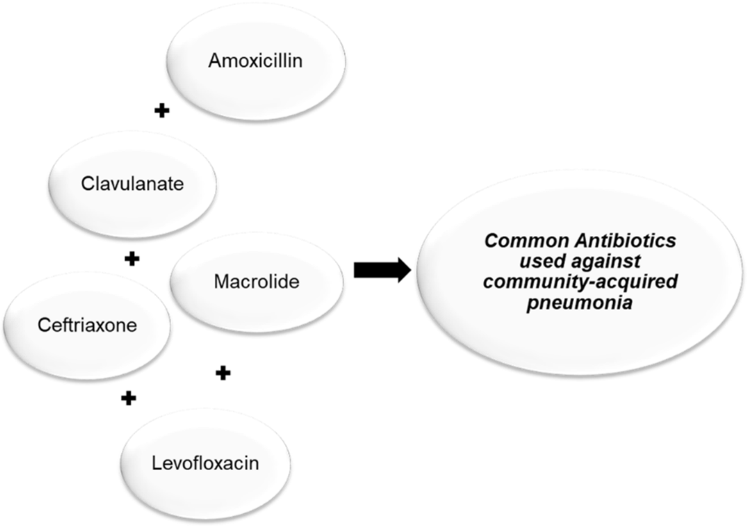

Figure 4: Commonly used Antibiotics against community acquired pneumonia

COVID19 patients. The outcomes of the study stated that Klebsiella and methicillin-sensitive Staphylococcus aureus were the two common species, reported in the samples respectively. All the bacteria were sensitive to amikacin, whereas oxacillin, erythromycin and clindamycin resistance was the highest. Antibiotic resistance strains healthcare systems, worsened by COVID-19's increased antibiotic misuse. Emerging trends include phage therapy, microbiome-based treatments and AI-driven drug discovery. Antimicrobial stewardship practices, such as precise diagnostics, restrictive prescribing and public awareness, are vital to curb resistance and ensure effective treatments in future pandemics [49].

CONCLUSION

This study made a comprehensive analysis of antibiotics resistance and new emerging diseases. The themes covered were phenomenon of antibiotics resistance, efforts of healthcare professionals, new and emerging diseases and effective response to antibiotics resistance. Antibiotic resistance imposes a severe economic burden, costing healthcare systems billions annually. In Europe alone, it leads to €1.5 billion in healthcare expenses and productivity losses. Globally, resistant infections increase hospitalization costs, prolong treatments and necessitate expensive alternatives, straining healthcare budgets and reducing economic productivity significantly.

The study highlighted the critical issue of antibiotic resistance, revealing that resistance among bacteria and other microorganisms is a natural, evolving process that presents significant challenges to healthcare systems. Findings emphasized how horizontal gene transfer exacerbates resistance, complicating treatment strategies. Moreover,

Table 2: Required Research Gaps

Topic	Current Knowledge	Research Gap	Potential Research Direction
Antibiotic Resistance and Global Surveillance [8]	Surveillance systems like ATLAS and EARS-net track antimicrobial resistance trends globally	Limited comparative data for low-income countries	Expand surveillance networks in underserved regions and assess regional variations
Environmental Contribution to Antimicrobial Resistance [22]	Identified environmental factors contributing to the spread of resistance	Inadequate understanding of long-term ecological impacts	Longitudinal studies on antibiotic persistence and microbial evolution in the environment
Efflux Pumps in Gram-Negative Bacteria [36]	Efflux pumps contribute to intrinsic resistance in pathogens like Pseudomonas aeruginosa	Limited availability of clinical efflux pump inhibitors	Development and clinical testing of novel efflux pump inhibitors
Antibiotic Resistance Genes in Waste Management [45]	Formation of resistance genes during decomposition of household waste is established	Lack of large-scale waste management solutions addressing resistance	Pilot studies on waste treatment strategies to reduce resistance gene formation
Mechanisms of Fusidic Acid Resistance [46]	Atomic-level insights into FusB-type resistance mechanisms	Insufficient clinical data on Fusidic acid-resistant strains	Clinical epidemiology studies on Fusidic acid resistance in infections
Antibiotic Resistance During COVID-19 [51]	Early antibiotic administration does not impact mortality in COVID-19 patients	Limited data on long-term effects of antibiotic use during the pandemic	Prospective studies to track resistance patterns post-pandemic

emerging trends indicate that COVID-19-related antibiotic misuse may have amplified the resistance problem. The study underscores the need for healthcare professionals to prioritize preventive measures, develop surveillance systems for resistant pathogens and promote the judicious use of antibiotics to mitigate the growing threat of antimicrobial resistance. Collaboration and awareness are essential for effective intervention. Antibiotic resistance threatens healthcare systems worldwide, driven by misuse and evolving pathogens. Global surveillance data reveal rising resistance rates, with multidrug-resistant infections surging. Emerging trends include rapid molecular diagnostics, AI-driven monitoring and novel antibiotics. Strengthened global cooperation, antimicrobial stewardship and innovative treatments are crucial to curbing this escalating crisis [16].

The study found that the process of developing resistance among germs is a natural and evolving process. When the germs, bacteria and fungi develop resistance, they also transmit this resistance to other bacteria. Research in antibiotics resistance is focused on two aspects. In the first aspect, researchers find out those bacteria that have become resistant. Some bacteria develop resistance to some antibiotics, in which case, the patients may be treated with other antibiotics. However, the study also found some bacteria that develop resistance against all antibiotics (Table 2).

This creates a complex situation for the healthcare professionals and they are compelled to create new antibiotics to kill those germs and bacteria. However, through a natural and evolutionary process, bacteria also develop resistance against new antibiotics. Limitations in addressing antibiotic resistance include insufficient global surveillance, limited novel antibiotic development and inadequate public awareness. Future studies should focus on enhanced monitoring systems, innovative antimicrobial therapies and robust stewardship programs. Strengthening policies, promoting alternative treatments and integrating AI-driven drug discovery can further mitigate resistance challenges effectively. Healthcare community has acknowledged this complexity and the focus is now on preventive measures because these measures not only prevent the infection but also reduce the spread of infection. Despite all these efforts, the healthcare professionals should be prepared for unforeseen circumstance as was observed in the case of coronavirus pandemic. When the knowledge about new resistant bacteria will be known timely and promptly in the public domain, the preventive measures can be implemented more effectively. Antibiotic resistance poses a severe threat to global healthcare, demanding urgent policy reforms and public health interventions. Strengthening regulations on antibiotic use, enhancing surveillance and promoting antimicrobial stewardship are crucial. Public awareness and research on alternative treatments must be prioritized to prevent a crisis that could render infections untreatable.

Self-medication has also contributed to the criticality of the issue. When antibiotics are taken in excessive quantity without prescription, bacterial resistance develops. Bacteria are trained to the attacks of the antibiotics and employ different defense strategies. Doctors and physicians also contribute to it by prescribing antibiotics where the cure was possible without them. The optimized use of antibiotics can also reduce the development of resistance in germs. The intake of drugs will also be more effective when they are taken only at the time of an acute need. Even if the resistance is not developed in germs, the excessive use of the same drug loses its effectiveness and the physician either increases the dose or changes the drug. Antibiotic resistance poses a significant threat to healthcare systems, yet there is a lack of focus on training healthcare professionals adequately. Integrating findings on resistance into educational curricula is crucial to equip future practitioners with effective prevention and treatment strategies. Therefore, the care receivers also have a role in contributing to the optimized use of antibiotics and reducing the development of resistant germs and bacteria. Pharmacies should also support this objective and provide medicines to the customers only on prescription. When the drugs are provided over the counter, the individuals are tempted to self-medication. Antibiotics resistance is a phenomenon that has highlighted the significance of joint efforts and collective wisdom. The resistance in bacteria may be caused by any individual. However, the negligence will have a cascading effect and it will also impact the lives of others. The health community should collaborate at a global level to address this issue. To combat antibiotic resistance, healthcare systems must enhance stewardship programs, promote rapid diagnostics and regulate antibiotic use. Public awareness campaigns, investment in novel antibiotics and global collaboration are crucial. Strengthening infection control, improving vaccination coverage and encouraging research on alternative therapies will help mitigate resistance and ensure sustainable healthcare solutions.

Future recommendations for combating antibiotic resistance should emphasize methodological improvements, including advanced genomic surveillance, AI-driven resistance prediction and standardized global reporting systems. Interdisciplinary collaboration between microbiology, public health and policy research is crucial. Strengthening antimicrobial stewardship, integrating microbiome research and promoting innovative drug discovery must be prioritized. Policymakers should enforce stricter regulations on antibiotic use, while public health initiatives should enhance awareness and vaccination programs. A holistic "One Health" approach, bridging human, animal and environmental health, is essential for sustainable solutions.

Acknowledgment

The Authors would like to express deepest gratitude to all those who helped during the writing of this manuscript.

Declaration of interest

The authors deny any conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

The authors declare no conflicts of interest regarding the publication of this paper.

REFERENCE

1. Frieri, Marianne, *et al.* "Antibiotic resistance." *Journal of Infection and Public Health,* vol. 10, no. 4, July 2017, pp. 369-378. http://dx.doi.org/10.1016/j.jiph.2016.08.007.
2. Abbara, S., *et al.* "Variable impact of an antimicrobial stewardship programme in three intensive care units: Time-series analysis of 2012–2017 surveillance data." *Journal of Hospital Infection,* vol. 104, no. 2, February 2020, pp. 150-157. http://dx.doi.org/10.1016/j.jhin.2019.10.002.
3. Howell L. World economic forum-global risks 2013. 2013.
4. Davies, Sally C, *et al.* "Annual report of the chief medical officer: Infection and the rise of antimicrobial resistance." *The Lancet,* vol. 381, no. 9878, May 2013, pp. 1606-1609. http://dx.doi.org/10.1016/s0140-6736(13)60604-2.
5. Mboowa, Gerald, *et al.* "Increasing antimicrobial resistance in surgical wards at mulago national referral hospital, Uganda, from 2014 to 2018—cause for concern?." *Tropical Medicine and Infectious Disease,* vol. 6, no. 2, May 2021,. http://dx.doi.org/10.3390/tropicalmed6020082.
6. Guo, Jianhua, *et al.* "Metagenomic analysis reveals wastewater treatment plants as hotspots of antibiotic resistance genes and mobile genetic elements." *Water Research,* vol. 123, no. 2011111, October 2017, pp. 468-478. http://dx.doi.org/10.1016/j.watres.2017.07.002.
7. Chu, Binh T. T., *et al.* "Metagenomics reveals the impact of wastewater treatment plants on the dispersal of microorganisms and genes in aquatic sediments." *Applied and Environmental Microbiology,* vol. 84, no. 5, March 2018,. http://dx.doi.org/10.1128/aem.02168-17.
8. Rossolini, Gian Maria, *et al.* "Trends of major antimicrobial resistance phenotypes in enterobacterales and gram-negative non-fermenters from atlas and ears-net surveillance systems: Italian vs. European and global data, 2008-2018." *Diagnostic Microbiology and Infectious Disease,* vol. 101, no. 4, December 2021,. http://dx.doi.org/10.1016/j.diagmicrobio.2021.115512.
9. Savoldi, Alessia, *et al.* "Prevalence of antibiotic resistance in *Helicobacter pylori*: A systematic review and meta-analysis in world health organization regions." *Gastroenterology,* vol. 155, no. 5, November 2018, pp. 1372-1382.e17. http://dx.doi.org/10.1053/j.gastro.2018.07.007.
10. Falardeau, Justin, *et al. Foodborne disease outbreak investigation: Surveillance and responses in the United States, Canada, the European Union and globally.* "Food System Transparency" CRC Press, 2021. pp. 93-116.
11. Bloom, Gerald, *et al.* "Antimicrobial resistance and universal health coverage." *BMJ Global Health,* vol. 2, no. 4, October 2017,. http://dx.doi.org/10.1136/bmjgh-2017-000518.
12. Maarten van der Heijden, *et al. When the Drugs Don't Work. Antibiotic Resistance as a Global Development Problem.* Uppsala, Sweden. https://www.reactgroup.org/wp-content/uploads/2019/02/When-the-Drugs-Don%E2%80%99t-Work-Antibiotic-Resistance-as-a-Global-Development-Problem-Feb-2019.pdf.
13. Cars, O., *et al.* "Meeting the challenge of antibiotic resistance." *BMJ,* vol. 337, no. 183, September 2008, pp. a1438-a1438. http://dx.doi.org/10.1136/bmj.a1438.
14. Laxminarayan, Ramanan, *et al.* "The lancet infectious diseases commission on antimicrobial resistance: 6 years later." *The Lancet Infectious Diseases,* vol. 20, no. 4, April 2020, pp. e51-e60. http://dx.doi.org/10.1016/s1473-3099(20)30003-7.
15. Klein, Eili, *et al.* "Racial and socioeconomic disparities evident in inappropriate antibiotic prescribing in the emergency department." *Annals of Emergency Medicine,* vol. 84, no. 2, August 2024, pp. 101-110. http://dx.doi.org/10.1016/j.annemergmed.2023.12.003.
16. Rong, Mingcong, *et al.* "Recent advances in optical sensing for tetracycline antibiotics." *TrAC Trends in Analytical Chemistry,* vol. 178, no. 2147483647, September 2024,. http://dx.doi.org/10.1016/j.trac.2024.117839.
17. Wan, Xingyu, *et al.* "Global burden of antimicrobial resistance in lower respiratory infections in 2021: A systematic analysis." *International Journal of Antimicrobial Agents,* vol. 65, no. 2, February 2025,. http://dx.doi.org/10.1016/j.ijantimicag.2024.107431.
18. Hasso-Agopsowicz, Mateusz, *et al.* "The role of vaccines in reducing antimicrobial resistance: A review of potential impact of vaccines on amr and insights across 16 vaccines and pathogens." *Vaccine,* vol. 42, no. 19, July 2024, pp. S1-S8. http://dx.doi.org/10.1016/j.vaccine.2024.06.017.
19. Pham, Thi Mui, *et al.* "Trends in infection incidence and antimicrobial resistance in the us veterans affairs healthcare system: A nationwide retrospective cohort study (2007–22)." *The Lancet Infectious Diseases,* vol. 24, no. 12, December 2024, pp. 1333-1346. http://dx.doi.org/10.1016/s1473-3099(24)00416-x.

20. Cox, Georgina and Gerard D. Wright. "Intrinsic antibiotic resistance: Mechanisms, origins, challenges and solutions." *International Journal of Medical Microbiology,* vol. 303, no. 6, August 2013, pp. 287-292. http://dx.doi.org/10.1016/j.ijmm.2013.02.009.
21. Choi, Byoung Jun, *et al.* "Phopq-mediated lipopolysaccharide modification governs intrinsic resistance to tetracycline and glycylcycline antibiotics in *Escherichia coli*." *mSystems,* vol. 9, no. 10, October 2024,. http://dx.doi.org/10.1128/msystems.00964-24
22. Fletcher, Stephanie. "Understanding the contribution of environmental factors in the spread of antimicrobial resistance." *Environmental Health and Preventive Medicine,* vol. 20, no. 4, April 2015, pp. 243-252. http://dx.doi.org/10.1007/s12199-015-0468-0.
23. Vance, Dennis E. and Jean E. Vance. *Biochemistry of lipids, lipoproteins and membranes*: 1st Edn., Elsevier Science, 1996. https://www.sciencedirect.com/book/9780444532190/biochemistry-of-lipids-lipoproteins-and-membranes#book-description
24. Madigan, Michael, *et al. Brock biology of microorganisms.* San Francisco, 15th Ed.,: Pearson/Benjamin Cummings, 2009, Pages: 1056. https://www.amazon.com/Brock-Biology-Microorganisms-Michael-Madigan/dp/0134261925
25. Schäffer, Christina and Paul Messner. "The structure of secondary cell wall polymers: How gram-positive bacteria stick their cell walls together." *Microbiology,* vol. 151, no. 3, March 2005, pp. 643-651. http://dx.doi.org/10.1099/mic.0.27749-0.
26. Scherrer, Rene and Philipp Gerhardt. "Molecular sieving by the *Bacillus megaterium* Cell wall and protoplast." *Journal of Bacteriology,* vol. 107, no. 3, September 1971, pp. 718-735. http://dx.doi.org/10.1128/jb.107.3.718-735.1971.
27. Randall, Christopher P., *et al.* "The target of daptomycin is absent from *Escherichia coli* and other gram-negative pathogens." *Antimicrobial Agents and Chemotherapy,* vol. 57, no. 1, January 2013, pp. 637-639. http://dx.doi.org/10.1128/aac.02005-12.
28. Ji, Ning, *et al.* "Lansoprazole (LPZ) reverses multidrug resistance (MDR) in cancer through impeding ATP-binding cassette (ABC) transporter-mediated chemotherapeutic drug efflux and lysosomal sequestration." *Drug Resistance Updates,* vol. 76, September 2024,. http://dx.doi.org/10.1016/j.drup.2024.101100.
29. Obst, S., *et al.* "Molecular dynamics simulations of six different fully hydrated monomeric conformers of *Escherichia coli* re-lipopolysaccharide in the presence and absence of Ca2+." *Biophysical Journal,* vol. 72, no. 3, March 1997, pp. 1031-1046. http://dx.doi.org/10.1016/s0006-3495(97)78755-1.
30. Vaara, M. "Agents that increase the permeability of the outer membrane." *Microbiological Reviews,* vol. 56, no. 3, September 1992, pp. 395-411. http://dx.doi.org/10.1128/mr.56.3.395-411.1992.
31. Bambeke, Françoise Van, *et al.* "Antibiotic efflux pumps." *Biochemical Pharmacology,* vol. 60, no. 4, August 2000, pp. 457-470. http://dx.doi.org/10.1016/s0006-2952(00)00291-4.
32. Ball, P.R., *et al.* "Accumulation of tetracyclines by *Escherichia coli* K-12." *Biochemical and Biophysical Research Communications,* vol. 77, no. 4, August 1977, pp. 1500-1507. http://dx.doi.org/10.1016/s0006-291x(77)80148-4.
33. Levy, Stuart B. and Laura Mcmurry. "Plasmid-determined tetracycline resistance involves new transport systems for tetracycline." *Nature,* vol. 276, no. 5683, November 1978, pp. 90-92. http://dx.doi.org/10.1038/276090a0.
34. Mcmurry, L, *et al.* "Active efflux of tetracycline encoded by four genetically different tetracycline resistance determinants in *Escherichia coli*.." *Proceedings of the National Academy of Sciences,* vol. 77, no. 7, July 1980, pp. 3974-3977. http://dx.doi.org/10.1073/pnas.77.7.3974.
35. Piddock, Laura J. V. "Multidrug-resistance efflux pumps ? not just for resistance." *Nature Reviews Microbiology,* vol. 4, no. 8, August 2006, pp. 629-636. http://dx.doi.org/10.1038/nrmicro1464.
36. Li, X Z, *et al.* "Role of efflux pump(s) in intrinsic resistance of *Pseudomonas aeruginosa*: Resistance to tetracycline, chloramphenicol and norfloxacin." *Antimicrobial Agents and Chemotherapy,* vol. 38, no. 8, August 1994, pp. 1732-1741. http://dx.doi.org/10.1128/aac.38.8.1732.
37. Poole, K, *et al.* "Multiple antibiotic resistance in *Pseudomonas aeruginosa*: Evidence for involvement of an efflux operon." *Journal of Bacteriology,* vol. 175, no. 22, November 1993, pp. 7363-7372. http://dx.doi.org/10.1128/jb.175.22.7363-7372.1993.
38. Chollet, Renaud, *et al.* "The acrab-tolc pump is involved in macrolide resistance but not in telithromycin efflux in *Enterobacter aerogenes* and *Escherichia coli*." *Antimicrobial Agents and Chemotherapy,* vol. 48, no. 9, September 2004, pp. 3621-3624. http://dx.doi.org/10.1128/aac.48.9.3621-3624.2004.
39. Peric, Mihaela, *et al.* "Effects of an efflux mechanism and ribosomal mutations on macrolide susceptibility of *Haemophilus influenzae* clinical isolates." *Antimicrobial Agents and Chemotherapy,* vol. 47, no. 3, March 2003, pp. 1017-1022. http://dx.doi.org/10.1128/aac.47.3.1017-1022.2003.
40. Dean, Charles R., *et al.* "Efflux-mediated resistance to tigecycline (GAR-936) in *Pseudomonas aeruginosa* PAO1." *Antimicrobial Agents and Chemotherapy,* vol. 47, no. 3, March 2003, pp. 972-978. http://dx.doi.org/10.1128/aac.47.3.972-978.2003.
41. Pagès, Jean Marie, *et al.* "Inhibitors of efflux pumps in gram-negative bacteria." *Trends in Molecular Medicine,* vol. 11, no. 8, August 2005, pp. 382-389. http://dx.doi.org/10.1016/j.molmed.2005.06.006.
42. Webber, M. A. "The importance of efflux pumps in bacterial antibiotic resistance." *Journal of Antimicrobial Chemotherapy,* vol. 51, no. 1, December 2002, pp. 9-11. http://dx.doi.org/10.1093/jac/dkg050.
43. Paulsen, I T, *et al.* "Proton-dependent multidrug efflux systems." *Microbiological Reviews,* vol. 60, no. 4, December 1996, pp. 575-608. http://dx.doi.org/10.1128/mr.60.4.575-608.1996.
44. Liang, Zhishu, *et al.* "The formation mechanism of antibiotic-resistance genes associated with bacterial communities during biological decomposition of household garbage." *Journal of Hazardous Materials,* vol. 398, November 2020,. http://dx.doi.org/10.1016/j.jhazmat.2020.122973.
45. Tomlinson, Jennifer H., *et al.* "A target-protection mechanism of antibiotic resistance at atomic resolution: Insights into fusb-type fusidic acid resistance." *Scientific Reports,* vol. 6, no. 1, January 2016,. http://dx.doi.org/10.1038/srep19524.
46. Rocha, Jaqueline, *et al.* "Inter-laboratory calibration of quantitative analyses of antibiotic resistance genes." *Journal of Environmental Chemical Engineering,* vol. 8, no. 1, February 2020,. http://dx.doi.org/10.1016/j.jece.2018.02.022.
47. Russo, Luigi, *et al.* "High-impact trials with genetic and -omics information focus on cancer mutations, are industry-funded and less transparent." *Journal of Clinical Epidemiology,* InPress, January 2025,. http://dx.doi.org/10.1016/j.jclinepi.2025.111676.
48. Langford, Bradley J., *et al.* "Bacterial co-infection and secondary infection in patients with COVID-19: A living rapid review and meta-analysis." *Clinical Microbiology and Infection,* vol. 26, no. 12, December 2020, pp. 1622-1629. http://dx.doi.org/10.1016/j.cmi.2020.07.016.
49. Covid N. COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital. London: National Institute for Health and Care Excellence (NICE); 2020 Oct 9. https://pubmed.ncbi.nlm.nih.gov/33400459/
50. Buetti, Niccolò, *et al.* "Early administered antibiotics do not impact mortality in critically ill patients with COVID-19.." *Journal of Infection,* vol. 81, no. 2, August 2020, pp. e148-e149. http://dx.doi.org/10.1016/j.jinf.2020.06.004.
51. Mahmoudi, Hassan. "Bacterial co-infections and antibiotic resistance in patients with COVID-19." *GMS Hygiene and Infection Control,* vol. 15, 2020. https://www.egms.de/static/en/journals/dgkh/2020-15/dgkh000370.shtml