CHARLES UNIVERSITY IN PRAGUE
FACULTY OF PHARMACY IN HRADEC KRALOVE
Department of Social and Clinical Pharmacy

Diploma Thesis

ANALYSIS OF SELF-MEDICATION WITH ANTIBIOTICS IN KOSOVO

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May 2015 *Ardita Veseli*

"I declare that this thesis is my original copyrighted work. All literature and other resources I used while processing are listed in the bibliography and properly cited. The thesis was not misused for obtaining the same or different academic degree."

Hradec Králové, 15/05/2015 Ardita Veseli

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Abstrakt

Název: Analýza samoléčení antibiotiky v Kosovu

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Úvod: Samoléčení je definováno jako činnost, při které je prováděna laická léčba u laicky diagnostikovaných symptomů nebo nemocí, nebo intermitentní nebo chronické užití léků předepsané pro jinou diagnózu nebo symptom než je nyní užíván. Samoléčba antibiotiky se rozumí laické užití těchto léčiv bez předchozí konzultace s lékařem. Jejich zdrojem je nákup ve veřejné lékárně, zbytky z předchozí farmakoterapie, velmi často je doporučena z řad příbuzných, přátel a sousedů. Antibiotika jsou považována za významné léky, protože jsou schopny eradikovat mikroby. Jejich nevhodné užití však může zvýšit riziko mikrobiální rezistence. Mikrobiální rezistence se zdá v současnosti jedním ze základních problémů zdravotnictví.

Cíl: Hlavním cílem teoretické části je popis stavu samoléčení antibiotiky ve světě, faktory, které jej ovlivňují a komplikace spojené s tímto druhem léčby. Dále je zpracována literatura týkající se faktorů ovlivňující antibiotickou rezistenci, nové diagnostické metody u infekčních onemocnění a popsány jsou i základní strategie léčby antibiotiky. V experimentální práci je hlavním cílem analyzovat frekvenci a důvody k samoléčbě antibiotiky u vybrané populace Kosova.

Metody: Hledání v literárních zdrojích bylo provedeno v PUBMED a k hledání byly využity tato klíčová slova: „antibiotics; drug consumption; resistence; self-medication“. Po validaci dotazníku, byl tento použit u 300 respondentů, návštěvníků lékárny v Prištině a ti jej sami vyplnili. Data pacientů byly sbírány v periodě dvou týdnů.

Výsledky: Prevalence samoléčby antibiotiky byla vysoká – u této skupiny 70,7% respondentů připustilo užití antibiotik. Nejčastějším zdrojem bylo předchozí užití stejného antibiotika v minulosti. Nejčastějším důvodem pro nákup antibiotika byl kašel 18,1%), poškození ledvin (17,3%) a chřipka (14,6%) následovány gastoenterologickými a gynekologickými záněty (obé po 12,2%). Na druhé straně 70,3% mají zásoby antibiotika doma, 58,3% vykazovalo nízké

znalosti týkající se antibiotické rezistence a 50,7% neví, že antibiotika poškozují mikrobiom pacienta ve střevě. Naproti tomu 63% respondentů se domnívá, že je nutno dokončit antibiotickou kůru a 55,7% se obává alergie a dalších nežádoucích účinků antibiotik. Byly nalezeny rozdíly v chuti se samoléčit – preferenčně u mladších věkových skupin a u nemocných s nižším vzdělávání.

Závěry: Neracionální užití a nadužívání antibiotik je problém Kosova i přes to, že zvyšují rezistenci bakterií a vedou k nežádoucím účinkům. Z našich výsledků se zdá, že používání antibiotik k samoléčbě je v Kosovu běžné. Možná by dobře cílená edukační kampaň zaměřená na antibiotickou rezistenci a správné užívání antibiotik mohla snížit jejich nevhodné užívání.

Abstract

Title: Analysis of self-medication with antibiotics in Kosovo

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Background: Self-medication is described as a behavior during which someone utilizes drugs for the purpose of treating self-diagnosed symptoms or disorders or the intermittent or continued use of a prescribed drug for chronic or recurrent disease or symptoms. When certain individuals self-medicate with antibiotics, they do it without any prior consultation with a physician. The antibiotics are bought from community pharmacies without a prescription, left-over antibiotics are used or they simply decide to follow the advice given from family members, neighbors or friends. Even though antibiotics are considered revolutionary therapeutic agents in order to eradicate microbes, the repeated and improper antibiotic consumption is contributing to the increased prevalence of antibiotic resistance which nowadays is one of the world's most pressing health problems.

Aim: The main goal of the theoretical part is to describe self-medication with antibiotics, the patterns influencing it and some complications associated with this behavior. Furthermore, the main factors influencing antibiotic resistance, new diagnostic approaches and prevention and management strategies are further described as well. In the experimental part the main goal is to analyze the rate and reasons of self-medication with antibiotics by a population in Kosovo.

Methods: Literature research was performed through using PubMed in order to achieve the goal in the theoretical part of this study. The main keywords which were utilized were: „antibiotics; drug consumption; resistance; self-medication". Additionally a validated, self-administered questionnaire was spread to a total of 300 randomly selected patients in a community pharmacy in Prishtina. Data from patients was collected during a period of two weeks.

Results: The prevalence of self-medication with antibiotics was high. In this group of patients 70.7% admitted to using non-prescribed antibiotics. Self-medication with antibiotics based on a previous experience was the most common source of non-prescribed antibiotic use.

Furthermore, the most frequent reasons for antibiotic consumption were cough (18.1%), urinary inflammations (17.3%) and influenza (14.6%) which were followed by gastrointestinal (12.2%) and gynecological inflammations (12.2%). On the other hand 70.3% of the patients store antibiotics at home, 58.3% have a poor knowledge regarding antibiotic resistance and 50.7% are not aware that antibiotics kill off normal flora. Nevertheless, in this group of patients 63% stated that it is important to complete an antibiotic course and except for that 55.7% of the patients were aware of the allergies/adverse effects associated with antibiotic consumption. Higher rates of self-medication with antibiotics were observed among younger respondents and respondents with a lower level of education.

Conclusion: Evidently, the irrational and overuse of antibiotics continues to be a significant problem in Kosovo despite the increased risks of antibiotic resistance and adverse drug reactions. According to these results it seems that unfortunately, self-medication with antibiotics is common indicating that there is a need for educational campaigns which will help the public understand the proper antibiotic use and diminish the inappropriate consumption of antibiotics.

CONTENTS

CHAPTER

1. INTRODUCTION

The present cross-sectional study consists of two parts: the theoretical and the experimental part both of which are related to self-medication with antibiotics. The main goal of the theoretical part is to define self-medication with antibiotics, describe the patterns influencing it, outline some complications associated with self-medication with antibiotics and additionally provide information regarding the epidemiology of antibiotic use. Furthermore, antibiotic resistance, the main factors influencing it, new diagnostic approaches and prevention and management strategies are further described as well. This goal was achieved through performing literature research from PubMed where the keywords like: „antibiotics; drug consumption; resistance; self-medication“were used.

On the other hand, in the experimental part the main goal is estimate the rate and reasons of self-medication with antibiotics by a population in Kosovo. This was accomplished by spreading a validated, self-administered questionnaire to a total of 300 patients in a community pharmacy in Prishtina. Demographic data, information regarding the attitude and knowledge of the patients concerning antibiotic use and their basic principles of antibiotic consumption were collected and analyzed. The main purpose of this collected information is to provide us with an idea of how well is the general public in Kosovo informed about the appropriate antibiotic use, their perception of antibiotic side effects, knowledge of resistance and of course estimation of the prevalence of self-medication with these agents.

Additionally, a discussion on how to prevent and manage self-medication with antibiotics will be mentioned and a general conclusion will be given in the end as well.

2. THEORETICAL PART-ANTIBIOTICS AND SELF-MEDICATION WITH ANTIBIOTICS

2.1. DEFINITIONS

2.1.1. ANTIBIOTICS

Antibiotics are important drugs which play an essential role in the treatment of bacterial infections. They prevent the spread of diseases and minimize serious complications of the disease. They are classified as bactericidal or bacteriostatic. Antibiotics that target the cell wall, cell membrane or interfere with essential bacterial enzymes have bactericidal effects. Those that target protein synthesis are usually bacteriostatic with the exception of aminoglycosides (Figure 1). Furthermore, they can also be divided as narrow or broad spectrum antibiotics. It is important to stress out that these agents are not used to treat viral infections. Common viral infections that do not benefit from antibiotic treatment include cold, flu, most coughs, viral gastroenteritis (stomach flu) and others [1].

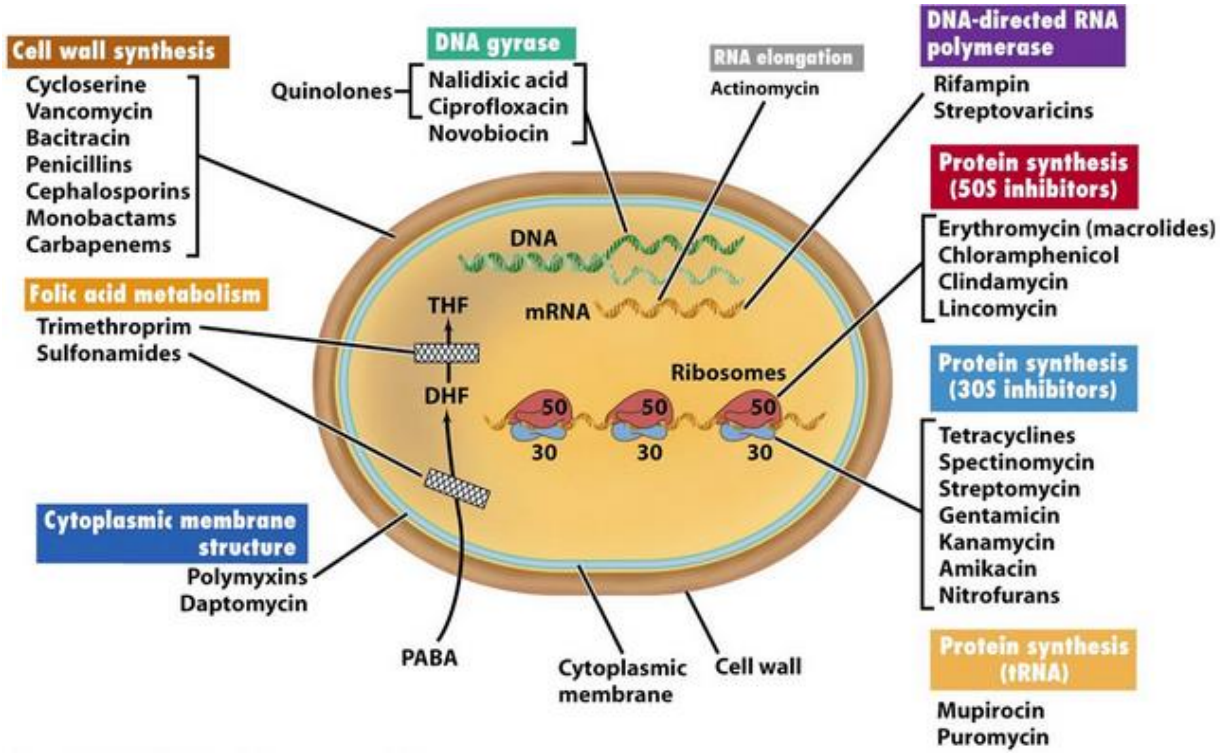


Figure 1: Molecular targets of antibiotics on the bacteria cell [2]

2.1.2. SELF-MEDICATION WITH ANTIBIOTICS

According to WHO, "Rational use of medicines requires that patients receive medications appropriate to their clinical needs, in doses that meet their requirements, for an adequate period of time, and at the lowest cost to them and their community" [3]. Unfortunately, nowadays during most occasions drugs are prescribed, dispensed and sold inappropriately worldwide while additionally patients fail to be compliant when it comes to taking their drugs correctly and on time. Examples of inappropriate use of medicines include polypharmacy, overuse of injections and of course self-medication with prescription only drugs such as antibiotics [3].

Self-medication is described as a human behavior during which someone utilizes drugs for the purpose of treating self-diagnosed symptoms or disorders or the intermittent or continued use of a prescribed drug for chronic or recurrent disease or symptoms [4]. When patients self-medicate with antibiotics, they usually do it without any prior consultation with a physician. Instead, they purchase them from community pharmacies without a prescription, overuse or underuse them, obtain them from family or friends or simply use left-over antibiotics.

Furthermore, self-medication is considered to be deleterious for the patient since it can lead to poor clinical outcomes and increases the probability of adverse drugs reactions. In the case of antibiotics, self-medication can lead to the wrong selection of the antibiotic, administration of insufficient doses and unnecessary treatment. Even though antibiotics are considered revolutionary therapeutic agents in order to eradicate microbes, the repeated and irrational antibiotic consumption is contributing to the increased prevalence of antibiotic resistance which nowadays is one of the world's most pressing health problems [3].

2.2. EPIDEMIOLOGY OF ANTIBIOTIC USE

The rates of antibiotic drug consumption are variable in different countries. One study assessed antibiotic consumption patterns from 2000 to 2010 for 16 groups of antibiotic drugs in 71 countries. The IMS Health MIDAS database which estimates antibiotic consumption from the volume of antibiotics sold in retail and hospital pharmacies was used. The study revealed that between 2000 and 2010 consumption of antibiotic drugs increased by 36% [5].

In 2010 India was the largest consumer of antibiotics with $12{\cdot}9 \times 10^9$ units followed by China with $10{\cdot}0 \times 10^9$ units and the USA with $6{\cdot}8 \times 10^9$ units. High income Asian countries such as Hong Kong, Malaysia, Singapore and South Korea all ranked as the top consumers of antibiotics per person. Substantial increase in antibiotic consumption was also seen among countries like Brazil, Russia, India, China and South Africa. Seventy-six percent of the overall increase in global antibiotic consumption between 2000 and 2010 was attributable to these countries [5].

Cephalosporins and broad-spectrum penicillins accounted for 55% of the total standard units consumed in 2010. Furthermore, a large absolute increase in consumption between 2000 and 2010 was observed for cephalosporins ($8{\cdot}4 \times 10^9$ standard units), broad-spectrum penicillins ($6{\cdot}1 \times 10^9$ standard units) and fluoroquinolones ($3{\cdot}0 \times 10^9$ standard units). An increase in the consumption of glycopeptides, carbapenems and monobactams was seen in France, Germany, United Kingdom, USA and China while on the other hand the consumption of cephalosporins and fluoroquinolones was higher mainly in middle-income countries such as India and China [5].

In several countries antibiotic consumption was also affected by seasonal patterns. In the northern hemisphere antibiotic consumption was highest between the months of January and March; however in the southern hemisphere consumption peaked between the months of July and September [5].

A similar study was conducted among European countries as well. The study showed that the volume of outpatient antibiotic use between 1997 and 2009 increased in most European countries. The total outpatient antibiotic use was the highest in Greece and lowest in Romania. A significant increase in penicillin and quinolone consumption was observed while the use of cephalosporins, tetracyclines and sulphonamides was either the same or decreased in most European countries [6].

2.3. FACTORS INFLUENCING THE PATTERN OF SELF-MEDICATION WITH ANTIBIOTICS

Even though the research interest in self-medication has been expanding, there is not a lot of information available about its major determinants particularly in developing countries.

For this reason more studies analyzing the factors that influence the pattern of self-medication should be conducted. Nevertheless, there are still several causes which are believed to contribute towards self-medication with antibiotics [7]. We are well aware that in many low and middle income countries there are not enforced policies that prevent antibiotic sales without a prescription and promote appropriate antibiotic use, an example includes Mexico where in private pharmacies until recently, antibiotics were the drugs which were sold the most and approximately 40% of the antibiotics were sold without a prescription [8].

Kosovo is currently confronted with a similar situation as well. The widespread practice of selling antibiotics over the counter is a very common problem in this country [9]. According to the law for medicinal products and medical devices in Kosovo (LIGJI Nr. 03/L-188 PËR PRODUKTE DHE PAJISJE MEDICINALE), antibiotics are categorized as prescription only drugs [10]. Unfortunately, even today this law continues not to be followed.

Furthermore, in Kosovo there is a lack of a sustainable health care system accompanied by a lack of medicines reimbursement system which leaves medicines as out of the pocket payments [8]. Even though the law for health care insurances (LIGJI Nr. 04/L -249 PËR SIGURIMIN SHËNDETËSOR) was approved, it has never been implemented due to the increased unemployment rates and poverty which are currently dominating in the country. This law is expected to be implemented by the year of 2018 [11]. Having to pay directly out of the pocket presents a major problem since many patients do not have sufficient finances to have access to a better health care [9]. The lack of proper health care and underuse of health care services in Kosovo seem to be factors that support self-medication with antibiotics.

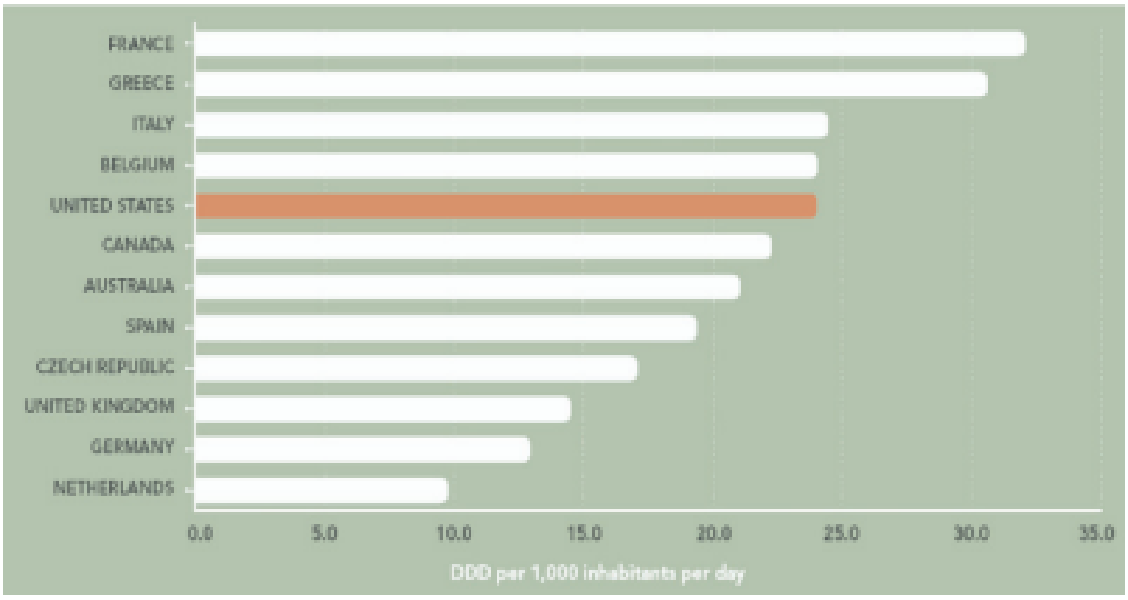
A lot of studies portrayed the use of antibiotics without a doctor's prescription as a "cultural artifact" which means that in countries where the sale of antibiotics is loosely regulated self-medication is perceived as normal and many people consider it to be familiar, cost-effective, safe and effective [12]. On the other hand, the concept of self-medication itself encourages people to take care and look after minor ailments for which they believe do not require any medical attention. One study that was conducted among an adult population in Nigeria revealed that people who self-medicated with antibiotics felt like they had a feeling of independence to take care of themselves [7].

Additionally, several studies found a significant association of antibiotic consumption with gender and age. One example includes a Lithuanian study which showed that self-

medication with antibiotics was reasonably affected by age. Except for that women were more prone to use these agents as compared to men [13]. On the other hand, in another Nigerian study antibiotic use among men was manifested to be higher in comparison to women [14].

Moreover, a study conducted in 11 European countries analyzed the attitude, beliefs and knowledge regarding antibiotic use and self-medication. It revealed that only half of the respondents were familiar with antibiotic resistance and the awareness was the lowest in countries with a higher prevalance of resistance. It also showed that respondents from countries like UK, Malta, Italy, Czech Republic, Croatia, Israel and Lithuania had significantly less appropriate attitudes, beliefs or knowledge for at least one of the dimensions compared with Swedish respondents [15]. If we further analyze and compare data from other European countries, it is shown that rates of self-medication in these countries are high as well. In countries like Greece, Spain and Italy the non-prescribed use of antibiotics ranges from 47 to 73% [16].

Inappropriate antibiotic prescribing continues to remain high even in the United States [29]. The figure displayed below shows antibiotic prescribing in the United States and other countries (Figure 2).



Note: DDD = Defined Daily Doses, a standardized measure of antibiotic consumption

Figure 2: Antibiotic prescribing in the United States and other countries [29]

Many people refuse to directly communicate with a health care professional due to the long waiting periods at the hospitals, shortage of doctors and they also want to save time and

money. Nowadays patients have also expressed concerns regarding the patient-physician relationship. Many patients believe that physicians do not act in the patient's best interest and that in their minds most physicians are businessmen first and physicians second. Except for that several patients were not satisfied with their physicians due to the fact that it was common for the physician to inappropriately prescribe antibiotics for the patients [7, 17].

According to "Medicines use in primary care in developing and transitional countries: Fact Book summarizing results from studies reported between 1990 and 2006" by WHO, the figure below (Figure 3) presents the types of health care providers who prescribed antibiotics inappropriately and in underdosage. Over 40% of the antibiotics were prescribed in underdosage by all health care providers, while the percentage of inappropriate antibiotic prescription was the highest when the prescriber was a medical doctor [3].

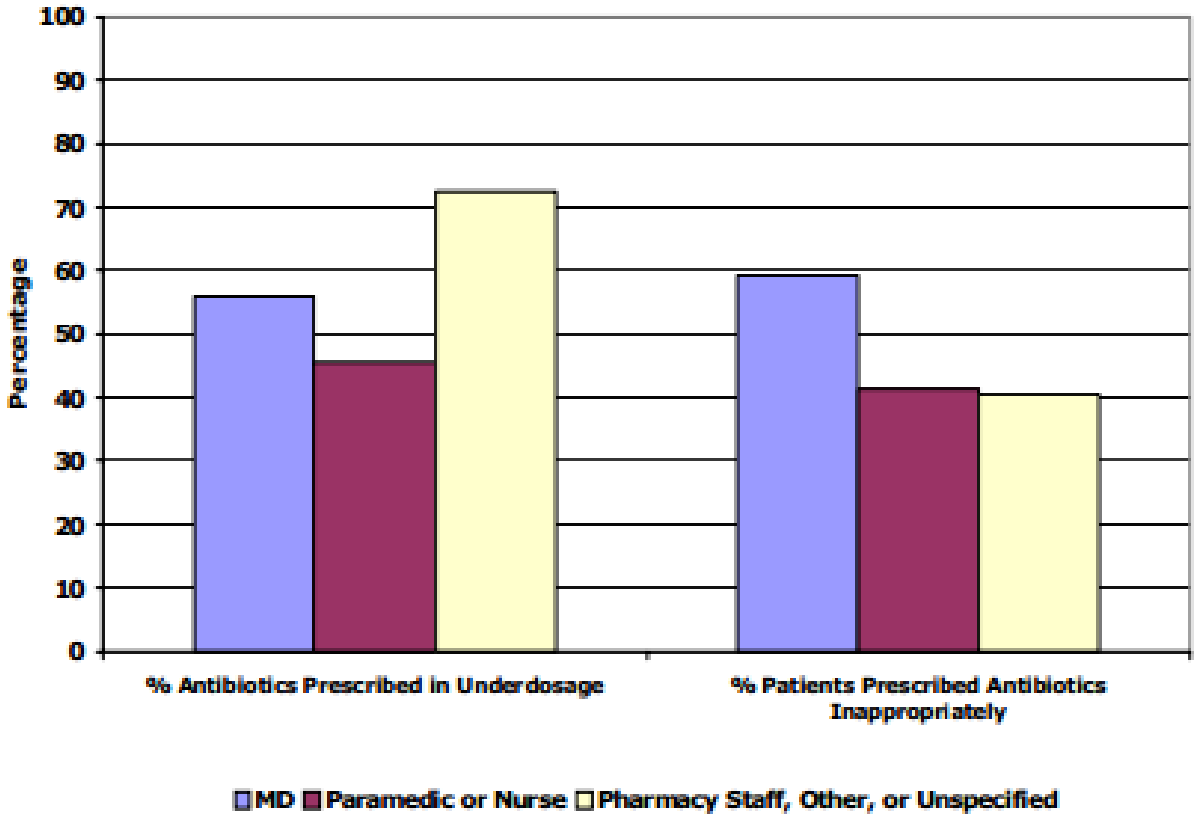


Figure 3: Inappropriate prescribing of antibiotics by type of prescriber [3]

The next figure illustrates the percentage of antibiotics prescribed in underdosage and the percentage of patients to whom antibiotics were prescribed inappropriately in different regions (Figure 4). It is clearly indicated that the inappropriate antibiotic prescription is a

common problem. In Latin America 67% of the prescribed antibiotics were dosed incorrectly while in South Asia over 50% of antibiotic prescriptions were inappropriate [3].

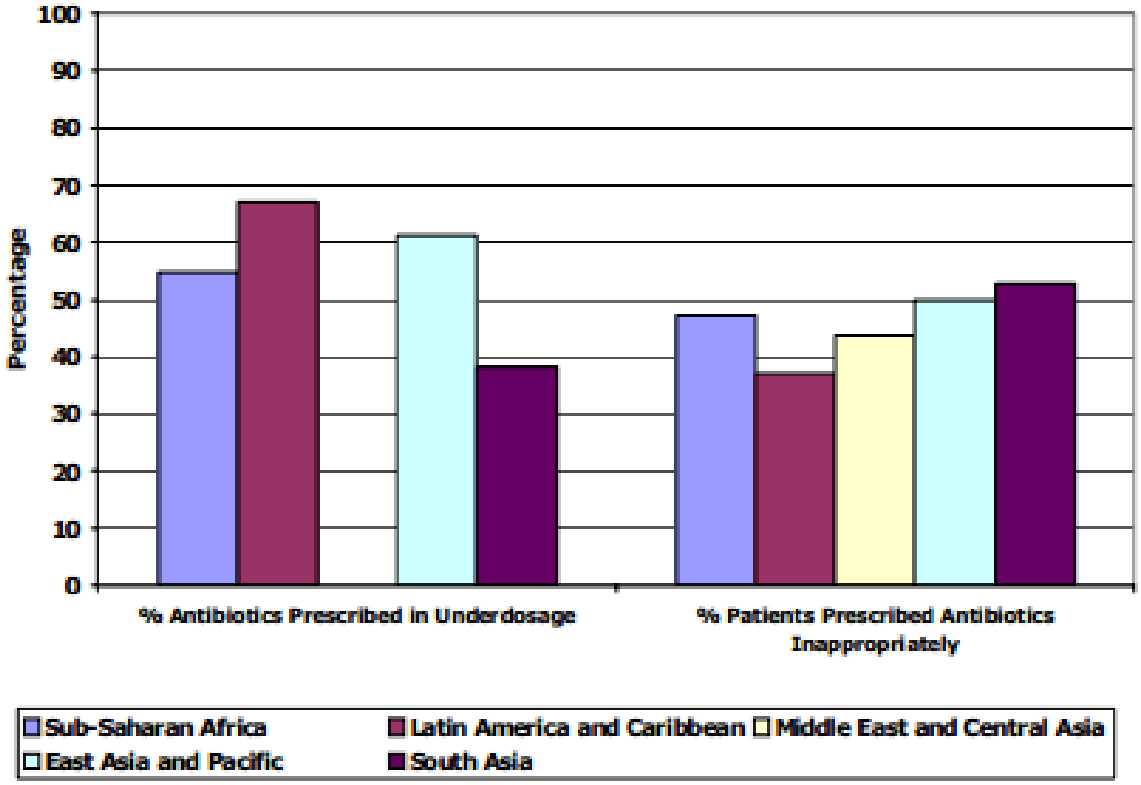


Figure 4: Inappropriate prescribing of antibiotics [3]

In some cases people tend to self-administer antibiotics through drug-identification. One common way of identifying drugs is through trade names, however, other means of identification such as identifying by generic name, action, colour and shape are used as well. Information about the drugs is usually obtained by family, friends, the internet or even health care providers such as pharmacists and medical practitioners [7].

Unfortunately, many people believe that antibiotics are able to heal different diseases including dyspepsias and headaches which pushes them towards using these drugs even in cases when it is not necessary [18].

Studies also imply that self-medication with antibiotics would decrease if the general public were given infortmation on how important it is to consult a doctor prior to self-treatement. This education could be delivered through community organizations or with the help and co-operation of doctors, nurses and pharmacists [12].

2.4. COMPLICATIONS OF SELF MEDICATION WITH ANTIBIOTICS

Self-medication continues to be a widespread problem especially in developing countries. It is of common belief that self-medication might not cause any serious harm. Nevertheless, that is a wrong perception because this activity negatively impacts the individuals's health and it is considered an economic burden too. If antibiotics are overused unnecessarily they can trigger an inappropriate patient demand and patients lose their confidence in the health care system as well [3].

It is generally assumed that antibiotics are degraded spontaneously; however, the indiscriminate use of these agents has caused water contamination while managing to destroy the fragile ecology of the microbial ecosystems [19]. As it was mentioned earlier on, self-medication increases the risk for side effects as well as allergic reactions. The most common side effects of antibiotics include nausea, diarrhea and stomach pain. Occasionally, these symptomps may proceed to dehydration and other problems. On the other hand, it is estimated that in the United States, every year there are approximately 140,000 emergency department visits for reactions to antibiotics and 79% of these visits are due to allergic reactions which range from mild rashes and itching to serious blistering skin reactions, swelling of the face and throat and breathing problems [20].

Minimizing unnecessary antibiotic use is the best way to reduce the risk of adverse drug reactions. Furthermore, self-medication with antibiotics is considered as the key driver of antibiotic resistance which nowdays has become a global phenomenon. At the same time treatment of diseases becomes more difficult and more expensive. It is necessary to develop new agents which unfortunately is expensive and time-consuming (Figure 5) [21]. Damages associated with antibiotic misuse include hospital and food-borne infections, enteropathy such as irritable bowel syndrome, antibiotic-associated diarrhoea as well as drug hypersensitivity [19].

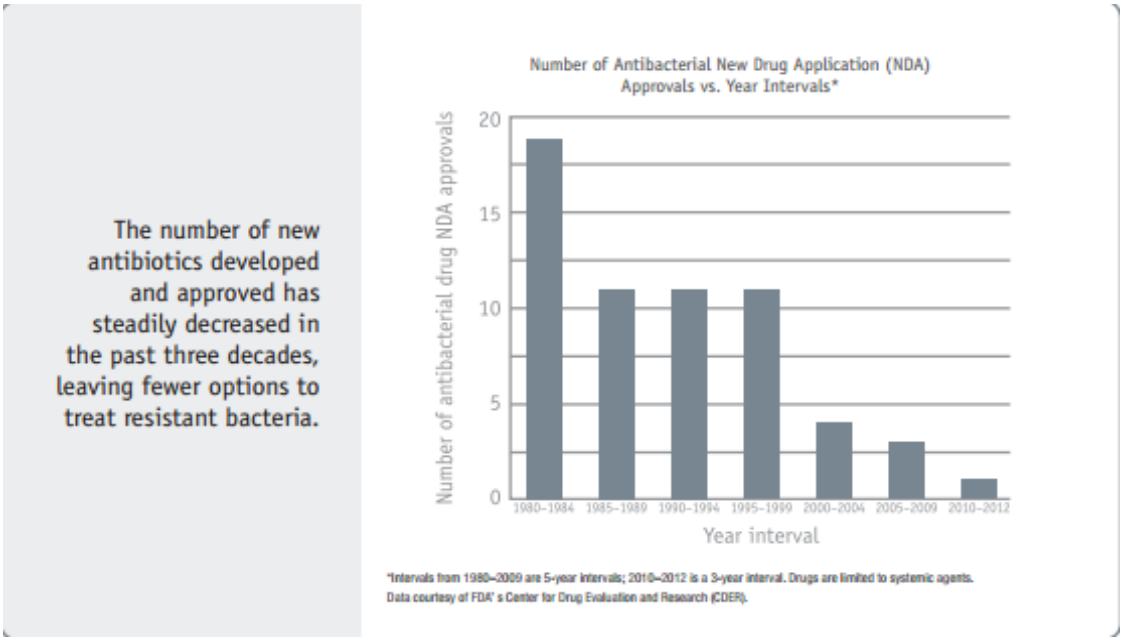


Figure 5: Number of Antibacterial New Drug Application (NDA) Approvals vs Year Intervals [20]

3. THEORETICAL PART- ANTIBIOTIC RESISTANCE

3.1. DEFINITION

Antibiotic resistance is a global problem of the public health with economic, social and political implications especially in developing countries which during the past few years has seriously endangered the efficient treatment of various diseases. Consequently, resistance leads to an increase in mortality, prolongs the duration of the disease and increases treatment costs. Since antibacterial agents are largely used in hospitals resistant bacteria were mainly found there, however today these bacteria are quickly spreading within the community as well [22].

Antibiotic resistance is described as the bacteria's ability to resist the antibiotic's effect, meaning that the bacteria are not eliminated and therefore they do not cease to grow. After their exposure to the antibiotic, the resistant bacteria manage to survive and proceed to proliferate in the body possibly causing more damage and continuing to spread to other individuals (Figure 6). Personal contact or coughing, are only a few examples of how these resistant bacteria can spread to other people. Resistance is something that cannot be completely prevented, the reason being that whenever antibiotics are used their effective lifespan is shortened. Additionally, nowadays antibiotics are so widely used that it has led to an increased prevalence of resistance to newer drugs as well. The way that these agents are used can easily affect the speed through which these pathogens are spread [23, 24]

According to the U.S. Food and Drug Administration (FDA), "Unless antibiotic resistance problems are detected as they emerge, and actions are taken to contain them, the world could be faced with previously treatable diseases that have again become untreatable, as in the days before antibiotics were developed" [25].

The phenomenon of antibiotic resistance will always be with us, however the main challenge which lies ahead is to transform this growing menace into a manageable problem.

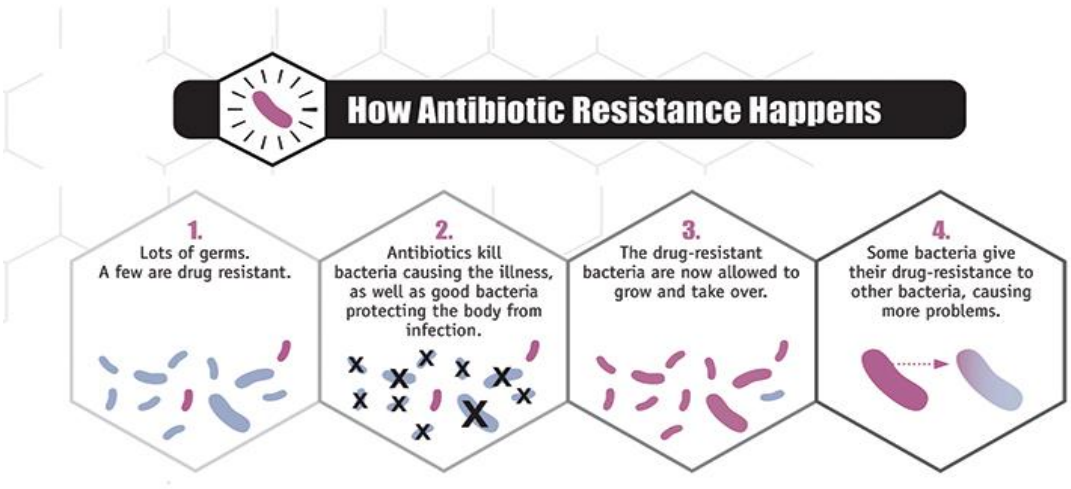


Figure 6: Illustration of the occurrence of antibiotic resistance [20]

3.2. EPIDEMIOLOGY

The incidence of resistance differs from one country to another and over time [19]. Unfortunately, as years pass by the situation keeps deteriorating where sexually transmitted diseases, respiratory, gastrointestinal and nosocomial infections have become the main cause of morbidity and mortality particularly in developing countries [22].

Streptococcus pneumoniae is a respiratory pathogen which is responsible for causing approximately 70% of acute respiratory bacterial infections that lead to the death of more than 3 million children in developing countries each year. *S pneumoniae* resistance to penicillin and erythromycin is becoming apparent in Asia, Argentina, Brazil, Mexico and in some parts of Kenya and Uganda. Furthermore, generally *S pneumoniae* resistance to macrolides and co-trimoxazole has increased while resistance to chloramphenicol and tetracycline has varied widely. On the other hand, it is estimated that about one-third of the world's population is infected with *Mycobacterium tuberculosis* which in comparison to other infectious bacterial species kills more people all around the world [22]. During 2012 approximately 450000 new cases of multidrug-resistant tuberculosis emerged worldwide. MDR-TB has been distinguished in 92 countries [26].

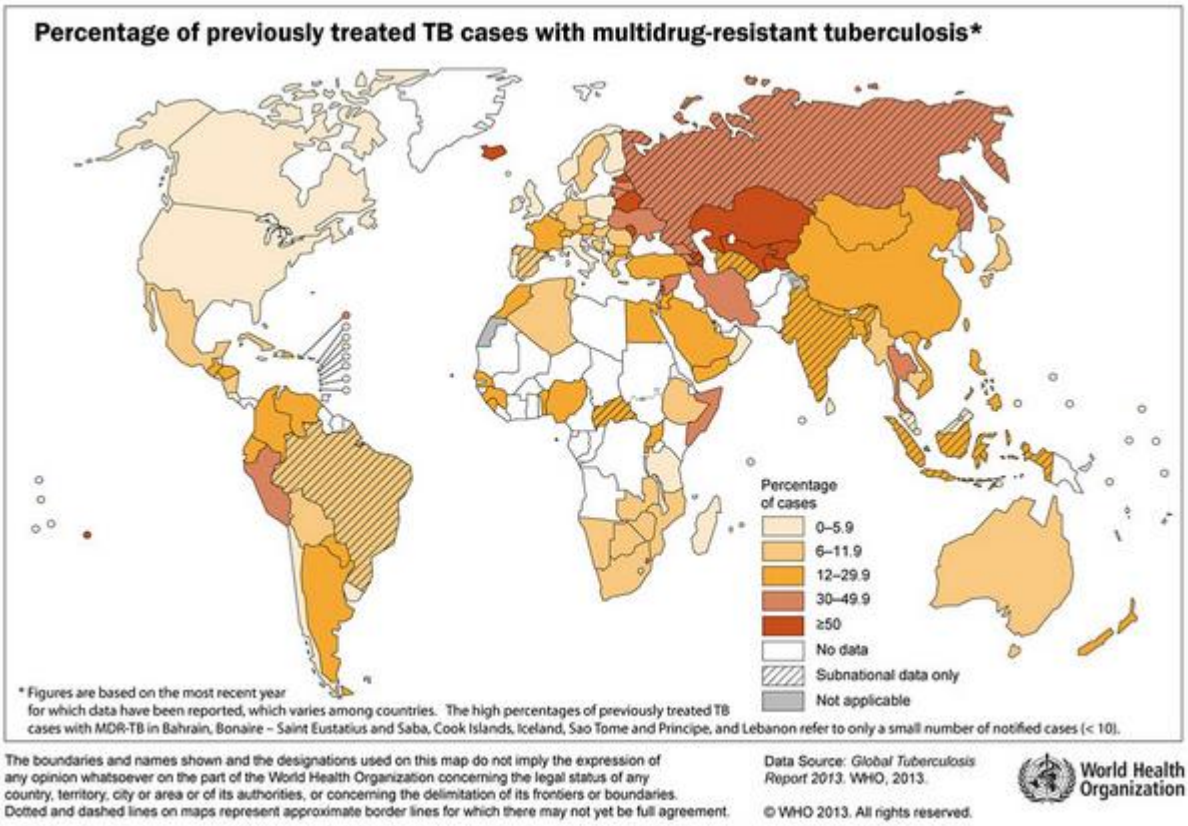


Figure 7: Percentage of previously treated TB cases with multidrug-resistant tuberculosis [26]

A few strains of *Escherichia Coli* which are known for commonly causing urinary tract infections are able to resist fluoroquinolones. In countries like China and parts of Southeast Asia, 60-70% of *E.Coli* are fluoroquinolone resistant while in the United States it is about 10% [27]. *Salmonella typhi* resistance to ampicillin, chloramphenicol and co-trimoxazole has presented serious public health related problems in developing countries and it has even become epidemic in South Asia. Unfortunately, this has elevated the disease's severity causing an increase in mortality and morbidity predominantly in South Asia, where fatality rates were reported to be as high as 10%. *Salmonella typhi* drug resistance has increased throughout the years in the United States too (Figure 8). Nevertheless, resistance seems to have spread to some different diarrhoeal pathogens such as *Campylobacter* species. *Campylobacter jejuni* isolates which were obtained from various Finnish travelers upon returning from countries from all around the world were analyzed and an increase in fluoroquinolone resistance was detected. In isolates from Asia the resistance ranged from 45% to 72% while the ones from Africa from 17% to 38% [22]. Furthermore, it is estimated that *Campylobacter* causes approximately 1.3 million

infections, 13,000 hospitalizations, and 120 deaths in the United States each year [20]. Additionally, *Campylobacter* resistance to ciprofloxacin has increased throughout the years in the Unites States as well (Figure 9).

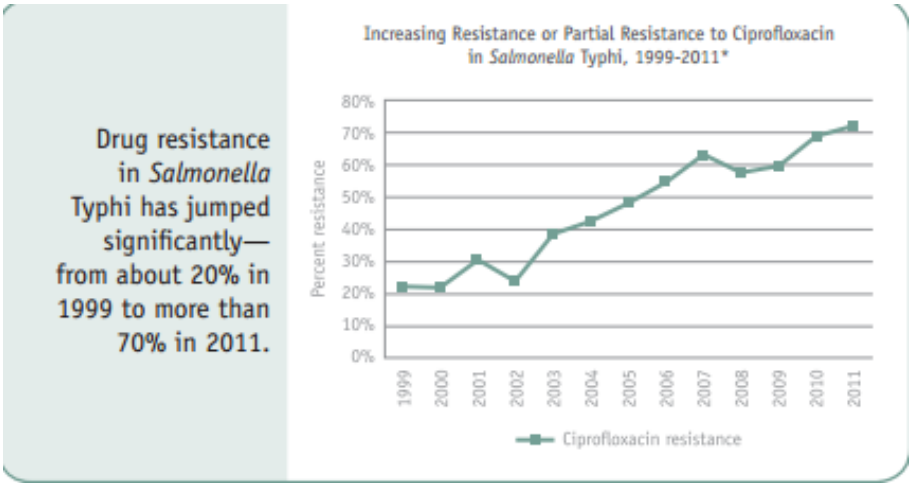


Figure 8: Increasing Resistance or Partial Resistance to Ciprofloxacin in Salmonella Typhi in USA [20]

Figure 9: Increasing Resistance to Ciprofloxacin in Campylobacter in USA [20]

Even today *Neisseria gonorrohoeae* continues to remain the most common cause of sexually transmitted disease in developing countries. Clinicians all around the world have been confronted with triple resistant *N.gonorrohoeae* strains to penicillins, tetracyclines and fluoroquinolones [22, 27]. This presents a big problem in the treatment of the disease because in case that the treatment fails then it leads to further complications, such as infertility and pelvic inflammatory disease in women and it may even increase the possibility of the transmission of HIV [22].

3.3. CAUSES OF ANTIBIOTIC RESISTANCE, PATIENTS AT HIGH RISK

Resistance has presented us with many disadvantages in both the health and economic aspects [28]. The most common and relevant factors which are believed to have influenced and contributed to antibiotic resistance are mentioned below.

3.3.1. IRRATIONAL USE OF ANTIBIOTICS BY THE PUBLIC

Today when patients suffer from an infection, they want a quick recovery and therefore they believe that an antibiotic is the fastest solution to their problem [29, 30]. In many developing countries patients are able to buy antibiotics without a prescription. They believe that antibiotics are not dangerous and therefore they proceed to self-medicate through using left-over antibiotics or receiving advice from family members, friends and pharmacists. Except for that, the patients might use the antibiotic to treat a viral rather than a bacterial infection not realizing that the antibiotic is ineffective in treating viral diseases, like common cold or the flu.

On the other hand, another dominant problem in developing countries is the poor patient adherence to antibiotics. A Mexican study revealed that 60% of patients failed to adhere and it is believed that one of the factors leading to this was the inadequate physician-patient interaction [12]. The overuse or underuse of antibiotics presents an increased risk for bacterial resistance. For this reason the relationship between patients and health care providers, needs to improve because this will improve the patient's understanding of the drug regimens respectively [23, 27, 28]

3.3.2. INAPROPRIATE USE OF ANTIBIOTICS BY UNSKILLED PRACTITIONERS

The quality of health care which is provided in each country is different. Unfortunately, in developing countries there is a lack of highly trained professionals who are not fully aware of the harmful effects of the inappropriate use of antibiotics [23]. It is quite common for these health care providers to inappropriately prescribe antibiotics while using incomplete information to diagnose an infection or by unnecessarily prescribing broad-spectrum antibiotics [31]. A broad spectrum antibiotic has a better probability to be more effective against an infection with unidentified bacteria; however, the disadvantage in this case is that these antibiotics select for resistance in several bacterial species at once. Except for that in the case of

busy clinical practices the physician may not have time to explain to the patient why they have chosen to prescribe or not prescribe antibiotic therapy which worsens the problem even further [27]. Even though in many developing countries pharmacists are not allowed to diagnose and prescribe, they often do it nonetheless. Sometimes they even have rooms which are special either for physical examination or injections. In countries like Mexico or the Philippines the pharmacy staff gives advice to the patients regarding the antibiotics they need to buy while in Egypt they refill the bottles of antibiotics without asking for a prescription [32]. Furthermore, there are doctors who are happy to prescribe antibiotics to patients who demand them just because this benefits their practice. However, neither the doctor nor the patient contemplate the fact that the misuse of antibiotics decreases the drug's effectiveness [29].

3.3.3. ANTIBIOTIC USE IN HOSPITALS

Hospitals have always been an important factor in the development and spread of antibiotic resistant bacteria [33]. In many hospitals there is a lack of infection control which is associated with poor hygiene and sanitation problems [28]. Consequently, this provides a fertile environment for the resistant bacterial strains to spread among patients. However, the most frequent way of transmission occurs during the contact between the patients and the contaminated hands of the health care staff [33].

3.3.4. USE OF ANTIBIOTICS IN ANIMALS FOOD AND AGRICULTURE

The chronic use of subtherapeutic quantities of antibiotics to promote growth in food animals has been banned in the EU nevertheless, this process is currently continuing in the USA. Organisms such as *Salmonella, Campylobacter, Listeria,* enterococci and some strains of *E.Coli*, initially grow among animals and afterwards infect people. This transmission can happen either through the food chain or animal handlers. Even though the animal contribution to resistance is small, we should not consider it as insignificant [27].

3.3.5. POOR QUALITY OF ANTIBIOTICS

The quality of several antibiotics in developing countries is considered to be below the standards [23]. In many African countries, due to the high temperature and humidity, the active constituents in some of these drugs have been degraded and additionally, the improper storage

conditions have led to the alternation of the physiochemical properties of these excipients which means that the dosage form can no longer protect and deliver the active compound. Degraded drugs contain less than the stated dose and some of the degraded products are even toxic [32]. Examples include countries like Nigeria where ampicillin, tetracycline, and oxytetracycline were found to be of substandard quality. This situation presents a high risk for therapeutic failure which unfortunately in the majority of cases is considered to be the only method to identify substandard drugs. Laboratories that analyze and distinguish substandard drugs are not commonly found and even when they exist in most cases we are unaware of them [23].

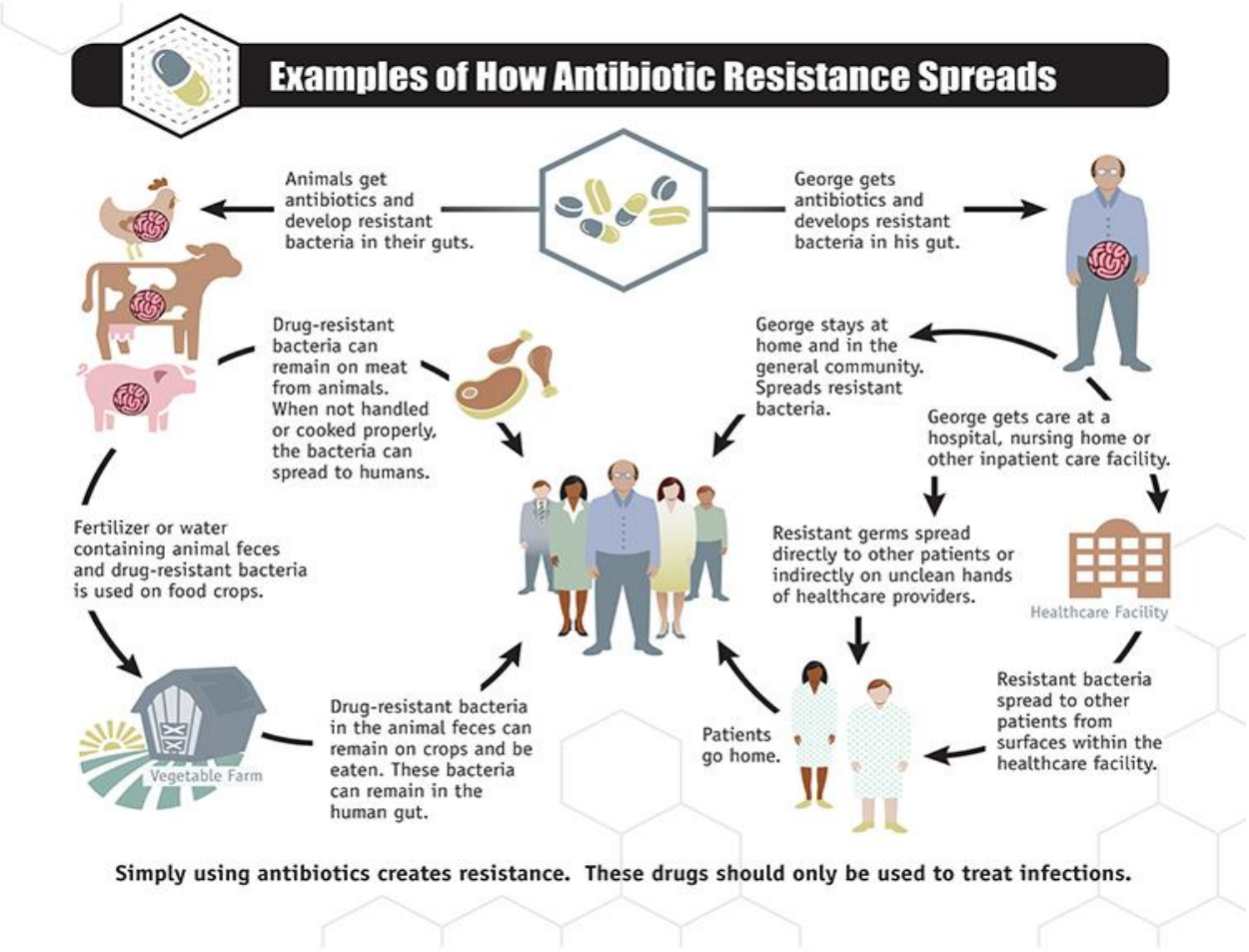


Figure 10: Examples of How Antibiotic Resistance Spreads [20]

As antibiotic resistance grows, the antibiotics that were once used to successfully treat infectious diseases do not work as well or at all. Once antibiotic treatments lose their effect, they will not only compromise the ability to fight infectious diseases but they will also undermine

treatment of infectious complications in patients with other diseases. Patients who are undergoing organ transplants, joint replacements, cancer therapy and the ones that are being treated for chronic diseases such as diabetes, asthma, rheumatoid arthritis, are dependent on the ability to fight infections with antibiotics. If that ability is lost then the possibility of offering patients various life-saving and life-improving modern medical advantages will be lost with it [18]. The figure below represents the group of patients who are at a high risk in case no antibiotics are available to treat infections (Figure 11).

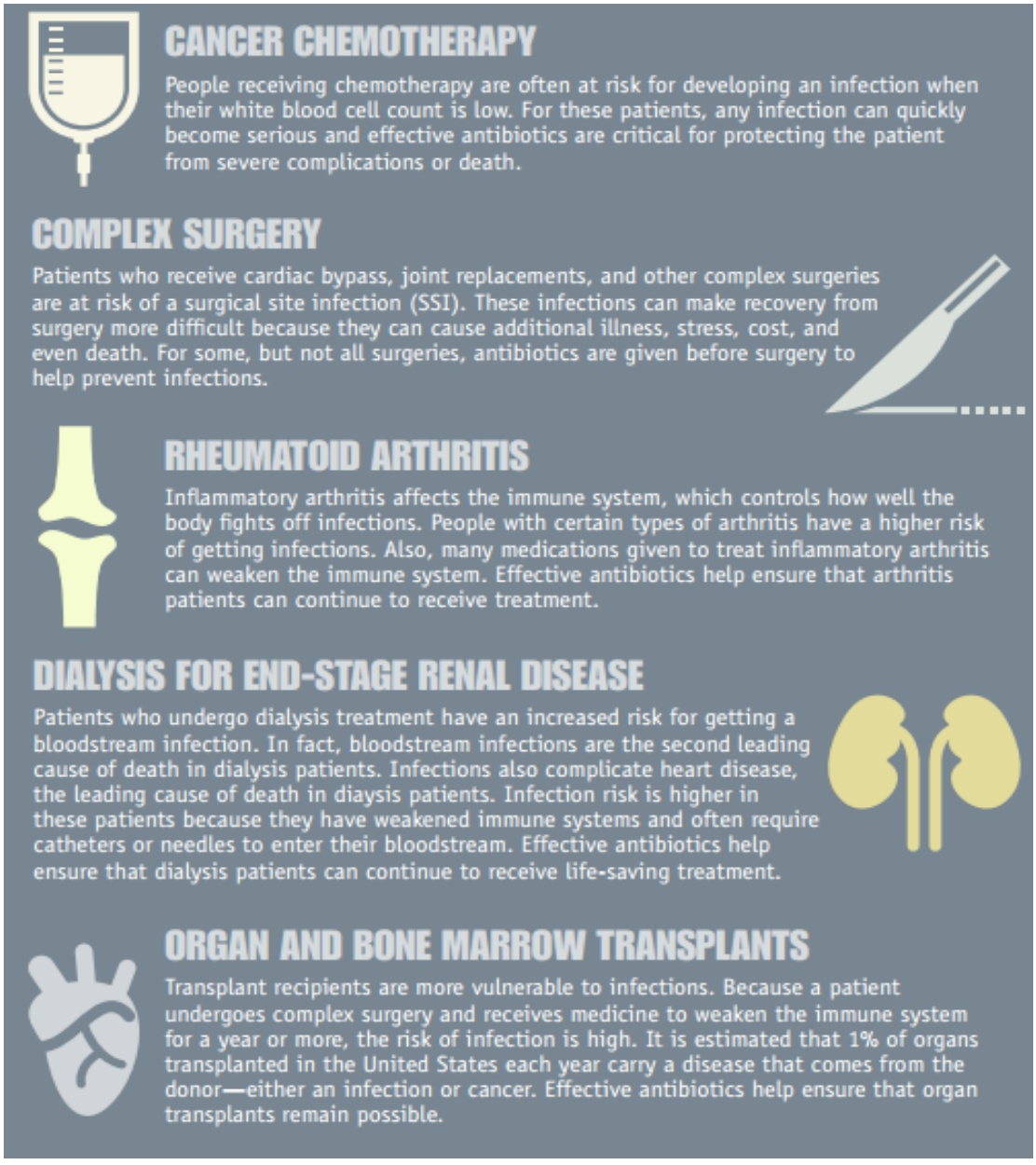


Figure 11: An illustration of the groups of patients at high risk [20]

3.4. DIAGNOSTIC METHODS CURRENTLY USED TO DETECT ANTIBIOTIC RESISTANCE

A few testing methods that have been used to detect resistance throughout the years include dilution methods, the disk diffusion method, the E-test, automated antimicrobial susceptibility testing systems as well as genotypic methods [24]. Unfortunately, most of these methods are considered time-consuming, costly and not totally reliable. Therefore, the research team from INSERM (INSTITUT NATIONAL DE LA SANTÉ ET DE LA RECHERCHE MÉDICALE) developed two tests that allow a rapid identification of antibiotic resistance. These works were published in September 2012 in two international reviews*: Emerging Infectious Diseases* and *The Journal of Clinical Microbiology* [34, 35].

These tests are known as the Carba NP test and ESBL NDP test. They are based on the acidification properties generated by the activity of the enzymes (ß-lactamases and carbapenemases) when they are in the presence of an antibiotic. If any of these enzymes is present, the medium becomes acid and the acidity indicator (pH) turns from red to yellow. These tests have excellent sensitivity and specificity and the use of these extremely efficient tests on a world-wide scale, would allow to adapt antibiotic treatments to the individual's needs and to be more successful in controlling antibiotic resistance, particularly in hospitals [36].

As Patrice Normann states "We can hope, in particular in many Western countries where the situation has not yet reached endemic proportions multi-resistances (France, in particular), to be able to preserve to a certain extent the efficiency of wide-spectrum cephalosporins and carbapenems, antibiotics used as a "last resource" [36].

Additionally, they have multiple benefits as well. They are non-invasive and can be done on bacteria taken from a urine or stool sample. Moreover, they are not time-consuming considering that the results are ready in 2 hours which is less time in comparison to other methods which normally take 24 to 72 hours. Except for that, the researchers consider these tests as 100% reliable, relatively simple and cheap to administer, since their estimated cost is about 4 to 5 euros each. These tests are regarded as an important breakthrough in the fight against antibiotic resistance [37].

3.5. MANAGEMENT OF SELF-MEDICATION WITH ANTIBIOTICS AND ANTIBIOTIC RESISTANCE

3.5.1. AIM

Self-medication with antibiotics supports irrational antibiotic use, which has consequently contributed to the increased prevalence of antibiotic resistance that in turn has managed to cause health and economic losses worldwide [28]. As a result, it is important to set aims in order to optimize antibiotic use, while increasing awareness of the threat that antibiotic resistance poses and encouraging immediate action to address the threat [20]. Several goals that we must aim to achieve include:

- Reduction of unnecessary antibiotic prescribing and elimination of antibiotic use especially in cases when they do not provide any medical effect. This would help in delaying the emergence of resistance and also maximize the benefit of antibiotics.
- Facilitate a more effective communication between health care providers such as the doctor or pharmacist and the patient in order to try and understand the patient's knowledge, attitude and practices towards antibiotic use.
- Identify subgroups of the population with high levels of antibiotic use and with misconceptions about antibiotic use, in order to evaluate the motivations, expectations and incentives that lead people to use or not use antibiotics.
- To try and understand which infectious diseases and resistance problems are important and which factors determine patterns of antibiotic use.
- Prevent infections from occurring and prevent resistant bacteria from spreading.
- Track resistant bacteria.
- Promote the development of new antibiotics and new diagnostic tests for resistant bacteria [19, 20, 29, 31].

3.5.2 STRATEGY

In order to achieve the goals mentioned above, it is essential to execute suitable strategies. For instance, it is important to encourage collaborations between governments, non-governmental organizations, professional societies and international agencies, in order to

recognize and present accurate messages regarding the importance of antibiotic resistance and the appropriate antibiotic use [19]. Additionally, educational interventions for prescribers, dispensers, patients and the general community should be implemented. These educational programs need to target doctors who often prescribe antibiotics unnecessarily or who frequently tend to prescribe broad-spectrum antibiotics rather than narrow-spectrum ones. Moreover, pharmacists need to be targeted also because, unfortunately, several pharmacists are willing to sell antibiotics without a prescription and for this reason community pharmacies nowadays are considered to be as one of the main sources of non-prescribed antibiotic use [28, 29].

Patients should be educated on the importance of proper antibiotic use and need to be discouraged to self-medicate with antibiotics. Except for that, emphasis should be put on the education regarding hygiene and disease transmission as well. In conclusion, successful educational interventions have shown to improve diagnostic quality, dispelling perceptions of patient pressure and reduce unjustified antibiotic prescription [19].

Another strategy in controlling bacterial resistance is the reduction in the transmission of bacteria. Since health care workers at hospitals are able to carry and transmit resistant bacteria to patients through contaminated hands, clothing or medical instruments. Some simple measures which can be taken in order to reduce transmission are hand washing, gloves, gowns and other barrier precautions. Some bacteria tend to be extremely persistent for weeks or even months on hospital equipment and therefore, resistance can be reduced through eliminating resistant bacteria that have colonized the hospital environment by improving cleaning procedures [29]. An important key element is also the utilization of aseptic techniques for medical and nursing procedures. It is also recommended that effective infection control teams consisting of physicians, microbiologists, nurses and pharmacists need to be established since they would help to recognize and investigate infection outbreaks and actively surveil bacterial resistance [19].

Hospitalized individuals with potentially dangerous resistant bacteria need to be isolated in special units. This is a process followed by hospitals in Australia which in turn has led to a decrease in the levels of MRSA and MDR staphylococci among all Australian hospitals. Similar measures are also followed in the Netherlands and Scandinavian countries [27]. However, it is important to consider the fact that in hospitals in different countries the antibiotic determinants

are specific and for this reason effective solutions will need to be tailored to local epidemiological circumstances and resources [33].

Last but not least, national governments and health care systems need to enforce legislation and policies concerning the development, licensing, distribution and sale of antibiotics. Government-initiated inspection of adherence to Good Manufacturing Practice (GMP), adherence to the product specifications agreed upon at the time of licensure and the elimination of unauthorized medicines from the market are essential. The efficacy, quality and safety of new drugs is determined by the US Food and Drug Administration (FDA), the European Commission, and the Japanese Ministry of Health, Labour and Welfare (MHLW). The content and conduct of preclinical and clinical development programs for pharmaceuticals has been highly influenced due to the release of individual regulations by these bodies. Therefore, countries that do not have similar systems to control the efficiency and safety of drugs need to establish them in order to avoid exposure to drugs of inferior efficacy and unacceptable toxicity, as well as a potentially higher market penetration of counterfeit drugs [19].

In many countries there is a lack of control over the supply, distribution and sale of antibiotics. For this reason a legislation should be implemented which does not allow the sale of antibiotics without prescription and restricts the antibiotic sale only to registered outlets which are staffed with personnel that have sufficient knowledge regarding antibiotic use. Ideally, these registered outlets should also have documentation of the quantities of antibiotics that they sell, so later on they can evaluate the amount of antibiotic sale and use [19].

4. EXPERIMENTAL PART

4.1. OBJECTIVE

The main aim of the experimental part of this cross-sectional study was to collect data from patients in one selected community pharmacy located in Kosovo, in order to estimate the rate and reasons of self-medication with antibiotics by a population in Kosovo and additionally, analyze the socio-demographic factors that affect this behavior.

4.2. METHODOLOGY

4.2.1. DATA EXTRACTION

The study was conducted during a period of 14 days, between the dates of December 16th to December 29th, 2013 in a community pharmacy in the city of Prishtina. A total of 300 patients that visited the pharmacy during these two weeks participated in this study. Data was collected through using a validated, self-administered questionnaire which was developed in English at the department of Social and Clinical pharmacy at Charles University, Faculty of Pharmacy in Hradec Kralove. In order to collect the data, the questionnaire was initially translated to the country's native language, which is Albanian, and afterwards the results obtained were back-translated to English for the purpose of data analysis and interpretation.

4.2.2. STUDY POPULATION

The study population consisted of participants of 5 different age groups (<20, 20-30, 31-40, 41-60, >60). The patients that visited the pharmacy were randomly selected and there was no additional criteria in the selection of these patients. Each patient was individually approached and was asked to participate. Additionally, they were informed that the study was being conducted for research purposes and therefore verbal consent was obtained from all of them.

4.2.3. DATA EVALUATION

Initially, the use of antibiotics without a prior consultation with a physician, the reasons for antibiotic consumption and the sources of non-prescribed antibiotic use were analyzed. Afterwards, the patient's attitude regarding the storage of antibiotics at home, their knowledge concerning antibiotic resistant bacteria and possible adverse effects associated with antibiotic

consumption were evaluated. Lastly, information related to the demographic data such as gender, age and the level of education of the patients was collected and evaluated. Furthermore, descriptive statistics were used to analyze and summarize the data.

4.3. RESULTS

All 300 patients that participated in this study provided complete information giving a 100% response rate. As it was referred earlier, one part of the questionnaire dealt with the collection of the demographic data which are presented in the table below (Table 1). When analyzing this data we can see that the amount of female and male participating patients was almost equal. The majority of respondents in this study were younger patients considering that 41% of the patients were in between the ages of 20 to 30 years old and 34% between 31 to 40 years old. Furthermore, after evaluating the level of education of the respondents it was concluded that this group of patients consisted mostly of well-educated adults.

Gender	**Total number of patients (N=300)**	**Percentage %**
Male	152	50.7
Female	148	49.3
Age		
<20	22	7.3
20-30	123	41
31-40	102	34
41-60	46	15.3
>60	7	2.4
Education		
Master's/Ph.D.	18	6
Bachelor's Degree	195	65
Secondary Education	87	29

Table 1: Demographic characteristics of the patients

The patients were initially asked if they self-medicated with antibiotics and 212 (70.7%) patients reported that they used non-prescribed antibiotics while 88 (29.3%) of the patients reported using prescribed antibiotics (Figure 12). Moreover, the rates of self-medication among individual groups of patients were analyzed. It seems that self-medication with antibiotics is higher among younger respondents and respondents with a lower level of education (Table 2). The sources of non-prescribed antibiotic use were further evaluated. Our results showed that 71 (33.5%) patients self-medicated based on a previous experience indicating that these patients might have either had an old prescription and used it to re-purchase the antibiotic or used left-over antibiotics. On the other hand, 58 (27.4%) patients self-medicated by their own initiative through obtaining information from various sources such as the internet, 50 (23.5%) of them received advice from their friends, neighbors or family members and 33 (15.6%) obtained antibiotics directly from the community pharmacy considering that in Kosovo the purchase of antibiotics over the counter is easily accessible (Figure 13).

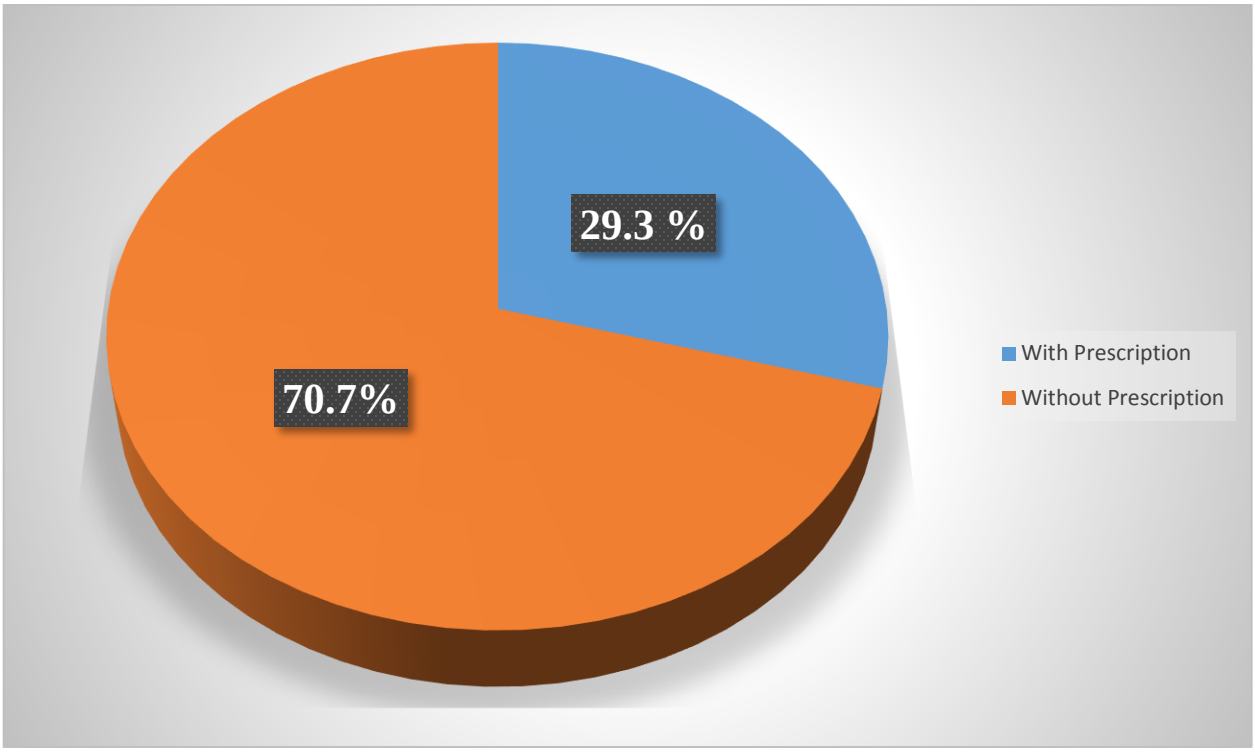


Figure 12: Percentage of patients that self-medicated with antibiotics (N=300)

Demographic Characteristics	Total number of patients (N=300)	Number of patients that self-medicated with ATB (N=212)	Percentage %
Gender			
Male	152	111	73
Female	148	101	68.2
Age			
<20	22	12	54.5
20-30	123	105	85.4
31-40	102	80	78.4
41-60	46	12	26
>60	7	3	42.8
Level of education			
Secondary Education	87	77	88.5
Bachelor's Degree	195	130	66.6
Master's/Ph.D.	18	5	27.8

Table 2: Number of patients that self-medicated with antibiotics according to gender, age, level of education

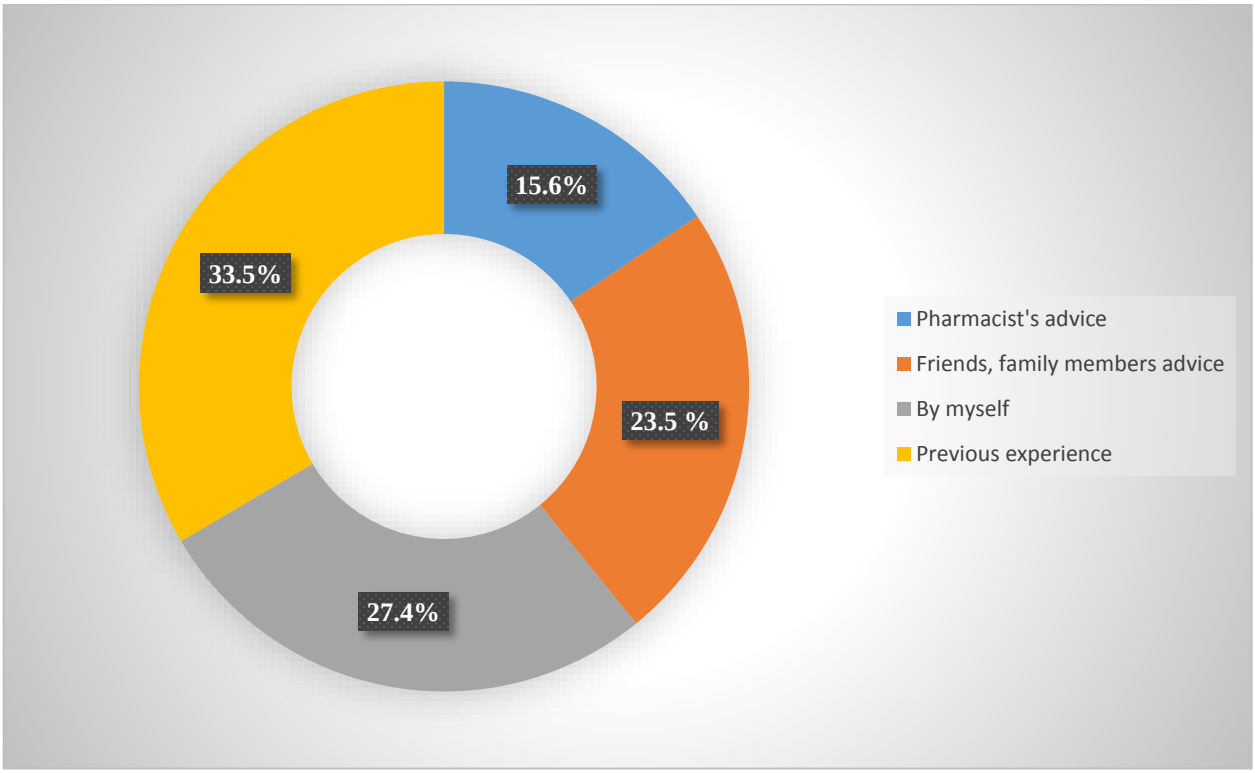


Figure 13: Sources of non-prescribed antibiotic use (N=212)

Additionally, the most common reasons for non-prescribed antibiotic consumption among this group of patients were assessed. The most frequent reasons for using antibiotics were cough, urinary inflammation and influenza which were followed by gastrointestinal and gynecological inflammations (Table 3).

Reasons	***Percentage %***
Cough	18.1
Urinary Inflammations	17.3
Influenza	14.6
Gastrointestinal	12.2
Gynecological Inflammations	12.2
Ear Infection	9.4
Respiratory Inflammation	8.7
Orthopedic Inflammation	5.1
After Surgery	2.4
Other Reasons	0

Table 3: Clinical indications of non-prescribed antibiotic use by patients (N=212)

One part of the questionnaire was used to analyze the principles of antibiotic use by all patients. Our findings showed that 137 (45.7%) of the respondents stopped taking the antibiotic once they felt better, indicating that this group of patients were not fully compliant during their therapy with antibiotics. On the other hand, 138 (46%) of the respondents claimed that they use antibiotics as prescribed by the physician or pharmacist. In this case, the patients used prescribed antibiotics and followed the physician's orders or simply purchased a non-prescribed antibiotic at the community pharmacy and followed the pharmacist's orders instead. Furthermore, only 25 (8.3%) of the respondents stated that they change the antibiotic if they do not feel better immediately (Figure 14).

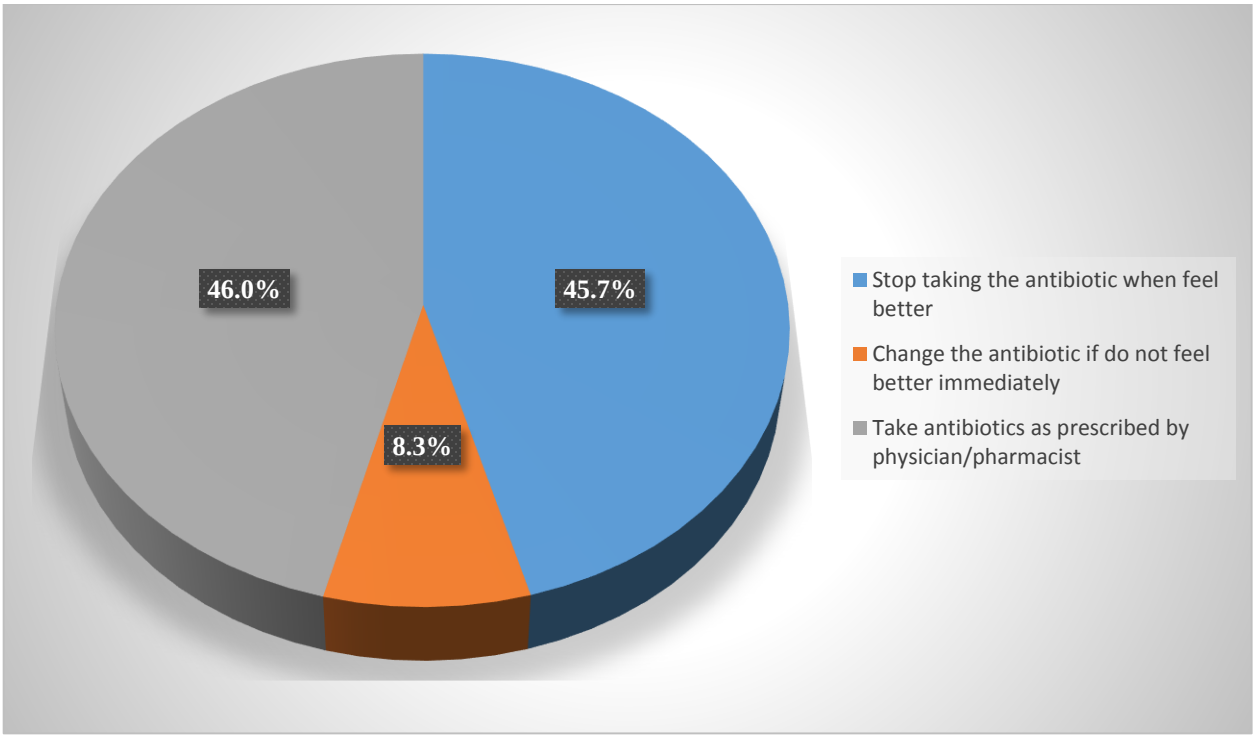


Figure 14: Principles of antibiotic use by patients (N=300)

Results regarding the general statements of patients about the storage of antibiotics, attitude, knowledge of antibiotic resistance as well as adverse effects and allergies associated with antibiotic use, are shown in the table below (Table 4). In this part both positive and negative statements can be seen.

A total of 70.3% of the patients admitted to storing antibiotics at home which unfortunately, seems to promote self-medication with antibiotics therefore supporting irrational antibiotic use. Our findings revealed that being younger and less educated were associated with keeping antibiotics at home (Table 5). Moreover, 58.3% of the patients had a poor knowledge regarding antibiotic resistance while additionally, 50.7% of the patients claimed that they were not aware that antibiotics can kill off normal flora. It seems that older and more educated patients were better informed and more aware of antibiotic resistant bacteria, in comparison to the younger and less educated ones. In addition, female patients had a higher level of knowledge regarding antibiotic resistant bacteria in comparison to the male patients (Table 6).

Nevertheless, it is important to stress out that in this group of patients 63% stated that they believe that it is important to complete an antibiotic course and except for that 55.7% of the patients were aware of the allergies/adverse effects associated with antibiotic consumption.

A higher level of awareness was found among older and more educated patients and even in this case female patients showed higher awareness and knowledge in comparison to the male ones (Table 7).

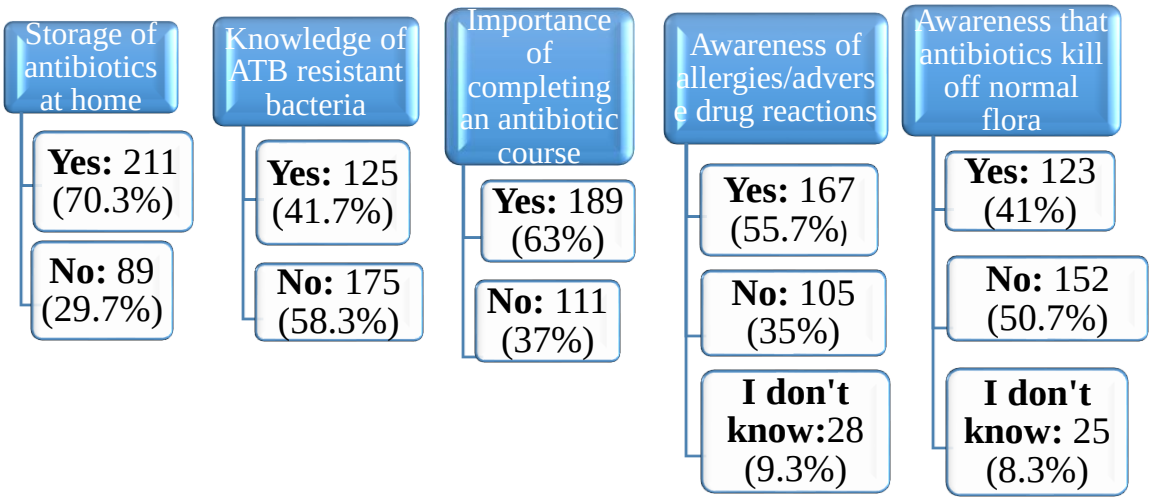


Table 4: Knowledge, attitude and behavior statements of patients

Demographic Characteristics	Total number of patients (N=300)	Storage of antibiotics at home	
		YES	NO
Gender			
Male	152	109 (71.7%)	43 (28.3%)
Female	148	102 (61.9%)	46 (38.1%)
Age			
<20	22	12 (54.5%)	10 (45.5%)
20-30	123	110 (89.4%)	13(10.6%)
31-40	102	81 (79.4%)	21 (20.6%)
41-60	46	6 (13%)	40 (87%)
>60	7	2 (28.6%)	5 (71.4%)
Level of education			
Secondary Education	87	79 (90.8%)	8 (9.2%)
Bachelor's Degree	195	126 (65%)	69(35%)
Master's/Ph.D.	18	6 (33%)	12 (67%)

Table 5: Storage of antibiotics at home according to gender, age and level of education

Demographic Characteristics	Total number of patients (N=300)	Knowledge of antibiotic resistance	
		YES	NO
Gender			
Male	152	56 (36.8%)	96 (63.2%)
Female	148	69 (46.6%)	79 (53.4%)
Age			
<20	22	3 (13.6%)	19 (86.4%)
20-30	123	36 (29.3%)	87 (70.7%)
31-40	102	51 (50%)	51 (50%)
41-60	46	33 (71.7%)	13 (28.3%)
>60	7	2 (28.6%)	5 (71.4%)
Level of education			
Secondary Education	87	30 (34.5%)	57 (65.5%)
Bachelor's Degree	195	81 (41.5%)	114 (58.5%)
Master's/Ph.D.	18	14 (77.7%)	4 (22.3%)

Table 6: Knowledge of antibiotic resistant bacteria according to gender, age and level of education

Demographic Characteristics	Total number of patients (N=300)	Awareness of allergies/ antibiotic side effects		
		YES	NO	I don't know
Gender				
Male	152	71 (46.7%)	64 (42.1%)	17 (11.2%)
Female	148	96 (64.9%)	41 (27.7%)	11 (7.4%)
Age				
<20	22	6 (27.3%)	10 (45.5%)	6 (27.2%)
20-30	123	51 (41.5%)	60 (48.8%)	12 (9.7%)
31-40	102	68 (66.7%)	26 (25.5%)	8 (7.8%)
41-60	46	39 (84.8%)	6 (13%)	1 (2.2%)
>60	7	3 (42.9%)	3 (42.9%)	1 (14.2%)
Level of education				
Secondary Education	87	44 (50.6%)	30 (34.5%)	13 (14.9%)
Bachelor's Degree	195	113 (58.5%)	68 (35.2%)	14 (6.3%)
Master's/Ph.D.	18	10 (55.6%)	7 (38.9%)	1 (5.5%)

Table 7: Awareness of allergies/antibiotic side effects according to gender, age and level of education

5. DISCUSSION

Research studies that analyze factors and patterns influencing self-medication with antibiotics are essential in order to diminish the irrational antibiotic use which in turn will help prevent the occurrence of antibiotic resistance in the future. As it was referred earlier, the selected community pharmacy in which this study took place is located in Prishtina which is the capital city of Kosovo. Prishtina is a relatively big city with around 210.000 inhabitants while Kosovo consists of approximately 1.9 million inhabitants. Additionally, 67.2% of the entire population is under the age of 64 years old and therefore Kosovo is considered as a country with a young population [38].

A total of 300 patients were assessed in order to analyze the rate and reasons for self-medication with antibiotics. As it was described earlier on, each patient was individually approached and was asked to participate. The advantage of the study is that all the patients were willing to participate and nobody refused the questionnaire. The questionnaire took an average of 5 to 10 minutes for each patient to complete. The short amount of time which was required to complete it, was convenient for all patients. Moreover, the questionnaire was understandable and no additional questions were asked by the patients.

On the other hand, our demographic data showed that secondary education was the lowest level of education in this sample of patients and no patients with only primary education were present. This community pharmacy is located in the center of the city and therefore people with a higher level of education and better financial income, are the ones with an easier access to the pharmacy. Furthermore, we believe that the lack of a medicines reimbursement system contributed to this situation as well. All patients have to pay for their drugs with out-of-the pocket money. Unfortunately, drugs in Kosovo are expensive and for this reason patients with primary education who have significantly lower incomes and in many cases are even unemployed, cannot afford to buy drugs on a regular basis therefore limiting their access to the pharmacy.

The present study indicated that antibiotic sale without prescription in Kosovo is widely available, leading to a high prevalence of self-medication with these agents. In this group 70.7% of the patients administered non-prescribed antibiotics. These rates can be compared with results conducted in Greece where 74.6% of the patients admitted using non-prescribed antibiotics,

Yemen (73.8%) and Uzbekistan (71.3%) [39, 40]. Nevertheless, these rates are considered high in comparison to other countries such as the Czech Republic (31.1%) [4]. According to our data it seems that the rates of self-medication with antibiotics are higher among younger and less educated respondents; however the rates of self-medication between males and females seem to be similar. In contrast to this study, another one conducted in Lithuania showed that women were more prone to self-medicating with antibiotics in comparison to men [13]. Furthermore the results from our study support the fact that the tendency for self-medication with antibiotics is increasing worldwide.

The high prevalence of self-medication that was found among the participants in our study is related to many factors. Poor enforcement regulation is considered as one of the leading factors influencing self-medication. Patients have easy access to non-prescribed antibiotics from community pharmacies even though there is a law which prohibits the antibiotic sale over the counter. Moreover, there are no punishments against the pharmacists who agree to dispense antibiotics without medical prescriptions.

On the other hand, poverty, cultural beliefs and the lack of a sustainable health care system are regarded as essential driving factors leading to self-medication with antibiotics in Kosovo as well. Several patients due to the lack of time are not able to attend consultations with a physician and express concerns regarding the cost of the consultations. Except for that, if the patients consider their condition as a minor ailment they believe that consulting with a physician is not necessary. In Kosovo, it is also believed that antibiotics are drugs with a high safety profile and with multiple purposes therefore patients do not hesitate to self-medicate even when it is inappropriate.

Non-prescribed antibiotic use is further associated with incomplete, short courses and unsuitable dose and drug selection [41-49]. Our study showed that this group of patients were non-compliant due to the fact that they stopped their antibiotic therapies once they felt better and therefore ended up not completing the entire course. Unfortunately, this kind of behavior results in the promotion of the occurrence of antibiotic resistance. Additionally, these findings are also supported by other studies which confirm that patients are frequently non-adherent to their treatment. A study analyzing non-compliance with antibiotic therapy was conducted among 11 countries worldwide and it revealed that 22.3% of the patients admitted not finishing their antibiotic therapy; however the results differed from one country to another where Asian

countries like China had the highest rates of non-compliance (44%) while European countries like the Netherlands had the lowest (9.9%) [50].

Furthermore, in several occasions patients tend to select the inappropriate antibiotic for treatment even when provided by a pharmacist, which increases the risk for adverse drug reactions or potential drug-drug interactions [44]. This means that when patients visit the pharmacy they may incorrectly describe their symptoms therefore leading to the inappropriate selection and provision of antibiotic by the pharmacist. In addition, the pharmacist does not ask about the patient's allergies or take the time to explain to them the possible side effects [50]. Except for that, the lack of a comprehensive medicines reimbursement system leaving medicines as out-of-pocket payments often guides patients into selecting a low quality antibiotic resulting in short duration of treatment and also, presenting a serious health problem because it undermines the principle of equity with respect to both financing and access to health care [9, 51].

In contrast to the studies conducted in the United Arab Emirates and Jordan, where patients reported that they were unaware of the side effects and consequences associated with inappropriate antibiotic use [4, 52], our study revealed that even though this group of patients self-medicated, 55.7% were aware of the potential side effects that might occur while consuming antibiotics. A possible explanation for this is that the patients might have learned about the possible side effects from a pharmacist, physician, and internet research or even from personal experience with antibiotic side effects.

Nevertheless, when this group of patients was asked about their knowledge regarding antibiotic resistant bacteria, 58.3% of the patients showed poor knowledge accompanied by a low awareness of the fact that inappropriate and irrational antibiotic use, are contributing factors leading to antibiotic resistance. Moreover, 50.7% of the patients did not know that antibiotics can kill off normal flora, thereby leading to superinfections. This was not entirely expected since this group of patients consisted mostly of well-educated adults. Results showed that younger and less educated patients had a lower knowledge regarding antibiotic resistance. In addition to that, male patients had a lower awareness of antibiotic resistance in comparison to the female patients.

Our study also showed that patients store antibiotics at home in order to self-administer them for self-diagnosed diseases or even give them to family members or friends. This indicates

that patients have developed beliefs that antibiotics should routinely be available at home, encouraging them to frequently use antibiotics even when it is not necessary. Moreover, this finding was consistent with results from other studies such as the one conduced in Russia, which showed that participants keep antibiotics at home in case they need them in the future [53].

Additionally, there are several studies providing evidence that antibiotics are administered inappropriately because they are used to treat infections which are more likely to be viral [54, 55]. In this case our study provides similar results as well. This group of patients stated that the main reasons for antibiotic consumption were cough, influenza and urinary inflammations. According to these findings, it seems that patients believe that with antibiotics it is possible to treat all kinds of infections irrespective of their origin.

Even though the major reasons for antibiotic consumption were evaluated, one of the limitations of our study is that the most commonly chosen antibiotic for self-medication in Kosovo was not determined. Nevertheless, another study which was conducted among 13 non-EU countries including Kosovo disclosed that amoxicillin followed by first-generation cephalosporins were widely used and consumed in high volumes (Figure 15) [9].

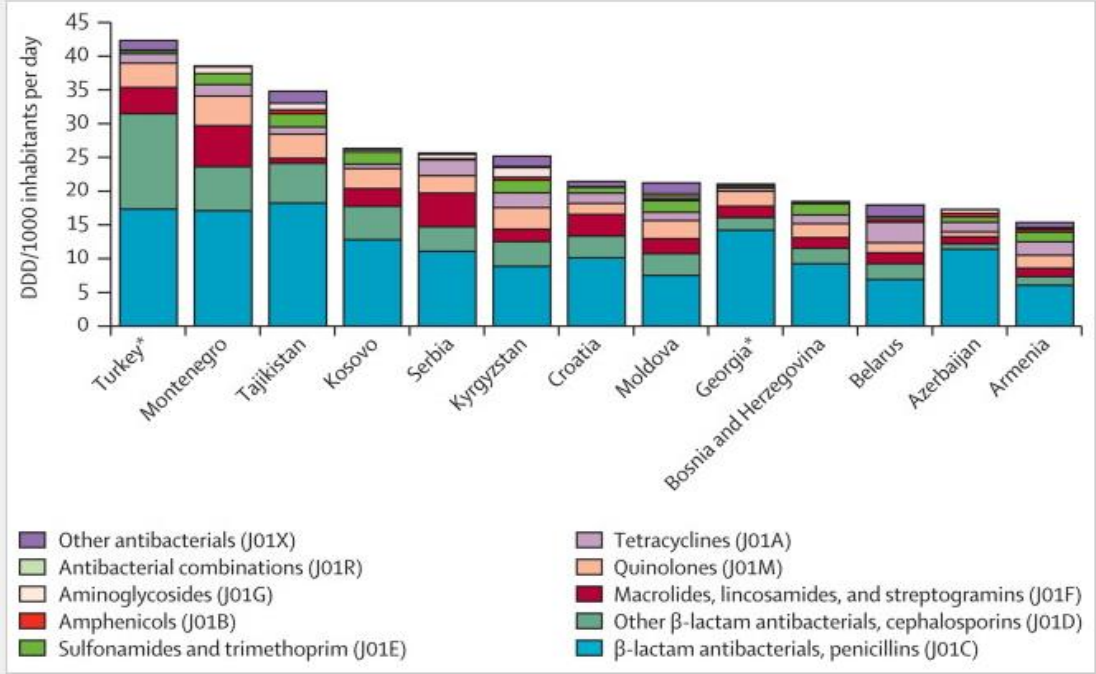


Figure 15: Total antibiotic use in 13 non-EU countries [9]

Except for the countries showed in the figure above (Figure 15), these results can also be compared with other countries such as Greece, Jordan and Sudan where amoxicillin was one of the most common antibiotics chosen for treatment [39, 43, 52]. In this study the rates of self-medication with antibiotics were estimated; however it is important to stress out that the rates and frequency of self-medication with oral or parenteral antibiotics were not analyzed or determined.

On the other hand, the cross sectional nature of this study is also considered a limitation. All of the participating patients were assessed only once. Moreover, the study itself was not designed to detect recent changes in opinion. Additionally, our study focused on analyzing self-medication with antibiotics among adults; however, it is essential to consider the fact that antibiotic consumption and misuse is high among children as well.

Last but not least, as it was mentioned several times earlier, 300 patients participated in this study which is a small number in comparison to the total population of the city. Data was also collected only from one community pharmacy. For this reason, even though this study proves that this group of patients in Kosovo self-medicates with antibiotics, the limitation of the study is that due to the small sample size used for research, the obtained results might not be representative of the whole country's behavior towards self-medication.

Consequently, in future studies it is necessary to assess a larger population size and ideally follow all the participating patients over time, so we can gain a better and deeper understanding of their self-medicating behavior and at the same time generate more accurate and representative findings.

6. CONCLUSION

In conclusion self-medication is a behavior which supports the irrational antibiotic use which on the other hand is considered as a relevant factor contributing to the increased prevalence of antibiotic resistance. The results of this study confirm that self-medication with antibiotics is a frequent problem and furthermore, the availability of these non-prescribed agents is leading to inappropriate antibiotic consumption in Kosovo. Additionally, we can also conclude that the knowledge and awareness regarding antibiotic resistance among these patients was poor.

In order to reduce the frequency of antibiotic misuse, interventions at different levels are required. Educational interventions encouraging appropriate antibiotic use and raising awareness about the problem of antibiotic resistance are essential and necessary. Emphasis should be put on the uses, limitations and negative effects of these medications. These interventions should target health care providers and the general public too. Strict policies regarding the sale of antibiotics should be implemented and punishments against those who do not follow these policies should be given to as well.

Nevertheless, the increased frequency of antibiotic use among adults and the widespread lack of awareness regarding resistance, indicate that this population-based study as well as future studies could be suitable in monitoring recent trends in antibiotic use. Moreover, by using surveys like this we are able to effectively monitor antibiotic knowledge, attitudes, and practices among demographic subgroups of concern. Knowing the extent of the problem and being aware of the groups of people that use antibiotics inappropriately more frequently, will help in the development and funding of intervention efforts, including public information campaigns [31].

7. ABBREVIATIONS

ATB = Antibiotic

CARBA NP TEST = Carbapenemase-Producing *Enterobacteriaceae* Nordmann/Poirel

ESBL NDP TEST = Extended-Spectrum-Beta-Lactamase-Producing *Enterobacteriaceae* Nordmann/Dortet/Poirel

EU = European Union

FDA = Food and Drug Administration

HIV = Human Immunodeficiency Virus

IMS HEALTH = Intercontinental Marketing Services Health

MDR-TB = Multidrug-Resistant Tuberculosis

MRSA = Methicillin Resistant Staphylococcus Aureus

WHO = World Health Organization

8. LIST OF FIGURES

9. LIST OF TABLES

10. REFERENCES

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