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# A situational analysis of antibiotic prescription, dispensing practices and resistance pattern in Nepal: Are we losing the battle?

Hemank K.C. <sup>1\*</sup>, Rashmi Shrestha <sup>2</sup>, Suraj Vaish <sup>1</sup>, Earnest Budhathoki <sup>3</sup>, Anisha Bhusal <sup>3</sup>, Ranjit Kumar Mahato <sup>4</sup> and Sanjeev Gurung <sup>1</sup>

<sup>1</sup> Valley College of Technical Sciences, Purvanchal University, Kathmandu, Nepal.
 <sup>2</sup> Kathmandu Multiple College, Purvanchal University, Kathmandu, Nepal.
 <sup>3</sup> HOPE International College, Purvanchal University, Kathmandu, Nepal.

<sup>4</sup> Om Health Campus, Purvanchal University, Kathmandu, Nepal.

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#### Abstract

**Background:** Antibiotics are widely utilized to treat infections and provide preventative and therapeutic benefits in animal and human healthcare. However, because of the emergence and spread of resistance mechanisms, which cause bacteria to become less susceptible to antibiotics and other treatments and less effective, antimicrobial resistance (AMR) has grown to be one of the most significant worldwide public health concerns. Low- and middle-income countries (LMICs) such as Nepal have a high rate of infectious illnesses and antibiotic resistance, which can lead to both human and financial losses.

**Methods:** The information for the scenario analysis was acquired through a review of published and grey literature, as well as interviews with important stakeholders from all sectors.

**Conclusion:** Besides knowing all the challenges of antibiotic resistance, the programs assuring towards AMR is conducted in Nepal in very infrequent way. The antibiotic use should be optimize by giving various personalized treatment approaches and accurate diagnosis which plays vital roles in minimizing unnecessary antibiotic prescriptions. We can organize different awareness programs to reduce antibiotic resistance that may enhance the proper use of antibiotic with proper dose and prescription in accordance health care professionals. Interpreting all the problems, government should give more priority to antibiotic resistance and should be able to minimize the problems. If antibiotic resistance is not taken in a very serious way by all the healthcare workers like doctors, nurses, pharmacists, lab technicians, etc. then the battle we are fighting leads to be defeated and problem will never end.

**Keywords:** Antibiotics; Antibiotic prescription; Antibiotic dispensing; Antibiotic resistance; Nepal; Situational analysis.

#### 1. Introduction

Antibiotics play a significant role in modern medicine, where they are widely utilized to treat infections and provide preventative and therapeutic benefits in animal and human healthcare. However, because of the emergence and spread of resistance mechanisms, which cause bacteria to become less susceptible to antibiotics and other treatments and less effective, antimicrobial resistance (AMR) has grown to be one of the most significant worldwide public health concerns. This has increased morbidity and mortality as well as prolonged hospital stays and increased healthcare costs (1). 76,704 tons of veterinary antibiotics were consumed worldwide in 2018, with a clinical consumption of 14.3 defined

<sup>\*</sup> Corresponding author: Hemank K.C.

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daily doses (DDDs) per 1000 people per day (2). Antibiotic-resistant bacterial (ARB) is to blame for almost twenty-five percent of healthcare-associated infections in healthcare institutions, and by 2050, it may be the cause of 10 million deaths (3).

Reducing the use of antibiotics might lessen risks to the public's health as well as "resistome" in the environment, animals, food chains, and healthcare facilities (4–6). Lower respiratory tract infections and diarrheal illnesses were among the top ten global causes of death in 2019, resulting in 4 million deaths overall, even after the development of the Global Antimicrobial Resistance Surveillance System (GLASS) in 2015 (7). High levels of resistance have been observed globally in 2020 in some dangerous bacterial diseases. This was common among several Gram-negative pathogens. Of these, the World Health Organization (WHO) 2017 priority list includes *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and extended spectrum  $\beta$ -lactamase-producing Enterobacteriaceae as critical priority bacterial infections (8). If AMR fails to be addressed fast, we will definitely be entering a post-antibiotic era in which the mortality rate from even common illnesses will continue to increase (9).

Low- and middle-income countries (LMICs) such as Nepal have a high rate of infectious illnesses and antibiotic resistance, which can lead to both human and financial losses (10-12). Antimicrobial resistance is caused by a variety of causes, including self-medication, the availability of antibiotics as over-the-counter (OTC) medications, using antibiotics for an extended period of time, and inadequate regulation (13).

The LMICs have been a major contributor to the 65% global growth in the usage and consumption of antibiotics. According to data, the daily defined doses (DDDs) of antimicrobial use have increased from 3.2 to 6.5 billion (14). The highest usage of broad-spectrum antibiotics in India was also indicated by another study (15,16). Data from Nepal is still being collected.

The widespread distribution of infectious diseases in Nepal, the inappropriate use of antibiotic therapy, the use of antibiotics as growth promoters in animals, and the absence of regulations governing the prescription and use of antibiotics are some of the causes that have contributed to AMR. Numerous research demonstrate that Nepal prescribes antibiotics needlessly (17).

Animal infections are treated with antibiotics in the same way as human infections. Although the health of animals is a significant source of productivity, every use also adds to the increase in resistance. Antibiotics are frequently added to animal feed in small amounts in order to stimulate growth or prevent illness. In the case of growth promotion, this suboptimal use has no positive impact on animal health; in the case of disease prevention, it is a preventable or minimized practice. Yet, it raises the likelihood of bacteria developing resistance (18).

The information for the scenario analysis was acquired through a review of published and grey literature, as well as interviews with important stakeholders from all sectors. There is currently no sufficient surveillance system in Nepal for tracking antibiotic resistance or documenting antibiotic use, making reliable reporting of trends impossible. To locate more papers, we searched the bibliographies of all relevant publications. Only papers that contained original data on antibiotic use, dispensing practice, and resistance in people were considered.

## 2. Antibiotic Prescription practices in Nepal

In hospitals across the globe, these are currently the most often prescribed medications. In poor nations where infectious diseases continue to be a major problem, antibiotics are especially important for preventing illness and preserving health. However because of an increase in antibiotic resistance, their benefit has been severely restricted lately. Inappropriate prescribing methods are the primary cause of the widespread resistance of microorganisms to the most widely used and effective first-line medicines (19–21). Although these prescribers' qualifications, training, and authority to prescribe medications vary, their prescribing practices must be studied on a regular basis. In Nepal, antibiotic prescription is governed by plenty rules and regulations, notably the Drug Act 1978; yet, it has not been found to be followed by a majority of practitioners (22). Antibiotics were defined in this regulatory framework as drugs that required a prescription to be dispensed. Similarly, the Nepal Pharmacy Council has developed a clear guideline for registered pharmacists to dispense prescription drugs (23). Yet, in fact, drug dispensers rarely follow proper pharmacy practice, and this sector is also extremely uncontrolled (20,24).

The study's demonstrates that the antibiotics prescribed do not fully follow the recommended standards. The issue of prescribing antibiotics excessively is also brought up in this study. Any type of illness, including fever, infections, etc., is treated using antibiotics. Examining the data for 2015, we find a significant 49.3% of the prescribed medication was ceftriaxone (antibiotic). During that period, antibiotics represented almost fifty percent of all prescribed

medications. However, in 2016, the largest percentage of all antibiotic prescriptions was for nitrofurantoin was 36.7% which is comparatively less. If we see all the data that was collected from 2015-2024, the use of antibiotics is more than 25% each year which is very high in amount. So, taking these data in account we reach in a conclusion that there is no appropriate prescription of antibiotics in Nepal also high proportion of people are practicing self-medication. Therefore, to prevent antibiotic resistance, unnecessary antibiotic prescriptions should be discouraged through raising awareness and implementing strict regulations.

Table 1 From 2015 -2024 yearly comparison commonly prescribed antibiotic pattern at Health care settings in Nepal

| Year | Name of the antibiotics/class | Prescription (%) | References |  |  |
|------|-------------------------------|------------------|------------|--|--|
| 2024 | Amoxicillin-clavulanate       | 26.11            |            |  |  |
|      | Azithromycin                  | 21.34            | (25)       |  |  |
|      | Metronidazole                 | 7.64             |            |  |  |
|      | Cefixime                      | 17.52            |            |  |  |
|      | Ofloxacin                     | 7.01             |            |  |  |
|      | Ciprofloxacin                 | 3.18             |            |  |  |
|      | Cefpodoxime                   | 5.10             |            |  |  |
| 2023 | Penicillin                    | 24.11            | (26)       |  |  |
|      | Macrolides                    | 11.61            |            |  |  |
|      | Quinolones                    | 17.42            |            |  |  |
|      | Cephalosporins                | 19.19            |            |  |  |
|      | Nitroimidazole                | 11.09            |            |  |  |
| 2023 | Ceftriaxone                   | 5.5              | (27)       |  |  |
|      | Cefixime                      | 7.5              |            |  |  |
|      | Cefazolin                     | 0.5              |            |  |  |
|      | Ampicilin                     | 0.5              |            |  |  |
|      | Amikacin                      | 13.5             |            |  |  |
|      | Levofloxacin                  | 14               |            |  |  |
|      | Ofloxacin                     | 0.5              |            |  |  |
|      | Nitrofurantoin                | 6.5              |            |  |  |
|      | Cefodoxime                    | 0.5              |            |  |  |
|      | Cefotaxime                    | 0.5              |            |  |  |
|      | Meropenem                     | 3                |            |  |  |
|      | Vancomycin                    | 1.5              |            |  |  |
|      | Polymyxin B                   | 1                |            |  |  |
|      | Gentamicin                    | 2.5              |            |  |  |
|      | Doxycycline                   | 0.5              |            |  |  |
| 2022 | Amoxicillin + clavulanic acid | 52.8             | (28)       |  |  |
|      | Clarithromycin                | 28.08            |            |  |  |
|      | Clotrimazole                  | 11.61            |            |  |  |
|      | Neomycin                      | 7.49             |            |  |  |

| 2022 | Ceftriaxone                  | 72.3  | (29) |  |  |
|------|------------------------------|-------|------|--|--|
|      | Azithromycin                 | 66.8  |      |  |  |
|      | Levofloxacin                 | 57.9  |      |  |  |
|      | Meropenem                    | 53.08 |      |  |  |
|      | Cepodoxime                   | 59.8  |      |  |  |
|      | Doxycycline                  | 51.0  |      |  |  |
| 2022 | Ceftriaxone                  | 32.7  | (30) |  |  |
|      | Levofloxacin                 | 15.3  |      |  |  |
|      | Piperacillin and Tazobactam  | 9.8   |      |  |  |
|      | Metronidazole                | 8.1   |      |  |  |
|      | Meropenem                    | 6.5   |      |  |  |
|      | Azithromycin                 | 5.4   |      |  |  |
|      | Amikacin                     | 5.4   |      |  |  |
|      | Cefuroxime                   | 3.8   |      |  |  |
|      | Ceftriaxone and Sulbactam    | 3.8   |      |  |  |
|      | Ceftriaxone and Tazobactam   | 3.2   |      |  |  |
|      | Cefotaxime                   | 2.1   |      |  |  |
|      | Gentamicin                   | 2.1   |      |  |  |
|      | Flucloxacillin               | 1.6   |      |  |  |
|      | Linezolid                    | 1.6   |      |  |  |
|      | Nitrofurantoin               | 1.6   |      |  |  |
|      | Vancomycin                   | 1.0   |      |  |  |
|      | Cotrimaxazole                | 1.0   |      |  |  |
| 2021 | Ampicillin                   | 4.4   | (31) |  |  |
|      | Meropenem                    | 3.84  |      |  |  |
|      | Aztreonam                    | 0.3   |      |  |  |
|      | Vancomycin                   | 3.88  |      |  |  |
|      | Cefotaxime                   | 48.74 |      |  |  |
|      | Ceftriaxone                  | 9.43  |      |  |  |
|      | Cefdinir                     | 0.94  |      |  |  |
|      | Cefixime                     | 6.91  |      |  |  |
|      | Cefipime                     | 0.62  |      |  |  |
|      | Ceftazidime                  | 1.25  |      |  |  |
|      | Ceftriaxone+ Tazobactam      | 31.76 |      |  |  |
| 2020 | Cefixime                     | 33.33 | (32) |  |  |
|      | Cefixime and Clavulanic Acid | 15.79 |      |  |  |
|      | Gentamycin                   | 12.28 |      |  |  |
|      | Nitrofurantoin               | 12.28 |      |  |  |

|      | Piperacillin and Tazobactam     | 8.77 |      |
|------|---------------------------------|------|------|
|      | Cefpodoxime and Clavulanic Acid | 7.02 | -    |
|      | Cefpodoxime                     | 5.26 | _    |
|      | Levofloxacin                    | 3.51 | -    |
|      | Ciprofloxacin                   | 1.75 | _    |
| 2019 | Amoxicillin                     | 16.6 | (33) |
|      | Ampicillin                      | 3.0  | _    |
|      | Cloxacillin                     | 1.8  | _    |
|      | Amoxicillin Clavulanate         | 0.69 |      |
|      | Doxycycline                     | 1.3  | _    |
|      | Ceftriaxone                     | 22.9 | _    |
|      | Cefixime                        | 3.9  |      |
|      | Cefpodoxime                     | 1.6  |      |
|      | Ciprofloxacin                   | 11.4 |      |
|      | Levofloxacin                    | 3.2  |      |
|      | Azithromycin                    | 4.4  |      |
|      | Cotrimoxazole                   | 7.2  |      |
|      | Metronidazole                   | 12.5 |      |
|      | Amikacin                        | 1.7  |      |
|      | Amikacin                        | 1.3  |      |
| 2019 | Azithromycin                    | 20.1 | (34) |
|      | Amoxicillin + Clavulanic acid   | 19.2 |      |
|      | Cefixime                        | 14.2 |      |
|      | Amoxycilin                      | 7.4  |      |
|      | Mupirocin                       | 5.0  |      |
|      | Levofloxacin                    | 4.4  |      |
|      | Cefadroxil                      | 3.2  |      |
|      | Clarithromycin                  | 3.0  |      |
|      | Cefpodoxime                     | 2.4  |      |
|      | Doxycycline                     | 2.4  |      |
|      | Metronidazole                   | 2.4  |      |
| 2018 | Ceftriaxone                     | 16.8 | (35) |
|      | Amoxicillin + Cloxacillin       | 12.9 |      |
|      | Azithromycin                    | 10.0 |      |
|      | Cefixime                        | 6.4  |      |
|      | Cloxacillin                     | 6.1  |      |
|      | Ciprofloxacin                   | 5.3  |      |
|      | Cefpodoxime                     | 4.5  | 1    |

|      | Amoxicillin + Clavulanic acid | 4.4  |      |
|------|-------------------------------|------|------|
|      | Amikacin                      | 3.9  |      |
| 2017 | Piperacillin + Tazobactum     | 28   | (36) |
|      | Cefoperazone + Sulbactum      | 7.33 |      |
|      | Ampicilin + Cloxacilin        | 4.66 |      |
| 2016 | Nitrofurantoin                | 36.7 | (37) |
|      | Ofloxacin                     | 20.4 |      |
|      | Cephalexin                    | 10.2 |      |
|      | Norfloxacin                   | 8.2  |      |
|      | Ciprofloxacin                 | 8.2  |      |
|      | Cloxacillin                   | 4.1  |      |
|      | Cefixime                      | 4.1  |      |
|      | Ampicillin                    | 4.1  |      |
|      | Amikacin                      | 2.0  |      |
|      | Levofloxacin                  | 2.0  |      |
| 2015 | Ceftriaxone                   | 49.3 | (38) |
|      | Cefotaxime                    | 26.2 |      |
|      | Cefixime                      | 24.3 |      |
|      | Azithromycin                  | 20.0 |      |
|      | Cefpodoxime                   | 14.3 |      |
|      | Erythromycin                  | 6.2  |      |
|      | Cefuroxime                    | 6.2  |      |
|      | Meropenem                     | 1.8  |      |
|      | Vancomycin                    | 1.2  |      |
|      | Ampicillin                    | 0.6  |      |
|      | Ofloxacin                     | 0.6  |      |
|      | Ceftazidine                   | 0.6  |      |
|      | Chloramphenicol               | 0.6  |      |

#### 3. Antibiotic dispensing practices in Nepal

Dispensers include both untrained medication dealers and competent pharmacists who sell antibiotics in pharmacies or drug stores. Dispensers work in 'drug shops', also known as 'Aushadi pasal' in Nepali, which refer to private or public pharmacies where antibiotics can be purchased (39). In Nepal, drug shops are regulated by the Drug Act of 1978. Pharmacists, assistant pharmacists, and pharmacy 'professionals' with minimal training can register with the Department of Drug Administration (DDA), which regulates medicine quality and use (40).

In addition, drug shops are poorly regulated and frequently manned by untrained employees. While there are gaps in antimicrobial policies, regulations, and implementation, there is insufficient engagement with policymakers and stakeholders to ensure optimal use (41–43). Dispensing antibiotics without a prescription is regarded one of the factors to the development in AMR in Nepal (44–46).

The study shows one of the main causes of antibacterial resistance is the unrestricted distribution of antibiotics. Our findings imply that this practice is still widespread in numerous parts of Nepal. Despite the lack of research on the dispensing rate, we were able to locate some data spanning a few years. The table no. 2 data shows there is more than 50-60% dispensing rate every year. Most of the time, pharmacy employees didn't ask about the patient's medical history or suggest that they see a doctor. The government must intervene through regulation and education to raise the level of expertise and conduct of drug salesmen, pharmacy assistants, and pharmacists. To stop self-medication, health education is also crucial for the general public.

 Table 2
 From 2015 - 2024 yearly comparison commonly dispensed antibiotic pattern at Health care settings in Nepal

| Year | Name of the antibiotics/ class | Dispensing (%) | Reference |  |  |
|------|--------------------------------|----------------|-----------|--|--|
| 2023 | Amoxicillin                    | 78.9           | (47)      |  |  |
|      | Azithromycin                   | 78.3           |           |  |  |
|      | Cefexime                       | 57.2           |           |  |  |
|      | Ciprofloxacin                  | 43.4           |           |  |  |
|      | Amoxiclav                      | 14.3           |           |  |  |
|      | Cefodoxime                     | 16.9           |           |  |  |
|      | Ampicillin                     | 12.7           |           |  |  |
| 2021 | Azithromycin                   | 67.6           | (48)      |  |  |
|      | Amoxicillin                    | 21.6           |           |  |  |
|      | Cefixime                       | 8.1            |           |  |  |
|      | Cipro                          | 1.8            |           |  |  |
|      | Cephalexin                     | 0.9            |           |  |  |
| 2020 | Cotrimoxazole                  | 7              | (13)      |  |  |
|      | Roxithromycin                  | 1              |           |  |  |
|      | Azithromycin                   | 69             |           |  |  |
|      | Ofloxacin                      | 16             |           |  |  |
|      | Ciprofloxacin                  | 11             |           |  |  |
|      | Ceftriaxone                    | 19             |           |  |  |
|      | Cefixime                       | 40             |           |  |  |
|      | Amoxicillin+Clavulanic Acid    | 35             |           |  |  |
|      | Ampicillin+Cloxacillin         | 43             |           |  |  |
|      | Amoxycillin                    | 68             |           |  |  |
| 2019 | Cefixime                       | 16.9           | (49)      |  |  |
|      | Amoxicillin                    | 12.2           |           |  |  |
|      | Cefpodoxime                    | 10.3           |           |  |  |
|      | Ampicillin+cloxacillin         | 8.7            |           |  |  |
|      | Ciprofloxacin                  | 8.7            | 1         |  |  |
|      | Azithromycin                   | 7.8            |           |  |  |
|      | Metronidazole                  | 7.6            |           |  |  |
|      | Amoxicillin+clavulanate        | 4.9            |           |  |  |

|      | Cefadroxil               | 2.5   |      |
|------|--------------------------|-------|------|
|      | Cephalexin               | 2.5   |      |
|      | Levofloxacin             | 2.2   |      |
|      | Ofloxacin                | 2.2   |      |
|      | Amoxicillin+cloxacillin  | 1.7   |      |
|      | Cefixime+clavulanic acid | 1.7   |      |
| 2017 | Penicillin               | 68.3  | (50) |
|      | Cephalosporins           | 69.8  |      |
|      | Fluoroquinolones         | 49.1  |      |
|      | Macrolides               | 57.1  |      |
|      | Sulfonamide              | 19.33 |      |

#### 4. Resistance pattern in Nepal

Antimicrobial resistance is a significant global public health issue. Beta-lactam antibiotic resistance in Enterobacteriaceae is increasingly being reported by both critically ill hospitalized patients and outpatients (51). Antibiotic use has increased since the discovery of penicillin in 1943. Tetracycline was discovered in 1950, but only nine years later, tetracycline-resistant Shigella was found (52). Methicillin antibiotic was discovered in 1960, but methicillin-resistant *S. aureus* was discovered two years later. Later on, penicillin-resistant pneumococcus, vancomycin-resistant enterococcus, levofloxacin-resistant pneumococcus, and cephalosporin-resistant organisms were identified, and their rates increased exponentially (53).

In 2015–2016, it was found that *E. coli* were resistant to third-generation cephalosporins, ciprofloxacin, and ampicillin, whereas in 2017, the alarming prevalence of antibiotic resistance was found in practically all samples of *E. coli*. The years 2018, 2019, and 2020 saw the discovery of an increased rate of resistance to commonly use and relatively safer antibiotics, such as cephalosporins and quinolones. These findings highlight the urgent need for alternatives to these classes of antibiotics, as *E. coli* demonstrated high resistance to ampicillin and all isolated strains showed 100% sensitivity to the drug nitrofurantoin, which was still the drug of choice for treating *E. coli* caused urinary tract infections. A third-generation cephalosporin called cefotaxime was found to be resistant to nearly one-sixth of the *E. coli* isolates in 2022. Colistin was more vulnerable to multiple medication resistance in 2023. Uropathogens showed significant resistance to ceftazidime in 2024, while respiratory and circulatory infections showed resistance to carbenicillin. (From table no. 3)

Based on the provided data (From table no. 4), it appears to be a report on the antibiotic resistance rates (%) of various antibiotics from 2015 to 2024. The resistance rate indicates the percentage of bacteria that were not affected by the antibiotic, meaning a higher percentage suggests more resistance. Gentamicin noticed a fluctuating trend, with a peak in 2021 (27%) and a significant drop in 2020 (4%). The rate in 2024 is 22.22%, indicating a recent increase. Piperacillin-Tazobactam and Amoxicillin has only one data point each in 2024, showing high resistance rates of 33.3% and 100%, respectively. Oxacillin (or Cefoxitin) resistance decreased over time, from a peak of 43% in 2017 to 11.4% in 2024. Ciprofloxacin increasing trend in resistance, peaking at 63.2% in 2023 before a slight decrease to 52.94% in 2024. Vancomycin remarkably consistent with a 0% resistance rate, except for a minor increase in 2017 (3%). Teicoplanin and Telavancin has limited data, but Teicoplanin had a 26% resistance rate in 2021 and then dropped to 0%, and Telavancin was at 6% with no follow-up data. Clindamycin a general increasing trend in resistance, peaking at 46.4% in 2024. Erythromycin increasing resistance over the years, reaching the highest rate of 64.3% in 2024. Chloramphenicol has limited data points but showed an increase from 3% to 20% by 2024. Penicillin is notable for its significant increase to 100% resistance in 2024, up from 44% in 2015. Cotrimoxazole (Trimethoprim/Sulfamethoxazole) resistance varied, with an increase to 67.8% in 2024. Ampicillin and Cloxacillin both show varied resistance rates, with Ampicillin hitting 100% in 2024. Doxycycline shows an increase in resistance, up to 23% in 2024.

Table 3 Antibiotic Resistance pattern of E. coli

| Antibiotics                 | 2015-<br>2016 | 2017 | 2018 | 2019 | 2020  | 2022 | 2023 | 2024 |
|-----------------------------|---------------|------|------|------|-------|------|------|------|
| Cefotaxime                  | 100           | -    | -    | 42.1 | 23.49 | 15.5 | 20.9 | 74.6 |
| Ceftazidime                 | 100           | 45   | 51.0 | -    | 23.49 | -    | 48.8 | 78.8 |
| Ceftriaxone                 | 100           | 45   | 50.0 | -    | 22.29 | 34.4 | -    | 68.6 |
| Cefixime                    | 94.4          | 71   | 53.0 | 60.5 | 36.14 | -    | 16.4 | -    |
| Cephalexin                  | 94.4          | 87   | -    | 59.8 | -     | -    | -    | -    |
| Nalidixic acid              | 94.4          | -    | -    | -    | 34.93 | -    | -    | -    |
| Norfloxacin                 | 944           | -    | -    | -    | 34.93 | -    | 64.4 | -    |
| Ofloxacin                   | 88.8          | -    | 41.3 | 46.5 | 36.14 | -    | 61.9 | -    |
| Cotrimoxazole               | 61.0          | 42   | 48.6 | 50   | 36.75 | 14.7 | 68   | 55.9 |
| Ciprofloxacin               | 88.8          | 78   | 45.2 | -    | 37.95 | 10.6 | 63.9 | 69.5 |
| Doxycycline                 | 72.2          | -    | -    | -    | -     | -    | -    | -    |
| Aztreonam                   | 47.0          | 43   | -    | -    | -     | -    | -    | -    |
| Amikacin                    | 35.0          | 14   | 9.9  | 13   | 7.83  | -    | 14.4 | 19.5 |
| Imipenem                    | 35.0          | 5    | 4.8  | -    | -     | -    | -    | -    |
| Meropenem                   | -             | -    | 4.7  | -    | -     | -    | 10.4 | 15.3 |
| Tigecycline                 | -             | 0    | 0.3  | -    | -     | -    | -    | -    |
| Amoxycillin                 | -             | 48   | -    | -    | 97.59 | -    | 82.5 | 39.0 |
| Gentamicin                  | 41.0          | 33   | -    | -    | 6.02  | 0.5  | 16.4 | 21.2 |
| Ampicillin                  | -             | 87   | 74.9 | 71.9 | -     | 40.5 | 92.5 | 93.2 |
| Nitrofurantoin              | -             | -    | 8.1  | 4.4  | 0     | -    | 30.4 | -    |
| Piperacillin-<br>tazobactam | 27.0          | 33   | 11.5 | -    | -     | -    | 19.8 | -    |
| Levofloxacin                | -             | 67   | -    | -    | -     | -    | 22.1 | 66.1 |
| Cefodoxime                  | -             | -    | -    | 60.5 | 21.08 | -    | -    | -    |
| Tetracycline                | -             | -    | -    | -    | 31.32 | 20.7 | -    | -    |
| Chloramphenicol             | -             | -    | -    | -    | -     | 3.5  | -    | 28.8 |
| Cefepime                    | -             | -    | -    | -    | -     | -    | 20.8 | 59.3 |
| Carbenicillin               | -             | -    | -    | -    | -     | -    | -    | 98.3 |
| Imipenem                    | -             | -    | -    | -    | -     | -    | -    | 31.4 |
| Ertapenem                   | -             | -    | -    | -    | -     | -    | -    | 13.6 |
| References                  | (54,55)       | (56) | (57) | (58) | (59)  | (60) | (61) | (62) |

# **Table 4** Antibiotic Resistance pattern of S. aureus

| Antibiotics                      | 2015 | 2017 | 2018  | 2020 | 2021 | 2023 | 2024  |
|----------------------------------|------|------|-------|------|------|------|-------|
| Gentamicin                       | 2    | 25   | 26.66 | 4    | 27   | 13.5 | 22.22 |
| Piperacillin-Tazobactam          | -    | -    | -     | -    | -    | -    | 33.3  |
| Amoxicillin                      | -    | -    | -     | -    | -    | -    | 100   |
| Oxacillin (or cefoxitin)         | -    | 43   | 39    | -    | -    | -    | 11.4  |
| Ciprofloxacin                    | 24   | 30   | 33.33 | 32   | 20   | 63.2 | 52.94 |
| Moxifloxacin                     | -    | -    | -     | -    | -    | -    | -     |
| Trimethoprim<br>sulfamethoxazole | 25   | -    | -     | -    | -    | -    | -     |
| Fusidic acid                     | -    | -    | -     | -    | -    | -    | -     |
| Vancomycin                       | -    | 3    | -     | -    | -    | -    | -     |
| Teicoplanin                      | -    | -    | -     | -    | 26   | -    | -     |
| Telavancin                       | -    | -    | -     | -    | 6    | -    | -     |
| Tigecycline                      | -    | -    | -     | -    | -    | -    | -     |
| Clindamycin                      | 5    | 21   | 56.66 | 13   | 21   | 39.9 | 46.4  |
| Daptomycin                       | -    | -    | -     | -    | -    | -    | -     |
| Erythromycin                     | 16   | 40   | 63.33 | 24   | 14   | 59.1 | 64.3  |
| Linezolid                        | -    | -    | -     | 12   | -    | -    | -     |
| Chloramphenicol                  | 3    | -    | -     | -    | -    | 10.7 | 20    |
| Fosfomycin                       | -    | -    | -     | -    | -    | -    | -     |
| Quinupristindalfopristin         | -    | -    | -     | -    | -    | -    | -     |
| Tetracycline                     | -    | 12   | -     | 20   | -    | -    | -     |
| Doxycycline                      | -    | -    | -     | -    | -    | -    | -     |
| Minocycline                      | -    | -    | -     | -    | -    | -    | -     |
| Penicillin                       | 44   | 58   | -     | 39   | -    | 91.6 | 100   |
| Amikacin                         | 0    | 10   | -     | -    | 25   | -    | 17.4  |
| Cefotaxime                       | 3    | -    | -     | -    | -    | -    | -     |
| Cephalexin                       | 14   | -    | 90    | -    | -    | 20.3 | -     |
| Cotrimoxazole                    |      | 30   | 30    | 21   | 13   | 39.5 | 67.8  |
| Ampicillin                       | -    | -    | 100   | 34   | 29   | -    | 100   |
| Cloxacillin                      | -    | -    | 93.33 | 9    | -    | 26.4 | -     |
| Azithromycin                     | -    | -    | -     | 34   | -    | -    | -     |
| Chlorpheniramine                 | -    | -    | -     | -    | 20   | -    | -     |
| Cetirizine                       | -    | -    | -     | -    | 5    | -    | -     |
| Doxycycline                      | -    | -    | -     | -    | -    | 28.8 | 23    |
| Meropenem                        | -    | -    | -     | -    | -    | -    | 50    |
| References                       | (63) | (64) | (65)  | (66) | (67) | (68) | (69)  |

### 5. Strategic taken by National Action Plan for AMR in Nepal

All antibiotics are antimicrobial but all antimicrobial are not antibiotics. The Global Action Plan (GAP) on Antimicrobial Resistance (GAP-AMR) outlines the commitment, perspectives, and roles of all relevant stakeholders, with clear and shared ownership and responsibilities, to address the intersectional dimensions of the problem. The goal of the GAP-AMR is to ensure the continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality- assured, used responsibly, and accessible to all those who need them. The success of the GAP depends on all countries developing their national action plans (NAPs) on AMR. The NAP-AMR clearly outlines the specific priorities and interventions to be implemented over the five-year period to tackle the public health challenge of AMR in Nepal (70). The five specific strategic priorities of the NAP-AMR are aligned with the GAP on AMR.

- Improve awareness and understanding of AMR through effective communication, education, and training,
- Strengthen the knowledge and evidence through surveillance,
- Reduce the incidence of infection through effective infection prevention and control,
- Optimize the use of antimicrobial agents in human, animal and food
- Promote investments for AMR activities, research, and innovations

#### 5.1. Improve awareness and understanding of AMR through effective communication, education, and training

Recognizing the Target Audience: Determine the main stakeholders and audience demographics in need of awareness regarding AMR, including healthcare practitioners, policymakers, veterinarians, agricultural workers, patients, and the general public.

Community Engagement: Encourage community involvement through grassroots efforts, involving local leaders, schools, and community organizations to distribute awareness and encourage responsible behavior.

Training and Education: Provide healthcare workers, veterinarians, and other interested parties with educational materials and training sessions on antibiotic caution, infection prevention, and antibiotic management.

#### 5.2. Strengthen the knowledge and evidence through surveillance

Tracking resistance pattern: Surveillance assists in monitoring the rise and spread of bacteria that resist antibiotics. It does this by examining samples from patients, animals, food items, and the environment. This helps surveillance systems recognize how resistance develops and spreads.

Supporting research: Surveillance data acts as a cornerstone for research on antibiotic resistance. It helps scientists explore how resistance develops, spreads, and how interventions can be effective. By analyzing this data, researchers can delve into the patterns of transmission, study genetic aspects, and conduct trials to develop strategies for combating antibiotic resistance

Strengthening labs in human, animal, food, and environmental sectors aids in collecting data for informed policymaking. Surveillance of AMR in these region provides crucial evidence for guiding policy decisions.

#### 5.3. Reduce the incidence of infection through effective infection prevention and control

Infection prevention and control measures are vital for curtailing the transmission of infections, including antibioticresistant bacteria, aiming to both prevent infections initially and contain their dissemination across healthcare facilities, communities, and various environments.

Alternative disease prevention: Promoting alternative disease prevention strategies, such as vaccination, biosecurity measures, and improved animal husbandry practices, offers a holistic approach to reducing the reliance on antibiotics in animals.

#### 5.4. Optimise the use of antimicrobial agents in human, animal, and food

Individualised Treatment: Personalised treatment involves selecting the most suitable antibiotics and doses for each patient, taking into account factors like age, existing health conditions, allergies, and prior antibiotic use. This customised approach enhances treatment effectiveness and reduces the chances of side effects and antibiotic resistance.

Accurate Diagnosis: Healthcare providers should conduct thorough clinical assessments and use relevant laboratory tests when required to precisely diagnose bacterial infections. This approach ensures antibiotics are only prescribed when necessary, preventing unnecessary use for conditions where antibiotics are ineffective, like viral infections or non-infectious illnesses.

Avoiding unnecessary uses: Avoid the unnecessary use of antibiotics for conditions where antibiotics are not indicated, such as viral infections like the common cold or influenza. Overuse of antibiotics in such cases contributes to the development of antibiotic resistance and can lead to adverse effects without providing clinical benefit.

#### 5.5. Promote investments for AMR activities, research, and innovations

Incentives for Innovation: Provide financial incentives, such as grants, tax credits, or prizes, to Incentivize private sector investment in research and development of new antibiotics, diagnostics, and vaccines targeting antimicrobial-resistant pathogens.

Research funding: Allocate financial resources to support research projects focused on understanding antimicrobial resistance mechanisms, developing new antibiotics and treatments, and exploring innovative infection prevention and control strategies.

Collaborations: Facilitate collaborations between government, academia, and private sector entities to combine resources and expertise, accelerating the research and development of antimicrobial solutions through enhanced access to funding, infrastructure, and intellectual property rights.

## 6. Way-Forward

As interpreting the current situation, the main problem in health sector of Nepal is antibiotic resistance. Besides knowing all the challenges of antibiotic resistance, the programs assuring towards AMR is conducted in Nepal in very infrequent way. The antibiotic use should be optimize by giving various personalized treatment approaches and accurate diagnosis which plays vital roles in minimizing unnecessary antibiotic prescriptions. Antibiotic resistance awareness programs should be conducted by health care institutions or other association like Nepal Pharmaceutical Association (NPA) etc. to reduce antibiotic use, reduce adverse consequences of antibiotic use and improve patient outcomes.

Lack of proper qualified laboratory personnel is the major disadvantage in Nepal to implement the antibiotic prescriptions in proper manner. Only a single laboratory having each and every facilities as per the guidelines cannot fulfill the need of everyone in a country. So, various laboratories and proper qualified staff is very necessary in maintaining or minimizing antibiotic resistance. As per the sources, there are many cases of people suffering from AMR which we are informed from various social media platforms like Pharma info Nepal, which is urged to be informed from different healthcare institutions or the government of Nepal. But, the government of Nepal lacks this ability. The antibiotic resistance cases are not collected properly and tracked which leads to the increment of antibiotic resistant in people. So, different health care institutions or association should be encouraged to provide awareness about antibiotic resistant.

Antibiotic resistance patterns in *E. coli* and *S. aureus* are increasing, posing a significant challenge in combating bacterial infections. *E. coli*'s resistance to critical antibiotics like cephalosporins and fluoroquinolones is concerning, while *S. aureus*'s escalating resistance rates to ciprofloxacin, erythromycin, and vancomycin are alarming, indicating the development of resistance mechanisms. As many people use antibiotics without prescription of health care professionals that may lead to major cause of antibiotic resistance.

Antimicrobial resistance is expected to lead to increased healthcare costs, reduced productivity, and a rise in poverty globally. So, we need to work together to ensure healthcare systems around the world are prepared for rising resistance and infection levels. We can also organize different awareness programs to reduce antibiotic resistance that may enhance the proper use of antibiotic with proper dose and prescription in accordance health care professionals. Health care professionals also need to provide proper counselling to the patients about the proper use and effects of antibiotic. Interpreting all the problems, government should give more priority to antibiotic resistance and should be able to minimize the problems.

If antibiotic resistance is not taken in a very serious way by all the healthcare workers like doctors, nurses, pharmacists, lab technicians, dispensers etc. then the battle we are fighting leads to be defeated and problem will never end.

#### 7. Take home messages

- Antibiotics are a limited and precious resource.
- Antibiotic resistance can affect anyone, of any age, in any country.
- Antibiotic resistance occurs naturally, but misuse of antibiotics in humans and animals are accelerating the process.
- Antimicrobial Stewardship Programs and appropriate use of antibiotics can contribute to reducing resistance and make a difference to patient safety and quality of care.

#### **Compliance with ethical standards**

#### Authors Contributions

HKC, SG and RS designed the study; SV collected the published paper. RKM and SG supervised the study. EB and AB analyzed the data. HKC, SV and RS wrote the original draft. HKC, SG and RKM reviewed the draft and finalized. All authors read and approved the final review.

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