Global Antibiotic Resistance Partnership

SITUATION ANALYSIS AND RECOMMENDATIONS

Antibiotic Use and Resistance in Nepal

Executive Summary

The GARP-Nepal National Working Group

Dr. Buddha Basnyat, Chairman

May 2015

GARP-Nepal National Working Group (NWG)

Dr. Buddha Basnyat, Chair GARP- Nepal, Researcher/Clinician, Oxford University Clinical Research Unit-Nepal\ Patan Academy of Health Science

Dr. Paras K Pokharel, Vice Chair- GARP Nepal, Professor of Public Health and Community Medicine, BP Koirala Institute of Health Sciences, Dharan

Dr. Sameer Mani Dixit, PI GARP- Nepal, Director of Research, Center for Molecular Dynamics, Nepal

Dr. Abhilasha Karkey, Medical Microbiologist, Oxford University Clinical Research Unit-Nepal\ Patan Academy of Health Science

Dr. Bhabana Shrestha, Director, German Nepal Tuberculosis Project

Dr. Basudha Khanal, Professor of Microbiology, BP Koirala Institute of Health Science, Dharan

Dr. Devi Prasai, Member**,** Nepal Health Economist Association

Dr. Mukti Shrestha, Veterinarian, Veterinary Clinics, Pulchowk

Dr. Palpasa Kansakar, Microbiologist, World Health Organization

Dr. Sharada Thapaliya, Associate Professor, Department of Pharmacology and Surgery, Agriculture and Forestry University–Rampur

Mr. Shrawan Kumar Mishra, President, Nepal Health Professional Council

Dr. Shrijana Shrestha, Dean**,** Patan Academy of Health Science

GARP-Nepal Staff

Santoshi Giri, GARP-N Country Coordinator, Global Antibiotic Resistance Partnership- Nepal/Nepal Public Health Foundation

Namuna Shrestha, Programme Officer, Nepal Public Health Foundation

International Advisors

Hellen Gelband, Associate Director, Center for Disease Dynamics, Economics & Policy

Ramanan Laxminarayan, GARP Principal Investigator, Director, Center for Disease Dynamics, Economics & Policy

Phone : 4-262534, Fax : 4-262565

Government of Nepal
Ministry Of Health & Population
Ramshahpath, Kathmandu, Nepal

Ref :

Hon'ble Khaga Raj Adhikari
Minister for Health and Population
Date : 07th December 2014

Foreword

In the developing country like ours, where the burden of treatable communicable diseases is very high and access to health facilities and laboratories not so easy, antibiotics have long worked as miracle drugs. Considering their effectiveness, antibiotics have for a long time been prescribed very regularly, and in many cases, randomly in the country. This has led to the emergence of antibiotic resistance as a silent epidemic in Nepal along with other countries of the world. The World Health Organization has already warned of the global threat posed by antimicrobial resistance. In the long run, AMR not only makes treatment difficult but also increases the health expenditure of people. In this regard, I am pleased to see that Global Antibiotic Resistance Partnership (GARP) Nepal, under Nepal Public Health Foundation has prepared this report "Situation Analysis and Recommendation: Antibiotic Use and Resistance in Nepal." This is a very important initial step towards bringing awareness on this issue.

The endeavor of GARP-Nepal to include the animal sector usage of antibiotics and publish this Situation Analysis is commendable as it also coincides with the "one health policy" of the Ministry of Health. Hence this document will bridge the information gap related to AMR in human and animal sector and will further serve as an important baseline document for developing plans, policies and programs in AMR for government and other allied agencies.

MOHP has recently endorsed "Antibiotic Treatment Guidelines, 2014" which aims to help with rational use of antibiotics in Nepal. In this context this Situation Analysis document will be important in helping to bring a clearer focus and hence strengthen the Guidelines.I thank the GARP Nepal team for their efforts in putting together this informative document and wish them every success in future AMR activities. MOHP looks forward to their continued hard work for Nepal in the field of antimicrobial resistance.

(Khaga Raj Adhikari)
Minister

SUMMARY AND RECOMMENDATIONS

Antibiotics are the 'miracle drugs' of the 20th century. They made possible great progress in turning many bacterial infections into illnesses rather than death sentences. Along with vaccines, they have transformed death in infancy and childhood from an ever-present danger into a rare event. Remarkably, Alexander Fleming, the discoverer of penicillin, warned of resistance eroding the drug's effectiveness in the year 1945. He made what may have been the first appeal for antibiotic stewardship: use penicillin only when necessary and do not 'under-dose'.

Unfortunately, the world has used penicillin and the rest of the available antibiotics, developed mainly in the 1940s and 1950s, at an ever-increasing rate, both when they are needed and when they are not, in human beings and in other animals. The result is that today, many antibiotics have lost their effectiveness against common bacterial infections, and antibiotic resistance is increasing in most countries before it is recognized as a major problem.

Antibiotic resistance is a natural evolutionary response to the exposure of bacteria to antibiotics. Every time an antibiotic is taken by a person or animal, bacteria come in contact with it and those that are naturally resistant, because of a mutation or natural variation have a survival advantage. When antibiotics are taken orally, a huge population of gut bacteria is exposed—pathogenic bacteria as well as bacteria living in equilibrium with the host, some of which may turn pathogenic at some point. Resistant strains of any of these bacteria may be selected for, and many exposed bacteria—both pathogenic and commensal—can pass on their resistant genetic material to other, even unrelated, bacteria.

Antibiotic resistance is no longer a concern for the distant future but is a pressing issue, both globally and in Nepal. As part of global effort to preserve the effectiveness of antibiotics, the Global Antibiotic Resistance Partnership (GARP)-Nepal was established to document the current state of antibiotic access, use and resistance in the country, and to identify policies and actions that could set a course for antibiotic sustainability.

This situation analysis is a first step in the GARP process, creating a baseline for what is known and identifying the important information gaps to be addressed in order to create responsible and effective recommendations for policymakers to consider.

ABOUT THE GLOBAL ANTIBIOTIC RESISTANCE PARTNERSHIP

Antibiotic resistance is a global concern strongly affected by local factors. Progress will be best made when national experts collaborate to understand all aspects of antibiotic access, use and resistance within their own country context, and then work together to craft policy solutions tailored to meet their own needs. With other health issues such as HIV/AIDS, tuberculosis, malaria, malnutrition and epidemics competing for global attention, antibiotic resistance has not been a priority in many low- and middle-income countries, though many scientists, clinicians and public health specialists are aware of and concerned about it.

This was the rationale for establishing GARP, a project of the Center for Disease Dynamics, Economics & Policy (CDDEP), a non-profit research and policy organization with offices in Washington, DC and New Delhi and funded by the Bill & Melinda Gates Foundation. GARP was created to enable local experts to occupy the multidisciplinary space to understand local conditions and identify policy opportunities related to antibiotics, especially (but not limited to) those affecting antibiotic resistance, and ultimately, to play a role in global deliberations.

GARP began in 2008 in Kenya, India, South Africa and Vietnam, where working groups continue to develop a deeper understanding of antibiotic issues and have become trusted sources of information for all sectors. The working groups are becoming largely independent of CDDEP for financial support, but they continue to collaborate and now serve as a resource for new members. After a successful initial 3-year phase culminating in the First Global Forum on Bacterial Infections, held in New Delhi in October 2011, the Gates Foundation supported the establishment of GARP in a second group of countries: Nepal, Tanzania, Mozambique, and Uganda.

Antibiotic Access

Despite GARP's emphasis on reducing the excessive use of antibiotics, we must keep in mind that in Nepal, as in so many countries, many people have little or no access to antibiotic treatment when it is needed. Pneumonia is still the leading cause of death for children under five and most of these children will have had no effective antibiotic treatment. These children—mankind—would clearly benefit from proper use. Although we are mainly concerned about resistance, the desire to preserve antibiotics must be balanced with the absolute need to get antibiotics to as many people who actually need them as possible. No saving of antibiotic resistance is worth losing lives that could have easily been saved with a few tablets.

DISEASE BURDEN AND ANTIBIOTIC RESISTANCE

Humans

As in many countries, no adequate surveillance system for tracking antibiotic resistance rates or documenting antibiotic use currently exists in Nepal. However, a number of individual studies have been carried out and are reviewed in detail in Chapter 4. These studies are summarized here, grouped by bacterial diseases that contribute to the morbidity and mortality burden in Nepal. These include respiratory infections, diarrheal infections, bloodstream infections, urinary tract infections, sexually transmitted infections and tuberculosis.

All of the studies identified reported relatively high rates of resistance. This is not surprising, as many studies worldwide tend to focus on patients with stubborn infections that are very likely to be antibiotic resistant. This body of literature is, therefore, unlikely to represent the situation in the general population. Nonetheless, it provides the only information available for assessing current levels of antibiotic resistance. Going forward, it will be important to establish some type of surveillance in order to reliably monitor antibiotic resistance trends in the population. In particular, if interventions to mitigate resistance are put in place, evaluating their effects will require tracking antibiotic resistance levels.

Burden of bacterial infections

The leading causes of premature mortality from infectious diseases in Nepal in 2010, were lower respiratory infections (pneumonia), diarrheal diseases, neonatal encephalopathy (birth asphyxia and birth trauma), preterm birth complications, and tuberculosis (GBD, 2010). Bacterial infections are implicated in all but the neonatal and preterm birth complications.

Rates of acute respiratory tract infections, diarrheal diseases, and bloodstream infections remain high. Diarrhea, pneumonia, and sepsis are major health risks for neonates and children under five, in spite of a significant decrease in infant mortality in Nepal of almost 70 percent over the past twenty years (World Bank, 2013).

Respiratory Infections

Infections of the respiratory tract are a major cause of death in Nepal, and are the most common cause of morbidity and mortality in children under five years of age.

Most common are upper respiratory tract infections (ARIs), which are primarily caused by viruses, with some bacterial infections. More serious are lower respiratory tract infections, including pneumonia, a leading cause of death of infants, children and the elderly. Lower respiratory tract infections are also caused by viruses and other organisms, in addition to bacteria.

The most common bacterial causes of pneumonia in Nepal (and worldwide) are several species of *Streptococcus, Staphylococcus aureus*, *Klebsiella pneumoniae*, *Haemophilus influenzae* type b, and *Pseudomonas aeruginosa*. Some bacteria, such as methicillin-resistance *S. aureus*, the well-known MRSA, are more likely to be acquired in hospitals or other healthcare facilities and are known as healthcare acquired infections (HAIs).

Eight studies were identified, all conducted between 2004 and 2011, reporting antibiotic resistance of *Streptococcus pneumoniae* and *K. pneumoniae* isolates from respiratory infections in Nepal. In all studies, more than half of all isolates were resistant to the commonly-used antibiotics cotrimoxazole and ciprofloxacin, with resistance increasing to both drugs from 2000 through 2008 (G. Shakya & Adhikari, 2012).

Diarrheal Infections

Diarrheal infections are also common, especially among children, and are the third leading cause of under-five mortality in Nepal. As with respiratory infections, most are caused by viruses (especially the genus *Rotavirus*), but an important minority are caused by bacteria, most commonly species of *Shigella*, *Campylobacter,* and *Salmonella* (including typhoid), *Escherichia coli*, and *Vibrio cholerae* (cholera). Most cases of viral and bacterial diarrhea can be treated with oral rehydration (and zinc, in some cases) and do not require antibiotics or other drugs for full recovery, with the exception of complicated, bloody diarrhea, or dysentery. However, antibiotics are often used to treat diarrheal infections, regardless of severity or cause.

Three studies were identified documenting antibiotic resistance among *Shigella* spp and three among *V. cholerae* in Nepal, all published since 2007. In the *Shigella* studies, most isolates were resistant to one or more of the antibiotics tested, which included ampicillin, nalidixic acid, cotrimoxazole and ciprofloxacin. In the largest study, out of 118 isolates, one-third were resistant to all four antibiotics (Kansakar, Malla, & Ghimire, 2007). Almost all *V. cholerae* isolates were resistant to nalidixic acid, cotrimoxazole, and furazolidone, the three drugs for which resistance levels were sought.

Bloodstream Infections

Major blood stream infections (often referred to as bacteremia) include neonatal sepsis, typhoid and meningitis. These infections are often very serious and require antibiotic treatment. These infections are prevalent in Nepal.

Neonatal Sepsis: Three out of the four sepsis studies, though all fairly small, reported resistance rates to antibiotics in bacteria that were responsible for neonatal infections in hospitals. Resistance rates of *S. aureus*, *K. pneumoniae*, *Pseudomonas* spp., *Acinetobacter* spp., and Gram-negative *Enterobacteriaceae* ranged from 50 to 100 percent for some drugs. Common drugs reported in these studies were ampicillin, cefotaxime, ceftriaxone, imipenem, ceftazidime, and piperacillin.

Typhoid and Paratyphoid (enteric fever): A comprehensive meta-analysis analyzed 32 antibiotic resistance studies conducted over 18 years (1993-2011) of *Salmonella* Typhi and *Salmonella* Paratyphi A., the main bacteria responsible for causing typhoid and paratyphoid.

Resistance of *S.* Typhi to ciprofloxacin increased from 2 percent in the 1998-2002 period to 11 percent in the 2008-2011 period. Resistance of *S.* Paratyphi A to ciprofloxacin increased from 4 percent between 1998 and 2002 to 14 percent between 2008 and 2011. From 2008-2011, resistance to nalidixic acid was 91 percent (Karki, Shakya, Cheng, Dumre, & Leder, 2013). In actual fact, nalidixic acid resistance better reflects ciprofloxacin resistance, hence this is staggering resistance to ciprofloxacin and calls into question treatment of enteric fever with ciprofloxacin.

Urinary Tract Infections

Urinary tract infections are common and can be appropriately treated with antibiotics, but resistance levels to first-line antibiotics can be very high. *E. coli* is the most common bacterial cause of these infections.

Nepal's National Public Health Laboratory reported on resistance rates from 2006 to 2010. Resistance rates were well above 50 percent for all the drugs tested, which included, in order of those with the most to least resistance; amoxicillin, cefixime, amoxicillin-clavulanic acid, nalidixic acid, ceftazidime and cefotaxime. Resistance to all drugs increased from 2006 to 2010 (G. Shakya et al., 2012).

Sexually Transmitted Infections

Antibiotic resistance studies on sexually transmitted infections remain limited in Nepal. The two identified studies reported expectedly high rates of resistance of *Neisseria gonorrhoeae* to penicillin, tetracycline and ciprofloxacin (Bhargava, Shakya, Mondal, & Rijal, 2010).

Healthcare Acquired Infections (HAIs)

Many patients acquire infections in hospitals and other health care facilities around the world, triggering heavy antibiotic use. These facilities are, thus, a potent breeding ground for antibiotic resistance. Most of the HAI studies in Nepal have reported a high prevalence of methicillin-resistant *S.aureus* (MRSA) and other resistant bacteria in patient isolates and on equipment. MRSA was frequently highly resistant to one or more of the common drugs used for treatment, such as cotrimoxazole, chloramphenicol and erythromycin. MRSA prevalence of up to 7 percent was also detected in studies looking at bacterial carriage rates (B. Shakya, Shrestha, & Mitra, 2010). The relatively few studies and lack of ongoing surveillance point to an underreporting of HAIs in Nepal.

Tuberculosis

Mycobacterium tuberculosis, the bacterial causative agent of tuberculosis in humans, is treated primarily with five first-line drugs: isoniazid, rifampin, ethambutol, pyrazinamide, and streptomycin. Reports of resistance to first-line drugs are discrepant, with some reporting relatively low resistance rates (3 and 18 percent, respectively for new and retreated cases) and others reporting rates that are quite high (35 percent and higher for each drug individually and up to 23 percent resistant to all first-line drugs. With increasing *M. tuberculosis* resistance to isoniazid and rifampin, two of the most powerful first-line drugs, MDR-TB is becoming more prevalent in Nepal.

World Health Organization Reported Antibiotic Resistance in Nepal

A recent World Health Organization report provided the first comprehensive review of the current state of global AMR surveillance (WHO, 2014). The report includes data from Nepal on antibiotic resistance rates for six combinations of bacterial pathogens and antibiotics. The bacteria were *E. coli*, *S. aureus*, non-typhoidal *Salmonella*, *Shigella* spp, *K. pneumoniae*, and *N. gonorrhoeae.*

Out of 140 isolates, 64 percent of *E. coli* isolates were resistant to fluoroquinolones and 38 percent were resistant to third-generation cephalosporins. Smaller data sets showed resistance rates of *S. aureus* to methicillin ranging from 2 to 69 percent. *K. pneumoniae* showed resistance to third-generation cephalosporins of 0 to 48 percent, while no resistance to carbapenems was detected (WHO, 2014).

Agricultural Animals

Animals are susceptible to infections just as humans are, and bacterial diseases in animals can require antibiotic treatment to prevent morbidity and to halt disease transmission. The livestock sector in Nepal is responsible for 11 percent of the total GDP, and animal health is important for sustaining productivity in this sector. However, inappropriate antibiotic use in animals can contribute to antibiotic resistance in humans. Epidemic investigations and disease surveillance of this industry are the charge of the Central Veterinary Laboratory.

The major diseases impacting animals in Nepal are foot and mouth disease, *peste des petits ruminants*, highly pathogenic avian influenza, and classical swine fever. The bacterial diseases of bovine and small ruminants are mastitis, black quarter disease and hemorrhagic septicemia, and common bacteria detected include Coagulase negative *staphylococci*, *Streptococcus* spp., *Staphylococcus* spp., and *E. coli*. The major diseases in poultry are salmonellosis, fowl typhoid and colibacillosis, while common bacteria detected include *Salmonella* spp. and *E. coli* (Thakuri, 2012).

In many countries, antibiotics are, or were in the past, used as growth promoters in food animals. The main reason for phasing out this practice (either voluntarily or by law) is to reduce the generation of antibiotic-resistant gut flora. Antibiotics are used both for growth promotion and as a disease preventive in Nepal, with low doses mixed with animal feed, with much the same result.

Very few studies of antibiotic resistant organisms in food animals and animal products have been carried out in Nepal, but those few do report a high prevalence of resistant organisms.

Consumption data can serve as a useful indicator for the potential overuse of antibiotics for therapeutic or sub-therapeutic purposes. Very few studies present such data, but their findings establish the need for stronger surveillance of antibiotic use in animals and the development of regulatory measures. A survey of distributors of veterinary medicine and feed supplements, reported in 2003, in six Nepali districts reported annual sales of NRs. 492 million (USD 6,739,726). Antibiotics represent 13 percent of

the total expenditure on veterinary drugs (Bhandari & Singh, 2003). In a recent survey, the volume of veterinary antibiotic sales rose more than 50 percent between 2008 and 2012. In that survey, 71 percent of veterinary drug sales were based on prescription by retailers, not veterinary professionals (Khatiwada, 2012).

INTERVENTIONS TO CONTAIN ANTIBIOTIC RESISTANCE AND THE NEPALI SITUATION

Antibiotics should be used whenever they might save a life or cure an infection that is unlikely to be self-limited, but even those appropriate uses lead eventually to antibiotic resistance emerging. In those cases, mankind (or animal kind) has benefited from the use. Equally, however, resistance emerges from inappropriate use. The ideal would be to use antibiotics only when a person or animal benefits. In practice, that is a difficult ideal to meet, because diagnoses are difficult to make and many suspected bacterial infections are caused by viruses or other conditions.

Reducing resistance requires limiting antibiotic use while ensuring access for those who need treatment. The six primary strategies to improve antibiotic use are to:

1. Reduce the need for antibiotics by improving public health;
2. Improve hospital infection control and antibiotic stewardship;
3. Rationalize antibiotic use in the community;
4. Reduce antibiotic use in agriculture;
5. Educate health professionals, policy makers and the public on sustainable antibiotic use; and
6. Ensure political commitment to meet the threat of antibiotic resistance.

1. Reducethe need for antibiotics by improving public health

The best way to reduce the need for antibiotics is to reduce the burden of bacterial disease treated with antibiotics which, ultimately, reduces resistance levels. The main benefit, of course, is a healthier populace. Vaccination is the most powerful engine of disease prevention available worldwide. Clean water, improved sanitation and adequate and safe food are also priorities. All of these have strong constituencies related to their main aims of improving the health of the population.

Situation in Nepal

The National Immunization Program in Nepal has achieved coverage rates of over 80 percent for most diseases, and remains a government priority. By 2009, the program

included routine immunizations for children and pregnant women against 10 diseases: tuberculosis, polio, diphtheria, pertussis, tetanus, hepatitis B, *H. influenzae* type b, measles, tetanus and Japanese encephalitis. The government has added a childhood pneumococcal vaccine to the national immunization schedule in 2015, but has not yet scheduled addition of *Rotavirus* vaccine. Other national prevention programs include control of malaria, tuberculosis, leprosy, and HIV.

2. Improve hospital infection control and antibiotic stewardship

Improving infection control in hospitals and other healthcare facilities can also reduce the need for antibiotics by reducing the spread of healthcare associated infection and therefore, the need for antibiotics. This also benefits patients immensely and at least in some instances, is cost-saving. Antibiotic stewardship programs in hospitals are designed to improve antibiotic prescribing through a number of mechanisms, which should be tailored to the facility. These can include guidelines for appropriate treatment, with consultations required for treatment outside of the guidelines, required cultures when antibiotics are started without a firm diagnosis and step down antibiotics to narrow-spectrum when appropriate, among others. Finally, the establishment of sentinel surveillance or point prevalence systems for antibiotic resistance can provide data to guide clinical decisions and policies at the hospital level.

Situation in Nepal

National infection control and antibiotic stewardship guidelines have not been established in Nepal. Some hospitals have developed manuals on nosocomial infection control and have appointed infection control committees and others have done neither (Ohara et al., 2013). This is an area with great potential for improvement.

Evidence of inappropriate prescribing in Nepal has been shown in several studies across different healthcare facilities, particularly for ampicillin, amoxicillin, ceftriaxone and gentamicin. In 13 studies of prescribing practices, nearly all found that antibiotics were the most frequently prescribed type of medication and most patients were prescribed more than one antibiotic at a time, usually without bacterial confirmation or susceptibility testing. Antibiotics were prescribed inappropriately in 10 to 42 percent of patients, and were prescribed for both therapeutic and prophylactic purposes.

There is also evidence that, especially in lower level health facilities, healthcare workers often do not give the correct dosages of antibiotics and often advise patients incorrectly on how to take them.

Appropriate antibiotic treatment requires trained staff and well-equipped facilities to ensure a correct diagnosis as well as surveillance for resistance. While there are a number of public and private laboratories located across Nepal, the availability of well-trained microbiologists, pathologists, and other higher level specialists and technicians to manage these labs remains limited (Mishara, Tiwari, & Yadav, 2012).

Nepal has made some progress in establishing AMR surveillance for infections in humans. The Ministry of Health and Population ran an AMR surveillance program from 1998-2003 and the Nepal Public Health Laboratory and the Epidemiology and Disease Control Division took over these efforts in 2004. The AMR surveillance network has grown to include 13 participating public laboratories. Their most recent report, with results from 1999 to 2012, includes *V. cholerae*, *Shigella* spp., *S. pneumoniae*, *H. influenzae*, *N. gonorrhoeae*, *Salmonella* spp. and *E. coli*. MRSA and other HAI-related bacteria are not included in the surveillance program. No private sector laboratories contribute to the network.

3. Rationalize antibiotic use in the community

Antibiotics may be prescribed by physicians and other healthcare workers inappropriately (e.g., without confirmation or for a common cold, usually caused by a virus and self-limiting) or they may be purchased directly by consumers without recourse to the healthcare system. Many patients self-treat with antibiotics, including prior to hospital admission, which can contribute to increased resistance rates.

Situation in Nepal

Antibiotics can be purchased routinely in the community, from pharmacies, drugs shops and informal drug sellers. It is likely that healthcare providers also prescribe antibiotics unnecessarily for coughs, colds and diarrhea.

The Community Based Integrated Management of Childhood Illness (CB-IMCI) program addresses major diseases that affect children from 2 months to 5 years old in all 75 districts of the country. The program aims to covers all children under 5 years old. Acute respiratory infections, pneumonia, and diarrhea are the most prevalent conditions, and each of these has important bacterial causes (in addition to viral and parasitic causes). However, neonatal mortality remains high, and the CB-IMCI program could be expanded to include detection and care for neonatal sepsis infections. This program should be improving antibiotic use in Nepal, but formal evaluation for this purpose has not been conducted.

4. Reduce antibiotic use in agriculture

Antibiotics are needed to treat bacterial infections in animals, just as they are in humans. However, it has become common practice to use antibiotics in food animals for two other purposes: 1) growth promotion and 2) to prevent disease. These two practices may be indistinguishable, as both rely on "sub-therapeutic" doses—small amounts of antibiotics are usually mixed with animal feed at the retail level. Farmers have also been using antibiotics to prevent disease in animals in place of improved sanitation and conditions for raising animals for decades. Use of antibiotics for growth promotion has been banned in Europe and some other countries, and has been deemed an inappropriate use of antibiotics.

Situation in Nepal

Although there is a great deal of anecdotal evidence of antibiotic use in animals, few studies have documented the specific formulations and quantities used. Therefore, the quality and quantity of veterinary antibiotics being used are difficult to assess. Antibiotics for animals are commonly bought from informal vendors with no training, and usually inadequate storage conditions.

Since the early 1990s, veterinary medicines and vaccines have been supplied by the private sector but the field suffers from lack of availability, high cost, poor quality, low awareness and poor distribution.

No veterinary AMR surveillance network exists. The Central Veterinary Laboratory conducts epidemic investigation and some disease surveillance. Nepal currently lacks veterinary drug use regulations and guidelines.

5. Educate health professionals, policy makers and the public on sustainable antibiotic use

In spite of the seriousness of the issue, antibiotic resistance is still not widely recognized as a problem, even within the health community. Raising awareness about resistance and educating health professionals, policy makers and the public on the diverse roots of resistance will support efforts to improve practices and build policies that improve rational antibiotic use.

Health professionals can be targeted through updates to curricula and to treatment guidelines, as well as through the implementation of hospital antibiotic stewardship

programs, as mentioned previously. Policy makers can be engaged through the dissemination of relevant research and participation in national and regional meetings. Finally, the public can be educated through awareness campaigns. Effective education should have an impact on many other areas, including improving rational use at the hospital and community level, reducing use in agriculture and building political commitment for the issue.

Situation in Nepal

Antibiotic resistance has received little attention in the education of professionals from community workers to physicians, and including nurses, pharmacists, veterinarians and the associated professions.

6. Ensure political commitment to meet the threat of antibiotic resistance

Addressing antibiotic resistance is a shared responsibility of health professionals, the private sector and the public. Ensuring a comprehensive response requires political commitment as well. Government cannot solve all the problems, but they can legislate, regulate and take a variety of other actions to lay the groundwork for action and represent the public interest.

Situation in Nepal

GARP-Nepal is the first multi-sectoral group working on antibiotic resistance in the country, and has engaged with key stakeholders from human, animal and environmental health. Further efforts to raise awareness and build cooperation between experts have the potential to improve antibiotic use as they engage in advocacy and take action in their respective sectors. In addition, increasing collaborative research will strengthen the knowledge base on which policies can be built. Creating policies to guide antibiotic use is the most sustainable way to ensure that changes are implemented and maintained. At present, though there are laws that guide drug purchasing, distribution and use, and a national formulary that outlines essential medicines and the type of health providers that may prescribe them, no national policies are in place to guide antibiotic use.

With this situation analysis and these recommendations, GARP-Nepal has the tools to begin building political and popular support to address this important issue.

From the situation analysis launch: participant observations and recommendations

The executive summary of this situation analysis was the focus of discussion at a launch meeting held in Kathmanduon December 15, 2014. More than 60 stakeholders and interested professionals from various sectors in Nepal, including the Minister of Health and Population, spoke or were in attendance. The reactions and recommendations offered by participants are summarized below.

Raise awareness about the public health crisis

Antibiotic resistance is a huge public health challenge and could quickly become a crisis if no action is taken to ensure the sustainability of these life-saving drugs. It should be of concern to clinicians, patients, government and the public at large. The dissemination of critical information on resistance to all audiences is important in building behavior change. The media can play a significant role in this process and should be involved in awareness raising campaigns. Efforts should be made to appeal to the public and policy makers by demonstrating the economic impact of antibiotic resistance in addition to the impact on human and animal health.

Collaborate with the government to improve guidelines and policies

Some national guidelines and policies are not sufficient to curb antibiotic resistance in their current form. For instance, the "National Antibiotic Treatment Guideline" is not consistent with technical standards for the treatment of infectious diseases and should be reviewed and updated in line with scientific evidence.

In addition, some policies currently in place may conflict with policies designed to encourage rational antibiotic use. For instance, female community health volunteers were authorized to distribute cotrimoxazole when treating respiratory infections at community level. While this policy may decrease the disease burden of ARI in children, treating infections without a laboratory diagnosis or clinician consultation may encourage the overuse of and resulting increase in resistance to cotrimoxazole. This policy should be revised and updated to promote the rational use of antibiotics.

Focus on antibiotic use and resistance in animals

Antibiotic use in livestock is currently uncontrolled, and the threat imposed by the irrational use of veterinary antibiotics is quite significant. It is important that activities to investigate and curb antibiotic use in animals be implemented.

Consistent with the recommendations of the International Federation for Animal Health, there should be a separate policy and agency responsible for regulating the use of veterinary antibiotics in country.

Ensure access

Many rural areas of Nepal lack access to health care, and increasing access to health services and personnel should be a major national focus to improve and safeguard human health.

Take an ecological approach

Antibiotic resistance is a multi-sectoral issue that requires the participation of many diverse partners and sectors. Efforts should target the individual all the way up to the societal level.

RECOMMENDATIONS AND NEXT STEPS

Recommendations:

Considering the information in this situation analysis and the pressing global need, the overarching recommendation of the GARP-Nepal Working Group is:

> **A national strategic plan for the use of antibiotics that preserves their effectiveness into the future and gains the maximum health benefits from their appropriate use.**

Developing and implementing such a plan will require the collaboration of all relevant sectors, including private and public sectors, and those involved with both human and veterinary health.

At the global level, the development of new antibiotics, alternatives to antibiotics and new diagnostics for bacterial and other infectious diseases is an important aspect of curbing antibiotic resistance, and these efforts should be increased.

Next steps

The development and implementation of a strategic plan will take time, and some activities can and should be implemented while this process is ongoing, providing more information and impetus. Financial and human resource limitations dictate that activities have to be staged. GARP-Nepal will initially focus on the development of curricula for healthcare workers and the implementation of studies to assess antibiotic use and resistance in animals. Concurrently, working group members will continue to use this situation analysis and other information to generate interest in and action on antibiotic use and resistance.

References

Bhandari, S., & Singh, S. (2003). Annual consumption of veterinary medicines and feed supplement in Nepal.

Bhargava, D., Shakya, B., Mondal, K., & Rijal, B. (2010). Emergence of penicillin resistant Neisseria gonorrhoeae. *Journal of Institute of Medicine, 32*(1), 15-18.

GBD. (2010). Global Burden Of Diseases Profile: Nepal Global Burden of Diseases, Injuries, and Risk factors Study 2010: Institute for Health Metrics and Evaluation.

Kansakar, P., Malla, S., & Ghimire, G. (2007). Shigella isolates of Nepal: changes in the incidence of shigella subgroups and trends of antimicrobial susceptibility pattern.

Karki, S., Shakya, P., Cheng, A. C., Dumre, S. P., & Leder, K. (2013). Trends of etiology and drug resistance in enteric fever in the last two decades in Nepal: a systematic review and meta-analysis. *Clinical Infectious Diseases, 57*(10), e167-e176.

Khatiwada, S. (2012). Trend of Antimicrobial use in Food Animals of Nepal

Mishara, S., Tiwari, B., & Yadav, B. (2012). Status of pathology professionals. *Journal of Nepal Health Research Council*.

Ohara, H., Pokhrel, B. M., Dahal, R. K., Mishra, S. K., Kattel, H. P., Shrestha, D. L., . . Sherchand, J. B. (2013). Fact-finding Survey of Nosocomial Infection Control in Hospitals in Kathmandu, Nepal—A Basis for Improvement. *Tropical medicine and health, 41*(3), 113.

Shakya, B., Shrestha, S., & Mitra, T. (2010). Nasal carriage rate of methicillin resistant Staphylococcus aureus among at national medical college teaching hospital, Birgunj, Nepal. *Nepal Med Coll J, 12*(1), 26-29.

Shakya, G., & Adhikari, B. R. (2012). Ten-years surveillance of antimicrobial resistance pattern of Streptococcus pneumoniae in Nepal. *African Journal of Microbiology Research, 6*(20), 4233-4238.

Shakya, G., Upadhayay, B. P., Rijal, N., Adhikari, S., Sharma, S., & Kansakar, P. (2012). Changing Trends of Antibiotic Resistance in Escherichia coli. *JHAS, 2*(1), 42-45.

Thakuri, K. (2012). Status of Animal Disease Outbreak and Identification of Provisional Disease Free Zone/ Area. *Vet Epidemiol Centre, DoHS, 2:3*.

WHO. (2014). *Antimicrobial resistance: global report on surveillance*: World Health Organization.

WorldBank. (2013). Child Mortality Estimates. 2015: UN Inter-agency Group for Child Mortality Estimation (IGME).

Meeting with veterinarians

Dissemination workshop, December 15, 2014

GARP-N inaugural meeting

About NPHF

Nepal Public Health Foundation (NPHF) was established in April 2010 with a mission to have concerted public health action, research, and policy dialogue for health development, particularly of the socio-economically marginalized population. NPHF has a vision to ensure health as the right and responsibility of the Nepali people with its focus on major public health issues such as Health Policy and Systems, Human Resource, Communicable Disease, Non-Communicable Disease, Malnutrition etc.

NPHF has been able to act as an umbrella organization to voice concern in public health thematic areas and at a same time developing as an academic organization by continuously supporting to individuals and organizations through training and workshops. NPHF board comprised of professionals from multiple disciplines.

Besides, NPHF acts as a watch dog to scrutinize Government policies and operations especially its adherence to national and international commitments such as commitments made in Interim Constitution, 2007 of Nepal and Health related Millennium Development Goals (1, 4, 5 and 6), aid harmonization, alignment and partnership including national level governance and accountability responsiveness and public private partnership.

About CDDEP

The Center for Disease Dynamics, Economics & Policy (CDDEP) was founded with the objective of using research to support better decision-making in health policy. The CDDEP team employs a range of expertise— including economics, epidemiology, disease modeling, risk analysis, and statistics—to produce actionable, policy-oriented studies on malaria, antibiotic resistance, disease control priorities, environmental health, alcohol and tobacco, and various other issues.

The strength of CDDEP derives from its researchers' experience in addressing national and regional health problems, as well as truly global challenges, while recognizing the circumstances in which the answers must fit. The outcomes of individual projects go beyond the usual models to inspire new strategies for analysis, and innovative approaches are shared through publications and presentations focusing specifically on methodology.

Founded in 2009 as a center of Resources for the Future, CDDEP is an independent non-profit organization. With offices in Washington D.C. and New Delhi, CDDEP works with distinguished academics and policy analysts around the world.

Cover Photo Credit: Alex Traedway, Nick Simon's Institute

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

नेपाल जनस्वास्थ्य प्रतिष्ठान
PREVENTION PROMOTION PROTECTION
NEPAL PUBLIC HEALTH FOUNDATION
ESTD:2010