Antimicrobial Resistance: A Global Threat to Health and Economic Stability

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Antimicrobial resistance is a naturally occurring, continuously evolving, phenomenon where pathogens develop resistance to medicines. Due to a lack of cohesive papers covering all aspects of the issue, this review timely focuses on the history, administrative involvement, impacts, causes, and cohesive solutions to the rising problem. It provides a collective account of the lack of diagnostic tools and surveillance systems, lack of country participation in WHO surveys regarding Antimicrobial Resistance (AMR), as well as a lack of awareness, and misuse as well as overuse of antibiotics, which extrapolate the issue of AMR. The objective of this paper is to cover all the aspects of antimicrobial resistance properties, especially focusing on the history of AMR over the years and the steps taken to mitigate the issue, at private and administrative levels. The secondary aspect is to focus on the propagation methods of AMR and how they play a significant role in understanding the increasing spread of resistance within pathogens. Then the paper focuses on providing a report of the costs of the problem in the form of health and patient care, economic impact, and mortality rates, followed by the reasons increasing the pace of resistance spread, inclusive of medicine abuse, poor sanitation and healthcare, and the agricultural use of antibiotics. Ultimately, education, improved diagnostic and surveillance systems, vaccinations, and steps taken at the national and global levels are the best and only methods of stemming the flow of AMR.

Introduction

Antimicrobial Resistance is a natural phenomenon which occurs when pathogens (specifically bacteria) develop resistance to drugs (medicines) used to cure them. It began shortly after antibiotics were introduced in the medical industry and progressed rapidly due to various causes including but not limited to poor healthcare services, unavailability of quality medicines, and abuse of medicines[1]. The rapid increase of AMR threatens the successful treatment of numerous diseases and medicinal processes such as chemotherapy, organ transplant, etc, while also increasing the vulnerability of patients[2].

The problem being addressed is the distinct lack of a compiled report providing a holistic outlook on the imminent problem of AMR. In this paper, we bridge the gap by giving a complete picture of the global issue of AMR, inclusive of its many causes of medicine abuse, poor sanitation, and excessive agricultural use of antibiotics, the numerous harmful effects inclusive of health and patient care, economic costs, and mortality rates. In continuance the paper also provides holistic evidence from surveys regarding the extent to which steps to mitigate and reduce AMR are being implemented and new solutions to improve upon the current situation. The major reason for the existence of the paper is the rising emergence of AMR as well as superbugs in the medicinal sectors around the world, while combating the lack of a literature review which provides detailed information regarding AMR, from its history to the current response to the issue.

Results

We went through a total of 27 reports, inclusive of WHO surveys conducted in the seven regions, peer-reviewed journals, individual reports focusing on area-specific propagation of AMR, and literature reviews focusing on the causes and effects of AMR. Papers covering the history of the issue along with a timeline of progress at international and national levels were coveted as reading material to provide a complete picture of the ever-evolving problem. Socio-economic, health and patient care, abuse of medicines, the effect of sanitation, and the methods of reducing the propagation of AMR were focused on and evaluated in much detail.

Discussion

The History

The first noted presence of AMR occurred during World War II with the emergence of sulpha drug resistance. Subsequently, *Staphylococcus aureus* was found to be resistant by British scientist Mary Barber during the late 1940s[3]. As a response to recurring resistance issues, the World Health Organisation held

a meeting of experts, in 1959, to discuss the issue of antibiotics and resistance; however, the discussion ended with a dispute over the laboratory definition of "resistance" and deliberation concerning the international role regarding AMR surveillance was not successful. There also existed a belief that pharmaceutical companies would always have the ability to make new medicines effective on resistant pathogens which led to the importance of the issue being sidelined[3].

After further investigation into the causes for resistance, E. S. Anderson and other fellow scientists at the Enteric Reference Laboratory in Colindale, England, in the 1950s reported that the spread of resistant superbugs was possible from animals to humans[3]. Their findings were published in the book *"Penicillin: Triumph and Tragedy"* by Robert Bud[4]. A further breakthrough into the cause for the rapid increase in resistance pathogens occurred in the 1960s when Japan introduced the idea that resistance could be transferred within pathogens of different species and strains, using plasmids. (Plasmids hold the genetic information of the bacteria. It was observed that often the mutated - resistant - section of plasmids transferred to other bacteria.) Subsequent alarming discoveries resulted in the WHO convening meetings and groups focused solely on antimicrobial resistance. However, the breakthrough occurred in 1981, when Stuart Levy, clinician-scientist at Tufts University, held a conference based on the *"Molecular Biology, Pathogenicity, and Ecology of Bacterial Plasmids."* The meeting ended with 147 scientists from 27 countries signing a joint *"Statement Regarding Worldwide Antibiotic Misuse."* This became the first global meeting to meet on and end with a collective goal[3].

The 1990s saw considerable progress regarding increasing awareness about AMR. Nobel Prize Winner Joshua Lederberg spoke on *"Medical Science, Infectious Disease, and the Unity of Humankind"* focused on the link between the pragmatic and moral necessity of confronting superbugs as a global concern. Following, *Emerging Infections: Microbial Threats to Health in the United States*, a book, discussed the importance of giving adequate attention to the problem of resistance. In the USA, the Infectious Diseases Society of America (IDSA) drew attention to the inability of the pharmaceutical industry in complying with expectations of new drugs to combat superbugs. The Pew Charitable Trust also lobbied for legislation to incentivise marketing companies to reengage with antimicrobial resistance. Eventually, AMR was framed as a shared global health concern requiring collaborative interventions in numerous sectors[3].

Administrative Role in Accepting AMR As a Global Concern

Ultimately, though, till the early 2010s, AMR was still not considered a problem of the present, but rather of the future. This idea was reinforced when Dame Sally Davies, the Chief Medical Officer of Great Britain released a report, *"Infections and the Rise of Antimicrobial Resistance,"*[5] which was framed around AMR being a less "present burden of disease" as compared to an upcoming emergency which might occur in the prospective future dependent on the choices of humans[3]. In 2013, the U.S. Centres for Disease Control released its own report on *"Antibiotic Resistance Threats in the United States, 2013,"*[6] and the Centre for Disease Dynamics, Economics and Policy drew attention to the link between the increase in resistance and consumption of antibiotics, displaying that there had been a 35% increase in global antibiotics consumption from 2000-2010. It also highlighted the need to improve access to antibiotics in the developing world to avoid inappropriate use[3].

Interestingly, it was noted that comprehensive data or research papers focusing on the era of 2010-15 in regard to Antimicrobial Resistance were not available despite extensive research on Google Scholar, Medline, and PubMed.

In 2015, under Director General Tedros Adhanom, the WHO also decided to increase efforts and released the *"Global Action Plan on Antimicrobial Resistance"*[3,7]. They declared that antimicrobial resistance was to be treated as a shared problem by all the member states of the organisation and would work towards individual action plans as well as coordinated mechanisms to improve education and awareness, sanitation and infection surveillance, and reduce unnecessary antibiotic usage in humans and agriculture sectors[3,7]. In 2016, economist Jim O'Neill chaired the *"Review on Antimicrobial Resistance,"*[8] on request of the British Prime Minister David Cameron, in cooperation between the UK Government and the Wellcome Trust. Being a member of the House of Lords and the person behind the term BRICS (Brazil, Russia, India, China, and South Africa), he was considered a trusted and learned person with enough resources to conduct the review in a fair, unbiased, and global manner. The review estimated that unless action was taken to stop the spread of AMR, the global economic cost by 2050 would reach 100 trillion USD. This was followed by the World Bank's report on *"Drug-Resistant Infections: A Threat to our Economic Future,"* in 2017, predicting that AMR could lead to an annual 3.8% global loss of GDP by 2050. In response to these statistics, the UN convened a meeting of the General Assembly on antimicrobial resistance, only the fourth meeting focused explicitly on the health concern[3].

It is important to note that government interest increased in the issue after AMR emerged as a threat to the national and global economies in the 2010s. Until then scientists working privately, and charitable trusts were focusing on investigating the problem and releasing reports and books based on their findings to increase awareness among the scientific society, with no involvement from the public sectors.

The Evolution of AMR Propagation: From A Single Cell to A Community Spread

Resistance occurs in bacteria either intrinsically or via mutation in gene structure. In both cases, drugs are unable to harm or destroy the bacteria, making it resistant to the medicine[9]. Drugs destroy bacteria in numerous ways, the primary being by binding onto an area of the cell wall to gain access to the inside. Interfering with the cell wall and nucleic acid synthesis is the most common method. The former prevents the bacteria from repairing or rebuilding the cell wall, allowing White Blood Cells to enter the bacteria and kill it. The latter, meanwhile, stops the reproduction of the bacteria by binding to enzymes which structure the DNA. The bacteria eventually die after completing the life cycle or due to a change in the genetic structure. Inhibition of protein synthesis to prevent sustenance of bacteria is another method medicines harm bacteria. Lastly, antibiotics hinder the bacteria by reducing the strength of the cell membrane. They do this by interfering with the metabolic pathways, eventually making it easier for White Blood Cells to attack the bacteria[9,10].

Therefore, bacteria have numerous mechanisms to become resistant. The most common implementation by colonies of bacteria is the build-up of biofilm. The thick sticky consistency of the biofilm makes it difficult for antibiotics to reach the bacteria[9]. Biofilm also reduces the rate of reproduction of bacteria, making drugs which target growing, dividing bacterial cells ineffective. Individual bacteria often alter the structure or number of penicillin-binding proteins (PBPs) which reduces the amount of drug which can bind to the cell wall. PBPs are involved in the construction of cell walls and so the change in their structure changes the construction of the cell wall. Often bacteria mutate the enzymes which are used to structure the DNA, so that drugs cannot bind to them. This makes them resistant to drugs targeting nucleic acid synthesis. Bacteria also possess efflux pumps which are used to rid the cell of toxic substances. Genetic modification of efflux pumps to identify drugs as toxic substances prevents the drug from staying in the system long enough to cause harm. Lastly, for drugs which inhibit metabolic pathways, resistance is formed by the mutation of enzymes near their active site where the drug binds. This structural change eliminates the binding site of the drug while retaining those necessary for the basic survival and function of the enzyme[9].

A resistance that occurs due to a mutation in the gene sequence is vertical evolution. It occurs during and via reproduction. The resistance that occurs due to bacteria acquiring genetic material from other resistant organisms, whether from the same or different species, is called horizontal evolution. It occurs during the life span of a bacteria, and not during reproduction[10].

Unfortunately, the number of resistant bacteria increases rapidly once one bacterial cell has acquired a mutation. This occurs because bacteria reproduce at a fast rate, and also have a high capacity of acquiring mutations via vertical or horizontal transmission. Therefore, even if there is one cell which is resistant and was not killed by the drug used as treatment, it will rapidly reproduce and there will be a colony of mutated bacterial cells which cause the same problem in the body but are not susceptible to the drug used to destroy them. This increases the number of mutated bacteria which exist[10].

Counting the Cost of Antimicrobial Resistance: From Health to the Economy

Major, and often irreparable damage, are the impacts of AMR in various sectors, including but not limited to the quality of health and patient care, the costs for mitigation and treatment of the problem, and a significant increase in mortality rates owing to the issue. These problems are becoming more difficult to tackle successfully over the years owing to a distinct lack of efforts undertaken by the pharmaceutical companies and the late response to governments in lieu of the problem[2,3].

Health and Patient Care : The cost of healthcare is substantially increased due to AMR[10]. Just in Europe, the cost of healthcare due to AMR is over Nine-Billion Euros per year. Further, AMR adds a surplus of Twenty-Billion dollars in the form of direct healthcare costs in the United States[11]. This is because the patient remains sick for a longer period and requires drugs which are not easily available and quite expensive. Further, after-surgery procedures to reduce infections, which require antibiotics, are often less effective due to AMR. Often specialised equipment is required for proper AMR treatment, which increases health care costs further[11–13].

Eventually, there is an increased death risk for patients undergoing chemotherapy, organ transplants, dialysis, joint replacement, Human Immunodeficiency Virus (HIV), etc. The number of HIV cases resistant to medicine are on the rise, particularly in Sub–Saharan Africa where 60% of patients with HIV have developed resistance to HIV medicine[11].

Economy : Aside from healthcare and patient costs, the cost of AMR alone is Fifty-five-Billion dollars in the United States, with an added Thirty-Five Billion dollars for loss of productivity. Studies on the healthcare costs for methicillin-resistant *Staphylococcus aureus* (MRSA) infections alone show that in the USA the costs are over $18,000 per case, in Germany the costs are nearly 9,000 per case, and in Switzerland there is an average added cost of over 100,000 Swiss francs per case[9].

AMR influences the number of people working in an industry, most specifically the labourers who are most susceptible to sickness and premature death owing to financial constraints. This also leads to the gap between developing and developed countries increasing because developing countries are not as well equipped to handle the effect of AMR[11]. In 2017, the World Bank's report *"Drug Resistant Infections: A Threat to our Economic Future"* also indicated that poorest countries

would be hit hardest if antimicrobial resistance continued to spread unchecked[9].

Mortality: There is an increased mortality rate owing to AMR, most specifically in developing countries like India, but also in countries with well-equipped healthcare systems like the United States. In the U.S, AMR adversely affects over 2 million people, and about 23,000 deaths occur per year. The Centre for Disease Control also reported that over 2 million people in the U.S become ill each year with antimicrobial-resistant infections[6,9].

This is similar to countries of the European Union where the mortality rate is 25,000 due to AMR. Further, there is an increasing number of HIV patients in Africa[11], and cancer patients vulnerable after chemotherapy. This adds to more of the world population likely to succumb to death as a direct or indirect effect of AMR[11–13].

Drivers of AMR Spread

The increase in AMR directly affects mortality rates, healthcare costs, and health and patient care. With the number of deaths increasing exponentially and the costs of treatment becoming too expensive for low to middle-income people to afford, the factors contributing to the increase in AMR are a significant starting point for understanding the problem in depth. The factors influencing the rise of AMR are numerous, including but not limited to misuse and overuse of medicines, lack of awareness, poor sanitation and health care facilities, and agricultural use of antibiotics.

Abuse of Medicines: Antibiotics are available over the counter without a prescription in many countries. This means that sick people self-prescribe medicines and take them without professional consultation[12,13]. Often, the medicine is not the appropriate one for the bacteria, and due to exposure, the bacteria develop a resistance against the drug, which is then passed on through horizontal transmission to other bacteria. A higher prevalence of self-medication with antibiotics was reported in South Europe (19%) in comparison with Northern Europe (3%) and Central Europe (6%). In some countries in Africa, 100% of antimicrobial use is without prescription and in Asia it reaches 58%[13,14].

Lack of awareness is also a significant factor in the abuse of medicines. Often people are not aware of the appropriate use of antibiotics and which pathogens they are effective against. Questionnaires and surveys conducted in Japan, Australia, the United States, Sri Lanka, and Gulf Cooperation Council countries showed that people have limited knowledge about the correct use of antibiotics. In Europe, a study revealed that 20% of the people admitted they had taken antibiotics to treat flu-like symptoms, although they knew that antibiotics do not act against viruses. 14% also said that they had taken antibiotics to treat a common cold. Further, a survey conducted in the United Kingdom showed that 38% of respondents did not know that antibiotics do not work against most coughs or colds[11–13].

According to a 2015 report by WHO, awareness about antimicrobial resistance was low in the African region. Only two of the reposting eight countries had conducted a public awareness campaign in the last two months, counterfeit and poor-quality medicines were a common problem in the region, and there was a high potential for misuse of antimicrobial medicines in the countries. To add to the lack of awareness, in the American Region, only 10 of 26 countries had conducted an awareness campaign in the last two years, and over-the-counter medicines were available in eighteen countries. Counterfeit medicines and inappropriate use of drugs was a common problem in this region also, despite it including some of the richest countries in the world. Additionally, self-medication was a common problem where only 11 countries reported that they could regulate prescriptions.

Continuing the trend, in the Eastern Mediterranean Region also, only 3 of 13 countries had conducted an awareness campaign and counterfeit medicines were a significant issue. Medicines were available without prescription in 9 countries, and there was a strong possibility of misuse of antibiotics indicated. The Western Pacific region also had a severe lack of public awareness as shown by only 4 of 26 countries that have conducted an awareness campaign. The public could buy antimicrobial medicines without a prescription in 52% of the countries increasing the harmful effect of unawareness.

On the contrary, awareness campaigns were common in the European region, with over 38 of 49 countries having implemented one in the past two years. Yet, about half the population believed that antibiotics are effective against viruses which was a major concern. It was also found that the quality of antimicrobial medicines provided in the region was high, but their effectiveness was hampered by medicines sold without prescriptions in over 20 countries. In the South-East Asian Region also, 5 of 11 countries conducted public awareness campaigns which was significant as it is one of the regions with the greatest number of developing countries. Unfortunately, medicines were available without prescription in more than 6 countries and healthcare workers were found to not comply with standard prescribing rules and guidelines. The monitoring of the use of antimicrobial medicines was limited in the region[15].

Further, antibiotics are often prescribed when they are not required for treatment. Unnecessary exposure leads to horizontal transmission of resistance. Moreover, physicians prescribe lengthy courses of antibiotics for financial gain or to reduce the chances of the infection recurring. Unfortunately, this overexposure to drugs eventually leads to an increase in resistance. Patients do not complete the antibiotic course, many times, stopping the intake of the drug once they feel relief from the problem[2].

At the hospital level, the inferior quality and unavailability

of medicines are other root causes for AMR. Unavailability results in other available antibiotics being used as a secondary resort which is overexposure of the drug to bacteria. In the United States, doctors and nurses prescribed over 2580 million courses of antibiotics (833 prescriptions per 1000 persons) in 2010[2,11–13,16].

Poor Sanitation and Healthcare Facilities: Poor sanitation and malnutrition increase a person's vulnerability to diseases and make the body ill-equipped to manage resistant bacteria. Further, healthcare facilities are underfunded in many developing countries, with an irregular supply of medicines which are eventually of inferior quality. Due to poorly trained and unlicensed doctors, there is often inappropriate use of antibiotics, with broad-spectrum antibiotics prescribed indiscriminately as a universal solution[2,11,12].

There is also an inherent bias within the system of purchasing antibiotics, with public hospitals buying less expensive older medicines, while private hospitals bought expensive newer ones. In developing countries with a majority of financially challenged population, public hospitals are favoured which means more people are exposed to old drugs. This is a cause for concern as most patients tend to go to public hospitals as they provide check-ups free of cost or at an extremely nominal fee. If public hospitals have an inconsistent supply of poor-quality medicines, the patients being treated are exposing pathogens to partially effective or poor-quality medicines which would not have as much impact as higher quality drugs. This exposure provides a base for Antimicrobial Resistance to build up in pathogens[11,12].

Agricultural use of Antibiotics: The use of antibiotics in livestock food results in the drug eventually entering the body of the consumer and being exposed to the bacteria in a diluted state. In fact, most of drugs sold over the counter are mixed with the food of animals. In the United States, approximately 80% of the antibiotics sold are applied to food that animals eat, with 63,200 tons of antibiotics being used in livestock production in 2013. These antibiotics include last level defence drugs, such as colistin, which is a critical drug to treat severe infections in humans but is also used in the growth of livestock. Studies have found that in Twenty-Six of the European Union countries, the sale of antibiotics for use (therapy or prophylaxis) in food-producing animals during 2012, amounted to 8000 tonnes, while in the US, it was 14, 800 tonnes. Currently, only 42 countries in the world record data of antibiotic use in livestock rearing.

This unnecessary overexposure of drugs to bacteria occurs because of human greed to rearing the best livestock to accumulate least losses and best prices[2,11,13].

Winning the War Against AMR

Educating the Population: Many countries still fail to accept AMR as a global health crisis. The African and Eastern Mediterranean regions had the least percentage of countries participating in the survey conducted by WHO, while the Southeast Asian region had 100% participation, with only one of the Western Pacific countries not participating in the survey. However, this is a major cause for concern as it sends a message that despite the vastness and urgency of the problem many countries are still unwilling to take part in surveillance efforts and accurate data collection. This is problematic because surveillance of antimicrobial resistance is the primary solution to contain the issue at local, national and global levels. Unless accurate information is known about AMR steps cannot be taken to properly mitigate it[17].

The WHO identified the need for enhanced laboratory testing capacities to test for the presence of resistance and also identify the pathogen causes disease for accurate prescribing of medicines; strengthening surveillance networks; promoting and supporting the use of standards and methods to test for susceptibility of bacteria towards medicines; encouraging the development of data systems which can be linked to clinical and pharmaceutical data, to come up with an effective way to combat AMR; and establish harmonisation in efforts to reduce the problem[17]. The organisation also recognises the need for a strong collaborative response including comprehensive national plans with sustainable financing to diminish the problem. One of the main solutions is also to make ready access to quality-assured antimicrobial medicines so that new resistant strains can be prevented from emerging[15].

Global Efforts: At the international level, efforts have been made by countries in Europe and the Americas as well. Organisations such as the European Centre for Disease Control and Prevention (EARS-net), the European Medicines Agency (EMA), the European Commission (EC), the Centre for Global Development (CGD), the European Federation of Pharmaceutical Industries and Associations (EFPIA) have been focusing on the issue of AMR more actively over the years2. ESAC-Net is a network of European countries aiming to provide data from the community and hospital sectors in relation to AMR so that comprehensive reports can allow for accurate analysis of trends. The European Union (EU) has also published major research papers and books addressing AMR and its public health threat including *The Race Against Drug Resistance, Extending the Cure, Innovative Incentives for Effective Antibacterial, Recommendations for Future Collaboration between the USA and EU, and The Bacterial Challenge: Time to React.*

In America, the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) was formed in 2009 to address the issue of AMR in collaboration between the European and Ameri-

can regions. It identifies concerning issues and provides workshops and publications to increase the knowledge base regarding AMR[2].

Local Efforts: An indirect solution to the issue is vaccination drives. During vaccination, a weak form of the pathogen is injected into the body. WBCs treat the pathogen as a foreign body and build up cells to fight against it. Some cells are stored in the memory, for future replication in case the pathogen enters the body again. Therefore, whenever the pathogen enters the body in full form, reserve WBCs to fight against it are already ready and present in the body. This reduces the need of using antibiotics, which means there are fewer chances for their abuse and so indirect reduction in AMR.

However, there still needs to be more research into strategies to reduce AMR based in developing and developed countries. National standard treatments and infection control guidelines need to be implemented, to promote rational use of medicines by doctors and patients, and education and awareness programs need to be advertised to increase the information ratio available to people. Rules are required in place to stop over the counter sale of drugs without prescription, and to control the use of antibiotics in animal rearing. Improved animal husbandry is another solution to reduce the use of medicines in livestock food. A sufficient and constant supply of good quality medicines is required in all countries so that partially effective antibiotics need not be prescribed and needlessly exposed to bacteria[11–13].

Diagnostics and Surveillance Systems

Diagnostics are methods to identify types of pathogens and their resistance percentage while Surveillance Systems are methods to identify AMR present in specific regions and index them with pathogens. Combined, they closely monitor the progress of AMR on local, national, and global levels and are essential for the compilation of all information available based on pathogenic resistance[2]. Diagnostics and Surveillance Systems play a major role in the increase of AMR because weak Surveillance Systems and inadequate national commitment lead to less information regarding AMR in the world. For example, at present, most conducted surveillance is based on *Staphylococcus Aureus* with information on other pathogens not widely available, hampering the search for common and global solutions. However, it was noticed that many low-to-middle-income countries do not have enough supply of diagnostic tools in laboratories as these are expensive to purchase and maintain. These tools are used to identify whether a disease is caused by bacteria or virus so that it can be determined whether antibiotics need to be prescribed. Advanced methods can also distinguish between different bacterial or virus types, helping make drug prescriptions extremely accurate and reducing the misuse of antibiotics[2].

Research has also shown a trend of countries not having a national database based on different bacteria showing resistance, nor are WHO-prescribed national plans in place. In Africa, only 6 of 8 countries undertook bacterial surveillance however it was not coordinated at the national level with common methods of analysis, making it ineffective. Only 1 country had conducted a surveillance of AMR in humans in the past 5 years. Only 13 of 26 countries of the Americas had compiled a surveillance report of AMR in humans during the past 5 years, and 10 countries had standard treatment guidelines. Few countries reported having a national plan (9%), a national coordinating mechanism (20%), and a national focal point (20%). To add on, the Eastern Mediterranean Region had only 8 of 21 countries with reports of surveillance of resistant bacteria, and none of the participating countries had a national action plan. Despite efforts to mitigate the problem, even Europe saw less than 20 of 49 countries with an action plan and around 30 countries collected data from surveillance of resistant bacteria. In the South East Asian area, 5 of 11 countries had a national action plan and 9 members had national reference laboratories for testing sensitivity to antibiotics. Lastly, only 4 of 26 Western Pacific Region countries had a national action plan but nearly 20 had reported surveillance of AMR in bacteria[17].

Additionally, the limited amount of data, with outdated, inaccurate or biased information, coupled with the refusal of countries to conform to a common method of tracking AMR, makes it difficult to assess patterns of resistance and find universal solutions. Government health policies have an important role in collecting and analysing the problem as well as the success rate of implemented solutions.

At a national level, it was found that national data based on AMR in different pathogens was unavailable which is problematic as the resistance levels of pathogens are dependent on the regions, they are located in. However, hospitals surveys in various parts of India have shown a rise in resistant pathogens, including *Salmonella, Shigella, Vibrio cholerae, Staphylococcus aureus, Neisseria gonorrhoeae, Neisseria meningitidis, Klebsiella, Mycobacterium tuberculosis,* and HIV. However, efforts are being made to rectify the issue. Organisations such as India Clen (Indian Clinical Epidemiology Network) have researched and produced data on AMR, IIMAR (Indian Initiative for Management of Antibiotic Resistance) was formed in 2008 as a collaboration between the WHO and various NGOs to promote the educated use of antibiotics, and INSAR (Indian Network for Surveillance of Antimicrobial Resistance) a network of 20 laboratories in the private and public sectors working to generate quality data on AMR. The WHO also supported local surveillance systems to collect data at a regional level and understand area-specific trends of pathogens[12]. A national programme focusing on the containment of AMR was recently introduced by the government which aimed at strengthening infection control guidelines, increasing awareness in healthcare workers regarding the appropriate use of antibiotics, and establishing a

laboratory-based AMR surveillance system[18].

Ultimately, national standardised treatment plans, laboratory surveillance of AMR in pathogens, regional and national plans to track AMR, government health policies, and awareness programs are essential to understand the issue further. Strong surveillance systems, the proper following of WHO guidelines, and a common method of tracking AMR is required to acquire information about resistant bacteria patterns. New vaccines are also required to reduce the prevalence of disease and, as a consequence, the need for antibiotics. More research is required at the hospital level regarding AMR, and national health plans and alliances need to be implemented with definite policies defining the appropriate use of antibiotics[11–13].

Conclusion

Antimicrobial resistance is a growing global problem due to several reasons including harm to various industries, socially and economically. Intensive research provided data on the trend of AMR and the causes of its rise, an interesting observation being that until negative economic aspects came to light, only private scientists were working on the issue. However, as soon as the economy became part of the equation, dormant governments and international health organisations decided to term it a global health concern requiring a collaborative approach. Despite this sudden surge, however, the period of 2010-15 witnessed no progress in the research or mitigation of AMR, until WHO surveys were conducted around the world. Another point of notice was that beyond 2015, worldwide surveys conducted by WHO on AMR were not available, showing a blatant disregard for a problem with severe consequences. Despite repeated calls for regional and national surveillance programmes, they were limited to the point of non-existence, painting a disproportionate image of the problem and not acting as a determinant for solutions.

However, with an increase in awareness programmes, vaccination drives, laboratory tests for the quality of antibiotics as well as the resistance in pathogens, detailed research on the topic being conducted, and surveillance systems steadily increasing, new solutions are being discovered and simultaneously implemented. With the Indian government's support, many organisations are working on the issue of surveillance and awareness. Eventually, the steady rise around the world regarding the issue of AMR provides a hopeful picture of understanding and ultimately conquering the issue at hand.

The author also suggests that solutions which can be implemented in day-to-day lives, such as introducing mandatory 30-second clips at the beginning of movies displaying patients' suffering owing to AMR would aid in spreading the message on a larger and more personal level. Warnings of "Self-prescription and Incomplete Dosage is injurious to health and may result in death" printed on antibiotic tablet packets would also remind people to be responsible in their usage of the drug and reduce the ignorance present in society.

Ultimately, we urge countries around the world to collaborate and work collectively towards providing an effective, comprehensive and universally implementable solution towards the rising problem of AMR. The exponential rise being witnessed in the world regarding the propagation of AMR is a worrying issue, not only due to the global impacts, but also due to the national and personal health and economic issues being faced by the world populace.

Methodology

Our plan is to review, chronologically, the phenomenon of AMR. We will first be looking at the history of the problem, the administrative interventions over the years, the methods of propagation causing it to be a persistent and evolving problem, the effects, and the causes of AMR. The report also provides holistic solutions for the issue, based on deep research. The below figure compiles data of the number of countries per region which participated in and provided information regarding AMR in their countries to the WHO Survey. The lack of participation by countries in the surveys conducted by the WHO causes a lack of accurate information which further hinders the steps which need to be chosen for mitigating the issue. All information was found using the tools of Google Scholar and the reports were selected based on their relevance to the issue. Using filtered Google Scholar searches, the authors chose the top hits, which covered the history as well as regional difficulties posed by AMR. The WHO reports were also specifically included due to their being the latest surveys conducted throughout the world and providing holistic information regarding the response of countries in the region to the threat of AMR.

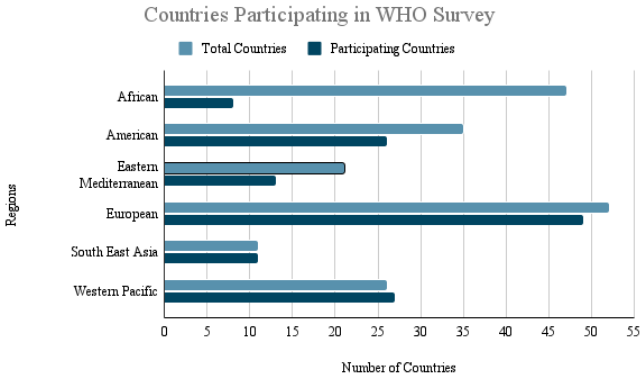

Fig. 1 Countries Participating in WHO Survey

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