ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL STEWARDSHIP PROGRAM- A KEY ROLE OF PHARMACIST

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ABSTRACT

India being the largely populated country and the largest consumer of Antimicrobials, the problem of irrational use of Antimicrobials and Antimicrobial resistance (AMR) is deep and multifactorial. India is one of the countries reported by WHO for its high unjudicial use of antimicrobial agents and high rates of drug resistance and poor surveillance. More than 50% of the prescriptions contain antimicrobial agents, without which many treatments may fall impossible. Rational use of such medicines is a crucial element for better health outcomes and for providing better patient medical care. But Antimicrobials has more chance of risk occurrence, such as disruption of naturally occurring micro biome in the human gut, antibiotic drugs taken to kill infection causing "bad" bacteria also kill "good" bacteria that protect against infection, followed by allergic reactions and drug interactions. Another serious issue mainly faced in the hospital setting is infections caused by resistant organisms to patients already on antibiotics. Above all risks antimicrobial resistance considered as the global emergency condition, which needs an immediate action. The pharmacist, due to their unique expertise over drugs, there is a paramount need of them for their active role in the health care team in country, where several other countries with the pharmacist collaboration are achieving success over AMR and irrational Antimicrobial use. Pharmacist led research on Antimicrobial use and stewardship

programs can be best solutions. Hence, the present paper describes about the Antimicrobial resistance, Antimicrobial Stewardship (AMS) Program and role of Pharmacist in AMS team.

KEYWORDS: Antimicrobials, Bacteria, Antimicrobial resistance (AMR), Antimicrobial Stewardship (AMS) Program, Pharmacist, Rational Use.

INTRODUCTION

Antimicrobial resistance (AMR), the result of irrational Antimicrobial use, has become a global health challenge.[1] This important feature was foreseen by Alexander Fleming who, in his speech when receiving the Nobel Prize in Medicine for the discovery of penicillin, issued a warning about the possibility of creating resistant organisms if antibiotics were used irresponsibly.[2] It is likely that AMR began as soon as mass use of antimicrobials by the population began, soon after industrialised production became possible.[3] It is predicted that by 2050 there will be more than ten million deaths per year attributed to AMR. Further, it is predicted that the greatest number of these deaths will be in developing countries.[4] Therefore, there is an urgent need to take action to minimize the emergence of antimicrobial resistant bacteria in developing countries.[5,6] India is the major contributor to global pharmaceutical production[7] and the antibiotics use as well as the prevalence of resistance is very high in India.[8,9] India mainly focuses on research and drug discovery, rather than on stewardship. Definitely, there is a need for new antibiotic discovery, but the present very serious issue is AMR, which is the result of irrational antimicrobial use. We have to treat the problem rather than searching from anew solution for the future.[10] The hospitals in India are making policies to improve the situation of antimicrobial use, but the time is running out and need urgent actions.[11] Indian government has come up with many national policies, action plans against AMR since 2010. The National Task Force on AMR also established in 2011. The country advanced by passing the Chennai Declaration, a 5-year plan to address antimicrobial resistance in 2012.[12] In spite of all the activities, the country has not gained success on AMR.[13,11] However, in the very recent years there was a tremendous awareness in the health care team with the publication of ICMR treatment guidelines for antimicrobial use. Then AMSP (Antimicrobial Stewardship Program) came in process and is recognised globally as a key strategy to help manage inappropriate use of antibiotics. Like many developed countries, now India also have their own treatment guidelines for antimicrobial use. The management of development and spread of AMR requires a multifaceted approach, including the participation of all healthcare workers.[14] Pharmacist is a profession, which

dedicates entire life to drugs, from discovery to dispensing. Nearly 40% of prescriptions containing antibiotics are inappropriate. The pharmacist, due to their unique expertise over drugs, when given a prominent role in AMS program can play a responsible role and fulfill the objectives like, promotion of the optimal antimicrobial use, reduction in the transmission of infections, and education of other health professionals, patients, and the public.[15,16] The pharmacist along with prescriber can best improve the situation by making appropriate use of antibiotics in their countries.[17]

DEFINITIONS

Infection: The invasion and multiplication of microorganisms such as bacteria, viruses, and parasites that are not normally present within the body. An infection may cause no symptoms and be subclinical, or it may cause symptoms and be clinically apparent. An infection may remain localized, or it may spread through the blood or lymphatic vessels to become systemic (bodywide). Microorganisms that live naturally in the body are not considered infections. For example, bacteria that normally live within the mouth and intestine are not infections.

Antibiotic: An agent or substance that is produced by or derived from a microorganism that kills or inhibits the growth of another living microorganism. Antibiotic substances that are synthetic, semi-synthetic, or derived from plants or animals are, strictly speaking, not antibiotics. However, for the purposes of the toolkit they are included. The term "Antibiotic" refers to an antimicrobial agent with the ability to kill or inhibit bacterial growth.[18]

Antimicrobial: An agent or substance derived from any source (microorganisms, plants, animals, synthetic or semi-synthetic) that acts against any type of microorganism, such as bacteria (antibacterial), mycobacteria (anti-mycobacterial), fungi (antifungal), parasite (anti-parasitic) and viruses (antiviral). All antibiotics are antimicrobials, but not all antimicrobials are antibiotics.[18]

Antimicrobial resistance (AMR): Microorganisms such as bacteria, fungi, viruses and parasites change when exposed to antimicrobial drugs such as antibiotics (antibacterial), antifungals, antivirals, antimalarial and anthelmintic. As a result, the medicines become ineffective. Therefore, Antimicrobial resistance is the ability of a microbe to resist the effects of medication that once could successfully treat the microbe. The term antimicrobial resistance is a subset of AMR, as it applies only to bacteria becoming resistant to antibiotics.[19]

Antimicrobial stewardship (AMS): A coherent set of actions which promote the responsible use of antimicrobials. This definition can be applied to actions at the individual level as well as the national and global level, and across human health, animal health and the environment.[20,21]

Antimicrobial stewardship programme (AMS programme): An organizational or system-wide health-care strategy to promote appropriate use of antimicrobials through the implementation of evidence-based interventions.

USES OF ANTIBIOTICS: Antibiotics or, more accurately, antimicrobials are active substances of synthetic or natural origin which destroy microorganisms (bacteria, viruses, fungi and parasites), suppressing their growth or their ability to reproduce in animals or humans.[22] Antibiotics are prescribed to treat wide range of infections, especially infections caused by bacteria. Without antibiotics, procedures such as surgery would carry a much higher risk owing to an increased likelihood of sepsis[23] therefore given as prophylaxis.

ANTIMICROBIAL RESISTANCE: Antimicrobial resistance (AMR) is a natural process. It occurs when microorganisms evolve to be able to resist the medicine that has been used to combat them.[24] Resistant microorganisms can survive or even grow in the presence of a concentration of antimicrobial that is usually sufficient to inhibit or kill non-resistant microorganisms of the same species. The increasing consumption of antibiotics is one of the key drivers of antimicrobial resistance.

Causes: People using antimicrobials, as on their own, without therapy realization, is one of the major cause particularly in developing countries, affect not only the individual but also the entire society. Some other factors driving antibiotic resistance in India include, use of high range broad-spectrum antibiotics, rather than narrow spectrum antibiotics, availability of high range of antibiotic fixed dose combinations in the market without a proven advantage over single therapeutic effect, safety and compliance(In India, approximately 118 fixed dose combination antibiotics are available) and drug prescribed by health care providers with lack of updated knowledge.[25] Other causes includes the disposal of wastewater from hospitals are poorly filtered, allowing the antibiotic-resistant bacteria escape in to local water bodies and flourish. People drinking this contaminated water or practicing poor hygiene are infected by this resistant bacteria.[26,27]

Apart from hospital sewage, residues produced from pharmaceutical industries containing antimicrobials also contributed for the development of resistance in microbes present in environment.[28] Quality of medicines is also a crucial factor in the prevention of AMR. Counterfeit medicines are a major threat to public health and antibiotics are one of the most counterfeited groups.[29] Counterfeit medicines may have no therapeutic effect or may even be toxic. Moreover, if the medicine has the correct active antimicrobial ingredient but it is not in sufficient quantity, this can increase AMR. Numerous studies have highlighted that inappropriate medication practices are relatively common in the community and hospital settings of developing countries.[30-32] Absence of qualified pharmacists is one factor that has contributed to these inappropriate practices in community pharmacies.[33] Similarly, overprescribing of antibiotics in hospitals especially in developing countries is common, and the lack of clinical pharmacists in hospitals in developing countries may be a contributing factor.[34]

Mechanism: The mechanism of drug resistance is grouped into three categories. They are permeability mechanism, enzymatic inactivation of antibiotic and altered target or pathway. In permeability mechanism the drug resistance may due to lack of entry/ decreased cell permeability or greater exit/ active efflux. In altered target mechanism the resistance may due to modification of drug receptor site or due to the synthesis of resistant metabolic pathway.[35]

Impacts: Many thousands of people die each year from infections caused by antibiotic-resistant bacteria. The increasing incidence of antibiotic resistance has been described as a global public health threat, and concerted efforts are required to address the problem.[36] It leads to worsen the clinical outcomes of patients who have infections caused by drug resistant bacteria and the medical procedure risks. AMR has a considerable impact on the healthcare system as it will result in a higher morbidity rate and prolonged duration of hospitalization.[37] It also results in treatment failure, additional side effects, psychological disorders due to reduced quality of life, burden on families and a greater likelihood of death as a result of inadequate or delayed treatment.[38] AMR also indirectly affects the treatment of non-communicable diseases, making it more difficult. AMR also affects patients who are not infected with resistant organisms. Because of the increasing rate of resistance among common pathogens, broader-spectrum agents are now required for the empirical therapy of many common infections. These agents are usually more expensive, have more deleterious effects on protective microflora, and can be more toxic or less effective.[39]

ANTIMICROBIAL STEWARDSHIP PROGRAM (AMSP)

According to the 30% Rule of Antibiotic prescribing Fact is that "30% of all hospitalised in-patient at any given time receive antibiotics, over 30% of antibiotics are prescribed inappropriately in the community, upto 30% of all surgical prophylaxis is inappropriate, 30% of hospital pharmacy costs are due to antimicrobial use, 10-30% of antimicrobial cost can be saved by antimicrobial stewardship programs".[40] The saying, "The right antibiotic for the right patient, at the right time, with the right dose, the right route, causing the least harm to the patient and future patients" is the moto of AMS.[41] It is a supervisory program over appropriateness of the treatment, like drug selection, correct dosing, duration of therapy, administration interval, therapeutic drug monitoring for certain antimicrobial agents. AMS program assure best clinical outcome in the treatment of infection by not only halting antimicrobial resistance, but also minimizing toxic effects to the patients and by decreasing adverse events, and controls health care cost.[42] Antimicrobial stewardship program (AMSP) helps clinicians to improve the quality of patient care, patient safety, reduced treatment failures, increasing frequency of prescribing appropriate therapy and prophylaxis, reduces the CDI rates and mainly it reduces antimicrobial resistance.

Evolution of AMSP: Decades of inappropriate use of antibiotics, combined with new development and discovery of antimicrobials, has led to AMR emerging as one of the most critical risks to global public health requiring action by governments around the world.[43,44] The World Health Organisation recognises that "Without harmonised and immediate action on a global scale, the world is heading towards a post-antibiotic era in which common infections could once again kill".[45] AMR has a number of negative consequences along with that the antimicrobial medicines are amongst the most commonly reported substandard falsified medicines.[46] An European research[47] has shown that a significant proportion of the population are unaware that antibiotics are ineffective against viruses (57%) and against colds and flu (44%). This research also demonstrated that the use of antibiotics is higher among those with lower levels of education (39%) and in worse economic circumstances (44%). The survey results point to the importance of increasing public awareness and understanding of antibiotics in order to help reduce demand for antibiotics for conditions where they would be ineffective. India is rich in pharmaceutical production; along with that the use of antibiotics is also very high. Indian government has come up with many national policies and action plans against AMR but all the activities have not gained success. However, in the very recent years there was a tremendous awareness in the health care team

with the publication of ICMR treatment guidelines for antimicrobial use. And then the AMSP (Antimicrobial Stewardship Program) came in process and is recognised globally as a key strategy to help manage inappropriate use of antibiotics. The term AMS is defined as 'an organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness'.[48]

Objectives: The main objectives of antimicrobial stewardship Program includes;

- To improve patient outcomes - Improve infection cure rates, reduce surgical infection rates, reduce mortality and morbidity.

- To improve patient safety by minimizing antimicrobial consumption, without increasing mortality or infection-related readmissions.

- To reduce resistance by restricting relevant agents that can reduce colonization or infection with Gram-positive or Gram-negative resistant bacteria.

- To reduce healthcare costs without adversely impacting quality of care. Savings achieved by reducing antibiotic costs can be greater than the cost of the intervention or program.[49]

Barriers in implementation of AMS program: Common barriers identified for the implementation of AMS in India include, lack of education and training related to antimicrobial usage, a prescribing culture in hospitals resistant to change, lack of resources, lack of feedback on institutional antimicrobial use[50], lack of funding and human resources, lack of information technology, lack of awareness in the administration and healthcare team.[51]

Antimicrobial Stewardship Team*:* It is well documented in the primary Antimicrobial Stewardship literature that a multidisciplinary team is an essential element to having a successful program. The guidelines highlight the interdisciplinary nature of Antimicrobial Stewardship teams, noting that each member has a unique area of expertise and background knowledge base that strengthens the team beyond individual members.[52,53]

*Infectious Diseases Physicians***:** A trained physician who dedicates a portion of their time to the design, implementation, and function of the AMS program. Supervision by an infectious diseases physician is necessary to ensure that therapeutic guidelines, antimicrobial restriction policies, or other measures are based on the best evidence and practice and will not put patients at risk. Although most (89%) infectious diseases physicians surveyed by Sunenshine et al. agreed that infectious diseases consultants should be involved in the approval process

for restricted antimicrobial agents.[54] The time involved in directly administering an intensive stewardship program at a medium- or large-sized hospital may leave little time for clinical consultations, research, or teaching. Thus, responsibility for the daily activities in such a program would either have to be shared among physicians or delegated to other personnel such as infectious diseases fellows in training or hospital or clinical pharmacists.

Clinical and Hospital Pharmacists: The origin of many antimicrobial stewardship programs as cost-saving measures initiated by the pharmacy department has put pharmacists at the forefront of many antimicrobial stewardship programs. Pharmacists often act as the effector arms for antimicrobial stewardship programs.[55] They are well positioned for this effort because of their role in processing medication orders and their familiarity with the hospital formulary. Different hospital-based pharmacists may play different roles in antimicrobial stewardship programs. Pharmacists whose primary role is in processing medication orders and dispensing drugs in the hospital may note when restricted antimicrobials are ordered and notify the prescriber that authorization is required. They may also flag orders for review by infectious diseases specialists, in addition to their usual role in assuring proper dosing and safety. However, the broad responsibilities of these pharmacists generally do not allow adequate time for a comprehensive review of antimicrobial therapy. In addition, these pharmacists may not have adequate training in infectious diseases to feel comfortable providing recommendations for complex cases. Thus, having a clinical pharmacist with specialized training in infectious diseases dedicated full- or part-time to the administration of the antimicrobial stewardship program is increasingly common. The next decades will likely see clinical pharmacists as increasingly important partners to infectious diseases physicians in implementation of antimicrobial stewardship programs.[56]

*Clinical Microbiologists***:** The clinical microbiology laboratory is a key component in the function of antimicrobial stewardship programs. Preparation of antibiograms specific to certain patient care areas, especially intensive care units, may allow identification of local problems and focused antimicrobial stewardship and infection control efforts.[57] Dissemination of antibiograms to clinicians may allow better selection of empirical therapy based on local susceptibility patterns. Timely and accurate reporting of microbiology susceptibility test results allows selection of more appropriate and focused therapy, and may help reduce broad-spectrum antimicrobial use.[58,59] The microbiology laboratory can also

encourage focused antimicrobial selection by cascade reporting of susceptibility results: depending on the organism's susceptibility.

Infection Control Staff and Hospital Epidemiologists: The problem of spread of antimicrobial-resistant organisms within hospitals has long been a concern of infection control professionals. While some resistant organisms have primarily been thought to be infection control problems and others antibiotic-use problems, an absolute distinction is artificial and both transmission and selection play important roles in the spread of antimicrobial resistance.[60,61] There are a number of avenues for collaboration between infection control and antimicrobial stewardship programs. Infection control staff gather highly detailed data on nosocomial infections which may assist in the antimicrobial stewardship team's evaluation of the outcomes of their strategies. Hospital epidemiologists have the expertise in surveillance and study design to lend to efforts studying the effect of antimicrobial stewardship measures. In turn, antimicrobial stewardship programs may be able to assist in efforts to control outbreaks by focused monitoring and/or restriction of antimicrobials in the targeted units. Any antimicrobial stewardship program should either be fully integrated with or work closely with a hospital's infection control program; such collaboration has the opportunity to synergistically reduce antimicrobial resistance and improve patient outcomes.

Hospital Administrators: None of the efforts of infectious diseases physicians, pharmacists, microbiologists, or infection control practitioners to establish an antimicrobial stewardship program are likely to be successful without at least passive endorsement by hospital leadership.[62] Program funding, institutional policy and physician autonomy are core issues in the development of antimicrobial stewardship programs that must be addressed by hospital administration. Without adequate support from hospital leadership, program funding will be inadequate or inconsistent since the programs do not generate revenue (although they may result in significant cost savings).

ROLES AND RESPONSIBILITIES OF PHARMACIST IN AMSP

A 2014 WHO report, "The role of pharmacist in encouraging prudent use of antibiotics and averting antimicrobial resistance: a review of policy and experience in Europe",[63,64] showed that the pharmacists have decisive role in AMR prevention and control. Pharmacists are the most accessible health care professionals, and are fully competent in all aspects of medicines. They possess scientific knowledge for the entire medicines-use process, including

procurement, preparation, storage, security, distribution, dispensing, administration and safe disposal. ASHP, statement recommends that, the pharmacist, due to their unique expertise over drugs, when given a prominent role in AMS program can play a responsible role and fulfill the objectives like, promotion of the optimal antimicrobial use, reduction in the transmission of infections, and education of other health professionals, patients, and the public.[65,66] Well-trained pharmacist, in the health care team and research areas can achieve success over AMR. Studies in hospitals have shown that pharmacist interventions improve appropriate antimicrobial use and reduce costs.[67-69] The CDC's recently released Core Elements of Outpatient Antimicrobial Stewardship, highlights the importance and impact of pharmacist involvement for a successful stewardship program.[71] However, the guidance on stewardship from IDSA, CDC, SHEA, ASHP and other key stakeholders makes it abundantly clear that a pharmacist is a resource that is vital to the success of any antimicrobial stewardship team.[52,53,70,71] As antimicrobials become an increasingly scarce resource, it will be imperative to have the input from the pharmacy professionals to guide in the increasingly challenging times. Each of the individual elements of stewardship can be enhanced with a pharmacist's assistance.

Prospective audit and feedback: Prospective audit with direct intervention and feedback is one of the two main core strategies employed by AST programs.[52,53] This is done by optimizing drug selection, dose, duration & route of therapy. It also involves concurrent review of patients who receive antimicrobials. It allows for providers to make their own treatment decision. It is thought that the education provided in these encounters may not only reduce inappropriate use for an individual patient, but the increase in knowledge can be applied to similar future encounters, thus decreasing the burden of inappropriate antimicrobial use.[70] The pharmacists are uniquely situated to intervene using prospective audits, as their workflow includes chart review for appropriateness and indication when approving inpatient orders, filling outpatient prescriptions, or doing medication reconciliation as part of their daily activities in their practice site. Pharmacists can promote optimal use of antimicrobials through individualized patient dosing when intervening on medication issues.[71]

Formulary restriction and preauthorization requirements: The second core strategy of many AST programs includes formulary restriction and preauthorization of selected antimicrobials.[52,53] These interventions may lead to immediate reductions in use and the

costs associated with these selected antimicrobials. Restrictions, additions, deletions to Formulary in the inpatient setting, development of drug therapy and disease state guidelines or pathways for appropriate use of antimicrobials are generally handled as part of the duties of the Pharmacy and Therapeutics (P&T) Committee.[70] These interventions are important components to promote optimal antimicrobial use. Pharmacist involvement for shepherding stewardship initiatives is vital to achieve the needed buy-in from members of the P&T Committee who may not have a level of comfort or understanding of the elements of stewardship.

Education: Education, targeting patients and the general public about antimicrobial stewardship is an important piece in the stewardship program to combat inappropriate use.[71] Pharmacists fulfils an important role in the community as well as in hospital pharmacy in providing unbiased and scientifically accurate information to their patients through counselling the patients, their families or carers on the appropriate use of antimicrobials and educating them on proper immunization. If appropriate, provide advice to prescribers for rational use of antimicrobials. Therefore, the pharmacist can act as liaison between the AMS team or AMS pharmacist and clinicians to advise on optimising the use of antimicrobials.[72]

Pharmacy-driven interventions: Antimicrobial therapy for patients with serious infections requiring hospitalization is generally initiated with parenteral therapy. Enhanced oral bioavailability among certain antimicrobials—such as fluoroquinolones, oxazolidinones, metronidazole, clindamycin, fluconazole, and voriconazole—allows conversion to oral therapy once a patient meets defined clinical criteria. This can decrease length of hospital stay and health care costs.[52,53] Pharmacist-driven other interventions include; individualized dose adjustments for patients with organ dysfunction (e.g. renal or hepatic adjustment), dose optimization based on therapeutic drug monitoring, detection and prevention of antibiotic-related drug-drug interactions[71], selection of drug to avoid unnecessarily duplicative therapy in patients simultaneously receiving multiple agents, or suggesting alternatives when a desired medication may be unavailable due to drug shortage.[70] This can be reviewed and actioned on by a trained pharmacist.

Regulatory compliance: The role of the pharmacist in an individual AST will vary based upon the structure and needs of the individual organization.[53,70] Pharmacists involvement helps to ensure compliance with the standards set by various regulatory agencies.[71] In

addition to compliance, collection and evaluation of antimicrobial utilization data is vitally important for assessing the impact of the stewardship interventions.

*Streamlining/ de-escalation***:** Excessively broad spectrum therapy contributes to the selection of antimicrobial resistant pathogens. This conflict can be resolved when culture results are available. Hospitalized patients are often empirically treated with antibiotics. However, prescribers often do not revisit the selection of antibiotics after microbiological data become available. All clinicians should perform a review of antibiotics 48 hours after prescription. But due to heavy workloads, the doctors may fail to review the antibiotic regimen. Therefore, in such condition the clinical pharmacist can interfere and assist physician in changing the therapy to targeted antibiotic choice (deescalate) to treat the infection with right antibiotic choice, dose, route of administration and duration. This intervention requires an expertise in antibiotic use and infectious disease and authorization to modify the antibiotic use in a timely manner. Some health care facilities restrict the use of certain antibiotics based on the spectrum of activity caused or adverse events and to ensure that the use must be discussed with an antibiotic expert before initiation of therapy.

Others: The pharmacists can also provide support to AMS program by;

- Advising and assisting physician in antibiotic cycling (Antimicrobial cycling refers to the scheduled removal and substitution of a specific antimicrobial or antimicrobial class to prevent or reverse the development of antimicrobial resistance).

- Maintaining antimicrobial order forms (Antimicrobial order forms decrease antimicrobial consumption through the use of automatic stop orders).

- Periodic assessment of antibiotic use for treatment of infection, performed to determine the quality of antibiotics use.

- Dose optimization according to PK/PD – characteristics, patient characteristics, causative organism and site of infection. PK monitoring and adjustment can reduce cost and decrease adverse effects.[40]

- Pharmacists protect the integrity of the supply chain, and procure medical products only from reputable sources. They are alert to differences in quality of packaging, labelling or leaflets and in physical appearance of medicinal products.[73] Thus pharmacists are a vital asset in assuring the safety of patients through their active participation in the fight against counterfeit medicines. The hospital pharmacists are also responsible for their purchase, manufacture and quality testing.[74]

- Participating in health promotion and infection prevention programs, AMS research works and relevant committees like PTC, Medication safety committee, Infection control committee etc., in order to develop antimicrobial prescribing guidelines/ algorithms and also in promoting infection prevention measures in hospitals as well as community.[72]

HOW TO OVERCOME AMR

By Health Care Professionals: Reducing AMR requires global action, education and promotion.

- Participate in hospital based programs dedicated to improving antibiotic use, commonly referred to as Antimicrobial Stewardship Program (AMSP), that have been found helpful in improving the quality of patient care and safety through increased infection cure rates, reducing treatment failures, and increasing the frequency of correct prescription for therapy and prophylaxis.

- Developing guidelines and policies can provide tools for physicians and dispensers to educate patients on antimicrobial use and the importance of adherence to prescribed treatments,

- Provide consumer education with main aim to fight against AMR and pharmacists can improve consumer's awareness of safe and appropriate medication practices concerning antibiotics.[75]

- Ensure that the patients receive medicines appropriate to their clinical needs at doses that meet their individual requirements for an adequate period and at the lowest cost to them and their community.[76]

- Surveillance of prudent use of antibiotics by medical, pharmacy, dental and veterinary professionals are urgently needed.

- Introduce public awareness campaign, reducing the unnecessary use of antimicrobials in agriculture and improving global surveillance of drug resistance in humans and animals.

- Educate public for limiting the over-the-counter use of antibiotics

- Provide awareness to the public about the importance of improving hygiene to prevent the spread of infection and in promoting the development and use of vaccines,

- Maintain effective and proper collaboration across the multidisciplinary team (MDT) in the implementation of AMS.

- Participate in education and training programs to keep up to date with the latest information regarding antibiotics.[77]

- Develop pharmaco-vigilance including prescription audit inclusive of antibiotic usage in the hospital and community.

By Public

- Avoiding overuse and misuse of antibiotics.
- Improve the understanding of antibiotics and inform their judicious use by direct contact with consumers in the community and in hospital.[78]
- Maintain proper personnel hygiene to avoid or prevent occurrence of infection.
- Avoid self-medication and sharing of antibiotics.
- Practice proper medication adherence, as mentioned by the healthcare professionals (especially Antibiotics).[79]

CONCLUSION

Antimicrobial resistance (AMR) is a major public health challenge, which is recognized as high priority area by the Government of India. Hospital based programs dedicated to improving antibiotic use, commonly referred to as Antimicrobial Stewardship Program (AMSP) have been found helpful in improving the quality of patient care and safety through increased infection cure rates, reducing treatment failures, and increasing the frequency of correct prescription for therapy and prophylaxis. Implementation of an effective AMSP requires a multidisciplinary approach involving a variety of experts. India being the largely populated country, it is difficult to control and educate the effects of irrational use of the antimicrobials. Possible ways for rational use of antimicrobials can be discovered with a sound research on antimicrobial use, resistance patterns, and drug related problems. A known fact is that most of the doctors are busy with their hectic schedules and they have less time for research and development in drug utilization. Strengthening and enhancing the pharmacists' role will have the positive impact on the global issue of AMR. Presence of appropriately trained pharmacists integrated into the health care system may have significant impact in minimising inappropriate antibiotic use in developing countries. ASHP recognizes the current shortage of advanced trained pharmacists in infectious diseases and supports the need for an evolutionary change in pharmacy education and postgraduate residency training on infectious diseases in order to produce adequate and well-trained pharmacists who can deliver essential services. As a result of introduction of Pharm-D program in 2008, the clinical pharmacist appointed in the hospitals has better control over the situation of AMR by implementation of stewardship programs and by sound research. Therefore, the need of clinical pharmacist in

hospital sector should be increased in order to fight against AMR and also, the government should consider only a small levy of pharmaceutical sector as the options to raise the development of new antibiotics.

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