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REVIEW

Antibiotic Consumption and Antibiotic Policies in Relation to Antibiotic Resistance: A Comparison of the Global Situation with that in Syria and AANES (Rojava)

Saify Nabiabad Haidar[1*], Abdou Houker[2]

[1] Ph.D., Department of Biotechnology and Biomedicine, Institute of Science and Modern Technology-Rojava University. North and East Syria

[2] MSc. candidate, Department of Biotechnology and Biomedicine, Institute of Science and Modern Technology-Rojava University. North and East Syria

Abstract

Antimicrobial resistance (AMR) and the inevitable evolution of super-bacteria pose a serious threat to human health worldwide. If this problem is not resolved immediately. As a result of the outbreak of antimicrobial resistance (AMR), many countries have adopted national action plans aimed at reducing the consumption of antibiotics. Here, we have reviewed several prominent studies on antibiotic consumption around the world, including Syria. A careful and comparative analysis of these studies indicate high prescription rates of broad-spectrum antibiotics in Outpatient Antibiotic Dispensing (OAD) and high percentage uses of the Watch group of AWaRE classification. By comparison antibiotic consumption rate in Syria and Autonomous Administration of North East Syria, known as AANES or Rojava, is comparable to that of average global consumption (20.9 DID) and much lower than those in neighboring countries such as Turkey (48,9 DID) and Iran (60 DID). Some recommendations regarding the situation in AANES (Rojava) have been presented. The purpose of this review is to summarize several important studies on worldwide antibiotic consumption with an emphasis on the Syrian situation and the effects of antibiotic consumption on the development of bacterial resistance, and point out how a proper public health policy can help curb antibiotic resistance.

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* - Corresponding Author: Haidar Saify homan_saify@yahoo.com

1. Introduction

It has been widely accepted that antibiotics are only pharmacologically active against foreign cells and bacteria, and are not active in our cells or tissues, except when they produce side effects. Several of the antibiotics become toxic when given only in large doses. As a result, their prescription can be less restrictive than that of other pharmaceuticals. They are often administered to patients who display signs of infection without strictly diagnosing the bacterial species. Antibiotic consumption has been highly affected by this, as can be seen from antibiotic sales numbers (Sköld 2011). Despite this, antibiotics are not benign interventions, and they can have adverse effects on patients and communities, including treatment failures and the development of antimicrobial resistance (AMR) (Denny et al. 2019). Microorganisms typically develop Antimicrobial Resistance (AMR) as a part of their evolutionary process, but widespread usage of antimicrobials accelerates this process (World Health Organization 2018). A major mechanism of resistance involves the inactivation of the antimicrobial by enzymes such as β-lactamases or aminoglycoside-modifying enzymes (Fernández and Hancock 2012). In addition, microorganisms can have mutations in the target molecules of antibiotics that may abrogate the binding and actions of the antibiotics, which makes these antibiotics ineffective. Moreover, genes can be inherited vertically from parental cells or can be acquired horizontally from other strains on mobile genetic elements such as plasmids (Ventola 2015). The horizontal gene transfer (HGT) can allow antibiotic resistance to be transferred among different species of bacteria (Read and Woods 2014). Furthermore, exposure to antibiotics kills sensitive bacterial cells sparing the resistant ones leading to the elimination of the competition and a higher chance for proliferation and spread of resistant bacterial strains. Therefore, the emergence and dissemination of resistance-causing bacterial strains are directly related to antibiotic consumption, according to epidemiological studies. There are many principal types of antibiotic resistance. First, the possession of a semipermeable outer membrane with low permeability, as is the case for the Gram-negative. Second, constitutive efflux pumps are observed in many bacteria. Third, the acquired resistance, in which an originally susceptible microbe can become resistant either by incorporating new genetic materials, such as plasmids, transposons, integrons, and naked DNA, or as a result of mutations (Fernández and Hancock 2012). A significant amount of the problem of antimicrobial resistance is also caused by the overuse of antimicrobial agents in farm animal, as the CDC has indicated that the use of antimicrobials in animals is associated with resistance in humans as antibiotics are transmitted to humans through animal products, such as meat and dairy products from the animals that have been treated with these antibiotics (Bartlett et al. 2013). Antimicrobial resistance (AMR) and the spread of multidrug resistant (MDR) pathogenic bacterial strains, so called super-bugs or super-bacteria, are posing a major threat to human health across the globe. If this problem is not tackled, the antibiotic resistance will further increase and lead to total failure of using them against bacterial infections. The United Kingdom government predicts that by 2050, 10 million deaths could occur annually due to the antibiotic resistance (Álvarez-Martínez et al. 2020).

The purpose of this review is to summarize recent studies on the antibiotic consumption and its relationship with increasing antibiotic resistance, with an emphasis on the Syrian, the importance of an effective public health policy to address increasing antibiotic resistance.

2. Antimicrobial Consumption

Antimicrobial resistance (AMR) and the inevitable evolution of super bacteria pose a serious threat to human health worldwide. Studies indicate that there is a high rate of inappropriate use of antibiotics worldwide and that this leads to an increased antibiotic resistance. In addition, more than two-thirds of antibiotics used in clinics are either not needed or inappropriate (Álvarez-Martínez et al. 2020). Widespread use of antibiotics provide an environment for rise and spread of AMR. If the antibiotic resistance issue is not resolved, the antibiotics that have been so far successful can become ineffective. According to UK government data, 10 million deaths may occur annually due to antibiotic-resistant bacteria in 2050, making it one of the main causes of death globally (Álvarez-Martínez et al. 2020). In this review, we have studied a group of publications around the world, including Syria, on the consumption of antibiotics. Careful comparison has shown a high correlation of antibiotic resistance with the high rates in the OAD (Outpatient Antibiotic Dispensing) of broad-spectrum antibiotics and high percentages of the Watch group of the AWaRE classification. These results are concerning as the increased consumption leads to notable increase in the bacterial resistance against antibiotics. By comparison, the antibiotic consumption rate in Syria (20.13 DID) is comparable to the global consumption rate (20.9 DID) but notably lower than Korea (23.12 DID) and much lower than Turkey (48.9 DID) and Iran (60 DID). This unexpected low consumption rate of antibiotics in Syria and AANES (Rojava) may be because Syria's study excluded children and inpatient care as well as limited data on antibiotic use. In addition, the prescription rate of extended-spectrum penicillins and third- and fourth generation cephalosporins have increased, while the prescription rate of first- and second-generation cephalosporins appears to have declined.

2.1. ATC/DDD methodology

The WHO methodology for antimicrobial consumption monitoring relies on the Anatomical Therapeutic Chemical (ATC)/ Defined Daily Dose (DDD) classification, which is a global standard for drug utilization research. This standardization allows comparisons of data across healthcare facilities, countries, and regions. The WHO Anatomical Therapeutic Chemical (ATC) classification system was used to classify antimicrobials. Among these drugs, antibacterial drugs are classified as the ATC J01 group; Antifungals are classified as the ATC J02 group; Antimycobacterial drugs are classified as the ATC J04 group; the antivirals are classified as the ATC J05 group.

2.2. WHO Classification of Antibiotics (AWaRe)

Access, Watch, Reserve **(AWaRe)** classification of antibiotics resistance was developed by World Health Organization (WHO) to assist in the development of tools for antibiotic steward-ship at local, national, and global levels and to reduce antimicrobial resistance. AWaRe classified antibiotics into different groups to emphasize the importance of their appropriate use (Tankeshwar 2021).

2.3. Antibiotic resistance and global antibiotic consumption between 2000 and 2015

Antimicrobial resistance has become a major public health crisis worldwide. Several factors influence antibiotic resistance, but one of the most important is antibiotic consumption (Olesen et al. 2018). The association between antibiotic consumption and resistance is well documented across spatial and temporal scales at individual hospitals, nursing homes, primary care facilities, and communities, as well as across countries. It is observed in many countries that national action plans have been adopted to reduce antibiotic consumption per capita (Klein et al. 2018). Between 2000 and 2010, antibiotic consumption increased by 36% in 71 countries, according to the largest prior study (Klein et al. 2018). It is however impossible to directly compare the results from this study with other studies since it used no defined daily doses (DDDs), the most commonly method used to measure antibiotic consumption (Klein et al. 2018). In this study, it was found that global antibiotic consumption increased by 39% from 11.3 to 15.7 DDDs per 1,000 inhabitants per day (DID). The mean antibiotic consumption rate across countries increased by 28% from 16.4 DDDs per 1,000 inhabitants per day to 20.9, and the median antibiotic consumption rate increased by 25% from 15.5 to 19.5 DDDs per 1,000 inhabitants per day.

Worldwide, broad-spectrum penicillin consumption increased by 36% between 2000 and 2015. While the antibiotic consumption rate of the next three most consumed classes is cephalosporins (20% of total DDDs), quinolones (12% of total DDDs), and macrolides (12% of total DDDs) (Klein et al. 2018). A careful comparison shows a high correlation of antibiotic resistance with the high rates in the OAD (Outpatient Antibiotic Dispensing) of broad-spectrum antibiotics and high percentages of the Watch group of the AWaRE classification. These results are concerning as the increased consumption leads to notable increase in the bacterial resistance against antibiotics.

2.4. Korean situation (from 2008 to 2012)

The recent trends in Korean antibiotic consumption at the national level have been evaluated in a few studies between 2008 and 2012. The results showed that the total consumption of antibiotics increased from 21.68 DID in 2008 to 23.12 DID in 2012. Penicillins were the most commonly used antibiotics (4.52 DID), followed by second-generation cephalosporins (4.47 DID) and macrolides (3.32 DID). There was a significant increase in the consumption of third generation cephalosporins, carbapenems, and glycopeptides (Choe and Shin 2019). A similar study conducted between 2007–2014 by Choe and Shin (2019) revealed additional information on trend changes for antibiotic classes in different age groups. Children younger than 6 years had the highest level of antibiotic use (59.21 DID) in 2014 with increasing trend each year from 2007, which is consistent with previous findings (Choe, & Shin, 2019). The prescription rate of extended-spectrum penicillins and third- and fourth generation cephalosporins showed an increasing trend, while the prescription rate of first- and second-generation cephalosporins seemed to have declined (fig. 1) (Choe and Shin, 2019).

In a study conducted between 2010 and 2014, a total: of 7,261,176 antibiotic prescriptions were provided to 1,039,756 patients. Most of these prescriptions (91.2%) were for the treatment of respiratory illnesses. The most frequent primary diagnosis was acute upper respiratory infection (24.4%), followed by acute bronchitis (22.2%). The antibiotic prescription rate was the highest for the 2–6 years-old patients, comprising 84.0% of all outpatient prescriptions for that age group in 2014. The antibiotic prescription rate for all pediatric patients increased from 34.8% in 2010 to 70.4% in 2014. Among drug classes, extended-spectrum penicillins were the most commonly prescribed antibiotic (Song et al. 2018).

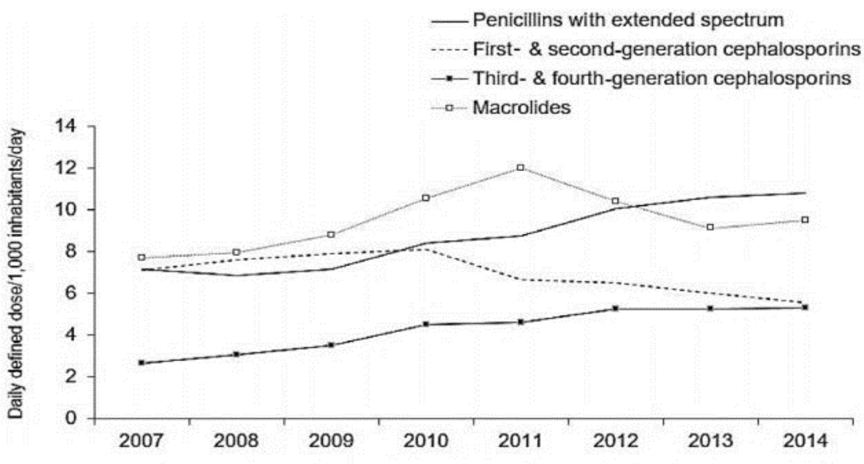

Figure 1. Trend of antibiotic consumption in children aged ≤6 years in Korea, 2007–2014 (Park et al. 2017).

2.5. Non-European countries

A survey of antibiotic usage in 2011 in 12 non-European countries, but including Turkey and Kosovo, showed that antibiotic use among the participating countries differed significantly, ranging from 15.3 DID in Armenia to 42.3 DID in Turkey (fig. 2). In a comparison of antibiotic use across 29 countries in 2011 penicillin (ATC group J01C) was the most commonly used antibiotic (Versporten et al. 2014). While provincial antibiotic consumption data in Turkey was detected to vary between 17.2 and 55.2 DID in Hakkari and Usak, respectively; regional AC ranged from 28.4 to 48.9 DID Middle Eastern Anatolia and Western Anatolia, respectively (Ayfer Sahin et al. 2017).

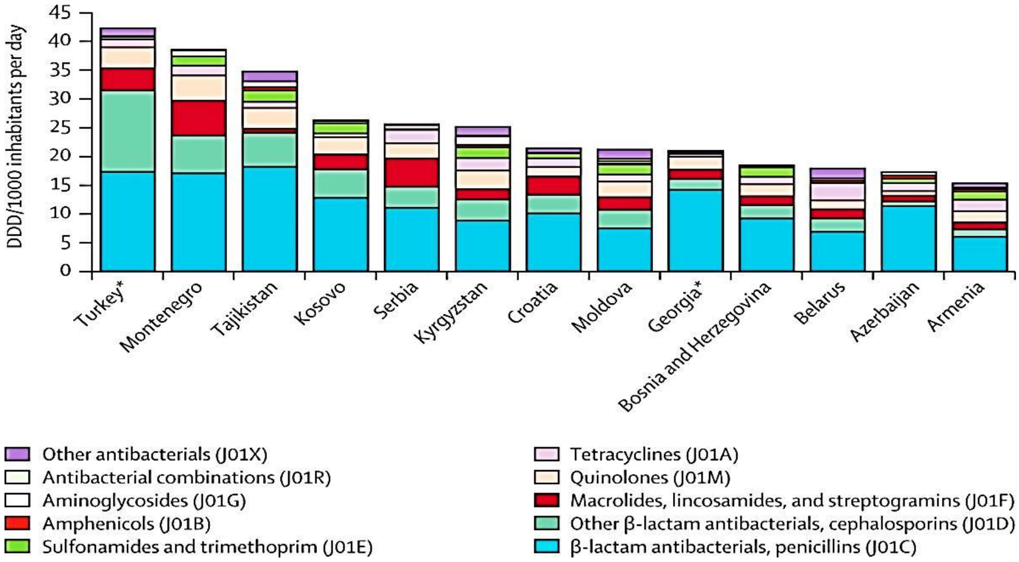

Figure 2. Total antibiotic use in 12 non-European countries and Kosovo, 2011 (Versporten et al. 2014). *Reported only outpatient antibiotic use.

2.6. Iran situation (2000–2016)

The systemic antibiotic consumption rate in Iran, as obtained from the IFDA (Iranian Food and Drug Administration) annual data, has increased from 33.6 DID in 2000 to 60 DID in 2016 (Abbasian et al. 2019). Consumption of cephalosporins increased from 3.2 DID in 2000 to 13.1 DID in 2016. Also, the macrolide consumption at the beginning of the study was equal to 1.2 DID and reached 8.8 DID in 2016. The use of Quinolones has also increased from 1.2 DID in 2000 to 4.4 DID in 2016, while the consumption of sulfonamides and aminoglyco-sides has decreased in the same period. Sulfonamides consumption has decreased from 3.5 DID in 2000 to 0.8 DID in 2016. Additionally, aminoglycoside consumption has decreased from 0.6 DID to 0.2 DID (Abbasian et al. 2019) (fig. 3). According to another study in Iran, 62.6% of children with acute cough during the previous two weeks had taken antibiotics. Based on similar studies conducted in other countries, such as the United States in 2011, Norway in 2003, and the United Kingdom in 2004, this figure is very high, compared to 21%, 27%, and 31%, respectively (Mostafavi et al. 2015).

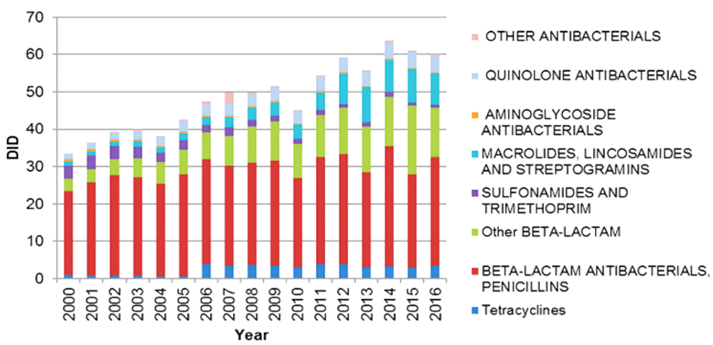

Figure 3. Consumption of antibiotics in Iran between 2000–2016 (Abbasian et al. 2019).

2.7. Syria situation (June 2018 to May 2019)

Prior to the Syria conflict, health indices for Syria showed many parallels with those of Western countries, such as the life expectancy in excess of 70 years. In contrast to Western countries, neither microbiology nor infectious diseases were recognized as specialty areas of training, nor were they financially rewarding. Little training was provided beyond medical school; there were few opportunities for continuing medical education. The laboratories established in public hospitals under the Ministry of Health (MoH) and Ministry of Higher Education were variably equipped with manual (Kirby–Bauer) and automated (Phoenix and Vitek) AMR testing (Abbara et al. 2018). A study published in Antibiotics Journal in 2020 presented outpatient antibiotic dispensing (OAD) patterns and rates for patients with health insurance using different indicators. This study was based on OAD data from thirteen Syrian government health insurance data that were used to cover 12 months from June 2018 to May 2019 to express annual OAD patterns and rates. The study included the OAD data of 81.314 beneficiaries. These beneficiaries were employed by the Syrian government (Aljadeeah et al. 2020). The most commonly used antibiotic was amoxicillin/clavulanic acid (5.76 DID), followed by clarithromycin (4.4 DID). Nine antibiotics accounted for 90% of the total dispensed antibiotics (table 1) (Aljadeeah et al. 2020).

Table 1. Outpatient antibiotic dispensing rates that accounted for 90% of total dispensed antibiotics among adults with health insurance in Syria expressed in the number of defined daily doses (DDDs) per 1000 people per day (DID).

Number	Antibiotic	AWaRe	DID	The proportion of Total DID
1	Amxicillin/Clavulanic acid	Access	5.76	28.62%
2	Clarithromycin	Watch	4.4	21.87%
3	Cefixime	Watch	2.66	13,05%
4	Cefuroxime	Watch	1.85	9.17%
5	Levofloxacin	Watch	1.09	5.4%
6	Azithromycin	Watch	0.72	3.59%
7	Cefdinir	Watch	0.63	3.15%
8	Cefprozil	Watch	0.55	2.71%
9	Ciprofloxacin	Watch	0.51	2.55%
Drug Utilization 90% (DU90%) 1-9			18.14	90.11%
Others 10-53			1.99	9.89%
Total			20.13	100%

The most commonly prescribed oral drug was amoxicillin/clavulanic acid (28.96%), followed by clarithromycin (22.17%). By injection, ceftriaxone was the most frequently dispensed antibiotic (34.27%), followed by ceftriaxone and sulbactam (31.32%). The most widely used group of antibiotics was cephalosporins, followed by penicillins (Aljadeeah et al. 2020). The highest incidence of OAD was found in AWaRe-classified Watch-class antibiotics (65.66%), followed by Access-class antibiotics (32.54%). Antibiotics in the Reserve category had the lowest percentage (0.83%). The remaining antibiotics were unclassified (0.76%) (Aljada et al. 2020). During the study period, a significant difference in the total OAD was observed between Syria's different governorates that are under the control of the Syrian government (fig. 4). According to the number of DDEDs in each governorate, Idlib (16.33 DDED), Quneitra (14.55 DDED), and Deer el-Zour (14.32 DDED) had the highest OAD rates, while Tartous (5.83 DDED), Lattakia (4.5 DDED), Al-Hasakah (7.56 DDED) and Al-Suwayda (3.63 DDED) had the lowest OAD rates (Aljadeeah et al. 2020).

These results are concerning as the increased consumption leads to notable increase in the bacterial resistance against antibiotics. By comparison, the antibiotic consumption rate in Syria (20.13 DID) is comparable to the global consumption rate (20.9 DID) but notably lower in Korea (23.12 DID) and much lower in Turkey (48,9 DID) and Iran (60 DID). This unexpected low consumption rate of antibiotics in Syria and AANES (Rojava) may be because Syria's study excluded children and inpatient care as well as limited data on antibiotic use. In addition, the prescription rate of extended-spectrum penicillins and third- and fourth-generation cephalosporins have increased, while the prescription rate of first- and second-generation cephalosporins appears to have declined.

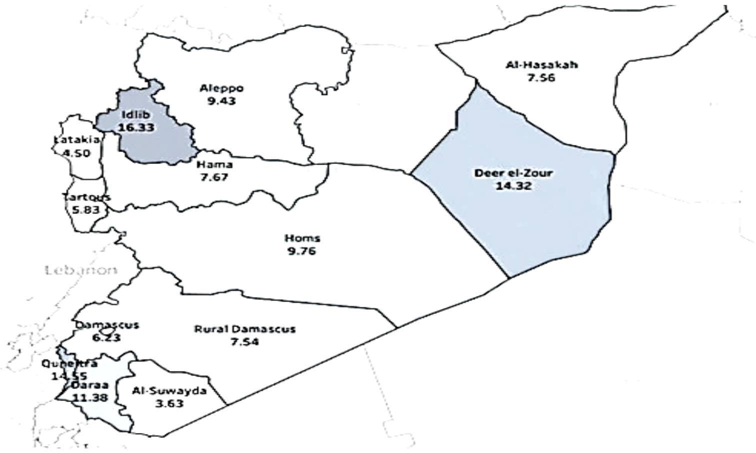

Figure 4. Adjusted outpatient antibiotic dispensing rates (DDD/1000 dispensing events/day) (Aljadeeah et al. 2020).

3. Resistance definition and breakpoints

Defining resistance is one of the most important issues in assessing antimicrobial use's impact on resistance. In essence, two agencies establish clinical breakpoints: CLSI (the Clinical Laboratory Standards Institute) and EUCAST (the European Committee on Antimicrobial Susceptibility Testing). International organizations have yet to harmonize clinical breakpoints, which has major implications for defining resistance and assessing its prevalence (Cantón et al. 2013). Defining resistance as a state in which an isolate has a protection mechanism that reduces its susceptibility as compared to other members of the same species without a protection mechanism. In order to identify microbiologically resistant isolates, the epidemiological cut-off value (ECOFF) is used, an MIC value that distinguishes wild-type isolates from isolates that have developed resistance as a result of mutation or horizontal gene transfer, regardless of whether the level of resistance is clinically relevant (fig. 5) (Cantón and María-Isabel 2011).

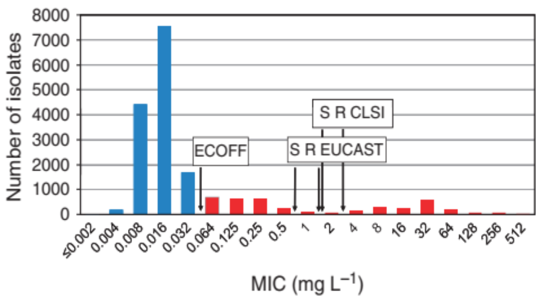

Figure 5. Ciprofloxacin MIC distribution of Escherichia coli isolates. Epidemiological cut-off (ECOFF) values and clinical susceptible (S) and resistant (R) breakpoints from CLSI and EUCAST committees are indicated (Cantón and María-Isabel 2011).

4. The minimum inhibitory concentration (MIC)

MIC is the lowest concentrations of antibiotics required to inhibit the growth of an organism. As a result of arbitrary breakpoint MIC values, bacteria are classified as sensitive, intermediate, or resistant based on how much growth inhibition by the antibiotic is achievable, the distribution of MICs for each organism, and their correlation with clinical outcomes. MIC values are influenced by a number of factors, including the type of bacteria, the composition of the media, the size of the inoculum, the duration of incubation, and the presence of resistant subpopulations (Smaill 2000). The indiscriminate dispensing use of antibiotics is the main driver of antibiotic resistance. The association between antibiotic consumption and resistance is well documented (Klein et al. 2018). Historically, the development and use of each new antibiotic have been followed by the emergence of resistance. Until the 1970s, many new antibiotics were developed to which most common pathogens were initially fully susceptible. Unfortunately, their introduction in clinical practice has been accompanied by the rapid appearance of resistant strains in most parts of the world. Since the 1980s, only a few new classes of antibiotics have been successfully brought onto the market and most of them target Gram-positive bacteria (WHO 2018). Most reports essentially describe the emergence of microorganisms that are resistant to different antimicrobial agents, and the frequencies of antibiotic resistances, and include surveillance studies collecting minimum inhibitory concentration (MIC) values of different drugs. The popularization of molecular techniques, including typing methods, resistance mechanisms, and the corresponding resistance genes have been widely documented (Cantón and Morosini 2011).

In 2015, WHO launched the Global Antimicrobial Resistance Surveillance System (GLASS) as a collaborative effort to standardize surveillance based on officially recognized data across countries and developed a common methodology for the measurement of antibiotic consumption. In response to the development of the methodology, WHO began collecting data on antimicrobial consumption for 2014–2016 worldwide (WHO 2018). According to the World Health Organization (WHO 2022) there are dangerously high levels of antibiotic resistance throughout the world. New resistance mechanisms are emerging globally and spreading, threatening our ability to treat common infectious diseases. Many infections such as pneumonia, gonorrhea, septicemia, tuberculosis, and foodborne illnesses are becoming more difficult and sometimes impossible to treat, because antibiotics become less effective. Furthermore, using unnecessary or inappropriate antibiotics; and self-medication with antibiotics, common in Syria and other less developed countries, can cause adverse effects, and lead to increasing numbers of resistant microorganisms (Gleckman and Czachor 2000; Muras et al. 2013). Several antibiotic resistant Gram-negative and several other MDR strains were found in samples taken from Syrian refugees in Germany and Italy in 2016 (Angeletti et al. 2016; Reinheimer et al. 2016).

On December 1, 1988 the Ministry of Health in Syria issued Law No. 2 / T, regulating the list of drugs that can be sold without prescription (Syrian Pharmacists Syndicate-Laws and orders that coordinate the profession of pharmacy in Syria), while the antibiotics were not included in this list. A second law number 2/T and enacted on January 23,1992 prevented pharmacists from reselling prescribed antibiotic to the same person without the permission of a physician and prevented physicians from prescribing an antibiotic more than twice for the same individual to treat the same infection (Syrian Syndicate for Pharmacists 1994). However, those regulations were not robustly enforced (Jakovljevic, et al. 2018). Study by Bahnassi in 2015 reported that 87 percent of pharmacists in Damascus sold antibiotics without a prescription, 10 percent accepted prescriptions, and only 3 percent refused to prescribe antibiotics without prescription (Bahnassi 2015). A high rate of self-treatment has been reported in neighboring countries, such as Jordan (39.5%) (Al-Azzam et al. 2007), as well as in some Eastern European countries such as 19.8% in Romania, and 21.0% in Lithuania (Grigoryan et al. 2006).

Due to the lack of laws limiting and enforcing the antibiotic consumption and the unfair competition among doctors for patients' trust, some doctors prescribe antibiotics belonging to the Reserve group of the WHO AWaRe classification such as Linezolid to treat minor ailments. There is a negative cultural impact on the medical practice in Syria and elsewhere. For example, In Syria, a doctor who does not prescribe antibiotics is considered unprofessional by some patients. In northern Israel, the pediatricians sometimes agree to prescribe antibiotics for children, in response to the pressure from parents believing in the efficacy of antibiotic treatment (Raz et al. 2005). In a study in the USA, it was found that about a third of antibiotics prescribed for three common respiratory conditions were incorrectly chosen (Hersh et al. 2016). If antibiotics are chosen that target only the bacteria most likely to cause a particular illness, resistance could be substantially reduced. Nearly 30 percent of the antibiotic prescriptions in outpatient settings were related to the three respiratory conditions in this study (Sorensen 2018).

The situation is even more complicated by the fact that most medicines, especially antibiotics, can be obtained from pharmacies without the need for a prescription in Syria. In a study from Greece, it was found that 74.6% of Greek urban adults used non-prescribed antibiotics (54.3% rarely, 12.7% often, and 7.5% very often) (Georgia Mitsi, et al. 2005). The reasons for the increased use of non-prescribed antibiotics in the population studied are not clear. However, one of the most important factors is the increased availability of over-the-counter antibiotics in Greece (Georgia Mitsi et al. 2005). Based on another study carried out by Mohanna in 2010 in Yemen, it was found that 312 (26% of patients) used a previous prescription to obtain antibiotics, while 888(74%) obtained the antibiotics from pharmacies and drug stores without any prescription required. An explanation for this may be to reduce the cost for patients and to pay only for drugs and not for medical examination. This probably may lead to many problems, and in addition to the misuse of antibiotics and antibiotic resistance (Mohanna 2010).

The non-specialization policy in the laboratory medicine in Syria has caused further complications in the field of laboratory diagnosis. A clinical medical laboratory in Syria is defined as a laboratory that practices at least all or two of the following clinical laboratory specialties: hematology and immunology, clinical biochemistry, microbiology and parasitology (Legislative Decree No. 42 of 2012). The lack of specialized microbiology laboratories under the supervision of microbiologists has resulted in non-standardized clinical outcomes. The main goal of antimicrobial susceptibility testing (AST) is to quantify the lowest concentration of an antibiotic that inhibits the visible growth of the microbe–the minimum inhibitory concentration (MIC). In the absence of attention to previous details by laboratory specialists, trust between the treating physician and the laboratories diminish, and antibiotics prescribe without laboratory testing.

In most Syrian laboratories, there is a lack of well-defined guidance for determination of the type of bacterial pathogens. It is incorrect to evaluate the results of antimicrobial susceptibility testing based solely on Gram staining. In order to determine whether the bacteria are resistant or susceptible, the following is used:

- If the inhibition zone diameter is greater than 15 mm, the bacteria are susceptible (S).
- The bacteria have intermediate susceptibility to antibiotics (I) if the diameter of the inhibition zone is less than 15mm.
- The absence of an inhibition zone diameter indicates resistance to the antibiotic (R).

However, EUCAST reports that each bacterial species has different breakpoints for antimicrobial susceptibility testing. MIC and zone diameter distributions for antimicrobial species combinations are available on the EUCAST. Furthermore, the economic situation has also a negative impact on the random increase in the use of antibiotics. In Syria, especially after the war, the economic situation was so bad that the treating physician avoided requesting medical tests as much as possible (due to the high cost) and prescribed antibiotics only based on clinical symptoms, resulting in the possibility of misusing the antibiotics. However, if an antibiotic is required to treat an infection, it is essential to prescribe the right one. An examination of antibiotic prescribed for three common respiratory conditions found that in about a third of cases, providers selected the wrong drug (Hersh et al. 2016). If antibiotics are chosen that target only the bacteria that most likely cause a particular infection, resistance could be substantially reduced.

5. Conclusion

In this review, we have reviewed a group of studies around the world including Syria on the consumption of antibiotics. A careful comparison of these studies show that Broad-spectrum antibiotics were over-prescribed in the OAD and the Watch group of the AWaRE classification was over-represented. These results are concerning as the consumption rate indicated in by the Watch group notably correlates with an increase the bacterial resistance against antibiotics. By comparing the results of antibiotic consumption in Syria with those in some other countries, we observed an unexpected low consumption rate of antibiotics in Syria. The reason for this low rate may be because Syria's study excluded children and inpatient care. Currently, available data on antibiotic use in Syria and implicitly in AANES (Rojava) are insufficient. Crucial stakeholders from the public, private, and nonprofit sectors must work together to ameliorate the quality and obtainability of data to expand antibiotic superintendence in human health care. It should be noted that the overuse of antimicrobial agents in animal agriculture contributes significantly to the problem of antimicrobial resistance. Whereas, the vast majority of antimicrobials used in animals are not for treating infections; instead, the animals are fed antibiotics to speed up growth and compensate for the unhealthy condition of these animals. The CDC has determined that antimicrobial use in animals is associated with resistance in human. Below we present some recommendations and proposals regarding the situation in AANES Priorities:

- Coordination between the Health Authority and the Agriculture Authority to reduce the consumption of antibiotics in the animal sector
- Legislate to limit the use of antibiotics without a prescription
- Conducting periodic statistics for the daily consumption of antibiotics and archiving the results
- Work in accordance with World Health Organization recommendations and dispensing antibiotics in accordance
- Consider the AWaRE to reduce the consumption of antibiotics
- Preventing antibiotic prescriptions for cases without a laboratory-proven bacterial infection
- Regularly sterilizing hospital departments to prevent the transmission of resistant bacteria between patients and the emergence of new antibiotic-resistant strains as a result of the transfer of resistance genes
- Taking periodic bacterial swabs from all hospital departments and identifying resistant strains
- Distributing laboratory work according to scientific specialization only (hematologist, clinical chemist, microbiologist, and pathologist)
- Establishment of international standards-based microbiology laboratories.

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