RESEARCH ARTICLE

ANTI-MICROBIAL RESISTANCE: A THREAT TO PUBLIC HEALTH

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ABSTRACT

The discovery of penicillin opened a new era in the treatment of infectious diseases, described as the "golden age" of antibiotic research (1940–1962). Discovery of other antimicrobials soon followed, and included widely used antibiotics like streptomycin, chloramphenicol and tetracycline. For the first time, many common bacterial diseases could be cured. However, with increasing use of antibiotics, more and more pathogenic bacteria developed resistance to their inhibitory effects. Currently, antimicrobial resistance threatens the effective prevention and treatment of an ever-expanding range of infections. It is an increasingly serious threat to global public health that requires immediate action. The major factors responsible for antibiotic resistance are (1) Inappropriate use & misuse of antibiotics (2) Indiscriminate use of antibiotics in agriculture and veterinary practices (3) Insufficient research and development. In order to combat the rising threat of antimicrobial resistance (AMR), the inappropriate and misuse of antibiotics by the general public should be discouraged by generating awareness regarding development of AMR and its consequences through IEC activities. There should be a check on over the counter sale of antibiotics. Guidelines on antibiotic use and infection control should be followed strictly by health care providers in health facilities and these guidelines should be timely updated.

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INTRODUCTION

The discovery of penicillin opened a new era in the treatment of infectious diseases, described as the "golden age" of antibiotic research (1940–1962). (Singh and Barrett, 2006) Discovery of other antimicrobials soon followed and included widely used antibiotics like streptomycin, chloramphenicol and tetracycline. For the first time, many common bacterial diseases could be cured. Moreover, the first antibiotics played a crucial role in the treatment and prevention of infections during World War II. (Lerner, 2004) Antibiotics were so successful that they were considered the ultimate cure, the "miracle drugs" which the medical world was craving for. However, with increasing use of antibiotics, large number of pathogenic bacteria developed resistance to their inhibitory effects. (Barriere, 2015) Currently, antimicrobial resistance threatens the effective prevention and treatment of an ever-expanding range of infections. It is an increasingly serious threat to global public health that requires immediate action and affects all parts of the world as new resistance mechanisms are emerging and rapidly spreading around the globe. (WHO 2014) The Centers for Disease Control and Prevention (CDC) estimates more than two million people are infected with antibiotic-

resistant organisms resulting in approximately 23,000 deaths annually in the United States, costing 20-35 billion dollars annually. In Europe, an estimated 25,000 deaths are attributable to antibiotic-resistant infections, costing 1.5 billion euros annually. In India, it is estimated that 58,000 neonatal sepsis deaths are attributable to drug resistant infections. (The State of the World's Antibiotics, 2015)

Antibiotic consumption

Human consumption

Between 2000 and 2010, consumption of antibiotic drugs increased by more than 30 percent worldwide. Brazil, Russia, India, China, and South Africa accounted for 76 percent of this increase. In most countries, antibiotic consumption varied significantly with season. (Van Boeckel *et al*., 2014) India consumed the maximum antibiotics during 2010 followed by China and the United States. However, during the same period, the per capita consumption of antibiotics was highest in the United States (22 SU per person) followed by 11 SU in India and 7 SU in China. (Van Boeckel *et al*., 2014) In most countries, about 20 percent of antibiotics are used in hospitals and other healthcare facilities, and 80 percent are used in the community, either prescribed by healthcare providers or purchased directly by consumers or care givers without prescription. (Kotwani and Holloway, 2011)

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Agricultural consumption

Increasing prosperity and population growth leads to an increasing demand for animal protein. To satisfy this need, many farmers are trying to increase their agricultural products and often use antibiotics for this purpose. (The State of the World's Antibiotics, 2015) Antibiotics are used not only to treat individual animals with bacterial infections and prevent infections in herds or flocks, but also to promote growth—a controversial and high-use application. Worldwide, in 2010, at least 63 thousand tons of antibiotics were consumed by livestock, likely to be more than all human consumption. (Van Boeckel *et al*., 2015) By 2030, this figure is projected to rise by another two-third to one lakh tons, to meet the demands of a projected 8.5 billion human population. (United Nations World Population Prospects:The 2015 Revision)
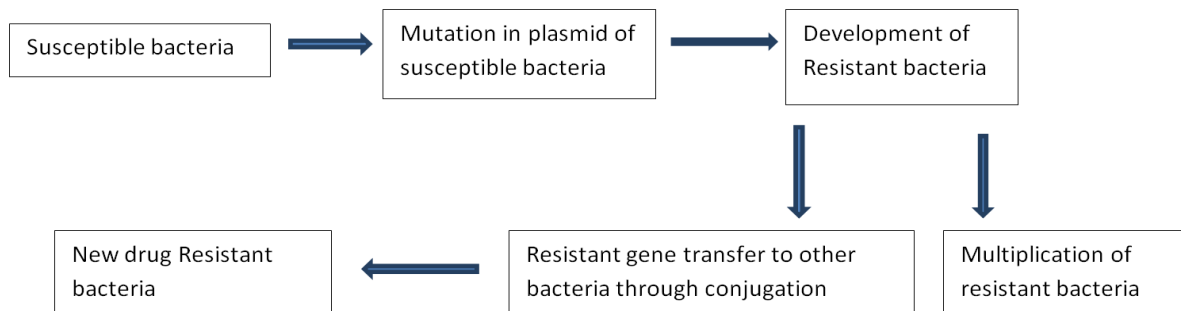
Causes of antibiotic resistance

Antibiotic resistance happens when bacteria convert and become resistant to the antibiotics used to treat the infections they cause. The major factors responsible for antibiotic resistance are

  a) Inappropriate use & misuse of antibiotics
  b) Indiscriminate use of antibiotics in agriculture and veterinary practice
  c) Insufficient research and development

Inappropriate use and Misuse of antibiotics

The three main types of misuse as underlined by the European Centre for Disease Prevention and Control (ECDC) include unnecessary prescription of antibiotics for viral infections, frequent prescription of "broad-spectrum antibiotics", instead of better targeted antibiotic, failure to adhere to regimens of prescribed antibiotics on part of the patient (Antimicrobial resistance and antimicrobial consumption).

Other Pharmacologically Active Substances' regulates the use of antibiotics in certain types of sea foods. The 'Export Inspection Council of India' prohibits the use of certain antibiotics in the feed and medication of poultry intended for export only. The Agriculture Ministry defends the antibiotic use in animal production as a way of earning money by better productivity ignoring their role in development of antibiotic resistance. This short term gain is not only affecting human health by leaving antibiotic residues in food products like milk, meat and milk products, but also affecting both animal and human health. (Mohanta, 2012)

Insufficient research and Development

Since antibiotics are are not as profitable as drugs that treat chronic conditions, such as diabetes, asthma, psychiatric disorders and used only for short duration, the pharmaceutical industries do not consider Research & Development on antibiotics as an economically wise investment. Other causes include poor infection control in hospitals and clinics and lack of hygiene and sanitation.

Mechanism of development of antibiotic resistance

Bacteria acquire resistance to antibiotics through mutations in plasmid.

Bacteria resist the effects of antibiotics by using genetic strategies, with thousands of variations such as producing destructive enzymes to neutralize antibiotics, modifying antimicrobial targets, by mutation, so that drugs cannot recognize them, removing antimicrobial agents by pumping them out (ef ux), preventing antibiotics from entering by creating a "bio lm" or otherwise reducing permeability and creating bypasses that allow bacteria to function without the enzymes targeted by antibiotics. (Penesyan *et al*., 2015)

Indiscriminate use of antibiotics in agriculture and veterinary practice

Indiscriminate use of antibiotics in agriculture and veterinary practice is one of the prime breeding grounds for tough, drug-resistant bacteria. The antibiotics are used in feed supplements given to farm animals to promote animal growth and to prevent infections rather than cure infections. Indiscriminate use of antibiotics in animal husbandry: Indian scenario. As such there are no regulations in India on the use of antibiotics in animal foods meant for cattle, buffaloes, swine and poultry which are raised for domestic consumption. The drugs banned or restricted in developed countries for use in animal feed are being rampantly used here. The Prevention of Food Adulteration Act (1995), Part XVIII: 'Antibiotics and

Spread of antibiotic resistance

Antibiotic resistance spreads in the community by the following ways:

  1. Patients suffering from non-bacterial infections receiving antibiotics develop resistant bacteria in their guts. If they seek medical treatment in a hospital or other in-patient health facility later on can spread the resistant bacteria directly to other patients. If the health care providers come in contact with these persons and do not follow precautions may spread the infections to other persons/patients. Apart from this, the fomites also get infected by resistant bacteria which in turn can infect the other persons/patients with resistant strains.

2. Farm animals receive antibiotics and growth promoters causing them to develop resistant bacteria in their gut. The meat products of these animals when not cooked properly, spread the resistant bacteria to humans.

3. Fertilizers and water contaminated with resistant bacteria are used in growing food crops and vegetables. When these contaminated food crops and vegetables are consumed by humans without washing them properly, they get infected with resistant bacteria.

Antimicrobial resistance – a global concern

Infections caused by resistant microbes fail to respond to treatment, resulting in prolonged illness and greater risk of death. Treatment failures also lead to longer periods of infectivity, with increased numbers of infected people moving in the community. This in turn exposes the general population to the risk of contracting a resistant strain of microorganisms. When these become resistant to first-line antimicrobials, the prohibitive high cost of the second-line drugs may result in failure to treat these diseases in many individuals. Most alarming of all are the diseases caused by multidrug-resistant microbes, which are virtually non-treatable and thereby create a "post-antibioticera" scenario. (Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines, 2011) Without effective antimicrobials for prevention and treatment of infections, medical procedures such as organ transplantation, diabetes management and major surgeries like hip replacement and caesarean section will become very risky. Antimicrobial resistance increases the cost of health care with longer stay in hospitals and more intensive care being required.

Problem statement

Antimicrobial resistance is considered to be the most serious health threats especially for the common infections like sepsis, diarrhoea, pneumonia, urinary tract infection, gonorrhea, malaria, tuberculosis, HIV, influenza. Presently, carbapenem resistance is reported worldwide in more than 50% of strains of Klebsiella pneumonia causing health care associated infections like pneumonia, blood stream infections, infections in the newborn and intensive care units. More than 50% of Escherichia coli strains causing urinary tract infections are reported worldwide to be resistant to fluoroquinolones. Similarly, patients suffering from gonorrhea are reported to be resistant to the last resort of antibiotics - third generation cephalosporins. High mortality (64%) was seen among patients infected with Methicillin resistant Staphylococcus aureus (MRSA). Over all, the antimicrobial resistance is associated with higher mortality rate, longer hospital stay, delayed recuperation and long term disability. Similar observations on the emergence of antimicrobial resistance in gram-negative and gram-positive bacteria are also reported from India. The published reports in the country reveal an increasing trend of drug resistance in common diseases of public health importance i.e. Cholera: showing high level of resistance to commonly used antimicrobials e.g. Furazolidone (60-80%), Co-trimoxazole (60-80%) and Nalidixic Acid (80-90%), Enteric fever: Chloramphenicol, Ampicillin, Co-trimoxazole (30-50%), Fluoroquinolones (up to 30%), Meningococcal infections: Co-trimoxazole, Ciprofloxacin and Tetracycline (50-100%), Gonococcal infections: Penicillin (50-80%), Ciprofloxacin (20-80%). Resistance is also seen in Meningococcal infections, malaria, leprosy, kala-azar, TB & HIV. Recently, New Delhi Metallo-beta-lactamase 1(NDM-1) positive bacteria have also been reported. (National Treatment Guidelines for Antimicrobial Use in Infectious diseases, 2016)

Resistance to anti-TB drugs

The development of resistance to anti-TB drugs begin shortly after the initial introduction of antibacterial drugs for the treatment of TB. Already, during the first randomized clinical trial (RCT) in the 1940s, resistance to streptomycin was detected in a large majority of patients treated with that drug. The spreadof drug-resistant strains was soon recognized and, despite the introduction of combination drug regimens throughout the world many years ago, the presence of drug resistance has been documented with increasing frequency from an ever wider geographic area. (WHO 2014) Drug-resistant TB threatens global TB control and is a major public health concern in several countries. In 2015, there were an estimated five lakh new cases of multidrug-resistant TB (MDR-TB), a form of TB that does not respond to at least isoniazid and rifampicin, the two most powerful anti-TB drugs and an additional one lakh people with rifampicin-resistant TB (RR-TB) who were also newly eligible for MDR-TB treatment. India, China and the Russian Federation accounted for 45% of the combined total of about six lakh cases. About 9.5% of MDR-TB cases had Extensively Drug Resistant TB (XDR-TB) in 2015. (WHO 2016) The two reasons why multidrug resistance continues to emerge and spread are mismanagement of TB treatment and person-to-person transmission. Most people with TB are cured by a strictly followed, 6-month drug regimen that is provided to patients with support and supervision. Inappropriate or incorrect use of antimicrobial drugs, or use of ineffective formulations of drugs (such as use of single drugs, poor quality medicines or bad storage conditions), and premature treatment interruption can cause drug resistance, which can then be transmitted, especially in crowded settings such as prisons and hospitals. (WHO 2016)

XDR-TB is a form of TB which is resistant to at least four of the core anti-TB drugs. XDR-TB involves resistance to the two most powerful anti-TB drugs, isoniazid and rifampicin, also known as multidrug-resistance (MDR-TB), in addition to resistance to any of the fluoroquinolones (such as levofloxacin or moxifloxacin) and to at least one of the three injectable second-line drugs (amikacin, capreomycin or kanamycin). MDR-TB and XDR-TB both take substantially long time to treat than ordinary (drug-susceptible) TB, and require the use of second-line anti-TB drugs, which are more expensive and have more side-effects than the first-line drugs used for drug-susceptible TB. (WHO 2016) XDR –TB may develop in a patient who is receiving treatment for active TB, when anti-TB drugs are misused or mismanaged, and is usually a sign of inadequate clinical care or drug management. It can happen when patients are not properly supported to complete their full course of treatment; when health-care providers prescribe the wrong treatment, or the wrong dose, or for too short period of time; when the supply of drugs to the clinics dispensing drugs is erratic; or when the drugs are of poor quality. The solution to control the resistant TB are to ensure adequate infection control in facilities where patients are treated, provide access to diagnosis, cure the TB patient with first line drugs and their proper dosages, and ensure the appropriate use of recommended second-line drugs.

Resistance to antimalarials

Drug resistant malaria has become a major problem in malaria control. Resistance in vivo has been reported against almost all antimalarial drugs except Artemisinin and its derivatives. Resistance to anti-malarials has been reported in both P. falciparum and P. vivax. Drug resistance in P. falciparum is not confined to chloroquine alone, but also to the other currently used antimalarials and is widespread. (Farooq and Mahajan, 2004) The problem of antimalarial resistance is more pronounced with Plasmodium falciparum. Resistance in Plasmodium vivax has emerged comparatively later and is seen mostly in South-east Asia. (Parija and Praharaj, 2011) Anti-malarial resistance first came into prominence at the end of 1950s when resistance to chloroquine was seen in South-east Asia and South America. In the 1970s and 1980s, chloroquine resistance became widespread and was responsible for the resurgence of malaria in the tropics and in Africa. There are very few countries in the world today, where chloroquine resistance to P. falciparum is not known. Compared to P. falciparum, P. vivax was considered relatively benign with insignificant antimalarial resistance till date. However, recent evidence points towards the increasing incidence of severe disease associated with P. vivax .There are various reports of treatment failure with chloroquine in patients infected with P. vivax. Treatment failure with chloroquine has been reported from Gujarat in India. (Parija and Praharaj, 2011) Resistance to antifolate drugs, pyrimethamine-sulfadoxine in P. falciparum was reported in the same year of introduction of the drugs. Antifolate resistance became widespread in the early 1980s. Southeast Asia, particularly, the Thai-Cambodian border has traditionally been the region from where antimalarial resistance was first observed. The recent observation of slow parasite clearance following artemisinin therapy in the Thai-Cambodian border is, therefore, a cause for concern and could be the harbinger of artemisinin resistance in this region. Although quinine has been one of the oldest antimalarials which is still in use, reports of quinine resistance have been sporadic and mostly confined to Southeast Asia [Parija and Praharaj, 2011]. Although the number of studies dealing with antimalarial drug resistance in India is very limited, available data suggests that drug resistance and decreased drug efficacy is an important deterrent in our fight against malaria. (Dash et al., 2008) Chloroquine resistance in P. falciparum in India was first reported in Assam by Sehgal et al in 1973. (Sehgal et al., 1973) This was followed by many reports of chloroquine resistance in P. falciparum from various parts of the country like Odisha, Madhya Pradesh, Gujarat and the north-eastern states. (Dash et al., 2008) Resistance to the second line drug sulfadoxine-pyrimethamine has also emerged in various parts of the country and molecular markers for the same have been detected. As far as quinine resistance is concerned, there is a paucity of studies dealing with it. Resistance against quinine has been reported from Kolar district in Karnataka. (Farooq and Mahajan, 2004)

Multidrug resistance in Malaria

With regard to P. falciparum, multidrug resistance has been defined as resistance to more than two operational antimalarial compounds belonging to different chemical classes. (Wernsdorfer, 1994) A few workers have modified the definition and have specified the degree of resistance to the third group of antimalarials. Areas where the third antimalarial is not operationally effective are classified as having established multidrug resistance. "Established multidrug resistance" is found in Thailand Cambodia border region. Areas where there is widespread loss of clinical efficacy of chloroquine and the antifolates along with a potential for emergence of resistance to a third antimalarial are said to have "Emerging multidrug resistance". (Wongsrichanalai et al., 2002) Fortunately, as of now, multidrug resistance in malaria parasites has not been frequently reported in India. A single case of "multi-drug resistant" P. falciparum malaria has been reported from Kamrup district of Assam. (Dua et al., 2003) Antimalarial drug resistance poses a very significant threat in the fight against malaria and if not taken care of well in time, could prove to undo most of malaria control activities. At present, Artemisinin Combination Therapy (ACT) seems to be effective in most of the cases. There is also need to encourage studies aimed at developing new antimalarials.[21] In conclusion, the control of drug resistance in malaria parasites requires reducing the overall drug pressure through more selective use of drugs and improving the ways the drugs are used and by prescribing the follow-up practices or using drug combinations which are inherently less likely to foster resistance or have properties that do not facilitate development or spread of resistant parasites.

Resistance to anti leprosy drugs

The emergence of drug resistance is a cause for concern in leprosy, a chronic disease with social stigma, as it poses a serious impediment especially at the stage where a dramatic decline in prevalence and new case detection has been achieved due to intensive and concerted chemotherapy interventions made by the national programme. (Guidelines for Global Surveillance of Drug resistance in Leprosy, 2009) Recent reports have indicated instances of rifampicin resistance in several endemic areas. Since rifampicin is the backbone of multi-drug therapy (MDT), it is important to monitor the emergence of rifampicin-resistant mutants. Resistance to dapsone has been reported since the late 1960s but convincing data supporting the existence of clofazimine resistant strains of M. leprae have not been reported. (Guidelines for Global Surveillance of Drug resistance in Leprosy, 2009)

To meet the challenge of containing the disease and to sustain the on-going declining trend of leprosy in endemic countries, it is essential to monitor drug sensitivity patterns in vulnerable settings. For the monitoring of drug resistance in leprosy, a two pronged strategy has been recommended by WHO for national governments which includes

- Close monitoring of trends in occurrence of relapses after treatment with MDT due to drug resistance, particularly to rifampicin.
- Promotion of research and development of new drugs for non-rifampicin containing regimens to limit and treat patients who relapse after completing one or more courses of MDT due to resistant strains of M. leprae (secondary resistance) and those new patients who are not responding to standard MDT regimen (primary resistance). Guidelines for Global Surveillance of Drug resistance in Leprosy, 2009

Resistance to Influenza drugs

Influenza A viruses that affect humans may originate from a variety of animal hosts, but primarily birds and swine. They are subtyped according to the combination of their

haemagglutinin (17 H subtypes) and neuraminidase (10 N subtypes) surface proteins. The A(H1N1) and A(H3N2) subtypes are currently in general circulation in human population. These viruses evolve continuously and the resultant new circulating viruses of the same subtype cause annual seasonal epidemics.(WHO 2014) Although vaccine remain the primary tool for influenza prevention and control but over the past 10 years, antiviral drugs have increasingly been used for the treatment of epidemic and pandemic influenza. Currently, two classes of antiviral drugs are available for the treatment of influenza: adamantanes and neuraminidase inhibitors. However, due to widespread resistance to the adamantanes, these antiviral drugs are currently not recommended for use against circulating seasonal influenza A and Bviruses. Adamantane resistance became fixed in A(H3N2) viruses after a rapid increase in prevalence during 2004–2005. For the 2009 pandemic influenzaA (H1N1) pdm09 virus, the adamantane resistanceM gene was acquired from its parental Eurasianswine virus. (WHO 2014) The neuraminidase inhibitors oseltamivir andzanamivir, developed in the 1990s, are effective against both influenza A and B viruses, and are widely available. However, the emergence and rapid global spread of oseltamivir resistance in 2007–08 in the former seasonal A(H1N1) viruses has shown that viruses resistant to neuraminidase inhibitors could pose a serious threat to public health and limit the control of influenza pandemics in the near future. (WHO 2014) The actual solution for swine flu lies in its prevention. Swine flu prevention can be achieved by following the simple steps like frequent hand washing, resisting all temptations to touch any part of the face (Hands-off-the –face approach), gargling twice a day with warm water, cleaning the nostrils once every day with warm salt water and drinking as much of warm liquids (tea, coffee) as these liquids will wash off the proliferating viruses from the throat to the stomach where the viruses cannot survive.

New Delhi metallo-beta-lactamase-1(NDM-1): SUPERBUG

New Delhi Metallo-beta-lactamase 1 (NDM-1) is a genetic element with multiple resistant genes that can be harboured by and transmitted between Gram-negative bacteria. It was first described by Yong *et al* in 2009. (Yong *et al*., 2009) It was first identi ed in a Swedish patient returning from New Delhi, India, in 2008. The infection was unsuccessfully treated in a New Delhi hospital and after the patient's repatriation to Sweden, a carbapenem-resistant Klebsiella pneumoniae strain bearing the novel gene was identified. The authors concluded that the new resistance mechanism 'clearly arose in India, but there are few data arising from India to suggest how widespread it is'.

Why NDM-1 is dangerous?

The World Health Organization (WHO) stated that "NDM-1 could be ushering in the dooms day scenario of a world without antibiotics" because NDM-1 gene causes bacteria to produce an enzyme called a carbapenemase which makes nearly every antibiotic ineffective including Carbapenems. Patients with NDM-1-related infections have been treated with a combination of medications, but there is no effective treatment available for many of the infections caused by NDM-1.

Combating antibiotic resistance

Increasing numbers of bacteria are becoming resistant to antimicrobials and there is a need to take urgent action. On

World Health Day (April 7, 2011), WHO introduced a policy package to combat antimicrobial resistance. This package reframes the critical actions to be taken by governments to stimulate change by all stakeholders. It includes commitment by national governments to a comprehensive national plan against antimicrobial resistance that brings together all the required recommended measures, strengthening of surveillance and laboratory capacity, ensuring uninterrupted access to essential medicines of assured quality, regulation and promotion of rational use of medicines, including those used in animal husbandry, ensure proper patient care and improvement of infection prevention and control in health care settings. (WHO 2011)

Four core strategies to prevent Antimicrobial resistance

1. Preventing infections and thereby preventing the spread of resistance

Avoiding infections in the first place reduces the amount of antibiotics that have to be used and reduces the likelihood that resistance will develop during therapy. There are many ways that drug-resistant infections can be prevented: immunization, safe food preparation, handwashing and using antibiotics as directed and only when necessary. (Centers for Disease Control and Prevention, 2013)

2. Tracking

The Government should take initiative to gather data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent these infections and prevent the resistant bacteria from spreading. (Centers for Disease Control and Prevention, 2013)

3. Improving antibiotic prescribing/stewardship

The single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Almost half of the antibiotics used for humans and much of antibiotic used on animals are unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case – is known as antibiotic stewardship. (Centers for Disease Control and Prevention, 2013) The governments and health sector should take necessary steps towards development of Antimicrobial stewardship programmes and develop a standard treatment protocol which can be followed in all health facilities by health care providers.

4. Developing new drugs and diagnostic tests

As antibiotic resistance occurs as part of a natural process in which bacteria evolves, it can be slowed but not stopped. Therefore, we will always need new antibiotics to keep up with resistant bacteria as well as new diagnostic tests to track the

development of resistance. (Centers for Disease Control and Prevention, 2013)

Role of Public in combating Antimicrobial resistance

Antimicrobial resistance is a public health problem which cannot be combatted only by doctors and scientists alone. It needs a concerted effort from the entire population.

What the public can do to help combat antibiotic resistance?

1. Ask the Right Questions. When the healthcare provider suggests treatment that includes antibiotics, the patient should ask if it is truly the best way to treat his/her infection is it really indicated.

2. Know what types of illnesses are most likely to respond to antibiotic treatment. Antibiotics will do nothing to fight off viruses like the common cold and flu. The public should be aware of the common conditions which respond to antibiotics and which do not. This needs efforts from the health sector to sensitize the population through health education.

3. Ask for the test. Ask the healthcare provider to order tests that will identify the source of illness. If necessary, the patients can also request an antibiotic susceptibility test to ensure that the antibiotic being prescribed is the correct one. This eliminates unnecessary use of incorrect antibiotics which can lead to unnecessary treatment and increased risk of resistant infections in the future.

4. If there is real need for antibiotics, follow the instructions and take the full course. Failure to follow the instructions of the prescription (how much to take and how often to take it) can lead to the development of antibiotic-resistance among the bacteria. Harmful bacteria that are exposed to antibiotics may begin to develop properties that allow them to survive – or become resistant to – exposure to antibiotics. Although it may be tempting to stop taking an antibiotic when you start to feel better, the full treatment is necessary to completely eliminate the cause of your illness. Stopping treatment early can result in the illness reoccurring later and help the proliferation and spread of antibiotic resistant bacteria.

How to protect against infections?

Light switches, door handles, table surfaces, public transport, aeroplane tray tables, keyboards on shared computers, toilet seats etc. usually contain disease causing germs. Hand washing with soap and water is the best way to get rid of disease causing microbes and prevent infections such as diarrhea, influenza, common cold etc. Soap doesn't kill organisms but helps remove them from skin surface so they can be washed away with water. Hands should be washed in running water. The importance of hand washing practices should be highlighted and general public, health care providers, doctors and nurses should be motivated for it. Hand sanitizers also work but are not as effective as hand washing with soap and water. Use alcohol based sanitizer (which contains at least 60% alcohol) if soap and water are not available. Wash and scrub fruits and vegetables so that dirt and surface contaminants are removed. Cook meat properly as viruses of bird flu and bacteria including campylobacter are killed by proper cooking. Kitchen is most contaminated area in a house even more than

the toilet. The washing sponge contains maximum number of germs followed by chopping board, dish cloth and cooking surface. Clean the sponge in boiling water and dry it every other day. As far as possible keep working area dry and wash your hands before and after handling food.

ICMR Observations and Guidelines

According to a recent ICMR survey, 50% hospital antibiotic uses are improper. ICMR has issued treatment norms for ten infectious syndromes. For the first time these guidelines are based on reliable Indian antimicrobial resistance data from health care settings. The reasons are irrational use of antibiotics by patients on their own and inappropriate use of antibiotics in health care settings. ICMR conducted a survey regarding use of antibiotics in health care institutions and found that most of them are not implementing the critical antimicrobial stewardship programme (AMSP) developed by it in 2013 to ensure effective antibiotic prescription and prevent drug resistance among pathogens. Treatment guidelines for ten syndromes have been provided by ICMR which include - onset of acute undifferentiated fever in adults, antibiotic associated diarrhea, device associated infections, infections in organ transplant recipients, obstetrics and gynecology related infections, patients with severe sepsis and septic shocks in Intensive care units (ICUs), Upper respiratory tract infections (URTI) and Urinary tract infections (UTI). (Treatment Guidelines for Antimicrobial Use in Common Syndromes, 2017)

National Programme on Containment of Antimicrobial resistance (AMR)

Government of India launched a "National Programme on Containment of Antimicrobial Resistance" under the 12th five year plan (2012-2017). The objectives of this programme include establishing a laboratory based AMR surveillance system involving 30 network labs in the country to generate quality data on antimicrobial resistance for pathogens of public health importance. This will strengthen infection control guidelines and will help in generating awareness among health care providers and in the general community about rational use of antibiotics. (National Programme on containment of Antimicrobial resistance, 2016)

Current status of the programme

A. AMR Surveillance:

National Centre for Disease Control (NCDC), New Delhi is the focal point for implementation of the programme. Ten network laboratories have been identified in the first phase to initiate antimicrobial resistance surveillance on four common bacterial pathogens (Klebsiella, Escherichia coli, Staphylococcus aureus, and Enterococcus species) of public health importance and to determine the magnitude and trends of AMR in different geographical areas of the country. As per trends obtained from the ten network laboratories for the year 2015, resistance rates to most of the antimicrobials (including fluoroquinolones, third generation cephalosporins and carbapenems) are high in these common pathogens. However, no resistance has been observed in reserve drugs such as vancomycin in S. aureusand colistin in gram negative pathogens. (National Programme on containment of Antimicrobial resistance, 2016)

B. National Treatment Guidelines:

A common unified National Treatment Guidelines for antimicrobial use in infectious diseases has been released which serves as a guide to all the hospitals to formulate their own guidelines on basis of which physicians will be trained. (National Programme on containment of Antimicrobial resistance, 2016)

C. Hospital Infection Control guidelines:

An interim concise guideline on infection control has been uploaded on NCDC website as a ready reference for the hospitals to start implementing infection control practices in their settings. National Infection control policy has been drafted and is in the process of finalization. (National Programme on containment of Antimicrobial resistance, 2016)

D. IEC Activities:

An International Conference on AMR was organized by MOHFW in February 2016 which was attended by Policy makers from Ministry of Health & Family Welfare, Ministry of Animal Husbandry, Agriculture, Environment, Clinicians and Microbiologists. (National Programme on containment of Antimicrobial resistance, 2016)

Activities planned for near future

1. Surveillance for hospital acquired infections, implementation of strengthening of Infection control practices, antibiotic use patterns in hospitals and IEC activities in the community as well as health care settings to spread awareness regarding rational use of antibiotics are being planned in phased manner. (National Programme on containment of Antimicrobial resistance, 2016)
2. Trainings will be carried out on Antibiotic Stewardship Program for different stakeholders for promoting rational use of drugs. (National Programme on containment of Antimicrobial resistance, 2016)
3. Expansion of network labs and inclusion of two more bacterial pathogens (Pseudomonas aeruginosa and Acinetobacter species) in AMR surveillance. Molecular characterization of resistant bacterial isolates from network laboratories will be carried out at the nodal centre. (National Programme on containment of Antimicrobial resistance, 2016)

Conclusion

Inappropriate and misuse of antibiotics by the general public should be discouraged by generating awareness regarding development of AMR and its consequences through IEC activities. There should be a check on over the counter sale of antibiotics. Guidelines on antibiotic use and infection control should be followed strictly by health care providers in health facilities and these guidelines should be timely updated. Government should also work on research and development of newer antibiotics to take care of development of resistance in pathogens despite above referred activities.

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