Antimicrobial Resistance; An Emerging Threat to Human Health

Khaizran Fatima Kamal[1], Hafsa Sehar[1], Afifah Anwar[2], Lubabah Numan[3,*], Muhammad Abdullah Qureshi[4] Zuha Fatima[4], Muqadas[4], Nouman Tariq[4] and Maria Shafaqat[1]

[1]Department of Pharmacy, Faculty of Health & Pharmaceutical Sciences, University of Agriculture, Faisalabad
[2]Department of Biochemistry, University of Agriculture, Faisalabad
[3]Department of Pathobiology, Faculty of Veterinary and Animal Sciences, Bahauddin Zakariya University Multan, Pakistan
[4]Faculty of Veterinary Science, University of Agriculture, Faisalabad
*Corresponding author: lubabahnuman@gmail.com

Abstract

Antimicrobial resistance is a major global health-threatening problem. It is because of the development of the resistance against antimicrobial drugs. Annual deaths which are caused by AMR reach up to 5 million people. Many microorganisms including bacteria, parasites, fungi, and viruses have the ability to adapt to the harsh conditions of the environment and harsh internal conditions of the body of the host organisms. This ability of the microorganisms makes them enable to resist the antimicrobial drugs. Microorganisms adopt multiple mechanisms of action to adapt to the changes for their survival. These mechanisms involve alteration of the genes, membrane permeability, and enzymatic degradation of the antimicrobial drug. However, there are multiple strategies to overcome this emerging threat in the whole world.

Keywords: Antimicrobial resistance, AMR, Antimicrobial drugs, Microorganisms

Cite this Article as: Kamal KF, Sehar H, Anwar A, Numan L, Qureshi MA, Fatima Z, Muqadas, Tariq N and Shafaqat M, 2025. Antimicrobial resistance; An emerging threat to human health. In: Zaman MA, Farooqi SH and Khan AMA (eds), Holistic Health and Antimicrobial Resistance: A Zoonotic Perspective. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 212-216. https://doi.org/10.47278/book.HH/2025.51

A Publication of Unique Scientific Publishers	Chapter No: 25-333	Received: 27-Jan-2025 Revised: 12-Feb-2025 Accepted: 08-March-2025

Introduction

Antimicrobial resistance (AMR) is defined as the resistance caused by microorganisms to cure the infection (Abushaheen et al., 2020). Microorganisms including bacteria, parasites, viruses, and fungi change over time and no longer respond to the drug that is given to treat specific infections or diseases (Uddin et al., 2021). These microorganisms or pathogens that become resistant to antimicrobial drugs can easily spread in humans as well as in multiple species of animals (Faridah et al., 2020; Hazards et al., 2021). These transmitted pathogenic organisms are harder to treat compared to the microorganisms that are drug-resistant (Velazquez-Meza et al., 2022). When we treat the organisms with drugs that the pathogen is resistant to, the disease may become more severe, and the chance of spreading the disease increases (Baker et al., 2022; Qureshi et al., 2023). However, if we keep giving drugs from which resistance has been developed illness may become so severe that even death of the organism may occur (Abushaheen et al., 2020). The major reason for the development of antimicrobial resistance is because of the alteration in the mechanism of action of the pathogen (bacteria, fungi, viruses, and parasites) (Holmes et al., 2016). Pathogens change their mode of action when we keep providing the same drugs for the infection over time (Schneider & Ayres, 2008). These same drugs have the same mechanism of action from which microorganisms escape (McManus, 1997; Jadimurthy et al., 2022). Improper management of antimicrobial drugs and their misuse is the primary source of the development of AMR (Baraka et al., 2021). However, AMR may also develop from genetic mutations naturally and from the spread of resistant genes (Hazards et al., 2021; Jian et al., 2021). Nowadays, AMR is reaching another level of threat for human beings as some single microbes are getting resistant to multiple antimicrobial drugs which is called as multidrug resistant microbes (Ahmad et al., 2021). Multidrug resistant microbes include mostly bacterial species as bacteria covers major portion of the AMR, and sometimes they are also called superbugs (Almutairy, 2024). Superbugs are those bacteria and fungi which get resistant to multiple types of antibiotics and antifungal drugs (Chen et al., 2020). Superbugs are formed because of the mutation by the microbe to survive the harsh conditions and repeatedly exposure to the same antimicrobial drugs (Mitra et al., 2022). These superbugs are the major public health threat to human society because the infection they cause is very difficult to cure and they can transfer from one human to another very easily even in the healthy ones (Bravo et al., 2018). Humans play a very significant role in the development of superbugs because of their improper use of antibiotics and consuming food which contains antimicrobial residues (Ghimpețeanu et al., 2022; Mohsin & Amin, 2023).

AMR is the most threatening problem to public health (Dhingra et al., 2020). The burden is increasing day by day as the annual deaths due to resistant infections become nearly equal to 5 million (Murray et al., 2022). This issue requires alternative treatment control, which is sometimes very expensive to be afforded by most of the community and it may have several other side effects (Ayukekbong et al., 2017). We can use multiple preventive measures to mitigate AMR which includes using narrow-spectrum drugs and avoiding misuse or overuse of the antimicrobials (Majumder et al., 2020; Rahman et al., 2022). In this chapter, we will briefly discuss the mechanism of the development of AMR, factors which significantly contribute to the rising issue of AMR, and different methods to combat AMR.

Mechanisms of Antimicrobial Resistance

Antimicrobial resistance to antimicrobial drugs develops through various mechanisms that have been adopted by the microbes or pathogens (Christaki et al., 2020; Uddin et al., 2021). There are multiple mechanisms through which organisms (bacteria, fungi, viruses, and parasites) develop resistance against the provided drug (Hughes & Andersson, 2015). The first mechanism involves the biodegradation of a given antimicrobial drug with the help of enzymatic activities (Caracciolo et al., 2023; Nguyen et al., 2024). This is the primary mechanism of the microorganisms through which they develop AMR. β-lactamase is the enzyme that is produced by the bacteria for the hydrolyzation of the cephalosporins and penicillin drugs (Fatima et al., 2021). However, some other enzymes may include N-acylases, O-phosphorylases, aminocyclitol, adenylases, and O-nucleotidylases which also play significant role to resist other classes of the antibiotic drugs (Setti & Micetich, 1998). Another mechanism that is responsible for the development of AMR is the alteration of the bacterial target proteins (Annunziato, 2019; Rosas & Lithgow, 2022). Many bacteria have the ability to alter the target proteins by which antimicrobial drugs will not be able to kill the bacteria or stop its proliferation (Gill et al., 2015; Baquero & Levin, 2021). This happens when we provide antimicrobial drugs, and the drug won't find a suitable site to attack the bacteria (Nizet, 2007; Mayegowda et al., 2022). However, one other mechanism of the development of AMR has also been reported by multiple researchers. This mechanism involves the alteration of the membrane permeability of the microorganism so that the antimicrobial drug cannot have the desired effect to kill the microorganism (Kadurugamuwa & Beveridge, 1997; Zhou et al., 2022). However, alternation in the bacterial proteins also makes it difficult for antimicrobial drugs to bind with the bacteria in order to kill or stop its proliferation (Baquero & Levin, 2021; Pontes et al., 2022).

Factors Contributing to AMR

There are multiple factors that significantly contribute to the development of the AMR (Ahmad et al., 2021). A list of the factors that are responsible for the antimicrobial resistance development in multiple microorganisms is given in Table 1.

Table 1: Factors contributing to the rise of AMR (Antimicrobial Resistance) and their explanation

Sr. number	Factors	Explanation	References
1.	Use of Antimicrobial drugs	Misuse or overuse of any antimicrobial drug leads to the development of AMR against the specific type of drug. Misuse of the antimicrobial drug includes not using the antimicrobial drug for a given period or using the drugs for more than recommended by the doctor. However, some people also add antimicrobial drugs in the feed of the animals which also leads to the development of AMR that can be easily transmitted to humans from animals by consuming contaminated food with the drug residues or drinking milk from the animal on which antimicrobials are overused. This factor is majorly contributing to the rise of the AMR.	(Woolhouse et al., 2015; Abushaheen et al., 2020; Mittal et al., 2020;)
2.	Environmental contamination	Residues and waste products from antimicrobial drugs can contaminate the water, food, and environment which will significantly contribute to the rising issue of antimicrobial resistance.	(Harris et al., 2012; Ahmad et al., 2021)
3.	Poor hygienic Measures	Poor sanitation and hygiene practices in different premises (including homes, farms, and healthcare facilities) contribute to AMR. This is because it can allow the easier spread of resistant pathogens in the environment.	(Davies & Wales, 2019; Endale et al., 2023)
4.	Mutation	Many microorganisms have the ability to adapt to multiple changes to survive according to the environmental conditions. Most bacteria adapt mutations in their genes which will allow them to survive harsh conditions. When some antimicrobial drugs are given repeatedly to some bacteria, they mutate themselves so that the antimicrobial drugs won't affect them. This mutation in the microorganism is responsible for AMR. It can also spread from humans to animals and vice versa. The mutated microorganisms are very hard to treat, and their infection is more severe than the normal microorganisms.	(Coates et al., 2002; Bleuven & Landry, 2016)
5.	Age, sex, and genetics	Age, sex, and genetics of the organism also contribute to the rise of AMR. These factors can cause low immunity in the individual which ultimately causes the pathogen to resist in the body.	(Baker et al., 2018; Waterlow et al., 2024)

Impact of AMR on Human Health

Antimicrobial resistance is the most emerging problem in the modern era as the number of deaths per year due to AMR reaches up to 5 million per year (Aslam et al., 2024). In 2019, deaths caused by antimicrobial resistance touched the digit of 1.27 million (Khan, 2021). However, it contributed to the death of more than 4.95 people and if this issue goes uncontrolled, the number of deaths will increase more dramatically (Khan, 2021). There is a severe need for methodology to control this life-threatening emerging problem (Saeed et al., 2023). AMR is of great importance because it has drastic effects on human health. Antimicrobial resistance has become the most important global health issue which is very hard to treat (Talebi Bezmin Abadi et al., 2019). The chances of the prevalence of the disease increase with the increase in the AMR (Allcock et al., 2017). Viruses, bacteria, fungi, and parasites are adapting so rapidly against the existing antimicrobial drugs (Caljon et al., 2016). AMR is also contributing to high economic losses to mankind (Ahmad & Khan, 2019; Dadgostar, 2019). The major drivers for the cause of AMR are unnecessary, overuse and not taking antimicrobial drugs for a specific period (Reghukumar, 2023). Not taking the antimicrobial drugs for the prescribed time makes the microorganism get stronger than before so it is strictly advised to take antimicrobial drugs for the given period as prescribed by the doctor (Costelloe et al., 2010).

Strategies to Combat AMR

To control the rising issue of AMR, we must adopt some strategies to overcome this emerging problem. If we don't do so, we will have to face some very difficult consequences. However, some scientists have already suggested some control measures that should be adopted in order to control this global health problem (Hernando-Amado et al., 2019). The list of some suggestions and control strategies is given as follows (Llor & Bjerrum, 2014; Sharma et al., 2018; Kasimanickam et al., 2021; Sweileh, 2021):

- Stop overuse and misuse of antimicrobial drugs
- Conduct awareness programs
- Minimize the use of antimicrobial drugs in food and milk animals
- Enforcement of legislation
- International collaboration
- Education and public awareness
- Conduct extensive research programs to develop new effective drugs
- Rotational use of antimicrobial drugs
- One health approach
- Use of nanomedicine

Conclusion

Antimicrobial resistance is a major global health-threatening problem. It is because of the development of the resistance against antimicrobial drugs. Annual deaths which are caused by AMR reach up to 5 million people. Many microorganisms including bacteria, parasites, fungi, and viruses have the ability to adapt to the harsh conditions of the environment and harsh internal conditions of the body of the host organisms. This ability of the microorganisms makes them enable to resist the antimicrobial drugs. Microorganisms adopt multiple mechanisms of action to adapt to the changes for their survival. These mechanisms involve alteration of the genes, membrane permeability, and enzymatic degradation of the antimicrobial drug. However, there are multiple strategies to overcome this emerging threat in the whole world. We can avoid a major part of AMR by only controlling the critical use of antimicrobial drugs.

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