NAME OF THE THESIS: ANTIBIOTIC RESISTANCE IN AFGHANISTAN

A thesis submitted in partial fulfilment of the requirement for the degree of

Master of Science in International Health

by

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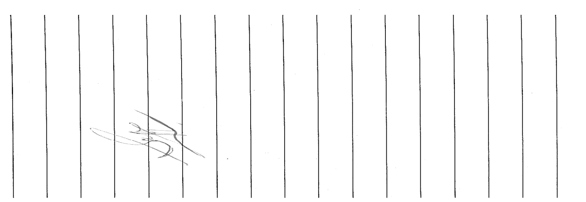
Afghanistan

Declaration: Where other people's work has been used (from either a printed source, internet, or any other source), this has been carefully acknowledged and referenced in accordance with departmental requirements. The thesis [Antibiotic Resistance in Afghanistan] is my own work.



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Master's In international health (9 September 2018 – 2 September 2021)

KIT (Royal Tropical Institute)/Vrije Universiteit Amsterdam, The Netherlands

September 2021

Organized by: KIT (Royal Tropical Institute) Amsterdam, The Netherlands

In co-operation with: Vrije Universiteit Amsterdam (VU) Amsterdam, The Netherlands

Antibiotic Resistance in Afghanistan

Summary/ Abstract

Anti-microbial resistance (AMR) is a global issue. A major contributing factor to this has been the increased and improper use of anti-microbial such as antibiotics. Issues such as use of antibiotics for the wrong intentions, and uncontrolled purchase of over-the-counter drugs. This study aims to look at AMR and especially antibiotic resistance in Afghanistan, its trends and contributing factors. Besides, it was aimed at reviewing the existing policies, strategies, and practices of AMR. Lastly, the study sought to review international guidelines and the best practices on AMR and make proper linkages to the country guidelines. This study was based on 2 approaches: 1) data collection and analysis from three reference laboratories and 2) literature review about antibiotic resistance in Afghanistan.

Data reviewed was obtained from three laboratories in different regions of Afghanistan, and they showed some of the most common pathogens, which are resistant to antibiotics. The available data (secondary data) for 2018 and 2017 from culture/Antibiogram tests from 3 reference laboratories in Afghanistan, Central Public Health Laboratory/Kabul, Regional Reference Lab of Jalalabad, and Regional Reference Laboratory of Kandahar were analyzed. Based on the data from the three regions, it is evident that resistant microorganisms are more prevalent in some regions than in others. For example, resistant *Pseudomonas aeroginosa (P. aeroginosa)* is common in Kandahar but not in Kabul. However, some resistant microorganisms are present in all regions. One of these is *Escherichia coli (E. coli),* which is found in all three regions. Information obtained from the literature review shows that for low-income countries such as Afghanistan, antimicrobial-resistant infections have become a major issue of concern. Since most of the population are low-income earners, an increase in the health care costs limits most of the population from accessing health care. Besides, due to the economic status of most of the population, they do not have a wide antibiotic choice. Afghanistan has developed a National Action Plan for Antimicrobial Resistance, but it is still not fully implemented in the country. Eventually, this may result in a higher burden from infectious diseases.

Keywords: anti-microbial resistance; antibiotics

List of Abbreviations and Acronyms:

AR: Antibiotic Resistance

AMR: Anti-microbial resistance

AST: Anti-microbial susceptibility test

CAPs: Community-acquired Pneumonias'

CDC: Center for Disease Control

CIP: Ciprofloxacin

CPHL: Central Public Health Laboratory

CTX: Ceftriaxone

CX: Cefotaxime

CVD: Cardiovascular Disease

CZX: Ceftizoxime

EMR: Eastern Mediterranean Region

GLASS: Global Antimicrobial Resistance Surveillance System

MRSA: Methicillin-resistant Staphylococcus aureus

NAP-AMR: National Action Plan on Antimicrobial Resistance

STI: Sexually Transmitted Infections

SXT: Sulfamethoxazole/ trimethoprim (Co-Trimoxazole)

TB: Tuberculosis

UTIs: Urinary Tract Infections

URTI: Upper respiratory tract infection

WHO: World Health Organization

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Chapter 1: Introduction

1.1 Background Information

When bacteria grow and adapt in an environment where antibiotics exist, antibiotic resistance develops. There are different definitions for Anti-Microbial Resistance, but the common one is; It is the capacity of bacteria, which can survive after exposure to a defined concentration of an antimicrobial substance (J. Acar(1) & B. Röstel (2)).

The development of resistance among bacteria is related to the extent and frequency of antibiotics use. It also depends on the environment: in hospitals (and hospital acquired infections) resistance is more common than in community acquired infections, due to the pressure of antibiotics; and probably it depends on the multiplication rate (growth rate) of the microorganisms. Resistance to one antibiotic can lead to resistance for other antibiotic from the same group when the antibiotics belong to the same class. The resistance among antibiotics also can rapidly spread from one microorganism, and one location to another microorganism and location through the exchange of genetic materials and treatment of such infections can be affected accordingly. Antibiotic-resistant bacteria are transmitted among human beings and animals through different means such as water, environment, and food. The spread of such bacteria is accelerated by human and animal movements, travel, and trade. It is essential to state that drug-resistant bacteria in different food products, may originate from plants or animals, which are consumed by human beings (J. Acar(1) & B. Röstel (2)) .

The Global Antimicrobial Resistance Surveillance System (GLASS) was developed in 2015 by World Health Organization (WHO) to support the Global Action Plan for Antimicrobial Resistance, and it should coordinate the actions for mitigating AMR at the national level in the member states (WHO, 2017). The overall goal of the GLASS is to ensure the availability of validated, standardized, and comparable data on AMR, which will be collected, analyzed, and shared with the countries for making informed decisions and provide evidence-based actions (WHO, 2017). Within the framework of the Global Antimicrobial Resistance Surveillance System (GLASS), data are collected on bacterial resistance, obtained from blood, stool, urine, urethral swabs, and cervical samples in human infections (Hajjeh & Mafi, 2016).

To understand the extent and impact of AMR on the populations, GLASS combines data from patients, epidemiological surveillance, and resistance from laboratories. To mitigate the existing challenges in data collection from the countries as advised by the GLASS, countries have been advised to implement the surveillance standards proposed gradually, based on their priorities and available resources (WHO, 2017).

The GLASS's primary focus is on the antibiotic-resistant bacteria, which are the major threats globally, specifically those bacteria, which are resistant to multiple drugs and that limit therapeutic options. The priorities vary in the different countries, so the components proposed by GLASS, the different pathogens to be surveyed, the specimens to be collected, are not fixed, and they are updated when necessary (WHO, 2017).

Afghanistan is one of the low-income countries, which has experienced about 40 years of war and conflict, and this has had an adverse effect on the health care system. The country has an overall sex ratio of 104 females to 100 males. The annual growth rate of the population is estimated at 2.2 %. The crude birth rate stands at 35 per 1000 persons while the general fertility rate is 159 per 1000 women (Ingle et al., 2018) In addition, the average household size of the country is 7.3. Although the life expectancy at birth has improved remarkably in the last decade, it remains low compared to the developing nations in the sub region. The life expectancy in Afghanistan stands at 63 years with females living longer than males (Ingle et al., 2018).

The demography of Afghanistan can be tabulated as follows (Year 2018, CSO Afghanistan)

Table 1:

Total population		34,940,837
Sex ratio at birth		104 males per 100 females
Crude birth rate		35/1000 population
Total fertility rate		5.1
General fertility rate		159/1000 women
Life expectancy at birth (years)		64
Country income group		Low income
Total expenditure on health per capita		87 USD
Gross national income per capita		560 USD

Data from Health Profile Afghanistan reveal that communicable diseases are the chief causes of mortality in the country, followed by diseases like maternal and neonatal complications, malnutrition, congenital anomalies, drug use and suicide. Non-communicable diseases cause about 20% of all the deaths in Afghanistan, and about 10% of deaths happen due to war, accident, or other injuries (WHO, 2017).

Data regarding non-communicable diseases reveal that cardiovascular disease (CVD) and stroke contribute to the greatest number of deaths in this category. Cancer is another ailment sharing about 11% of deaths from NCD's (WHO, 2017). Kidney diseases, Endocrine disorders including diabetes, and Gastroenterology, including liver together, share about 21% of deaths equally distributed among each of them (Ingle et al., 2018). Chronic respiratory disease causes approximately 6% of deaths among non-communicable diseases with neurological disorders contributing about 1% to the mortality from NCD's.

1.2 Anti-Microbial Resistance (AMR) and Antibiotic Resistance (AR):

From a global health perspective, the general topic is Anti-Microbial Resistance (AMR), so let us elaborate first on AMR then we will focus on Antibiotic Resistance. AMR refers to the expression of microorganism's ability to neutralize drugs, which are commonly used for the treatment of associated infections (World Health Report, (2007)). The microorganisms develop resistance through different mechanisms such as efflux pump (removing anti-microbials penetrating the microorganism), or enzymatic changes of anti-microbial drugs (e.g., by production and release of beta-lactamases by bacteria that break down the structure of antibiotics). The AMR includes different microorganisms Wsuch as virus, bacteria, fungus and all the products that are used to control them.

Antibiotic Resistance (AR) may occur naturally, where microorganisms that develop resistance become harder to control using ordinary antibiotics. Antibiotic resistance is to some extent a normal biological or evolutionary phenomenon, that under the pressure of antimicrobial use, resistant strains emerge. Additionally, human beings have been seen as some of the greatest contributors to antibiotic resistance. Where people buy antibiotics without a proper prescription, they contribute to making the microorganisms more y resistant to drugs (World Health Report, (2007). AR only includes bacteria and antibiotics, so it has a narrow spectrum.

1.3 Problem Statement

Anti-microbial resistance (AMR) is a global health problem and a kind of big threat to human beings. The global AMR rates have become alarming, where over 700 000 deaths worldwide can be attributed to anti-microbial resistant species due to tuberculosis (TB), human immune-deficiency virus (HIV), and malaria (Hajjeh & Mafi, 2016). During the last two decades, anti-microbial resistance became a global threat to public health systems. From the day, the first antibiotic was discovered, which provided significant benefits for the health and human medicine, the abuse and misuse of anti-microbial in human and veterinary medicine and microorganisms' biological processes have accelerated the worldwide growing phenomenon of AMR (WORLD HEALTH REPORT, (2007)).

The resistance against antibiotics has become an epidemic, which has been described in many pathogens within different contexts. Still, some of the infections such as methicillin-resistant Staphylococcus aureus (MRSA) and Streptococcus Pneumonia have shown a global spread of drug resistance (Spellberg et al., 2008).

The appropriate use of antibiotics is an issue that is addressed by every nation in the world. The reason for this is that the level of antibiotic resistance has gone up. Every country has experienced antibiotic resistance in one or another form, making it necessary to address this issue. For example, in 2000, records indicate that more than 54 billion standard units of antibiotics were consumed. In ten years from 2000, the figure increased gradually by 36% (Naimi et al., 2017). The increase has been continuing, and this has brought about a public health crisis. The problem is not only affecting middle-income countries where the use of antibiotics is considered a right that cannot be denied. Important reasons for the increase in antibiotic resistance are an increase in over-the-counter sales of antibiotics, inappropriate prescribing, and high consumption of antibiotics among people even for diseases and conditions that are supposed to be treated by other means or drugs and use of antibiotics in agriculture and veterinary (J. Carlet, 2015).

Recently resistance among microorganisms has become a global public health problem, where we are all in the battle to evade microbial resistance, and it has become a global public health problem (Felmingham, 2002).

Another consequence of AMR is that it leads to increasing costs, as newer antibiotics are often much more expensive. This is particularly worrisome for LMIC's, as cheap first-line antibiotics are no longer effective.

Antibiotics enable and reinforce the modern medicine of today, from major surgery to the cesarean section as well as the treatment of cancer (Felmingham, 2002). Antibiotics are overused and misused, both in human and animal health, which can threaten the effectiveness of anti-microbials (Felmingham, 2002). In addition, the prevention and treatment of various infections caused by fungi, parasites, and bacteria is threatened by AMR.

Anti-microbial resistance (AMR) stands as a growing threat to global public health, which transcends socioeconomic divisions as well as national boundaries. Anti-microbial resistance (AMR) does not only affect human beings but also affects animals and environmental health. While AMR may be viewed from one perspective, the best thing is to view it as a multi-faceted problem, which has economic, health, environmental, food security and safety, as well as human implications. This approach is referred to as the "one health" approach. Thus, there is a need to address the threat that is posed by AMR as a global health and multi-sectoral priority (I.Roca1, M. Akova2, 2015).

The reported rates of AMR in the Eastern Mediterranean Region (EMR) have reached dangerous levels both in health facilities and in the community, which can threaten the response of public health to many communicable diseases, such as pneumonia, malaria, TB, HIV/AIDS, healthcare-acquired infections and STI (Hajjeh & Mafi, 2016). At the south Asian level, antibiotic resistance is also a concern for the health care sector. Southeast Asian countries have employed locally relevant policy structures to drive the antibiotic resistance agenda. There is a need to look at the strategies which have reduced the burden of antibiotic resistance in developed countries to apply them in the countries within the South Asian countries. Thus, such strategies need to be evaluated before they are implemented to ensure that they fit the Asian context.

There are also cases where some countries experience higher rates of resistance than others. Usually, countries with poor health care systems are likely to experience higher rates of resistance than those with an advanced health care system. While this is not always the case, it may be so where variables such as the strength of health care system is considered. Poor countries, with weak health systems, may continue longer using relatively old antibiotics for which resistance has already developed as newer antibiotics may be more expensive. A study in Pakistan has highlighted that Low- and Middle-Income Countries (LMICs) seem to be a reservoir for AMR (*Mishal S Khan1, Anna Durrance-Bagale. 2019*). Additionally, in LMICs, where standard treatment guidelines either don't exist or are badly adhered to, there is usually the possibility of the health care workers over-prescribing drugs, and this leads to over usage of drugs, thus resulting in antibiotic resistance. A study in Pakistan has shown that AMR is a public health challenge, and it has revealed the trend of AMR in one of the hospitals in Lahore (Carly Ching1, Summiya Nizamuddin2, 2018)

1.4 Justification

Human bodies have always been faced with different challenges that make them vulnerable to diseases and infections. These range from infections such as TB and pneumonia to other diseases such as cancer, among others. To treat these conditions or reduce pain and suffering in cases such as surgeries, antibiotics have been used. Some antibiotics have been used for quite a long time before resistance developed, other and newer antibiotics may have taken much shorter, also depending on the way they are used. Antibiotics are part of the essential drugs needed to address many priorities public health problems, and resistance to antibiotics is a global threat that needs to be addressed by all countries.

Antibiotic Resistance is also a public health problem in Afghanistan, although there is hardly any data at country level, some small studies have revealed that Antibiotic Resistance is existing, which is due to misuse and overuse of antibiotics that are very common, and additionally, all antibiotics can be easily acquired over the counter without prescription (Bahrmand et al., 2009). It is worth mentioning that Afghanistan has developed national action plan (NAP) for AMR, but it has been implemented partially.

In Afghanistan there is some knowledge and information about irrational use of antibiotics, but there is little information about the resistance of microorganisms against antibiotics in Afghanistan. Therefor it is important to understand better about the situation of AR in Afghanistan, by the case, I would like to conduct this study to address this issue and reveal some facts about the situation of resistance of microorganisms against antibiotics in Afghanistan. The results of the study will help the public health authorities and policy makers for informed decision making.

1.5 Objectives

This study was guided by a general objective and specific objectives, as indicated below.

1.5.1 General Objective

To review the public health situation in Afghanistan in relation to antibiotic resistance and guide policy formulation to address this problem.

1.5.2 Specific Objectives

- i) To describe the burden of AR, its trends and contributing factors.
- ii) To analyze data about AR from 3 reference laboratories in Afghanistan.
- iii) To review international guidelines and best practices on AMR and make comparisons to the country guidelines.
- iv) To make recommendations on policies in relation to AMR.

Chapter 2: Methodology:

This study focuses on two main parts; 1) Literature Review and 2) Data Analysis; so, the methodology for every part has been described below:

2.1: Methodology for Literature Review:

The literature on AR was reviewed at global, regional, and then at country level in terms of the existing data about the burden of AR, Risk Factors, existing policies, strategies, and action plans. In order to support the UN General Assembly (UNGA) declaration on AMR in 2016, an Interagency Coordination Group (IACG) was established. The IACG developed a framework for addressing AMR in 2017, called The "Framework for Action Supported by the Interagency Coordination Group", which was used as a framework for the literature review of this research (AMR Framework, 2017).

The AMR framework consists of 14 content areas, which are divided in 3 groups:

1. Reduce need for antibiotics or unintentional exposure to antibiotics.

2. Optimize use of medicines.

3. Invest in innovation, research, supply, and access of antimicrobials:

For each of the above group, different content areas have been identified as illustrated in the below table 1. Totally there are 14 content areas (AMR Framework):

Table 2: Content Areas from AMR Framework:

Group area	Content areas
1. Reduce need for antibiotics or unintentional exposure to antibiotics:	Human infection prevention and control
	Clean water and sanitation
	Animal Infection Prevention and control
	Food and Safety
	Environmental Contamination

2. Optimize use of medicines	Human Use
	Animal and agriculture use
	Laboratory capacity and surveillance
3. Invest in innovation, research, supply, and access of antimicrobials:	Basic Research
	Development of new Therapeutics
	Access to all Therapeutics
	Diagnostic development and access
	Vaccine development and access
	Quality and Falsified Medicines

Content areas with Next steps: In the AMR Framework developed by IACG, for each one of the content areas mentioned above, next steps have been identified as illustrated in the below table 2, to enable the countries how to work on the content areas and achieve the main areas. In this study only the following content areas from the above have been reviewed in the literature review chapter based on Afghanistan context, because these areas have been prioritized in Afghanistan National Action Plan for AMR or some work has been done for the content areas as they are in the health sector, while no action or very little has been done for the other content areas.

Table 3: Next Steps for Content Areas from AMR Framework:

Group Area	Content Areas	Next Steps
1. Reduce need for Antibiotics	**Human Infection Prevention and control:**	Allocate & integrate (into national budgets) funding to develop proper health infrastructures across the world
		Allocate funding for research to understand implication of AMR in IPC
		Develop & improve IPC education and training for health workers, and continuously assess their IPC skills
2. Optimize Use of Medicine	**Human Use**	Encourage countries to undergo JEE assessment
		Include AMR in education and training for health workers
		Develop & roll out tailored awareness campaigns for public, patients and Professionals
		Develop & roll out evidence-based treatment and prophylaxis guidelines for health care workers tailored to countries resistance
		Expand and link existing surveillance systems (e.g., GLASS)
3. Invest in Innovation	**Access to all Therapeutics:**	Develop innovative mechanisms to ensure access without limiting incentives to develop and make new drugs available.

		Promote affordable access of old and new antimicrobials to those who need them

Based on above contents recommended by the IACG in the AMR Framework, the literature review was carried out for Afghanistan to find out the areas already completed and the areas, which still need more efforts to be achieved. The sources for this research were obtained from different databases. The below table illustrates the sources and the search criteria for the literature review:

Table 4: Searching criteria literature review.

Sources	Searching terms	Year of Publication	Language
Google Scholar PubMed World Health Organization Lancet	Antimicrobial Resistant, antibiotic resistance, Afghanistan and Antimicrobial Resistance policies and Strategies for Antimicrobial Resistance, Consequences of Antibiotic Resistance, Antibiotic Resistance at global level, Practices for addressing Antimicrobial Resistance	2001 – 2019	English

2.2: Methodology for Data Analysis (Secondary data):

The data for use in this research was collected from secondary sources that are relevant to the topic. This study used the lab results from specimens having been analyzed in these 3 labs, or surveillance based on routinely collected data for clinical purposes. The three Reference Laboratories from where data was analyzed are Central Public Health Laboratory (CPHL) in Kabul, Regional Lab in Jalalabad, and Regional Lab in Kandahar. Data on AMR was collected through the GLASS by specific database system created by WHO called "whonet". The participating labs provide data on AST to GLASS. Afghanistan is also included in the countries, that have been reporting on AMR to GLASS; so far only one Reference Lab from Afghanistan; the Central Public Health Lab (CPHL) has been identified to report to GLASS. In this study beside the CPHL, two other reference labs, which are not part of GLASS, also have been included to be able to get more representative data on AR from the country. According to Afghanistan National Action Plan for AMR, they will expand more reporting sites to GLASS in the future. These two other laboratories (Kandahar and Jalalabad Reference Labs), which are not part of reporting to GLASS, are reference labs in the regions, but so far not included in the GLASS reporting.

These methods are information about the national surveillance system status through a global questionnaire survey, collection of AMR data through case finding surveillance system, where the specimens are routinely sent to the laboratories, and collection of data on patient and population from national surveillance sites for monitoring the AMR in the different risk groups.

Afghanistan has the Drug and Food Quality Control Laboratory, but they are not performing culture and Antibiogram. Only that laboratory is dedicated to the analysis of food and medicine quality control.

Under this method, the available data (secondary data) for 2017 and 2018 from culture/Antibiogram tests from 3 reference laboratories in Afghanistan; Central Public Health Laboratory/Kabul, Regional Reference Lab of Jalalabad, and Regional Reference Laboratory of Kandahar were analyzed.

As being WHO AMR Focal Point in Afghanistan, I have been working with collecting routinely AMR data from reference laboratories, so I used this data (secondary data) from the microbiology unit of the 3 reference laboratories (Central Public Health Laboratory (CPHL), Kandahar and Jalalabad) to conduct my study. As all the data had been recorded manually in the register books of the 3 reference labs, so specific data sheet forms were developed to enable us to compile the anonymized data, organize the data, enter the data smoothly into the computer and analyze them accordingly.

The available data with at least one positive pathogen was reviewed for 2017 and 2018 from the 3 reference labs and were analyzed. The data from the labs was analyzed based on the kind of pathogens that were found to be present. The analysis showed the commonest pathogens and the least common pathogens in each of the samples from the labs. The pathogen that was most common was accurately reviewed to find out its resistance against various antibiotics and if it was the most resistant. Data was also analyzed based on the ages of the patients from whom it was collected. The purpose of this was to determine whether a specific pathogen is common among different age groups or affects a specific age group.

2.2.1 Inclusion and Exclusion Criteria

The inclusion criteria used were as follows:

i. Culture and Antibiogram test results from blood, stool, urine, Semen, Vaginal Swab, or cerebrospinal fluid (CSF).
ii. Age: Any age group
iii. Only samples with a positive result after the culture and antibiogram susceptibility test.

Note: Due to lack of electronic registration system in the reference labs, the collection of data on all the tested samples, was challenging.

Chapter 3: Literature Review

3.1 Introduction

Literature has looked at the methods of estimating the burden of anti-microbial resistance (AMR). Anti-microbial resistance (AMR) leads to some economic impacts, which researchers have been trying to study. The lack of studies on the topic arises from the fact that anti-microbial resistance (AMR) remained an issue of very little concern until recently when it has been studied deeply following the realization that its impact was increasingly becoming influential especially in the economic sector as well as in the hospital settings by the delayed recovery of patients (Poke et al., 2013).

3.2 Background to Antibiotic Resistance

Anti-Microbial Resistance is a common concept with almost all drugs that have been (over)used. Even the earliest drugs such as Penicillin, which was discovered in 1928 by Alexander Fleming has also experienced resistance by some microbes, thus rendering it ineffective (O'Dowd, 2014). Research has shown that germs will always look for ways to survive and resist new drugs (O'Dowd, 2014). Thus, the first few years of the usage of a new drug may turn out to be very effective. However, with time, the germs develop resistance to the drug as they seek to survive. Additionally, germs are sharing their resistance, and this is making it very difficult for people to treat the conditions caused by such germs. Resistant germs identified for Penicillin are Penicillin-resistant *Staphylococcus aureus, Streptococcus pneumonia* and *Neisseria gonorrhea.* For Vancomycin there are *Enterococcus faecium* and *Staphylococcus aureus (*Woolhouse et al., 2015). For Methicillin there is Methicillin-resistant *Staphylococcus aureus.*

3.3 Patient Burden of Antimicrobial Resistance (AMR) or Clinical Outcomes of Treatment

Anti-microbial resistance (AMR) affects patient recovery. A study by "Lynn Peters (2019)" showed that AR is risky to the recovery of the patient and has been a cause of a higher mortality rate among neonates with Health Care Associated Infections. The trend of AMR has been increasing both in human and veterinary medicine. A study conducted by the University of Kentucky Diagnostic Laboratory found out high levels of resistance among Staphylococcus spp to some antibiotics in canine specimens, also they highlighted the increasing temporal trends of resistance among the microorganisms. The major growing temporal trends of resistance were detected against antibiotics of Beta-Lactam class ($P<0.001$) (amoxicilline-clavunate, oxacillin, cephalothin and penicillin ($P=0.024$) (Julia G Conner 1, Jackie Smith. 2018). Additionally, it has revealed that when microorganisms become resistant to antibiotics, the treatment is needed with other antibiotics, which are less effective or may have more adverse effects.

Mousavi (2018) observed that when antibiotic resistance increases, cases of ineffective treatment increases.

3.4 Estimating the Economic Burden of AMR

Researchers have been grappling on the question as to whether anti-microbial resistance (AMR) is associated with any economic impacts (Shallcross et al., 2015). Nations like Afghanistan have overlooked issues such as anti-microbial resistance (AMR), which have the capability of affecting the economy. The money dedicated to repeated treatments could have been used to develop other areas of the economy. Studies have also shown that there exists a relationship between anti-microbial resistance (AMR) and psychosocial impact. This is majorly observed in the case of Tuberculosis patients (Lesho et al., 2014). In Afghanistan, multidrug resistant tuberculosis has affected many patients. This type of tuberculosis is resistant to drugs that used to treat it before. Many patients are rushing to using these drugs to no avail. As a result, stigma and social isolation increase for such patients. Due to the increased stigma and self-isolation, such patients find it hard to engage in economic activities, and this affects the economy adversely (Ghafur, 2013).

While studies have looked at the economic impacts of anti-microbial resistance (AMR), there have not been credible attempts to quantify this effect by giving an exact figure. However, a few studies have looked at the amount of money lost as a result of anti-microbial resistance (AMR).

According to a study carried out in Thailand (Hadi et al., 2006), about 38,481 patients died, who had hospital acquired infections of AMR in 2010. The same study also estimated the cost of about 202 million USD for the treatment AMR infections in 2010, and the amount of 1.3 billion USD was the cost of AMR related morbidity and premature deaths in 2010. In Thailand, a further study also suggested that in 2010, additional 43% of deaths were due to hospital acquired multi drug resistant bacterial infections. (Hadi et al., 2006). However, such exercise or data is not available in Afghanistan.

3.5 Antibiotic Prescription in Kabul, Afghanistan

Kabul is the capital city of Afghanistan and has a population of more than six million people who depend on private and public hospitals in Kabul for medical services. Mousavi's (2018) study found out that 66% of the prescriptions given in Kabul are antibiotics. Some of the commonly prescribed antibiotics are ceftriaxone, metronidazole, amoxicillin, azithromycin, ciprofloxacin, cefixime, levofloxacin, and clarithromycin, among others. Out of these, ceftriaxone and metronidazole are the mostly prescribed drugs.

A study carried out by Mousavi (2018) looked at the way antibiotics were being prescribed in Kabul, Afghanistan. The study found out that antibiotics are among the most used drugs. Due to their wide usage, they ought to be prescribed in an appropriate manner for them to be adequately effective. It also highlighted that improper, unsystematic prescribing, prevalent use, illogical and abuse of antimicrobials can be the crucial elements for the growth of antimicrobial resistance (Mousavi. 2018) For low-income countries such as Afghanistan, antimicrobial-resistant infections have become a major issue of concern. Since most of the population are low-income earners, an increase in the health care costs limits most of the population from accessing health care (Shallcross et al., 2015). Besides, due to the economic status of most of the population, they do not have wider antibiotic choices. The result of this is that they experience higher rates of infectious diseases.

One of the major causes of antibiotic resistance in Kabul is inappropriate and indiscriminate prescribing. Doctors and other health care providers have been accused of not following the right procedures when prescribing drugs to patients (Ancillotti, et al., 2018). It is reported that more than 70% of the patients who present themselves in the hospitals are likely to be given antibiotics even before the condition is tested and determined (Hutchinson et al., 2014). The widespread misuse of antibiotics has contributed to many of them having become ineffective.

The overuse of antibiotics is not a problem in Kabul only. Studies on other provinces show similar practices. Mousavi (2018) reported that studies from other parts of Afghanistan showed that overuse, as well as the irrational use of antibiotics, is common. Although the curricula of medical and pharmacy schools have specific sessions on rational use of medicine, it has not been well observed in the practice, Thus, this is a problem that affects the entire country. Other countries also show similar reports. Studies conducted in Iran on the use of antibiotics show that vancomycin and third-generation cephalosporin were being overused (Ikram et al., 2014). By this, it means that they were either given too often for the diseases they are supposed to treat or prescribed even for diseases that they are not supposed to treat. Another similar study conducted in New Delhi, India, revealed that antibiotics were being used for the treatment of acute, uncomplicated respiratory tract infections. It is to be noted that most of these are viral diseases, and they do not respond to antibiotics. As such, it would have been better to prescribe drugs that are able to treat such viral diseases or none, and only treat these conditions symptomatically.

Mousavi (2018) also analyzed another study from China. The study revealed that the Chinese health care facilities frequently prescribed antibiotics. While this is not medically right, what is more, is that most of these prescriptions were found to be inappropriate. Studies conducted in Jordan, Malaysia, and Nigeria realized similar results (World Bank, 2014). The World Health Organization has provided guidelines on how antibiotics should be used and the diseases for which they should be used to treat. However, research has revealed that many countries are not using them as recommended.

The misuse of antibiotics is termed as one of the greatest causes for antibiotic resistance. To ensure that antibiotics resistance is delayed or controlled, the WHO states the need to rationalize, control, and regulate the usage of antibiotics. This requires a concerted effort from all the concerned persons ranging from the prescription process, distribution, and administration (Goossens et al., 2005). Similar to other countries, Afghanistan is also facing improper practices on the usage of antibiotics. One of the major ways of achieving this is by identifying the major challenges related to the prescription of antibiotics as well as the pattern of prescription of these drugs in Kabul. Mousavi (2018) stated that if the antibacterial resistance war must be won, then the antibiotic prescribing pattern in Kabul should follow the laid down procedures and guidelines by the WHO.

3.6 AMR in Disease-Specific Programs

it is usually difficult to detect resistance with routine laboratory procedures. There have been cases of artemisinin-resistant strains that have been identified in countries such as Vietnam, Cambodia, Thailand, and Myanmar (Kotwani & Holloway, 2011).

3.7 How MOPH/Government in Afghanistan Addresses AMR

Literature suggests that the Afghanistan government has developed several measures aimed at addressing the issue of anti-microbial resistance (Hajjeh & Mafi, 2016). The government developed a policy whose major aim was to look at the effective ways of combating anti-microbial resistance in the country since it is an issue that poses a public health threat. The policy was dubbed National Action Plan on Antimicrobial Resistance (NAP-AMR) and was meant to run from 2017 to 2021. This policy majorly addresses the resistance goal and has several objectives, which are supposed to be followed to ensure that it is successful. Some of the objectives touch on the strategic priorities, indicative budget, and timeline, which are aimed at slowing the emergence of AMR in Afghanistan. Besides, it is aimed at strengthening the organizational as well as the management structures.

The National Action Plan on Antimicrobial Resistance (NAP-AMR) 2017-2021is committed to combating AMR which is a public health threat. In conjunction with The Ministry of Public Health in Afghanistan, NAP-AMR is keen on combating AMR. The NAP-AMR has focused on the content areas of human use of medicine, infection control and access to therapeutics from AMR Framework, while other content areas from the Framework, still need to be addressed (AMR Framework). Despite this commitment, challenges such as political issues, and lack of adequate control of smuggling of medicine in the country make it hard to deal with AMR. Other related issues include presence of remote areas and poor economic state.

Looking to the implementation of National Action Plan for AMR, it has been implemented very partially, because no budget was allocated for the plan from the government of Afghanistan (Interview with Dr Nasir Stanikzai the AMR National Focal Point). Also, the NAP-AMR was looked to find out that which content areas from AMR Framework 2017 were implemented (fully or partially). The below table shows the implementation of the content areas of the AMR Framework:

Table 5: Content Areas from AMR Framework:

Group area	14 Content areas	Implementation status
1. Reduce need for antibiotics or unintentional exposure to antibiotics:	Human infection prevention and control	Partially implement
	Clean water and sanitation	Partially implemented
	Animal Infection Prevention and control	Not implemented
	Food and Safety	Partially implemented
	Environmental Contamination	No action taken
2. Optimize use of medicines	Human Use	Partially implemented
	Animal and agriculture use	Not implemented
	Laboratory capacity and surveillance	Partially implemented
3. Invest in innovation, research, supply, and access of antimicrobials:	Basic Research	No action
	Development of new Therapeutics	Not Implemented
	Access to all Therapeutics	Partially implemented
	Diagnostic development and access	No action
	Vaccine development and access	No action
	Quality and Falsified Medicines	Partially implemented

The National Action Plan for AMR will expire in 2021, based on the decision made by the National Advisory Committee of AMR, it will be revised in 2021(reference to the interview held with Dr Stanikzai the National Focal Point for AMR in Apr 2021).

3.8 Best Practices on Antibiotic Use globally:

AMR is also a public health problem in the region, where overuse and misuse of antibiotics contribute to the resistance of microorganisms against antibiotics as well. We would like to review some of the best practices and actions made by other countries for addressing the AMR in their countries.

For combating and reducing AMR in Singapore, they introduced different recommendations, but they found the interventions for appropriate use of antibiotics (Antimicrobial Stewardship Unit) in hospitals settings, effective for the reduction of AMR incidence and hospital acquired infections (Antimicrobial Stewardship Unit).

WHO recommends some proper practices for reducing AMR at Primary Health Care facilities such as improving basic water, sanitation, and hygiene, because the primary care facilities are the points of exposure to infection, for both patients and staff, so Such facilities can play an important role and as primary source for AMR transmission in the community and other places. Also, WHO recommends other practices at PHC level such as improving supply chain of antibiotics, training of PHC centers on rational use of Antibiotics, promoting simple diagnostics tests for the patients and furthermore working on community awareness on antibiotic usage (World Health Organization 2014).

3.9 Common Risk Factors

There exist various risk factors for anti-microbial resistance. The risk factors range from one drug to another and are also dependent on the proper use of drugs, the monotherapy versus combined treatment, the use of antibiotics in other sectors, among others. For example, an invasive procedure is considered a risk factor for ciprofloxacin resistance. Besides, an indwelling urinary catheter is also associated with anti-microbial resistance. Patients with preexisting conditions are also considered more vulnerable to anti-microbial resistance since they are more likely to have used antibiotics earlier, or they are more at risk of having been hospitalized (where hospital environments are places where more resistant bacteria dwell, because of the many antibiotics used in a hospital environment).

Research has shown that in the Intensive Care Units, anti-microbial resistance rates are seen to be increasing rapidly due to inappropriate microbial usage as well as the prolonged length of stay in the hospital. It is also essential to mention that even when antibiotics are appropriately used, you expect higher resistance problems in an IC unit; this is comparable to a hospital environment compared to community infections: there is more use of antibiotics, and when there is more pressure from antibiotics, resistant strains tend to selectively develop. It is like evolution in a relative short time. The longer one stays in the hospital, the higher the likelihood of developing anti-microbial resistance. For example, *P. aeruginosa* is among the pathogens that were found to develop a high rate of resistance, specifically in immunocompromised patients.

Besides *E. coli* is another pathogen that was found to develop a high rate of resistance. The presence of this pathogen was common across the three regions in Afghanistan, perhaps, an indication of how severe the pathogen is. It is expected that in accordance with the WHO guidelines on the control of pathogens, the Afghanistan government and other health agencies should develop stronger measures to control the spread of *E. coli* resistance. As shown in the data analysis, *E. coli* was found to be present in both adults and the young population.

Chapter 4: Data Analysis and Findings

In this section we will focus on the analysis of secondary data coming from three reference laboratories (bacteriology section); Central Public Health Laboratory in Kabul, regional Laboratory in Kandahar, and regional laboratory in Jalalabad.

In the following table, positive samples refer to the samples that were collected and showed the presence of at least one pathogen.

Table 6. Positive samples from 3 reference labs.

No.	Reference Lab	Total No. of positive Samples in 2017	Total No. of Positive Samples in 2018
1	CPHL/Kabul	703	0
2	Kandahar	554	756
3	Nangarhar (Jalalabad)	228	0

The following table shows the Positive samples with at least one pathogen disaggregated by the type of specimen from the 3 reference labs:

Table 5: Positive Samples with at least one pathogen from different specimen.

No.	**Lab**	**Urine samples**	**Blood Samples**	**Stool Sample**	**Vag. Swab**	**ENT Swab**	**Sputum**	**SEMEN**	**Others**	**Total**	**Remarks**
1	CPHL 2017	447	4	22	136		1	85	8	**703**	
2	Kandahar Reg. Lab 2017	45	18	40	10	359	6	3	73	**554**	
	Kandahar Reg. Lab 2018	71	17	74	18	372	2	2	200	**756**	
3	Jalalabad Reg. Lab 2017	70	6	14	9	44	0	6	79	**228**	
Total		**633**	**45**	**150**	**173**	**775**	**9**	**96**	**358**	**2239**	

Data collected from the three laboratories were analyzed to detect the anti-biotic resistance of different microorganisms for various antibiotics. It is worth mentioning that due to lack of an electronic registration system, it was not possible to get the total number of samples sent to the laboratories. Since all the samples were sent from the hospitals to the laboratories, so the laboratories were only responsible for the testing of the samples and sending back the results to the hospitals, therefore there was no information with the laboratories about the outcome of the patients.

Table 7: List of resistant pathogens from the different specimen in 3 laboratories:

Lab	**Bacteria identified**	**Sample**	**Total positive cases/ Antibiotic (s) Resistant to**	**Total Resistant cases**	**Age Bracket(years)**
CPHL/Kabul	1.E. Coli	Urine/Semen	152 (CRO,CZX,CXM,CAZ)	624	9 to 60
	2.Psedomonas aeruginosa	Urine	112 (CRO, SXT)		4 to 37
	3.Citrobacter frundii	V. Swab	98 (CX, CTX)		11 to 60
	4.Streptococcus Species	Urine	107(CRO)		19 to 92
	5.Protues mirabillis	Urine	46 (CX, CTX)		2 to 47
	6.Staphylococcus aureus	Urine/blood	13(AML,CRO,CIP)		11 to 92
	7.Candida Albicans	Urine	32(E,P)		16 to 76
	8.Morganella moriganii	Urine	64 (CXT)		6 to 42
Nangarhar	1.Entero. coc	Urine	32 (AML, CIP, PIP)	96	18 to 72
	2. Staphylococcus aureus	Urine/pus/blood	12(VA, AML)		29 to 89
	3. E. coli	Semen/urine/pus	43(AML,CRO,CIP)		14 to 35
	4.Salmonella	Stool	6(CRO,CZX,CXM,CAZ)		13 to 43
	5. Klebsiella	Urine	3(CX)		27 to 60
Kandahar	1. E. coli	Urine	69 (CRO,CZX,CXM,CAZ)	153	3 to 37

	2.Staphylococcus aureus	Blood	23(E,P)		34 to 56
	3.Salmonella	Stool	33(AML,CRO,CIP)		11 to 45
	4.Staphylococcus aureus	Urine	17(P,SXT,GM) 2years		12 to 65
	5.Psedomonas aeruginosa	Urine	11(AML,CXM)		13 to 47

Analysis of Data from CPHL:

Based on data acquired from CPHL laboratory, resistance of microorganisms presents in various specimens have been detected in many patients. According to WHO (2014), AMR has led to infection of bacteria in all patients irrespective of their age. Minor cases of *Serratia species*, which were present in males, were also recorded in CPHL. In addition, *Pseudomonas aeruginosa* was present in urine samples; however, very few cases were recorded.

Bacteria such as *proteus mirabilis*, which is not common, were found to be resistant in some patients, whereby urine samples were tested. Resistant in some rare cases such *hafnia alvae* was also recorded after her urine sample was tested. Although not many blood samples were tested, the two that were tested showed that resistant *Staphylococcus aureus* was present in the blood.

Analysis of Data from Nangarhar Reference Laboratory:

Nangarhar lab presented data that showed how different people had various bacteria in the samples. Specimens used in the lab included urine, stool, ear, nose, and wound pus. The age group was also a factor that was also analyzed when analyzing the data collected. Additionally, *Staphylococcus bacteria* were also present in patients of all age groups. For instance, the nose pus of a 2-year-old boy that was tested revealed that the bacteria were also present in young children.

Most of the urine samples that were tested in the hospital also show that *E. coli* bacteria are common in the region and were resistant to antibiotics such as CIP, CRO, and CTZ. Besides, the bacteria were present in all genders and did not necessarily affect adults. Stool tests were also performed, and different cases of bacteria were recorded. *Salmonella bacteria* were present in the stools of some participants. *E. coli* was also present in many people, which was also recorded in CPHL.

Citrobacter was also present in some samples that were collected. *Klebsiella,* which is not common in many regions, was also recorded in Nangarhar. Also, *shigella bacteria* were recorded in the samples that were tested in the hospital. Although *shigella* is closely related to *E. coli*, shigella is not common in the area compared to *E. coli*.

In many cases, practitioners fail to test bacteria in the pus of patients since pus consists of debris and tissue destroyed by the infection, whereby the bacteria have already been killed. Despite this, pus was still tested to ensure that adequate data were obtained regarding bacteria in pus. Most of the tests involved ear pus and wound pus, whereby *E. coli* was the most common bacteria in the ear and wound pus. *Staphylococcus aureus* was also present in some ear pus samples. *Salma spp* is also other bacteria that was recorded during data collection. *Proteus bacteria* was also found in the ear pus of a child who was tested. The bacteria are mainly found in decomposing animal matter, sewage, and human and animal faces.

Analysis of Data from Kandahar Laboratory:

The samples that were used include ear pus, urine, blood, sputum, and stool. Children and adults were also tested. *Staphylococcus aureus* is one of the bacteria that was largely recorded in many samples. Based on the data collected, the bacteria were mainly present in ear pus. *E. coli* was also present in some various samples, which shows that *E. coli* is the most common bacteria in the region. Besides, many cases of E. coli bacteria in the other two laboratory results were noted. *P. Vulgaris* was also present in some of the samples that were tested. *P. Vulgaris* bacteria were also mainly found in the ear pus.

The test of sputum also showed the result that the sputum had *S. aureus* bacteria. Other bacteria that were common in most samples include *Pseudomonas aeruginosa (P. aeruginosa)* and *Proteus merabilius (P. merabilius)*. *P. Aeruginosa* was mainly found in pus. On the extreme*, P. merabilius* was found in pus and blood samples. AR also largely contributed to more cases of various bacteria in the region. For instance, *Klebsiella oxytoca* was found in some samples, such as fluid and ear pus. Bacterial infection in the hospital also involved people of different age groups.

Data analysis revealed that *E. coli* was the most common bacteria in urine based on the samples used in the region. The microorganisms were resistant to antibiotics such as CZX, CRO, and AML. Among the urine samples, *staphylococcus coagulase* was also common although not in many samples compared to *E.coli*. Moreover, the researcher noted that urine tests and pus tests showed that many people in the region have different types of bacteria. In the CPHL hospital data, out of about 700 positive samples, more than 150 showed the presence of resistant *E.coli.*

The analysis of different sex and age groups also showed detection of microorganisms in different groups. For instance, CPHL data shows that people aged 25 to 55 years had various infections with most people having the *E.coli* and *Staphylococcus aureus* in urine and stool. The analysis also entailed examining data from each laboratory to determine the resistance of microorganisms. For instance, analysis of resistance in Nangarhar Lab shows that more males were infected with various bacteria compared to females. Moreover, most of the people tested aged 2 to 30 years. On the extreme, the analysis of Kandahar Lab shows that more males had bacteria compared to females. The analysis of the three regions shows that more cases of teenagers infected with bacteria was experienced in Kandahar compared to other regions. The following chart shows percentage of various bacterial infection based on the samples presented.

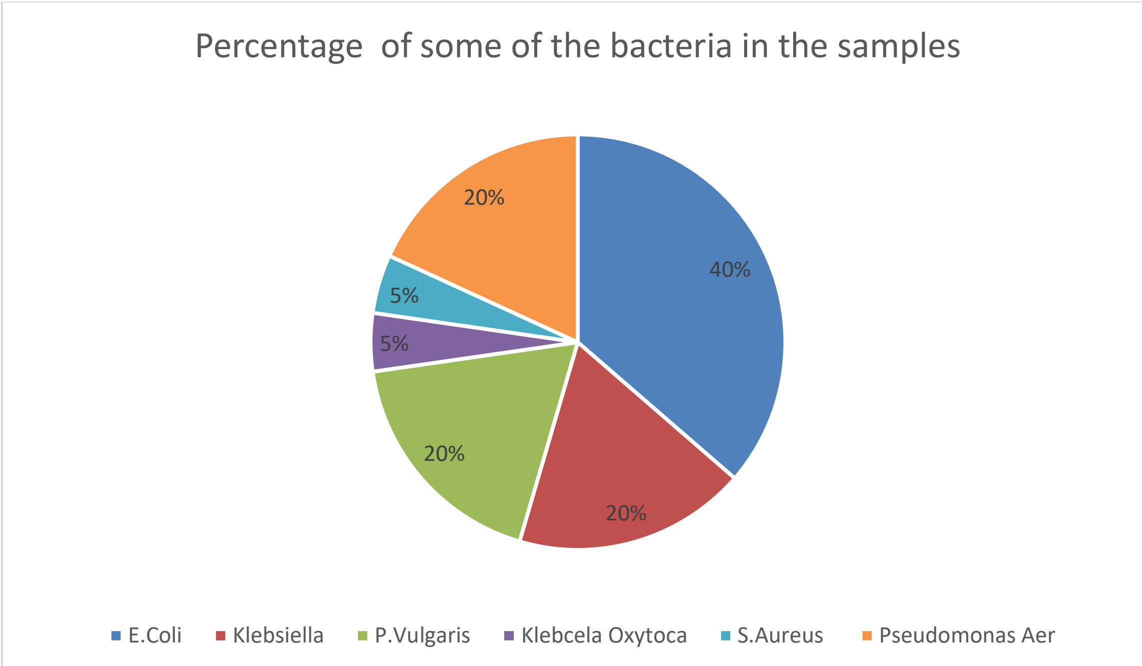


Fig 1. Percentage of some of the commonest bacterial infection based on the samples presented.

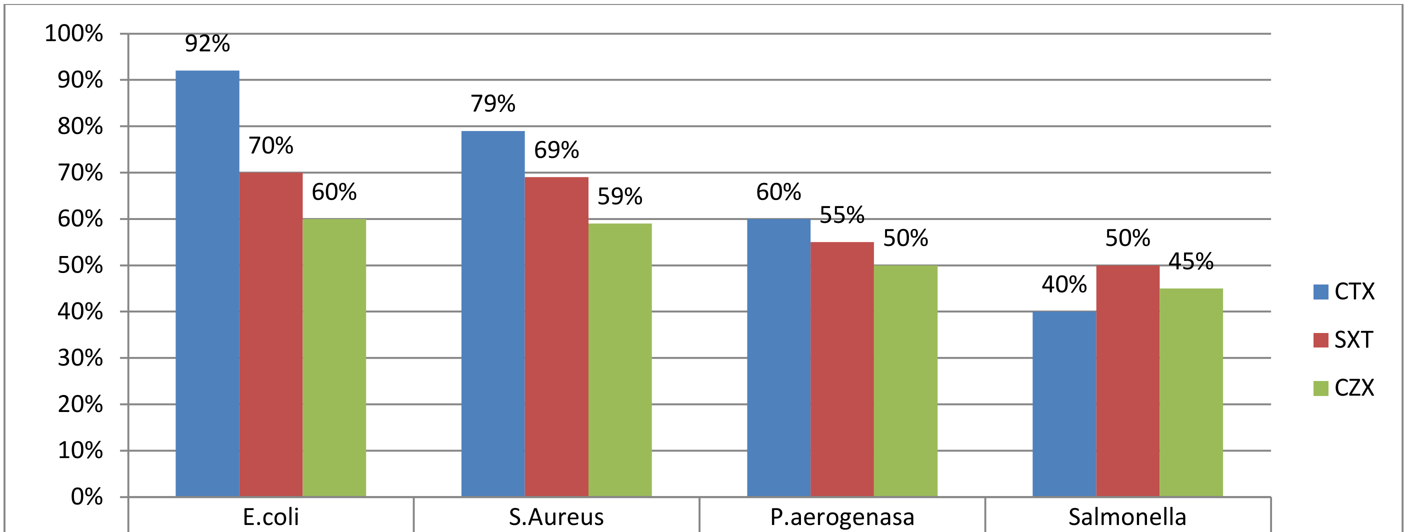
Resistance of microorganisms against some antibiotics was also analyzed. For instance, data collected in Kandahar show that *S. Aureus* was highly resistant to Ciprofloxacin (CIP) and Ceftriaxone (CTX) antibiotics. Most of the bacteria were also resistant to ceftizoxime (CZX) in the three laboratories. Other bacteria that were not common in the three hospitals also showed resistance to some antibiotics. For example, *Klebsiella oxytoca* and *Citrobacter* were resistant to various antibiotics such as CTX and CIP. Many bacteria in the three laboratories also showed resistance to sulfamethoxazole/ trimethoprim (SXT) antibiotics. For instance, *Hafnia alave* and *Edwarsell trada* were resistant to the SXT despite them being rare in the three locations. The following table has more information regarding some of the microorganisms and their resistance to some of the antibiotics.

The below table shows the resistance of microorganisms against different antibiotics only urine samples, where it reveals that E. Coli is the highest in terms of resistance (40%) compared to other bacteria detected from 200 Urine samples.

Table 8: Resistance of Microorganisms against antibiotics in Urine Samples:

		Resistant to:					
Urine samples	**Total samples: 200**	**CIP**	**CTZ**	**CTX**	**SXT**	**FOX**	**CX**
E.coli	80 (40%)	30	21	13	12	1	3
Klebsiella	40 (20%)	17	8	1	11	1	12
Pseudomonas Aer.	40 (20%)	13	12	1	2	11	1
P.Vulgaris	20 (10%)	2	1	13	2	1	1
S.Aureus	10 (5%)	4	1	2	1	1	1
Klebsiella Oxytoca	10 (5%)	5	2	1	1	0	1

The below chart (Fig 2) shows the percentage of resistance among four common microorganisms against antibiotics in the total positive samples of urine, blood, and pus in 3 laboratories. It reveals the highest proportion of resistance in E. coli comparing in other 3 common bacteria.



	E.coli	S.Aureus	P.aerogenasa	Salmonella
CTX	92%	79%	60%	40%
SXT	70%	69%	55%	50%
CZX	60%	59%	50%	45%

Fig 2. Representation of the percentage of resistance of microorganisms against the antibiotics in all the **positive samples** in the three laboratories. The specimen used is urine, blood, and pus.

Key:

Green represents pus

Blue represents urine

Red represents blood

4.1 Comparison of Resistance in Three Regions in Afghanistan:

In Nangarhar, about 226 samples were collected for analysis. Out of these samples, it was evident that there were several microorganisms, which were resistant to antibiotics. Some of those that were identified included *Enterococci, Pseudo.Aerga, Stuph. A., E. coli, Enterobacter, P.Valgaris* and *Salmonella* among others. The microorganism, *E. coli* is rampant and has developed the highest resistance. The other common microorganism in Nangarhar is *Stuph. A. (aureus)*. This microorganism is also common in Nangarhar, and it seems to have developed great resistance. Other common microorganism that has developed antibiotic resistance in Nangarhar include *Pseudo Aerga* and *Enterococci.* The microorganism *Enterococci* was found to be present among the aged people. For example, some of the affected patients were aged 67 years, 39 years, and 52 years, among others. However, a few cases showed younger patients showing the presence of *Enterococci.* In one case, the patient was aged 26 years and another case, a female aged one year. This distribution shows that although the highest distribution is in the elderly individuals, it is also present in the young population.

The most common microorganism, *E. coli* seems to be most rampant among the population aged 30 years and below. Some of the patients who showed the resistance of *E. coli* were a female-aged 21 years, another female-aged 25 years, another female-aged 3 years, a female-aged 17 years, a male-aged 27 years, and a male-aged 3 years. Thus, based on the specimens sent for analysis, the distribution was highest among individuals aged below 30 years. Despite this, there were a few instances of individuals aged above 30 years who showed the presence of the microorganism. There was a male aged 35 years, another aged 40 years and another a female aged 67 years. Thus, measures to curb the resistance should be addressed to the relevant population to develop viable mechanisms.

From Kandahar, the data obtained also showed specific results for the region. Some of the antibiotic resistance microorganisms from this region include *P. aeroginosa, S. aureus, E. coli, P. aureus* among others. Some of the most common microorganism identified were *P. aeroginosa, E. coli,* and *S. aureus.* The latter affected individuals within a mixed age bracket. There was no specific age bracket for patients with this microorganism. Some of the examples picked from the data obtained are a male aged 55 years, a female aged five years, a male aged 31 years, a female aged 9 years, a male aged 38 years, a male aged 50 years, and male aged 30 years to mention but a few.

The spread of *P. aeroginosa* is also mixed up. There are aged patients who show its presence and other young patients. However, based on the samples used, most of the population lies below the age of 30. For instance, the data obtained showed examples of the age of the patients who showed the presence of *P. aeroginosa* as follows; a male patient aged 3 years, a female patient aged 20 years, a female aged 20 years and a male patient aged 9 years.

Chapter 5: Discussion

As highlighted earlier under the objective section, we will discuss; i) the burden of AR, its trends and contributing factors. ii) discuss the findings from data analysis about AR from 3 reference laboratories in Afghanistan. iii) discuss the international guidelines and best practices on AMR and make comparisons to the country guidelines.

5.1 The burden (prevalence) of AR, trends and contributing factors:

The prevalence of anti-microbial resistance in Afghanistan is not evident due to the lack of enough data to make a conclusion. According to data provided by the WHO, the anti-microbial resistance is high in both high and low-income countries. For instance, the new Global Anti-microbial Surveillance System (GLASS) shows a widespread occurrence of antibiotic resistance among people who have suspected bacterial infections (O'Dowd, 2014). The data reported to GLASS from one Lab in Afghanistan (CPHL) also has shown resistance to antibiotics. So far Afghanistan has introduced only one reference lab (CPHL) to report to GLASS. Some bacteria that have been deemed resistant across the world include *Escherichia coli*, *Klebsiella pneumonia*, *Staphylococcus aureus*, and *Streptococcus pneumonia*, followed by *Salmonella* spp.

The consequences of anti-microbial resistance are common across the globe. This means that the consequences experienced in Afghanistan are the same as those experienced in Iraq, Iran, and other high economic countries such as the UK, Germany, Italy, and the US. One of the major consequences is increased risk of worse clinical outcomes. In extreme circumstances, this is followed by death. Many countries across the world are experiencing high mortality rates arising from anti-microbial resistance. Anti-microbial resistance also leads to high costs as the patients consume more healthcare resources than they would have spent if they did not have anti-microbial resistance (Kotwani et al. 2012). Patients with non-resistant strains of the same bacteria spend lesser than the patients with anti-microbial resistance. This is an indication that anti-microbial resistance strains the economy of a nation. Thus, with controlled anti-microbial resistance, it is possible for low-income nations to flourish.

Based on the data from the three regions, it is evident that there are some microorganisms which are more prevalent in some regions than in others. Data presented also shows that there is the need for more tests in various labs since different regions have recorded different microorganisms. For example, *P. aeroginosa* is common in Kandahar but not in Kabul. However, there are some microorganisms, which are present in all regions. One of these is *E. coli, which* is found in all the three regions. This shows that its resistance to antibiotics is prevalent and there should be bolder measures developed to control it.

5.2 Common Resistant Microorganisms

The data obtained from 2017-2018 from different labs in Afghanistan showed that the country experiences anti-microbial resistance for various strains of microorganisms. The samples came from the specialize hospitals; IPD, OPD and it came from individuals referred from outside the hospitals and from patients referred from PHC centers as well. Antimicrobial Resistance is not an isolated issue in one or two countries. It affects the entire world and thus termed as a global concern. From the data obtained from laboratories in Afghanistan, different microorganisms were found to have developed resistance. Some these are *Staphylococcus aureus, Escherichia coli, Klebsiella pneumonia, Candida Auras,* and *Pseudomonas aeruginosa,* among others. In data obtained from Kandahar, the number of cases resulting from *Staphylococcus aureus* resistance were high and affected both male and female patients within the age of 18 to 45. The specimen collected on 1/11/2017 and reported on 3/11/2017 showed that *Staphylococcus aureus* was a resistant microorganism. The specimen used to determine this was a pus swab. Other specimens used to conclude that *Staphylococcus aureus* is a resistant microorganism were right ear swab, left ear swab, and pus. To determine that *Pseudomonas aeruginosa* is a resistant microorganism, the specimen types used were left ear swab and right nasal. To determine that *Escherichia coli* is a resistant microorganism, the specimen observed from Kandahar was blood, pus, and stool.

Data collected from Central Public Health Laboratory also shown some common microorganisms. While microorganisms such as *E. Coli* and *Staphylococcus aureus* was common in different specimens collected, *Staphylococcus coagulase* was rarely found in the tests conducted. Tests conducted on the month of February 2017 indicated negative for *Staphylococcus coagulase.* Most of the samples taken were from urine and they did not show the presence of *Staphylococcus coagulase.* There also samples from semen, and V. swab and all of them showed the absence of *Staphylococcus coagulase.* This may mean that *Staphylococcus coagulase* is not a common microorganism, and it is possible that it has not developed resistance against antibiotics.

However, data collected from Nangarhar Lab showed some common microorganism present in the samples that were taken. The conclusion that can be drawn from their presence is that such microorganism has developed resistance and therefore, it becomes difficult to control them by use of antibiotics. Some of the most common microorganisms identified include *E. coli, Stuph. A.* and *Salmonella.* The samples used to test for *Stuph. A*. was obtained from the pus, E. Pus, W. pus, urine, and blood. These samples showed the presence of *Stuph A.* an indication that the microorganism has developed high resistance against antibiotics. Other microorganisms such as *Salmonella* were also present in different sample that were collected. Samples included the stool. This is an indication that the microorganism mostly resides in the stool.

As stated earlier, data for this study was collected from three regions in Afghanistan. However, one cannot conclude that the samples sent in can be used as a representative for the country since there exist many other hospitals in Afghanistan. Samples used were acquired from different hospitals and health centers (OPD and Inpatient) and private sector, which involved specimen of people of different ages and gender. The samples were received for the purpose of clinical diagnosis by the reference laboratories. There was no specific guideline for receiving the samples by the laboratories, but most of the samples were analyzed by the laboratories to support the diagnosis. Proper recording of data collected during testing was also encouraged to ensure that credible information was obtained during the research. The three regions are Kabul, Kandahar, and Jalalabad. Based on the samples used in Kabul, some of the commonest microorganisms found were *E. coli,* and *Candida albicans*. From the close to 700 samples collected, about 80% of them shown that *E. coli* was the most resistant microorganism in Kabul. Cognizant of these findings, a more systematic survey would be warranted since quite some resistance is present in the samples used and the concerned health agencies in Afghanistan may develop measures to curb the resistance of *E. coli* against antibiotics. With such a visible pattern, it is possible to develop ways of controlling further spread. The distribution of *Staphylococcus aureus* was also a factor for consideration. The spread of the microorganism resistance in Kabul is also common. Although it is not as spread as *E. coli*, there is the need to develop mechanisms of curbing the spread. However, microorganisms such as *Hafnia alvae* and *Staphylococcus Coagulase* are the least found in Kabul based on the samples used.

5.3 Consequences

The consequences of anti-microbial resistance are common across the globe. This means that the consequences experienced in Afghanistan are the same as those experienced in Iraq, Iran, and other high economic countries such as the UK, Germany, Italy, and the US. One of the major consequences is increased risk of worse clinical outcomes. In extreme circumstances, this is followed by death. Many countries across the world are experiencing high mortality rates arising from anti-microbial resistance. Anti-microbial resistance also leads to high costs as the patients consume more healthcare resources than they would have spent if they did not have anti-microbial resistance (Kotwani et al. 2012). Patients with non-resistant strains of the same bacteria spend lesser than the patients with anti-microbial resistance. This is an indication that anti-microbial resistance strains the economy of a nation. Thus, with controlled anti-microbial resistance, it is possible for low-income nations to flourish.

5.4 Existing Policies, Strategies, and practices:

Currently, there exist various strategies and policies to mitigate antibiotic resistance in Afghanistan. Some of the existing policies and strategies in Afghanistan are steered by the WHO. There exist similar policies and strategies the in world over. For example, the CDC has initiated several surveillance efforts coupled with prevention and control activities to support applied research. In some cases, CDC has initiated efforts such as the Campaign to Prevent Antimicrobial Resistance in Healthcare Settings (O'Dowd, 2014). This is a program that is targets clinicians, health care organizations, and patients as a means of educating them on the need to curb anti-microbial resistance (Ingle, 2018). This is achieved by practicing measures that reduce infections to reduce the need for anti-microbial exposure as well as the selection of resistant strains. Besides, it is aimed at ensuring that patients are properly treated, and this will reduce the opportunity for development and selection of resistant microbes. Additionally, people are educated on how to use anti-microbials wisely as proper use of them will reduce unnecessary exposure and unnecessary treatment (Ingle, 2018). Besides, people are educated on preventing transmission of resistant organisms from one person to another.

As a response to the call by WHO, the Afghanistan government is working on strengthening its surveillance capabilities and health systems to limit anti-microbial resistance. There are also moves to develop new legislation and regulations which are meant to control how drugs are used. For example, the purchase of over-the-counter drugs without prescription has been cited as a leading contributor to anti-microbial resistance (Kotwani et al. 2012). To curb this, chemists and pharmacies have been warned against giving some types of drugs without prescription. The Afghanistan government has also moved with speed to establish functional and sustainable laboratories for anti-microbial resistance surveillance.

Looking to the existing practices for rational use of antibiotics and combating AMR in Afghanistan, and comparing to the practices in other countries, there are poor practices in Afghanistan, although the issues have been documented well in the National Action Plan of AMR and other documents. Beside other factors such as poor awareness, the lack of a department or an entity for combating AMR in the country could be a significant factor.

5.5 Limitations to the Study

Just like any other study, this study faced different limitations which may had the possibility of affecting the outcome of the study. However, the researcher employed all possible means ensure that the limitations did not affect the findings of the study. One of the limitations that the researcher had to grapple with is on the obtained data. The data that was obtained from the three reference laboratories was not primarily collected by the health care providers for the purposes of AMR. The data was mainly meant to determine the diagnosis of certain diseases and conditions. It is expected that if the health care providers in those hospitals had decided to collected data in relation to AMR, there would have been some variations in the data that would have been available.

The other limitation for this study is that it did not use information from interviews of health care providers and policy makers about AMR. This was not done because it would have entailed the use of a lot of time seeking permission to interview health care workers. That would have delayed the completion of this thesis. Besides, the interview with health care providers and policy makers were not done, because the researcher reviewed the National Action Plan for AMR in Afghanistan, which included all the gaps, challenges and plans for AMR, so he thought that the interview will not give more information than what is stated in the document of the Ministry of Public Health. Data from interviews would have been obtained through interviewing health care providers and policy makers to ensure that the researcher gets firsthand information from these essential subjects in such a study. However, to ensure that this did not affect the outcome and the findings of the study, the researcher used credible sources of information some of which had revelations from health care providers themselves. Sources from credible health institutions such as the WHO were used to ensure that the information and data obtained are credible.

Chapter 6: Conclusions and Recommendations

6.1 Conclusions

Anti-microbial resistance (AMR) is a global issue Disease-causing microorganism to become resistant to the drugs that used to treat them. As seen in the study, some of the causes of this include where the bacteria grow and adapts to the environment antibiotics exist, thus developing resistance. As stated earlier, the microorganisms develop resistance through different mechanisms such as efflux pump (removing anti-microbials penetrating the cell), enzymatic changes of anti-microbial drugs (e.g., by production and release of beta-lactamases), new pathways of metabolic (altered enzymes synthesis), alteration of bacterial proteins alteration, which is acting as anti-microbial) targets. Afghanistan is one of the countries that have recorded increased cases of anti-microbial resistance, making the treatment of diseases and conditions which were previously treatable, difficult. Anti-microbial resistance (AMR) makes it difficult for it to treat diseases that are caused by fungi, parasites, bacteria, and viruses. The effects of anti-microbial resistance (AMR) are that it results in reduced efficacy of the drugs and treatment methods used as antiparasitic, antiviral, and antifungal. Anti-microbial resistance (AMR) has resulted in an increase in the cost of treating patients.

It is noteworthy to mention that the challenge of antibiotic resistance is a global problem that requires concerted efforts to address. As much different governments may be in the frontline towards addressing this issue, that is not enough. There is the need to include all the stakeholders to ensure that the battle is won. In the prevention and control of antibiotic resistance, there is the need to involve individuals, policymakers, and the health professionals to ensure that the problem is dealt with in the best manner possible. The individuals can do several things to prevent and control the spread of antibiotic resistance. Some of the steps they can take include the use of antibiotics only when they have been prescribed by a permitted health care provider. This way, the problem of buying antibiotics anyhow will stop. Additionally, individuals should desist from requesting for antibiotics especially when the health care provider says that it is not necessary. There is also individual who tend to use antibiotics even when they have not been guided by health care professionals. Such individuals must desist from such behavior and follow the advice provided by a health care professional on the use of antibiotics. This will limit unnecessary use of antibiotics, which leads to resistance. As stated earlier, there are also people who share their leftover antibiotics with others. This habit increases the chances for antibiotic resistance. Were such people to desist from such unwarranted sharing, then the problem of resistance would have been solved.

The WHO advises individuals to wash hands regularly, avoid close contact with sick people and prepare food hygienically to decrease the chances of getting sick hence lowering the usage of drugs.

The policy makers are also tasked with a great role of limiting the antibiotic resistance. Policy makers can engage in such activities as ensuring that there is a robust national action plan aimed at tackling antibiotic resistance that is put in place. Besides, they need to improve surveillance of antibiotic-resistant infections. The policy makers are also at a better position to strengthen policies and programs that are aimed at preventing infections. Currently, there is very little information available to the public about antibiotic resistance. The limited information makes it difficult to address the issue adequately. It is prudent for policy makers to make information available to the public about the impact of antibiotic resistance. This way, it will be easier to address issues related to antibiotic resistance among the people.

On their part, health care professionals need to prevent infections by making sure that they operate in clean environments. In addition, they need to prescribe antibiotics only when they are needed and desist from prescribing antibiotics that are not needed. In doing this, they need to keep themselves updated on the current guidelines as provided from time to time by the WHO and other related agencies and bodies. In cases where there have been reports about increased antibiotic resistance, the health care professionals need to report such information to surveillance teams. The health care professionals are also mandated with the greatest task of educating the patients about proper usage of antibiotics. Thus, they ought to educate the patients on how to use antibiotics correctly as well as the dangers for misuse. This way, the problem of antibiotic resistance will have been addressed to a proper extent. The health care providers may also talk to the patients about the different ways that they can use to prevent infections thus limiting their use of drugs. Such ways may include covering the nose and mouth when sneezing, timely vaccination and washing hands thoroughly.

6.2 Recommendations

Following the above findings, there are several recommendations that this study gives to ensure that anti-microbial resistance in Afghanistan and the world over is limited and the effects mitigated. One of the recommendations is to improve tracking antibiotic-resistant bacteria. The rationale behind this is that the more the knowledge there is on the antibiotic-resistant bacteria, the easier it is to develop measures to curb the spread. The second recommendation is for the governments and responsible health bodies to increase the life of the existing antibiotics by way of improving their use and implementing various interventions. This will ensure that the current antibiotics are put into proper use. It is also recommended that governments increase the speed to research on, discover, and develop new antibiotics as well as related interventions.

It is also recommended that the Afghanistan government invests more in studying about resistance patterns in a bid to develop better mechanisms of handling the issue of antibiotic resistance. Worthwhile to note is that resistance patterns are usually highly heterogeneous in several infections. For instance, in the upper respiratory tract infections, the upper tract infections as well as the Urinary Tract Infections (UTIs) are limited when compared with Community-acquired Pneumonias (CAPs). In CAPs, antibiotic resistance may have a significant role in avoiding the development of life-threatening diseases. Antibiotics are not recommended in the treatment of upper respiratory tract infections, but they are used by many people. Such people lack the understanding that antibiotics are not recommended for the treatment. As a result, antibiotic resistance rates increase steadily. It is impudent upon the government to gather enough information on resistance patterns to ensure that the use of antibiotics is limited to the necessary conditions.

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