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Antibacterial Resistance Menace: A Global Cause of Concern?

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ABSTRACT

Antibacterial resistance (ABR) is defined as bacteria that are not inhibited by an agent's usually achievable systemic concentration with a standard dosage schedule and fall in the minimum inhibitory concentration ranges. ABR act as a major threat by the World Health Organization (WHO) due to the lack of new antibiotics in the development pipeline and infections caused by multi-drug resistant pathogens becoming untreatable. ABR posed a major threat to human health around the world and occurs when changes in bacteria reduce or eliminate the potency of drugs or chemicals designed to treat or prevent the infection. This systematic review discussing the true burden of resistance, particularly in developing countries where surveillance is minimal and data are sparse, its method of spread, and ways to prevent ABR. GLASS developed by WHO monitors progress in implementing national surveillance systems worldwide and fosters the standardized collection, analysis, and sharing of official data on ABR and antimicrobial consumption (AMC), as well as information on crucial ABR epidemiological indicators.

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KEYWORDS:
Antibacterial resistance, Antibiotic- emergence, Global survillance, Antibiotic menace

INTRODUCTION

It is easy to forget what the world was like before the first antibiotic penicillin, was discovered by observations of Alexander Fleming in 1928, when diseases like pneumonia and insignificant abrasion and infections often caused fatality owing to septicemia. Another landmark in the history of the development of antibiotics was the synthesis in 1935 by Gerhard Domagk of the first sulfonamide, prontosil, which was effective against streptococcus infections.[1] Since then, the use of antibiotics for various bacteria has appreciably contribution to the be in command of infectious diseases by declining the associated mortality and morbidity rate in humans and animals and contributed to the advance of technology.[2] Also, antibiotics significantly increased life expectancy in the latter part of the last century. Antibacterial compounds are small molecules with a low molecular weight (150-5000 Dalton) commonly classified based on their chemical origin into natural (antibiotics produced by bacteria and fungi, e.g. penicillin), semisynthetic (like methicillin) and synthetic substances (chemotherapeutic agents obtained by modifications of various natural compounds, like sulfonamides). A new classification is based on their biological effect on microorganisms. It comprises two broad groups: bactericidal agents able to kill bacteria and bacteriostatic agents that stop bacterial growth. The term 'antibiotic' has a limited meaning compared to antimicrobial. The latter includes substances against all microorganisms (bacteria, viruses, parasites, and fungi). The most significant evolution in different classes of antibiotics took place in the period between 1949 and 1980. In the succeeding period, often defined as an "antibiotic discovery void", no new

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significant antibiotics were developed. More accurately, looking at the timeline of dates of discovery of distinct classes of antibacterials (as opposed to dates of introduction), there have been no successful discoveries of novel agents since 1987 (Lynn, 2011). [3] Only three new antibiotics for systemic administration active against Gram-positive bacteria have been developed after 1970. A new antibiotic (the first in nearly 30 years), teixobactin, has recently been discovered as having the potential to work against a wide range of fatal infections such as pneumonia, and chronic diseases caused by Staphylococcus aureus (MRSA, a so-called "superbug") and tuberculosis.[4]

Antibacterial resistance (ABR) posed a major threat to human health around the world and come out as one of the leading public health threats of the 21st century.[5] Antibiotic resistance occurs when changes in bacteria reduces or eliminates the potency of drugs or chemicals designed to treat or prevent the infection. Therefore, bacteria survive and continue to multiply, causing more harm.[6] ABR is an expression of the ability of microorganisms to counteract drugs commonly used to treat associated infections by emergent mechanisms that provide them resistant and permit for the transferring of resistant genetic character to the community. Widespread use of antibiotics promotes the spread of antibiotics resistance in the emergent microorganisms. Susceptibility of bacteria to antibacterial agents is achieved by determining the minimum inhibitory concentration that inhibits the growth of bacteria.[7] Antibacterial resistance is defined as bacteria that are not inhibited by an agent's usually achievable systemic concentration with a standard dosage schedule and fall in the minimum inhibitory concentration ranges. Likewise, multiple drug resistance is defined as the Resistance to two or more drugs or drug classes.[8] Acquiring resistance to one antibiotic conferring resistance to another antibiotic to which the organism has not been exposed is called cross-resistance.[9] Nowadays, approximately 70 % of the bacteria that cause infections in hospitals are resistant to at least one of the antibiotic agents mainly used for treatment. Some micro-organisms are resistant to all approved antibiotics and can only are treated with experimental and potentially toxic drugs. A frightening increase in the resistance of bacteria that cause community-acquired infections has also been documented.[10] ABR occurs when changes in bacteria because the drugs used to treat infections become less effective. According to Center for Disease Control and Prevention (CDC) data, every year in the United States, at least 2.8 million people get infected with antibiotic-resistant germs, and at least 35,000 die. A similar report by the United Kingdom (U.K.) The government argued that ABR could kill 10 million people annually by 2050. [5, 6] Current burden of bacterial ABR, trends in different parts of the world, and the leading pathogen–drug combinations contributing to the bacterial ABR burden are crucial. If left uncontrolled, the spread of ABR could make many bacterial pathogens much more lethal in the future than they are today.[5,6,7]

One major challenge to tackle ABR understands the true burden of resistance, particularly in developing countries where surveillance is minimal and data are sparse. The CDC and prevention in the USA have estimated that some 50 millions of the 150 million prescriptions every year are unnecessary. For instance, the United States (U.S.) The CDC has published a 2019 report on ABR infections and deaths in the USA for eighteen ABR threats using surveillance data, while Cassini and colleagues estimated the burden of eight bacterial pathogens and sixteen pathogen–drug combinations in the E.U. and European Economic Area for 2007–15.[11,12] Lim and colleagues estimated the burden of multidrug Resistance in six bacterial pathogens in Thailand in 2010, and Temkin and colleagues in 2014 estimated the burden of resistance in Escherichia coli and Klebsiella pneumoniae to third-generation cephalosporins and carbapenems in 193 countries.[13,14] In the Indian scenario, with 700,000 people losing battle to ABR annually and another 10 million estimated to die from it by 2050, ABR alone is killing more people than cancer and road traffic accidents combined.[15] Economic prediction suggests that by 2050, ABR can decrease Gross Domestic Product (GDP) by 2-3.5 percent with a drop in livestock by 3-8 percent, costing US 100 trillion dollars to the world.[16] The rise of ABR has attracted the attention of the WHO and several other organization. With WHO announcing ABR as a priority area and several world leaders from Europe framing their Action Plans for the containment of ABR.[17,18,19] It is obvious that sincere efforts are being directed against this common enemy. India has also framed its National Action Plan (NAP) for ABR.(20) Some estimates of the economic effects of ABR have been attempted, and the findings are disturbing. For example, the yearly cost to the U.S. health system alone has been estimated at the U.S. $21 to 34 billion dollars, accompanied by more than 8 million additional days in the hospital. Because the effects of ABR were far beyond the health sector, it was projected nearly 10 years ago to cause a fall in real GDP of 0.4% to 1.6%, translating into lots of billion dollars globally. ABR is a complicated global public health challenge. No single or straightforward strategy will suffice to contain the emergence fully and spread of infectious micro-organisms that become resistant to the available antimicrobial drugs. [19]

The development of ABR is a natural phenomenon in microorganisms and is sped up by the selective pressure exerted by the use and misuse of antimicrobial agents in animals and humans. The current lack of newer antimicrobial to replace those that become ineffective brings added urgent need to protect the efficacy of existing drugs. [20] The development and implementation of effective methods to decrease the emergence and spread of ABR and evaluate the effect of interventions depend on collecting precise representative data on the degree of the problem and its impact. WHO has always raised the global monitoring of

ABR and taken steps for awareness of the impending public health crisis it can cause. Among the scope of WHO initiatives, in 2001, the Global strategy for containment of Antibacterial resistance was issued, and ABR was the focus of World Health Day in 2011 when a 6-point ABR policy package was issued.[21,22] The World Health Assembly, through several resolutions over the years, has called to boost the implementation of the global strategy, emphasize the need for strengthening surveillance of ABR and escalate laboratory capacity to carry it out and lessen the inappropriate use of antimicrobial drugs. The ability to perform antimicrobial susceptibility testing, which can inform surveillance of ABR, also falls within the scope of the International Health Regulations, which stipulate the requirement for access by States Parties to the capacity for investigation of any disease outbreak that may represent an international public health threat.[23]

Many holes are still left in the efforts to contain ABR. Many diversified bacterial, viral, fungal, and parasitic pathogens show resistance to antimicrobials. For some specific diseases (e.g. tuberculosis [T.B.], HIV, influenza, and malaria), programs are in place that address Resistance. Many of the immediate and urgent concerns are related to antibiotic resistance in common bacteria. The ABR involves bacteria that can cause many life-threatening infections in hospitals and the community, for which treatment is becoming challenging or, in some cases, unfeasible. Despite the importance of these infections, there are notable gaps in information concerning the extent, spread, evolution, and impact of ABR. There is urgency due to the lack of new treatment options available to replace those that lose their effectiveness as bacteria become resistant to them. Thus, the main center of this report is on ABR, for which knowledge, support, and concerted action are inadequate. [23]

Although ABR surveillance has been tackled for many years in several high-income countries, there are still significant gaps in understanding the condition of ABR surveillance positions worldwide, particularly in resource-limited settings. This report aims to map ABR surveillance status in the Member States, specifically the availability of data from official national sources. WHO has assembled the accessible information on national ABR surveillance and its data for a set of common pathogenic bacteria to evaluate the global situation as it appeared in 2013. Their action of plan was an examination of the evidence base regarding the health and economic brunt of ABR. The information gathered highlights the strengths and weaknesses in both the collection of data and the quality of data collected in the Member States and demonstrates the need for further effort and investment. [22,23]

1. How Resistance Spreads?

Five areas where Resistance emerges and spreads are given below: [24]

In Healthcare Facilities – microorganisms will be capable of entering our body and causing infections through procedures and medical devices (e.g., catheters). It may spread to people on surfaces like bed rails or by the hands of healthcare workers. It may move with patients when they are transferred from one hospital to another or into the community when patients go home. If not stopped, these resistant healthcare-associated germs can spill over into communities, and become much harder to control Germs can also spread in other ways. Fecal waste can carry traces of previously consumed antibiotics and antibiotic-resistant micro-organisms. The combination of antibiotics and resistant micro-organisms in hospital wastewater allows these resistant micro-organisms to survive in plumbing systems (e.g., toilets).

In the community – Germs are part of everyday life. Many germs do not cause harm; some even help us stay healthy. Only a tiny portion of germs are known to cause infection. Unfortunately, there have been rising antibiotic-resistant conditions in U.S. communities.

Reasons for antibiotic-resistant germs in the community: Community-acquired infections can happen to healthy people who have not had a recent interaction with health care (healthcare-associated micro-organisms tend to impact sicker, more vulnerable people while they receive care). The Infections rate in the community can be challenging to identify and control the spread. New forms of resistance can develop and spread quickly; especially resistance shared among germs through mobile genetic elements Antibiotic-resistant micro-organisms can share their resistance genes with other micro-organisms, making them more challenging to treat.

In water and soil: Human activity can contaminate the environment (water, earth) with antibacterial and antifungals, which can escalate the development and spread of resistance. Contamination can occur from Human and animal waste, the use of antibacterial and antifungals as pesticides on plants or crops, and pharmaceutical manufacturing waste.

Food supply: The U.S. food supply is one of the safest in the world, but people can still become ill from foodborne infections or contact with animals and their environments. CDC estimates that each year 48 million people get sick from a foodborne illness. Antibiotic-resistant bacteria can cause these infections. Germs like Campylobacter, Salmonella, and Shigella cause an estimated 742,000 antibiotic-resistant infections yearly. The number of drugs these germs are resistant to seems to be increasing.

2. People can get infections from food in various ways: The various modes of transmitting the infections from food like handling or eating meat, seafood, milk, eggs or undercooked and contaminated with resistant bacteria, eating fruits and vegetables contaminated with resistant bacteria, contact with untreated or un-composted animal waste, directly or when it gets into the water and the environment and from touching or caring for animals without proper handwashing.

3. Across the world: Antibiotic resistance has been identified in all regions. The degree of resistance and number of infections are different globally, along with the antibiotics use, access to safe water, adequate sanitation, and approach to quality healthcare.There are significant knowledge gaps regarding how much antibiotic resistance occurs worldwide. This is mainly seen in low- and middle-income countries lacking laboratories for resistance testing and systems to collect infection data. According to the review on antibacterial resistance, resistant infections caused around 700,000 deaths worldwide in 2016. Without proper action, antibiotic resistance will lead to approximately 10 million deaths worldwide by 2050 and can cost up to $100 trillion. Germs will naturally find ways to resist antibiotics, which is why aggressive action is needed to keep new resistance from developing and prevent the existing resistance from spreading.

4. Actions to Fight against Antibacterial resistance

Antibacterial resistance happens when micro-organisms like bacteria and fungi develop the ability to overcome the drug action. That means the micro-organisms are not killed and continue to grow. Antibacterialr has been found in every U.S. state and country. Addressing this threat requires continued aggressive action to [24].

i. **Prevent infections** in the first place
ii. **Improve antibiotic use** to slow the development of Resistance
iii. **Stop the spread** of Resistance when it does develop

5. Prevention of Antibacterial resistance

We all have a role to play, from travelers, animal owners, and caregivers to patients and healthcare providers. The various ways to help them are as follows:

Protect yourself and your family - Infections caused by antibiotic-resistant germs are complex and sometimes impossible to treat. ABR happen when bacteria develop the ability to defeat the drugs deliberate to kill them.

i. Ask your healthcare provider about risks for certain infections and sepsis. Keep all abrasion and wounds clean and enclosed until healed, and take good care of chronic conditions, like diabetes or heart disease.
ii. Keeping all hands clean is one of the greatest behavior to prevent infections, avoid getting unwell, and prevent spreading microrganisms.
iii. Vaccines are an essential step in preventing infections, including resistant infections.
iv. Talk to your doctor about how to recognize early signs and symptoms of infections. If an infection isn't stopped, it can lead to complications like sepsis, a life-threatening medical emergency.
v. Talk with your healthcare provider or veterinarian about the management when you, your family, or your animal is sick.
vi. Antibiotics save lives, but any time they are used, they can cause side effects and lead to antibiotic Resistance.
vii. Always wash your hands after touching, feeding, or caring for animals, and keep your animals healthy.
viii. Follow these four steps to avoid foodborne infections. Clean your hands, cooking utensils, and surfaces. Separate raw meat from other foods. Cook foods to safe temperatures. Chill leftovers and other foods promptly.

(a) Healthcare providers : Follow infection prevention and control recommendations, like screening at-risk patients when indicated. Ask patients if they recently received treatment in another facility or traveled to another country (germs can be spread quickly across borders). Follow clinical and treatment guidelines. Support Antibiotic Stewardship to ensure appropriate antibiotic use. Consider fungal infections for patients with respiratory infections that do not respond to antibiotics. Be aware of infections and resistance patterns in your facility and community. Ensure that we are notified by the concerned laboratory immediately when antibiotic-resistant bugs are identified in your patients. State and local health departments fight antibiotic Resistance, but more support is needed as new resistance continues to emerge.

6. Lab Data are Enhancing Local Response

Rapidly detect ABR through CDC's Antibiotic Resistance Laboratory Network. Inform local responses to prevent the spread.

(a) Prevention & containment are stopping spread**:** Support aggressive responses to all unusual Resistance. Work with local partners¡ and healthcare facilities to track and prevent healthcare- associated, foodborne, and community infections caused by antibiotic-resistant germs.
(b) Improving antibiotic use slows development of ABR. : Use data to improve antibiotic use and keep antibiotics effective for life-threatening infections, including those that can lead to sepsis. Support improvements to antibiotic use in humans, animals, and the environment.

7. Veterinarian practices

Veterinarians are stewards in conserving the effectiveness of antibiotics for both animals and people. Working with animal owners, veterinarians can decrease antibiotic resistance by administer disease prevention strategies and improving the use of antibiotics while also promising high-quality medical care for animal patients.

i. 8.1 Prevent Disease: Implementing leading practices for animal husbandry, vaccination, nutrition, and biosecurity (e.g., infection control). Educating people who engage with animals on how to prevent disease.
ii. 8.2 Maintaining accurate records of treatment & their outcomes, documenting and review diagnostic test results and patient response to therapy and reevaluate the reason for prescribing, dose, and duration as needed.
iii. 8.3 Stay current: Always Stay up-to-date on disease prevention tools and prescribing guidelines; local and state requirements; and professional standards for antibiotic use.

8. Livestock and poultry producers: Livestock (e.g., cattle, sheep, goat) and poultry producers are vital in helping to reduce the development and spread of antibiotic resistance. Adopt these practices to protect the health of animals and people who work on farms, the community, and our food supply.

i. Work Closely with Your Veterinarian- Communicate often with your veterinarian, who will decide when antibiotics are needed to treat, control, and prevent animal disease. Ask for advice on preventing antibiotic-resistant infections specific to your farm size, animal species, and environment.
ii. Keep Animals Healthy- Follow good husbandry practices and implement biosecurity practices and techniques to prevent diseases on the farm, during transport, and in production units. Adhere to animal health standards, including a clean drinking water, good nutrition and remove overcrowding. Give veterinarian-recommended vaccinations to prevent fatal diseases and isolate sick animals to prevent the disease spread. Adopt proper practices in waste management and follow manufacturer recommendations to clean equipment.

9. Global Antibacterial resistance and Use Surveillance System (GLASS)

GLASS monitors progress in implementing national surveillance systems worldwide and foster the standardized collection, analysis and sharing of official data on ABR and antimicrobial consumption (AMC), as well as information on crucial ABR epidemiological indicators. GLASS activities are grouped into several technical modules. [25] These modules comprise surveillance activities built on routinely available data (for example, patient samples collected for clinical purposes or national sales of antimicrobials) and focused surveillance activities aimed at generating information for specific goals based on countries' needs. GLASS is also engaged in designing and implementing surveys and studies aimed at helping countries collect data on crucial ABR epidemiological indicators. GLASS and the regional networks, with the support of WHO Collaborating Centers, also contribute to building national laboratory capacities through technical support to primarily low-resource settings in the development and operation of national reference laboratories (NRL), such as external quality assessment (EQA), quality management, continuous training for the performance of ABR testing, and the reporting and interpretation of ABR results. Several guidance documents have been recently developed to support laboratory functions. For example, in 2020, GLASS published "GLASS whole-genome sequencing for surveillance of Antibacterial resistance" and "GLASS guidance for national reference laboratories". [26, 27]

The GLASS-Antimicrobial consumption provides:

(a) At the national level: A methodology that can be integrated into the package of tools to assist the national strategy on optimizing AMU (for example, national action plans on ABR). A methodology that can produce information on quantities and types of consumed antibiotics Antimicrobials to guide the decisions of policy-makers and prescribers and thus monitor the impact of national actions to optimize the access and rational use of antimicrobials.
(b) At the regional and global level : A methodology common to all countries for collecting, analyzing, and reporting national AMC data. The comparable data with animal and agricultural consumption data.

10. National Programme on Containment of Anti-Microbial Resistance.[27]

India has given due recognition to the problem of ABR and to tackle this issue. Antibacterial resistance in pathogens causing important infectious diseases has become a matter of public health concern worldwide, which includes our country also. Antibacterial resistance has emerged even to newer & more potent antimicrobial agents e.g. carbapenems. The quick spread of multi-resistant bacteria and the lack of newer antibiotics to treat infections caused by these organisms pose an increasing threat to public and animal health and need to be taken forward if we are to contain the problem and prevent untreatable illness from becoming a reality.

The main objectives of this program are:

(a) To set up a laboratory-based ABR surveillance system of 30 network laboratories in our country and to create quality data on antibacterial resistance for pathogens of public health importance.
(b) To build up infection control guidelines and practices and promote rational use of antibiotics.
(c) To create awareness among healthcare providers and the community about the rationale for the use of antibiotics.

Activities to be carried out under the national programme.

i. Surveillance for Containment of Antibacterial resistance in several geographical regions.
ii. Rationalizing the use of antibiotics.
iii. Implementation & Development of national infection control guidelines.

iv. Training and capacity building of professionals in related sectors.
v. IEC for dissemination of information about the rational use of antibiotics.
vi. Development of National Repository of Bacterial strains/cultures.

CONCLUSION

This chapter highlights the emerging threat of antibacterial resistance in the community as well as in healthcare settings and its dissemination to environmental reservoirs such as rivers and water bodies. Some of the major causes of ABR include poor awareness about ABR, irrational use of antibiotics due to weak control measures, and lack of adherence to prescribed drugs due to financial restrictions. Rising ABR indicates the urgent need for strict implementation of national drug regulations to limit the over-the-counter sales of antibiotics. Moreover, awareness campaigns should be started with the help of multimedia to educate people on ABR.

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Conflict of Interest: Nil

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Appendices:

ABR: Antibacterial resistance
WHO: World Health Organization
GLASS: Global Antibacterial resistance and Use Surveillance System
AMC: Antimicrobial consumption
CDC: Centres for Disease Control and prevention
GDP: Gross domestic product
NAP: National Action plan
NRL: National Reference Laboratory
EQA: External quality Assurance.

REFERENCES

1. Tortora JG. Microbiology: an introduction. 7th ed. Redwood City, CA: The Benjamín Cummin Publishing Company; 2001. p. 491–509.
2. Arakawa Y. Epidemiology of drug-resistance and clinical microbiologists in the 21st century. Rinsho Byron. 2000 Jan; Suppl 111:1-8.
3. Lynn L. Silver. (2011). Challenges of Antibacterial Discovery. Clin Microbiol Rev. 2011 Jan; 24(1): 71–109.
4. http://www.independent.co.uk/life-style/health-and-families/health-news/first-new-antibiotic-in-30-years-could-bekey- to-beating-superbug-resistance-9963585.html.
5. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. London: Review on Antibacterial resistance, 2016.
6. O'Neill J. Antibacterial resistance: tackling a crisis for the health and wealth of nations. London: Review on Antibacterial resistance, 2014.
7. Bari SB, Mahajan BM, Surana SJ. Resistance to an antibiotic: A challenge in chemotherapy. Indian Journal of Pharmaceutical Education and Research 2008; 42 (1): 3-11.
8. Roger FG, Greenwood D, Norbby SR, Whitley RJ. Antibiotic and Chemotherapy, The problem of Resistance, 8th ed. Churchill Livingstone; 2003. p. 25 – 47.
9. Tripathi KD. Essentials of Medical Pharmacology, Antimicrobial Drugs: General Consideration, 5th ed. Jaypee brother's Medical publishers (P) Ltd; 2003. P.627-640.
10. Bacterial Resistance to antibiotics, 2008 Kenneth Todar University of Wisconsin- Madison Department of Bacteriology. (http://www.textbookofbacteriology.net/ resantimicrobial.html)
11. US Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, 2019.
12. Cassini A, Högberg LD, Plachouras D, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibioticresistant bacteria in the E.U. and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis 2019; 19: 56–66.
13. Lim C, Takahashi E, Hongsuwan M, et al. Epidemiology and burden of multidrug-resistant bacterial infection in a developing country. eLife 2016; 5: e18082
14. Temkin E, Fallach N, Almagor J, Gladstone BP, Tacconelli E, Carmeli Y. Estimating the number of infections caused by antibiotic-resistant Escherichia coli and Klebsiella pneumoniae in 2014: a modelling study. Lancet Glob Health 2018; 6: e969–79.
15. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. Review on Antibacterial resistance; 2016. Available from: https://ABR-review.org/ sites/default/files/160518_Final%20paper_with%20 cover. pdf, accessed on April 15, 2017.
16. O'Neill J. Antibacterial resistance: Tackling a crisis for the health and wealth of nations. Review on Antibacterial resistance; 2020.

17. World Health Organization, Regional Office for South-East Asia. Jaipur declaration on Antibacterial resistance; 2011. http://www.who.int/iris/handle/10665/205397, accessed on April 15, 2017.
18. Smith E, Lichten CA, Taylor J, MacLure C, Lepetit L, Harte E, et al. Evaluation of the action plan against the rising threats from Antibacterial resistance. Final Report. European Commission; 2016. Available from: https://www.ec.europa. EU/health/ABR/sites/ABR/files/ABR_final-report_2016_rand. pdf, accessed on April 15, 2017.
19. Department of Health, Department for Environment Food and Rural Affairs. U.K. Five Year Antibacterial resistance Strategy 2013 to 2018. Government of U.K.; 2013. Available from: HTTPS:// www.gov.uk/government/publications/uk-5-year-antimicrobialresistance-strategy-2013-to-2018, accessed on April 15, 2017.
20. Government of India. National Action Plan on Antibacterial resistance (NAP-ABR) 2017 - 2021; 2017. Available from: http://www.searo.who.int/india/topics/antimicrobial _ resistance/nap_ABR.pdf, accessed on April 15, 2017.
21. Higgins J, Green S. Cochrane handbook for systematic reviews of interventions, version 5.1.0. West Sussex, Wiley-Blackwell, A John Wiley & Sons, Ltd, 2011.
22. GA Wells BS, D O'Connell, J Peterson, V Welch, M Losos, P Tugwell, The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. www.medecine.mcgill.ca, 2000.
23. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Letter Y, Alonso-Coello P et al. GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. BMJ (Clinical Research Ed.), 2008, 336(7650):924-926. (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cm d=Retrieve&db=PubMed&dopt=Citation&list_ uids=18436948, accessed 29 January 2014).
24. Center for disease control and prevention. https://www.cdc.gov/drugresistance/index.html.
25. WHO. Global Antibacterial resistance and use surveillance system (GLASS) report Early implementation 2020. 2020 (https://apps.who.int/iris/bitstream/hand le/10665/332081/9789240005587-eng.pdf, accessed 08/04/2021
26. WHO. GLASS whole-genome sequencing for surveillance of Antibacterial resistance. 2020 (https://cms.who.int/publications/i/item/9789240011 007, accessed 08/04/2021
27. WHO. GLASS guidance for national reference laboratories. 2020 (https://cms.who.int/publications/i/item/9789240010 581, accessed 08/04/2021.