

Antibiotic Resistance: A Universal Issue of Concern

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Abstract

The antibiotic resistance forthwith is the worldwide severe health problem. Clinical and economically, outcomes are harmed by the antibiotic resistance, along with consequences ranging from a patient's failure to respond treatment and the expensive and alternative drugs costs higher morbidity and mortality rates, preponderant hospital stays and the need for changes in standard therapy. The usage of antibiotic in the population as a whole a few leading sources of antibiotic resistance. Patients who do not have a prescription are frequently given 'prescription-only' medications like antibiotics by pharmacists in undeveloped nations like India. There is a lack of information on how community pharmacists use antibiotics which is critical for developing a viable and long-term intervention programmed to encourage judicious antibiotic use. Antibiotics are one of the most effective weapons to fight against life-threatening illnesses. Their discoveries have a significant impact on human as well as animal health. Consequently, because of the advent and spread of antimicrobial resistance, people all around the world including Americans are sinking due to intractable diseases. In this review, we will look at the trapping of antibiotic resistance on the general public health, community, society and health care system. Resistance to antibiotics is a danger sign that is putting strain on healthcare systems and resulting in severe health loss; we must continue to monitor and support activities aimed at preventing and controlling the infection.

Keywords: Clinical Pharmacist, Infection Control Team, Prescribers.

INTRODUCTION

Antibiotic resistance takes place when bacteria substitute in some way that decrease or eliminates the efficacy of drugs, chemical or other agents planned to cure or prevent the infection. As a result, the germs endured and multiply causing superlative damage.

The use of antibiotic espouses the spread of antibiotic resistance in the worldwide population. Antibacterial susceptibility is determined by the minimal inhibitory concentration that stops bacteria from growing.¹ Antibiotics are mostly used for bacterial infection and infectious disease prevention. Antibiotics are cytostatic or cytotoxic to bacteria, allowing the body as a natural defence such as immune system to eliminate them. Antibiotics act by inhibiting the synthesis of a bacterial cell, synthesis of proteins, deoxyribonucleic acid (DNA), Ribonucleic Acid (RNA) and by membrane disorganizing agent or other specific actions. Antibiotics generally enter the cell wall of micro-organisms by binding to them, using the energy-dependent transport mechanisms in ribosomal sites, as a result of which protein synthesis is inhibited.^{1,2} Approximately 70% of bacteria that cause illnesses in hospitals are now resistant to one of the most often used antibiotics. Antibiotics resistance in bacteria is a global challenge associated with mortality and morbidity.³ The Centre for Disease Control and Prevention in USA has estimated that 50 millions out of 150 millions prescriptions every year are superfluous.¹⁻³ Antibiotic resistance is a worldwide public health issue. Antibiotic resistance can also be caused by hospital-acquired infections

and poor public health.⁴ Antibiotic resistance is a result of drug-resistant micro-organisms that have developed new resistance mechanisms, posing a threat to the capacity to treat common bacterial infections. The rapid global expansion of multi- and pan-resistant bacteria, which cause diseases that are resistant to current antibiotics is particularly pertaining.⁵ Antibiotic resistance has increased day by day as a result the widespread use of antibiotics and related problems has been arise to be accomplished for the treatment and cure of these contamination emerged due to the resistant bacteria. Now days many researches trying to formulate a new drugs while the other there is also tortuous in treatment as a result the spread of antibiotic resistance increases rapidly. The development of resistance to antibiotics is a main worldwide health issues.⁶

History

Antibacterial compounds were first observed in action in the late 1800s. A German physician named Paul Ehrlich noticed that some chemical dyes coloured due to some bacterium cells but not the other micro-organisms. He came to the conclusion that is based on this idea; it must be able to design a compounds that can selectively kill bacteria causing germs without disturbing the other cells of the body. He discovered that arsphenamine, a chemical was an excellent therapy for the treatment and cure of syphilis in 1909. Although Ehrlich referred to his finding as 'chemotherapy' - the

employment of a chemical to cure a disease- it became the first modern antibiotic. Over 30 years later, the Ukrainian-American inventor and microbiologist Selman Waksman, who discovered over 20 antibiotics throughout his lifetime coined the term “antibiotics”. Alexander Fleming’s work was apparently a little haphazard, and he found penicillin by mistake. In 1928, he returned from a vacation in Suffolk and discovered that a fungus - *Penicillium notatum*, had infected a culture plate of *Staphylococcus bacteria* that he had left uncovered. Wherever the fungus grew on the plate, it generated bacteria-free zones. The Fleming separated the mould and cultured it in pure culture. He discovered that *P. notatum* was highly effective even at low concentrations for preventing *Staphylococcus* growth even after being diluted 800 times and was less toxic than the disinfectants in use at the time.⁷⁻⁸ During the treatment of patients with streptomycin which was the first used in 1944 to treat tuberculosis (TB; “The Great White Plague”), mutant strains of the *Mycobacterium tuberculosis* resistant to therapeutic amounts of the antibiotic were discovered. A similar chain of events has occurred as different antibiotics have been discovered and put into the clinical practice. The discovery of genetically transferable antibiotic resistance in Japan in the mid-1950s (which was initially met with scepticism in the West) changed everything by introducing the heretical genetic concept that collections of antibiotic resistance genes could be disseminated throughout an entire population of bacterial pathogens by bacterial conjugation (with a few notable exceptions).⁷⁻⁸ The usage of streptomycin and tetracycline was found in the late 1940s and early 1950s and the period of antibiotic chemotherapy became the highly tolerated in clinical medicine.

These medications were efficient and effective against bacillus TB and other dangerous bacteria.⁹

Causes

The extensive usage of antibacterial medications is a main cause behind the antibiotic resistance. Antibiotics are used to treat or prevent infections in more than half of patients in acute care hospitals. Approximately 80% of antibiotics for human use are consumed in the community and at least half of them are prescribed inaccurately generally for viral infection. Antibiotics are often and clumsily prescribed by hospital physicians. The misuse of antibiotics in patient-related factors, prescriber prescriptions, monotherapy, hospitals, veterinary prescriptions, commercial promotion, over-the-counter antibiotic sales, inadequate microbiological testing and globalization are all factors that contribute to the emergence of antibacterial resistance. Antibiotics are abolished when they are used for long-term, at a low dose or with insufficient potency. The intricate genesis of antibiotic resistance is now being influenced by a number of variables. Inadequate restrictions and usage imprecisions, a lack of awareness of recommended practices that leads to inappropriate antibiotic use, the use of antibiotics as a growth booster rather than to manage infection in poultry and animals and online marketing that made low-grade antibiotics widely available. Overuse of antibiotics is the primary driver of resistance evolution as Alexander Fleming predicted when he said that “the public will desire [the drug] and then will begin a period... of excesses. “Antibiotics kill susceptible germs, but they leave resistant pathogens alone which proliferate and prosper as a result of natural selection. Despite the fact that overuse of antibiotics is severely prohibited there is still an over-prescription problem.^{1,10-11}

Impact of resistance on Public Health

Antibiotic resistance has been named as one of the top ten worldwide public health problems facing humanity by the World Health Organization (WHO). Antibiotic resistance has a number of implications, including the inability to

Steps Involved in causes of antibiotics resistance	
Factors	Example
1. Poor drug quality	Sub-inhibitory quantities of these low-quality antibiotics can occur <i>in vivo</i> , boosting the selection of resistance micro-organisms.
2. Prescribers	Prescription practice varies by health-care practitioner. Sometimes the wrong medicine, the inappropriate dose or an antibiotic that isn't needed are prescribed.
3. Dispensers	Medications are usually purchased in small aliquots from a roadside stand, and quacks are often in charge of storage and delivery.

treat infections effectively, resulting in more severe or prolonged sickness, death, productivity losses, and negative consequences for livelihoods and food security in worldwide populations. Antibiotic resistance has secondary effects that go beyond health concerns and lost productivity such as treatment and healthcare expenses as well as draining national and global economies (conference). The effects of Antibiotics resistance on health and economic are expected to be 10 million annual human deaths and a 2 to 3.5 percent reduction in worldwide Gross Domestic Product (GDP) or \$100 trillion USD by 2050. Although the actual impacts of antibiotics resistance are still remains unclear, low-income nations will be hit harder by these declines due to increased disease incidence with a predicted increase of 6.2 to 18.7 million in the next decade.¹² Individually the cost for the treatment of patient increasing as a result of the increased expensive second-line therapies, longer hospital stays, and more intensive care and diagnostic tests, high rates of complications and the costs of infection control measures.

Resistance frequently causes delays in the administration of effective therapy with the most significant factor in delaying effective therapy being a mismatch between empirical therapy and future antibiotic susceptibility test findings.¹²⁻¹⁴ According to recent research studies, the death rate from bacterial antibiotic resistance around worldwide in 2019 reached 1.2 million. In terms of deaths that could have been avoided, 1.27 million individuals could have been saved if drug-resistant to the infections had been replaced with infectious diseases that were susceptible to present antibiotics. Moreover, if drug-resistant illnesses were replaced by no infections, 4.95 million fewer people would have suffered, according to the researchers. Indeed, the research studies shows that Antibiotic resistance is now a leading cause of death of a patients across worldwide.

Role of Clinical Pharmacist to minimize antibiotic resistance

Pharmacists are the healthcare professionals and they play an important role in the usage of medications provides guidance on how to use the medications safely by having direct interaction with the patients in the hospitals as a healthcare Professionals they are well positioned to promote understanding of antibiotics and inform their prudent use. Patient education is an vital part of the fight against antibiotics resistance and pharmacists helps the patients to understand the safe and appropriate use of antibiotic medication, pharmacists helps in counseling of a patient on usage of antibiotic including drug selection, dosage and duration.¹⁵ By conducting the various program related to the usage of medicines among patient’s reduce the burdens of antibiotic resistance, how to use antibiotics in an appropriate manner,¹⁶ The pharmacist are involved in control and prevent from infectious diseases increases important as antibiotic and vaccine regimens get more sophisticated as the epidemiology of infections evolves. Due to the decline in drug research, it is more important to preserve currently available antibiotics, emphasising the importance of pharmacists in optimising the value of available medications.

While certain pharmacist roles in combating antibiotic resistance may require more practical training and knowledge about the infectious illnesses.¹⁷

1. **Education and Public Awareness:** Increase public awareness and understanding as well as professional education and training.
2. **Monitoring and Surveillance:** Antibiotics Resistance and Antibiotics use should be Monitored Continuously and the Signs of Change and Spread of Antimicrobial Resistance should be accurately recognized.
3. **Infection Control and Prevention:** Implement Appropriate Infection Prevention and Control to Prevent the Spread of Antimicrobial-Resistant Organisms.
4. **Rational use of antibiotics:** Encourage appropriate antibiotics use in healthcare e.g, out patient department and in Patient department in Hospitals.
5. **Research and Development:** To secure the means to prevent, diagnose and treat antibiotic resistant infections promote research on antibiotics resistance and development.¹⁷⁻¹⁸
6. **By Conducting awareness program:** Creating scientific proof local antibiotic prescribing recommendations.
7. **Ensuring good Prescribing Practice:** Providing teaching and training programmes in antibiotic therapy for doctors, nurses, pharmacists, and medical and pharmacy students; monitoring antibiotic use in terms of volume or 'defined daily dosage' and expenditure^{1,17-18} So that the pharmacist's play a vital role to promote proper antibacterial medicine usage and to participate in patient treatment.
Furthermore, because good antibacterial drug use and effective PK-PD parameter utilization reduce the emergence of resistant bacteria.¹⁹

Control and Prevention

Several societies have released guidelines for optimising the antibiotic use and reducing antibiotic resistance in hospitals. So Antibiotics resistance is spreading that cause both community-acquired and nosocomial illnesses, raising awareness of the need for efficient preventative and control methods.

The following are some of the most important aspects of these guidelines.^{1,21}

1. On a multidisciplinary basis, the hospital administration, clinicians, infection control team, microbiology, and hospital pharmacy collaborate.^{1,16}
2. Antibiotics should only be taken if a doctor advises it.
3. According to accepted criteria, antibiotics should only be administered and supplied when absolutely essential.
4. Report antibiotic-resistant infections to surveillance teams.²⁰
5. Controlling antibiotic usage, developing practice guidelines and other institutional restrictions, and responding to data from the monitoring system are all priorities.
6. Set up a mechanism to keep track of bacterial resistance and antibiotic usage.

7. Adopt the Centers for Disease Control and Prevention's (CDC) recommendations
Guidelines for hospital isolation precautions in the case of patients colonized or infected with resistant bacteria.
8. Antimicrobial stewardship, which includes antibiotic use control and optimal treatment selection, dose, and duration, will prevent or slow the emergence of resistance among micro-organisms.²²
9. Despite the fact that the occurrence of resistance genes appears to be stable even in the absence of antibiotic exposure, a few studies suggest that reducing antibiotic use to reverse bacterial resistance in human populations is possible, both in the community and in hospitals.
10. Local anti-infective therapy and prophylactic recommendations based on the formulary, teaching and management of prescriptions by consultant specialists, monitoring and auditing drug use, and observation and reporting of hospital bacteria resistance patterns.^{1,23}

Consequences

Microbes that are resistant to antibiotics have serious effects. Resistant microbe infections fail to react to therapy, resulting in extended illness and a higher risk of death, longer hospital stays and infections all of which increase the number of infected people moving around in the community. When a first-line antibiotic fails to treat an illness, second- and third-line antibiotics must be used, which are always more expensive and sometimes more harmful.¹

Strategies for promoting judicious use of antibiotics

Increased demand for antibiotics is caused by patients' lack of knowledge and previous experience.

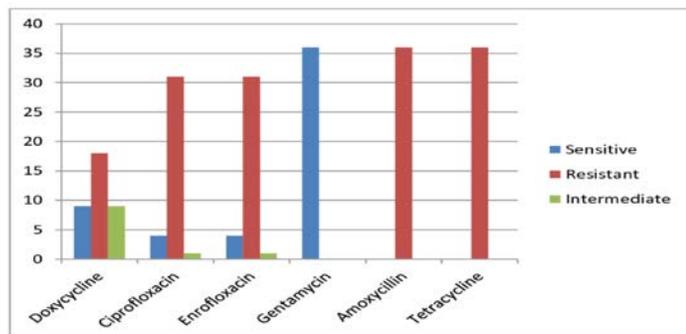
Antibiotics were given to a large number of individuals with viral respiratory illness, and these treatments were thought to be beneficial because the infections were self-limiting. Antibiotic use and upper respiratory infections appear to be the most misunderstood by patients with lower educational levels so, antibiotic prescribing must be done with greater prudence via

1. **By educating Patients and the Public:** Lack of education, prior experience, patient expectations, and economics are all these factors are required to know the patients
2. **Clinical Practice Guidelines:** To promote and develop the good clinical practice guidelines with the help of local governments.
3. **Direct mailing of lectures and information:** This would facilitate the flow of vital information as well as differing viewpoints from opinion leaders and professional groups.

Materials Available

1. Antibiotic stewardship principles for paediatric illnesses.
2. One-page summary of the fundamentals of antibiotic use are provided on academic sheets.
3. Banners for educating Patients

- For viral respiratory diagnosis, there are question and answer papers.
- A “prescription pad” with symptomatic treatment advice for people with viral respiratory infections.
- A letter to childcare providers stating that the youngster is no longer in need of antibiotics and can return to day care.²⁴



Percentage of resistance to different antibiotic with different classes via graph

As the graph shows Tetracycline is consider most resistant antibiotic in the above graph so its very important to avoid irrational use of this antibiotic.

CONCLUSION

The proliferation and development of resistance to most common bacteria to most inexpensive generic antibiotics has made the issue of antibiotic overuse a global concern. Antibiotic resistance is now widely recognized as a serious problem, and a strategy to tackle resistance should be created, if antibiotics in not effective so the infections will not be appropriately treated, hence it effects the goal of therapy of the patients. Improving the quality of medication, not simply the quantity, would necessitate public and professional education on the proper use of antibiotics. In public health, antibiotic resistance causes antibacterial drugs to lose their efficacy to the point where they are no longer used therapeutically, worse infection outcomes, treatment and prophylactic failures, and secondary cost impacts on both health services and treatment methods. Antibiotics used inappropriately or indiscriminately may cause bacteria to develop resistance in community-acquired and nosocomial illnesses, Micro-organisms can propagate antibiotic resistance in a variety of ways. The high prices and time it takes to introduce new antibiotics against resistant germs, as well as the high expenses and requirements As a result, rather than discovering new antibiotics, the most key parameters are the rational use of antibiotics (the proper indications, dosage, method, and time), In hospitals, strong infection control measures are implemented, as well as antibiotic resistance training and community-based antibiotic use. Health care Professionals e.g. Clinical Pharmacist, Nurses, Physicians should Conduct an Antimicrobials stewardship Program and give a Continue Medical Education to other health care professionals to implement a rational use of antibiotics. Another Initiation Should also take by Ministry of Health and Welfare is there is no dispensing and compounding of antibiotics without the Prescription of Registered Medical Practitioners. This initiation also helps to avoid resistance of antibiotics.

REFERENCES

- Bisht R, Katiyar A, Singh R, Mittal P. Antibiotic resistance –A global issue of concern. *Asian J Pharm Clin Res.* 2009;2(2):24-39.
- Ventola CL. The antibiotic resistance crisis: Part 1: Causes and threats. *PT.* 2015 Apr;40(4):277-83. PMID 25859123.
- Frieri M, Kumar K, Boutin A. Antibiotic resistance. *J Infect Public Health.* 2017;10(4):369-78. doi: 10.1016/j.jiph.2016.08.007, PMID 27616769.
- Laxminarayan R, Chaudhury RR. Antibiotic resistance in India: Drivers and opportunities for action. *PLOS Med.* 2016 Mar 2;13(3):e1001974. doi: 10.1371/journal.pmed.1001974, PMID 26934098.
- W.H.O. *Antimicrob Resist.* 2021.
- Cesur S, Demiröz AP. Antibiotics and the mechanisms of resistance to antibiotics. *MJIWAS.* 2013;21(4):138-42. doi: 10.12816/0002645.
- Microbiology Society. Antimicrobial resistance [online]; n.d. [cited Mar 2 2022]. Available from: <https://microbiologysociety.org/our-work/antimicrobial-resistance.html>.
- Davies J, Davies D. Origins and evolution of antibiotic resistance. *Microbiol Mol Biol Rev.* 2010 Sep;74(3):417-33. doi: 10.1128/MMBR.00016-10, PMID 20805405.
- Kourkouta L. 2018. History of antibiotics. xxxx-xxxx.
- Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH, et al. Antibiotic resistance: A rundown of a global crisis. *Infect Drug Resist.* 2018 Oct 10;11:1645-58. doi: 10.2147/IDR.S173867, PMID 30349322.
- Ayukekpong JA, Ntemgwa M, Atabe AN. The threat of antimicrobial resistance in developing countries: Causes and control strategies. *Antimicrob Resist Infect Control.* 2017 May 15;6:47. doi: 10.1186/s13756-017-0208-x, PMID 28515903.
- Regea G. Pharmacology and clinical research review on antibiotics resistance and its economic impacts. 10.19080. *JPCR.* 2018.05.555675. 2018.
- Tula MY, Iyoha O, Iruolaje F. Antibiotic resistance: Challenges and prospect for therapy in developing countries. *Br J Pharm Res.* 2015;8(3):1-16. doi: 10.9734/BJPR/2015/19061.
- Friedman ND, Temkin E, Carmeli Y. The negative impact of antibiotic resistance. *Clin Microbiol Infect.* 2016 May;22(5):416-22. doi: 10.1016/j.cmi.2015.12.002, PMID 26706614.
- Sakeena MHF, Bennett AA, McLachlan AJ. Enhancing pharmacists' role in developing countries to overcome the challenge of antimicrobial resistance: A narrative review. *Antimicrob Resist Infect Control.* 2018 May 2;7:63. doi: 10.1186/s13756-018-0351-z, PMID 29744044.
- Kotwani A, Wattal C, Joshi PC, Holloway K. Irrational use of antibiotics and role of the pharmacist: an insight from a qualitative study in New Delhi, India. *J Clin Pharm Ther.* 2012 Jun;37(3):308-12. doi: 10.1111/j.1365-2710.2011.01293.x. PMID 21883328.
- Mansour O, Al-Kayali R. Community Pharmacists' Role in Controlling Bacterial Antibiotic Resistance in Aleppo, Syria. *Iran J Pharm Res.* 2017 Fall;16(4):1612-20. PMID 29552070.
- Muraki Y. [The role of pharmacists in antimicrobial stewardship]. *Yakugaku Zasshi.* 2019;139(4):557-64. Japanese. doi: 10.1248/yakushi.18-00181-3, PMID 30930388.
- Kohno E. [The role of the pharmacist in the proper use of antibacterial drugs]. *Rinsho Byori.* 2013;61(2):118-26. PMID 23672089.
- WHO guidelines of Control and Prevention of antibiotic Resistance.
- Yalew ST. Review on antibiotic resistance: Resistance mechanisms, methods of detection and its controlling strategies. *Biomed J Sci Tech Res.* 2020;24(5). doi: 10.26717/BJSTR.2020.24.004121.
- Shlaes DM, Gerding DN, John JF Jr, Craig WA, Bornstein DL, Duncan RA, et al. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: Guidelines for the prevention of antimicrobial resistance in hospitals. *Clin Infect Dis.* 1997 Sep;25(3):584-99. doi: 10.1086/513766, PMID 9314444.
- Gould IM. A review of the role of antibiotic policies in the control of antibiotic resistance. *J Antimicrob Chemother.* 1999 Apr;43(4):459-65. doi: 10.1093/jac/43.4.459, PMID 10350373.
- Belongia EA, Schwartz B. Strategies for promoting judicious use of antibiotics by doctors and patients. *BMJ.* 1998 Sep 5;317(7159):668-71. doi: 10.1136/bmj.317.7159.668, PMID 9728003.
- McNamara D. Antimicrobial resistance linked to 1.2 million global deaths [online]; 2022. *Medscape* [cited Mar 2 2022]. Available from: <https://www.medscape.com/viewarticle/966910>.
- WHO. Antibiotic resistance [online]; 2020 [cited Mar 2 2022]. Available from: <https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance>.