Antibiotics Resistance: A Global Health Challenge

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Abstract: Infectious diseases have been the leading cause of morbidity and mortality worldwide, particularly in low-income countries, especially in children. The development of antibiotics led to the improvement of life expectancy by about 8 years as they could be used to treat infections that were previously life-threatening. They have also made possible complex surgeries that could otherwise kill the patients. However, a number of pathogens have developed resistance to antibiotics, rendering the drugs ineffective in treatment of infections. The level of antibiotics resistance is rising dangerously, threatening the ability to treat even common infections. Worst still, antibiotics resistance is not limited to a given locality. Resistance to antibiotics can develop in one area and spread worldwide due to interconnected trades and travels. Thus, antibiotics resistance is a global health crisis and a silent tsunami that unless urgent steps are taken, many infectious diseases that could easily be treated will become difficult to manage, leading to increase in mortality and morbidity. This paper discusses antibiotics, their mode of action, development of resistance and its effect on global health and the means of preventing/controlling resistance.

Key word: Antibiotics, global health, resistance, infections, antibiotics misuse

INTRODUCTION

One of the major global health threats has been infectious diseases, usually associated with poor hygiene and poor sanitation. Infectious diseases remain among the leading causes of morbidity and mortality on our planet. The concept of resistance in microbes—bacteria, viruses, or parasites—to therapeutics, while not surprising nor new, poses a great challenge due to its burden. About 700,000 deaths per year are attributed to antimicrobial resistance worldwide and "if not properly addressed, the number could grow to 10 million per year by 2050 (Abebe, 2020). However, the scope and scale of this phenomenon is an ever-increasing multinational public health crisis as drug resistance accumulates and accelerates over space and time (US Institute of Medicine, 2010). There have been threats of new diseases emerging due to the evolution/adaptation of microbes and the re-emergence of old diseases due to the development of antimicrobial resistance. This has been recognized as one of the transnational challenges that do not emanate from the policies of individual states (Brower and Chalk, 2003). Razzaque (2020) asserts that resistance to antimicrobials is a global health problem causing high morbidity and mortality as well as enormous economic burden worldwide.

Antimicrobials are medicines used to prevent or treat infections in humans, animals and plants (WHO, 2021). They are chemical substances of natural or synthetic origin with ability to suppress the growth of microbes or destroy them (Vintola, 2015). They are usually derived naturally from bacterial or fungal sources or synthesized. The term antibiotics is used for drugs used against bacteria while antifungals are used against fungi. Antivirals are used against viruses and antiparasiticals are used against protozoa and helthminths (Werth, 2020).

This paper takes a look at antibiotics and their uses, development of resistance, and the implications of resistance in global health, and the way forward.

Antibiotics: Antibiotics, in the strictest sense, are substances (medicines) produced by microorganisms that are capable of killing or inhibiting the growth of other microorganisms at low concentrations (Ojide, 2019). Only substances that target bacteria are called antibiotics, while the name antimicrobial is an umbrella term for anything that inhibits or kills microbial cells including antibiotics, antifungals, antivirals

and chemicals such as antiseptics. They are drugs used to treat bacterial infections (Shiel, 2004).According to Lalitha (2004), antibiotics are powerful medicines that fight certain infections and can save lives when used properly. Antibiotics either stop bacteria from reproducing or destroy them.

According to Ojide (2020), antibiotics can be classified on the basis of their origin, range of activity, biological activity or mechanism/site of action. On the basis of **origin**, antibiotics may be: (i) natural (obtained strictly from natural sources); (ii) semisynthetic (derived partly from natural sources and partly synthesized); (iii) synthetic (derived completely from synthetic sources). On the basis of **biologic activity**, they may be (i) bacteriostatic (inhibit the growth/multiplication of bacteria); (ii) bactericidal (they kill the bacteria out-rightly). On the basis of **range of activity**, antibiotics may be (i) narrow spectrum (act against a small number of bacterial species); (ii) broad spectrum (act against a large number of bacterial species). On the basis of **mechanism/ site of action**, antibiotics can be classified as (i) cell wall inhibitors (they interfere with the bacteria's ability to synthesize its cell wall, leading to its death); (ii) protein inhibitors (interfere with the bacteria's ability to synthesize its proteins); (iii) nucleic acid inhibitors; (iv) folate synthesis inhibitors and (v) cell membrane inhibitors/destruction) (Ojide, 2020).

The introduction of antibiotics into medicine revolutionized the way infectious diseases were treated. Between 1945 and 1972, average human life expectancy jumped by eight years, with antibiotics used to treat infections that were previously likely to kill patients. Today, antibiotics are one of the most common classes of drugs used in medicine and make possible many of the complex surgeries that have become routine around the world (The Microbiology Society, 2019)

Resistance: Resistance is a means whereby a naturally susceptible microorganism acquires ways of not being affected by the drug. Antimicrobial Resistance (AMR) occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines, making infections harder to treat and increasing the risk of disease spread, severe illness and death (WHO, 2021). According to Scott (2019), resistance can be defined from two perspectives: the clinical and the microbiological points of view. From the clinical point of view, resistance is seen as a state in which a patient infected with a specific pathogen, is treated with an adequate antimicrobial dosage and administration schedule, but the clinical criteria of cure (at a clinical and/or a microbiological level) are not reached. Microbiologically, resistance is a state in which an isolate has a resistance mechanism rendering it less susceptible than other members of the same species lacking any resistance mechanism. Microbes, such as bacteria, can develop resistance to antimicrobials meaning that a drug such as an antibiotic is no longer effective in treating the infection. The development of resistance is caused by the incorrect use of these drugs, for example, using antibiotics (which help to treat bacteria) for viral infections like flu, or as a growth promoter in agriculture (WHO, 2020).

Alexander Fleming who discovered penicillin, observed as early as in 1943 that some bacteria were resistant to the drug and warned that indiscriminate use of penicillin would lead to the proliferation of resistant pathogenic bacteria. By 1946, medical staff at a London hospital estimated that 14 percent of the staphylococcal strains isolated from their patients were resistant to penicillin (US National Institutes of Health, 2007).

Microbial resistance to antimicrobial agents is not a new phenomenon; it has been going on in soil microorganisms since the dawn of time, as competitive/survival mechanisms by microorganisms against other microorganisms. In humans, microbes acquire resistance as a consequence of their adaptation to exposure to antimicrobials used in humans, or agriculture, and the

widespread use of disinfectants at the farms and the households. It is now accepted that antimicrobial use is the single most important factor responsible for increased antimicrobial resistance. Antibiotic resistance is accelerated by the misuse and overuse of antibiotics, as well as poor infection prevention and control (WHO, 2018). Mutations leading to drug-resistant and multi-drug-resistant strains of *Mycobacterium tuberculosis*, Enterobacteria, pneumococci, malaria parasites, and other agents occur continuously. Drug resistance is becoming a major obstacle to the control of these infections in many parts of the world, including the Americas (PAHO, 1996).

Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhea, and food-borne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective (WHO, 2018).

Causes of resistance: Several studies have demonstrated that patterns of antibiotic usage greatly affect the number of resistant organisms which develop (Science Daily, 2019). Ventola (2015) underscores the following as the causes of antibiotics resistance in pathogens: overuse of antibiotics: Epidemiological studies have demonstrated a direct relationship between antibiotics consumption and the emergence and dissemination of resistant bacteria strains; inappropriate prescribing**:** Incorrectly prescribed antibiotics also contribute to the promotion of resistant bacteria; poor patient adherence to antimicrobial regimens increases selective pressure. Lack of ability to pay and shortages of antimicrobials "promote under-dosing, the substitution of available but unsuitable drugs, procurement from inappropriate sources, and drug counterfeiting. Therefore, to avoid compromising therapy and promoting resistance, antimicrobials may need to be made more (rather than less) available in certain instances, provided their availability is intelligently controlled and effective therapeutic doses are adhered to"; Extensive agricultural use**:** In both the developed and developing world, antibiotics are widely used as growth supplements in livestock. The transfer of resistant bacteria to humans by farm animals was first noted more than 35 years ago, when high rates of antibiotic resistance were found in the intestinal flora of both farm animals and farmers. More recently, molecular detection methods have demonstrated that resistant bacteria in farm animals reach consumers through meat products. This occurs through the following sequence of events: 1) antibiotic use in food-producing animals kills or suppresses susceptible bacteria, allowing antibiotic-resistant bacteria to thrive; 2) resistant bacteria are transmitted to humans through the food supply; 3) these bacteria can cause infections in humans that may lead to adverse health consequences.

According to WHO (2021), antibiotic resistant organisms can spread from person to person or between people and animals, including from food of animal origin. The main drivers of antimicrobial resistance include: The misuse/overuse/underuse of antimicrobials; Lack of access to clean water, sanitation and hygiene (WASH) for both humans and animals; Poor infection and disease prevention and control in health-care facilities and farms; Poor access to quality, affordable medicines, vaccines and diagnostics; Lack of awareness and knowledge; and Lack of enforcement of legislation (WHO, 2021).

Global Health Challenges of Antibiotics Resistance: According to Sriskantharawjah (2022), antimicrobial resistance is a global crisis, but it is not given much 'air time' by world leaders, the media, and the public in general. The World Health Organization (WHO) has declared antibiotics resistance as one of the top 10 global public health threats confronting humanity. However, because the

impact is slow and often in conflict with economic interests, it is unrecognized and does not receive the attention it needs from public health leaders (Egwuenu, 2022).Due to antibiotics resistance, the world is running out of effective antibiotics to treat infectious diseases, and unless appropriate action is taken, decades of progress in health and medicine risk being undone (WHO, 2020).

Antibiotics are becoming increasingly ineffective as drug-resistance spreads globally, leading to difficult-to-treat infections and death (WHO, 2021). Today, diminishing antimicrobial effectiveness represents a formidable threat to human and animal health and therefore to overall global development. Deaths from drug-resistant infections are projected to increase from currently 700,000 to 10 million annually and cost estimates are as high as US$100 trillion worldwide by 2050 (Jasovsky *et al.*, 2016). The Ventola (2015) reports a study carried out to estimate the burden of antibiotics resistance. From the findings, an estimated 4.95 million deaths were associated with antimicrobial resistance in 2019, with the highest rate occurring in western sub-Saharan Africa. The leading pathogens associated with the deaths were *E. coli, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinebacter baummanii* and *Pseudomonas aeruginosa.* Of these, methicillin-resistant *Staphylococcus aureus* caused more than 100,000 deaths. Another study estimated that 200,000 babies die each year as a result of drug resistance (Jorgensen, 2016).

According to Health News (2022), the further antibiotic resistance spreads, the more often common antibiotics—including many available as generics—must be retired, meaning that ridding patients of infection will require longer time and more expensive forms of therapy. Kraker and Lipsitch (2021) aver that other effects of antibiotics resistance include: more-serious illness; longer recovery; more-frequent or longer hospital stays; more health care provider visits and more-expensive treatments.

Of special concern is the rapid global spread of multi-resistant bacteria, for some of which there is no available treatment. The prospect of the world entering a 'post-antibiotic era', where common infections can no longer be cured, is therefore a real possibility (Jasovsky *et al.,* 2016). CDC (2018) also reports WHO's assertion that the pandemic of antibiotics resistance is becoming a global health crisis and a silent tsunami that roars over the whole world without noise and pulling down pillars upon which modern medicine is built. This situation requires immediate action which is a responsibility of all.

There are trillions of beneficial bacteria that are essential for our bodies and Earth's living resources. Unfortunately, overuse is increasingly depleting this global common resource and replacing it with increasingly hard-to-treat resistant microbes. With global transport and increasing rates of international spread, antimicrobial resistance is increasingly becoming a global problem in need of coordinated systemic action.

Antibiotics resistance easily spreads across borders around the globe due to modern travels of people, animals and goods. According to CDC (2018) antibiotics resistant bacteria know no territorial borders. Thus, resistance developed in one space can rapidly spread worldwide due to interconnected world trades and travels.

There have been threats of new diseases emerging due to the evolution/adaptation of microbes and the re-emergence of old diseases due to the development of antimicrobial resistance (Shrivastava *et al.,* 2013).

In September 2015, the General Assembly of the United Nations adopted the 2030 Agenda for Sustainable Development that includes 17 Sustainable Development Goals (SDGs). The number three of these goals advocates for "good health and wellbeing" (UN, 2021). The concept of antibiotics resistance poses a serious threat to this number three SDG of the United Nations and by implication, the rest of the 17 goals. A critical look also reveals that SDG number

6 which is on "clean water and sanitation", if properly pursued can go a long way to reduce the menace of antibiotics resistance.

The way forward: The World Health Organization (2021) asserts that unless serious and urgent steps are taken, even new antibiotics that may be developed later will still become ineffective, leading to a serious health crisis. According to WHO (2021), the problem of antibiotics resistance is complex and requires a multisectoral approach to resolve, including individuals, policy makers, as well as those involved in human, animal and plant health. It also involves government and non-governmental agencies involved in design and implementation of programs, policies, legislation and research for public health outcomes.

Jorgensen (2016) avers that the approach of developing new antibiotics to replace the resistant ones tends to downplay important solutions such as hygiene, sanitation, vaccines, or even cultural changes. Jasovsky *et al*. (2016) avers that WHO in 2015 adopted a 5-objectives global action plan on antimicrobial resistance. These included: to improve awareness and understanding of antimicrobial resistance; to strengthen the knowledge and evidence base through surveillance and research; to reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures; to optimize the use of antimicrobials in humans and animal health; to increase investment in new medicines, diagnostic tools, vaccines and other interventions.

In order to accomplish this, WHO (2020) outlined actions by individuals, policy makers, health professionals, healthcare industries as well as the agricultural sector.

To individuals, WHO (2020) advocated as follows: only use antibiotics when prescribed by a certified health professional; never demand antibiotics if your health worker says you don't need them; always follow your health worker's advice when using antibiotics; never share or use leftover antibiotics; prevent infections by regularly washing hands, preparing food hygienically, avoiding close contact with sick people, practicing safer sex, and keeping vaccinations up to date; Prepare food hygienically, following the WHO Five Keys to Safer Food (keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials) and choose foods that have been produced without the use of antibiotics for growth promotion or disease prevention in healthy animals.

To policy makers, WHO (2020) that: ensure a robust national action plan to tackle antibiotic resistance is in place; improve surveillance of antibiotic-resistant infections; strengthen policies, programmes, and implementation of infection prevention and control measures; regulate and promote the appropriate use and disposal of quality medicines; make information available on the impact of antibiotic resistance.

The health professionals should: prevent infections by ensuring your hands, instruments, and environment are clean; only prescribe and dispense antibiotics when they are needed, according to current guidelines; report antibiotic-resistant infections to surveillance teams; talk to your patients about how to take antibiotics correctly, antibiotic resistance and the dangers of misuse; talk to your patients about preventing infections (for example, vaccination, hand washing, safer sex, and covering nose and mouth when sneezing).

The Healthcare industry should invest in research and development of new antibiotics, vaccines, diagnostics and other tools.

To the Agriculture sector, WHO (2020) directed that: only give antibiotics to animals under veterinary supervision; not use antibiotics for growth promotion or to prevent diseases in healthy animals; vaccinate animals to reduce the need for antibiotics and use alternatives to antibiotics when available; promote and apply good practices at all steps of production and processing of foods from animal and plant sources; improve biosecurity on farms and

prevent infections through improved hygiene and animal welfare.

CONCLUSION AND RECOMMENDATIONS

One of the major global health threats has been infectious diseases, which the advent of antibiotics had brought hope that they could be eliminated. However, more and more infectious agents are developing resistance to antibiotics, making it difficult to treat such infections. The difficulty in treating such infections therefore entails longer days of stay in hospitals, increased cost of treatments, increase cost in development of new antibiotics, increased rate of morbidity and mortality.

The development of resistance in pathogens is usually due to misuse (overuse, undersuse, wrong prescription) as well as use in agriculture. Worst still is the fact that these resistant infectious agents can spread quickly across territorial borders due to international trades and travels. A phenomenon WHO describes as a silent tsunami that is likely going to consume the globe.

In order to put antibiotics resistance under check, it is recommended that the WHO 5-objectives global action be pursued earnestly with passion by mass awareness on the public and healthcare givers on how resistance can be prevented. Government should enact laws to govern the administration of antibiotics. Administrators of healthcare institutions should ensure that health personnel adhere to WHO guidelines for antibiotics use. Tests should also be carried out on travelers (international) to ensure they are not carrying any of the common resistant strains of infectious agents.

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