Turkish Medical Journal, 2025; 10(2),65-75.

Derleme / Review
https://doi.org/10.70852/tmj.1530388

OVERVIEW OF ANTIMICROBIAL RESISTANCE AND EPIDEMIOLOGY OF TÜRKİYE WITH A ONE HEALTH APPROACH

Tek Sağlık Yaklaşımıyla Türkiye'nin Antimikrobiyal Direnci ve Epidemiyolojisine Genel Bakış

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Geliş / Received: 09.08.2024
Kabul / Accepted: 21.10.2024

Cite as:
Kurum, S., Balcı, A. İ., Çuhadar, A. H., Aydemir, E., Erkal, E., Bulut, M., Ünal, E., Gökler, M. E. (2025). Overview of Antimicrobial Resistance and Epidemiology of Türkiye with a One Health Approach. Turkish Medical Journal, 10(2),65-75. https://doi.org/10.70852/tmj.1530388

ABSTRACT

Since their discovery, antimicrobials have saved countless lives and formed the foundation of modern medicine. In addition, their use in veterinary medicine, agriculture, and livestock has provided great convenience. However, despite all these benefits, antimicrobial resistance (AMR), resulting from excessive and inappropriate use, threatens the global achievements made against diseases and thus public health. The World Health Organization (WHO) included AMR in its "Ten Threats to Global Health" list published in 2019 and encouraged the joint participation of all nations and stakeholders for effective action. This issue, which has become a global concern for many organizations, is also emerging as a growing problem in Türkiye. According to current AMR reports, Türkiye is one of the countries with the highest resistance rates in the WHO European Region. These findings highlight the urgency and importance of the fight against AMR. The misuse of antimicrobials in the food industry and veterinary medicine, as well as their environmental effects, should be considered priority issues, and policies should be shaped through intersectoral cooperation. In this review, AMR is evaluated through the One Health approach, and Türkiye's AMR data obtained from reports are analyzed.

Keywords: Antimicrobial Resistance, One Health, Surveillance

ÖZET

Antimikrobiyaller keşfedilmeleriyle birlikte sayısız hayat kurtarmış ve modern tıbbın temelini oluşturmuştur. Ayrıca veterinerlik, tarım ve hayvancılıkta kullanımı büyük kolaylık sağlamıştır. Ancak tüm bu faydaların yanı sıra aşırı ve uygunsuz kullanım sonucu oluşan antimikrobiyal direnç (AMD); antimikrobiyaller ile hastalıklara karşı elde edilen küresel başarıları ve böylelikle toplum sağlığını tehdit etmektedir. Dünya Sağlık Örgütü (DSÖ), 2019 yılında yayınladığı "Küresel Sağlık İçin On Tehdit Listesi"ne AMD'yi dahil ederek, etkili mücadele için tüm ulusların ve paydaşların ortak katılımını teşvik etti. Dünya çapında birçok kuruluşun odak noktası haline gelen bu konu, Türkiye'de de giderek büyüyen bir sorun haline geldi. Güncel AMD raporlarına göre Türkiye, DSÖ- Avrupa Bölgesi'nde en yüksek direnç yüzdelerine sahip ülkelerden biridir. Bu sonuçlar mücadelenin aciliyetini ve önemini gösteriyor. Gıda endüstrisinde ve veteriner hekimliğinde antimikrobiyallerin yanlış kullanımı ve çevreye olan etkileri de öncelikli konular arasında ele alınmalı ve politikalar sektörler arası iş birliği yoluyla belirlenmelidir. Bu derlemede AMD, Tek Sağlık yaklaşımıyla değerlendirilmiş ve Türkiye'nin raporlardan elde edilen AMD verileri incelenmiştir.

Anahtar Kelimeler: Antimikrobiyal Direnç, Sürveyans, Tek Sağlık

INTRODUCTION

One Health is a critical approach that establishes connections among humans, animals, and the environment by emphasizing their interdependence. It not only examines each discipline individually but also addresses the intersections between them. One common issue faced collectively due to cohabitation is the emergence of infectious diseases. The One Health approach should encompass all necessary components for identifying risk factors of infectious diseases, inter-community transmission dynamics, emerging resistant microorganisms, appropriate antibiotic management, and policy development. The use of antimicrobials involves numerous stakeholders, including doctors, nurses, pharmacists, patients, families, medical delegates, distributors, pharmaceutical companies, regulators, and policymakers. (Babu Rajendran et al., 2023). Since their identification in the 20th century, antibiotics have exerted a profound influence on human and animal well-being by facilitating the treatment of infectious diseases. Presently, industrial agriculture heavily depends on the utilization of antimicrobials (such as antibiotics, antifungals, and antiprotozoals) to manage and prevent diseases, enhance animal welfare, and boost productivity. Nevertheless, the extensive use of antimicrobials on a large scale may lead to the emergence of resistance in bacteria.AMR denotes the capability of microorganisms to develop resistance to antimicrobials they were previously susceptible to, diminishing the efficacy of treatments. Even though the development of AMR is a natural occurrence, excessive and inappropriate usage of antimicrobials can significantly exacerbate it, resulting in the rapid dissemination of communities resistant to bacteria (Berman et al., 2023). There are numerous factors and investors contributing to the issue of AMR. One such factor is excessive clinical use and misuse. Non-adherence to treatment by patients can also impact this. Also poor drug quality can lead to increase of resistance. The proliferation of fraudulent and adulterated antibiotics contributes to the selection of resistant strains. Absence of AMR action plans in some developing countries is another factor. Healthcare providers also play a role in the increase of resistance. Additionally, excessive and indiscriminate use of antimicrobial drugs in the agriculture and livestock sectors can lead to the transmission of resistant bacteria to humans through food or the environment. Distributors who often supply drugs to these sectors lack sufficient knowledge about the indications, contraindications, or dosages of the drugs (Ayukekbong et al., 2017). According to the WHO, AMR is recognized as one of the top 10 global public health threats facing humanity (WHO, 2023). The emergence and spread of drug-resistant microorganisms threaten global public health, the foundation of modern medicine, and our ability to perform life-saving procedures, like cancer chemotherapy, organ transplantation, and other surgeries. Furthermore, drug-resistant infections affect the health of animals and plants, reduce productivity on farms, and endanger food safety. The widespread and systematic overuse of these drugs, in both human and food production, could lead to a resurgence of common infections that may become deadly once again. Therefore, effective collaboration among all national and international workers in human and veterinary medicine, agriculture, environment, and finance sectors is needed to implement an efficient 'One Health' approach (Global Action Plan on Antimicrobial Resistance, 2015). AMR, a growing problem both worldwide and in Türkiye, is a subject that needs to be evaluated with intersectoral cooperation. This review provides an overview of AMR from a one-health approach and evaluates the relevance of AMR to veterinary medicine, agriculture, livestock, the environment and their economic aspects. It also summarizes studies on AMR surveillance and reviews Türkiye's situation based on data from global AMR reports.

MATERIALS AND METHODS

The study aimed to conduct a literature review of current AMR reports and stakeholders, and to provide an overview of Türkiye's situation. The keywords "Antimicrobial Resistance, One Health, Surveillance" were searched in PUBMED and TRDIZIN databases, and WHO reports were utilized. As this research was conducted as a literature review, ethics committee approval was not required.

AMR Surveillance

According to the WHO, public health surveillance involves the continuous and systematic collection, integration, and evaluation of relevant data, followed by timely dissemination of findings to the relevant stakeholders. (WHO EMRO | Public Health Surveillance | Health Topics, 2024). AMR surveillance facilitates the early detection of resistant strains that may pose public health threats by monitoring microbial populations. Sensitivity tests are performed on bacteria isolated from regional samples, and the results are collected through surveillance systems. The obtained data are then evaluated based on the demographic and clinical structure of the surveyed population, alerting relevant units to prevent outbreaks and facilitating the implementation of necessary measures. Additionally, surveillance data guide treatment decisions and support policy implementation. (Johnson, 2015) (Surveillance and Monitoring for Antimicrobial Use and Resistance IACG Discussion Paper, 2018). Exposure to antimicrobials can be assessed from two perspectives: antimicrobial consumption (AMC) and antimicrobial use (AMU).AMC indicates the consumption at a national level, which can be estimated from data on imports, wholesalers, or health insurance, with estimations varying significantly depending on the measurement method. On the other hand, AMU defines the patient-level use of antimicrobials and can be derived from clinical, pharmaceutical, or hospital records. Data on AMC and AMU provide a valuable understanding into the emergence of AMR at different geographical scales and can be utilized to inform the development of empirical treatment guidelines. However, antimicrobial exposure is often assessed only through AMC, as AMU data are not readily available in many countries. (GLASS-AMC Module, 2024; Global Action Plan on Antimicrobial Resistance, 2015; Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report 2022, 2022).In 2017, WHO developed the AWaRe (Access, Watch, Reserve) classification to identify the levels of antibiotic groups consumed nationally and optimize their use. This regularly updated list divides antibiotics into 3 groups. The Access group includes antibiotics with activity against commonly encountered pathogens and lower resistance potential compared to other groups. The Watch group includes antibiotic classes with higher resistance potential and contains most of the highest priority agents among Critically Important Antimicrobials (CIA) for Human Medicine. The Reserve group includes antibiotics reserved for the treatment of confirmed or suspected infections caused by multidrug-resistant organisms and should be considered as a "last resort" option. One of the WHO targets is that at least 60% of the overall antibiotic usage at the country level should be Access group antibiotics (WHO, 2023). In its latest reports, the United Nations suggests that current surveillance systems are disjointed and insufficiently developed, emphasizing the urgent need for the strengthening of international AMR surveillance systems (No Time to Wait: Securing the Future from Drug-Resistant Infections, 2019). Isabel Frost and colleagues have discussed the challenges in current surveillance studies under five headings; First, one of the reasons is that information systems are often paper-based, making data collection and integration difficult. Even when electronic records exist, laboratory management systems are typically not connected to hospital or pharmacy information systems. Secondly, if both AMR and AMC are not reported at the same geographic level, consumption data cannot be correlated with resistance data (WHO, 2018). Thirdly, the use of different measurements as consumption metrics in databases can make comparisons between surveillance systems difficult. Additionally, estimations made using sales data may differ from actual consumption. Purchased antibiotics may not always be consumed, and antibiotics taken without a prescription cannot be tracked through prescription data. (Morgan et al., 2011). Fourthly, the financing of AMR control activities is industry specific and often focuses on human health. In many low and middle income countries, AMR control activities either underfunded or underdeveloped. Fifthly, weak connections between human health, animal, and environmental sectors lead to an underestimation of the burden of AMR. Therefore, establishing robust surveillance systems requires close coordination among all stakeholders, standardization of methodologies, capacity building, adopting a One Health approach, and strong political will (Frost et al., 2021).

Global Actions Addressing the AMR

At the 2015 World Health Assembly, it was decided to develop a Global Action Plan (GAP) on AMR to address the issue globally and to create multisectoral national plans. By the end of 2023, 178 countries had developed national AMR action plans aligned with the GAP. Since 2016, countries have been reporting their progress every year through the Tracking AMR Country Self-Assessment Survey (TrACSS). To standardize the stages of AMR surveillance, WHO established GLASS in 2015 as the first global collaborative effort. GLASS aims to monitor the status of countries' national surveillance systems and develop their capacities. It encourages the transition from systems based solely on laboratory data to those incorporating epidemiological, clinical, and population-level data. GLASS aims to gradually integrate surveillance data from human health with AMR data concerning food and the environment. It cooperates with regional AMR networks such as CAESAR in Central Asia and Europe, EARS-Net in Europe.Under the GLASS umbrella, various surveillance activities are conducted through grouped modules. In the Routine Surveillance section, GLASS-AMR collects national AMR data from samples routinely taken from pathogens causing common infections using a standardized approach. GLASS-AMC collects standardized reports on AMC at the country, regional, and global levels. The Emerging AMR Reporting (GLASS-EAR) module involves early detection, reporting, risk assessment, and monitoring of newly emerging resistance. The GLASS-FUNGI module, another Focused Surveillance tool, monitors invasive fungal bloodstream infections caused by Candida spp. (Global Antimicrobial Resistance and Use Surveillance System (GLASS), 2024).

AMR and Epidemiology of Türkiye

To collect comparable and reliable data on resistance in Türkiye, the "National Antimicrobial Resistance Surveillance System (UAMDSS)" was established in 2011 and remains active todayunder the General Directorate of Public Health (HSGM). Additionally, it is a part of the WHO's European Office's "Central Asian and European Surveillance of Antimicrobial Resistance Network (CAESAR)" (GLASS-AMC Module, 2024; Ulusal Antimikrobiyal Direnç Sürveyans Sistemi, 2024; World Health Organization GLASS Dashboard, 2022). Türkiye is part of the WHO European Region and joined GLASS-AMR in 2022; however, it is not enrolled in GLASS-AMC. (Global Antimicrobial Resistance and Use Surveillance System (GLASS), 2024). Also, there is no data for the antibiotic groups used according to the AWaRe classification for Türkiye. The WHO European Region has a high prevalence of AMR. The data revealed a clear pattern: resistance increased from north to south and from west to east, reaching its highest levels in southern and eastern Europe. Türkiye has some of the highest AMR percentages in the WHO European region according to the 2023 ECDC (European Centre for Disease Prevention and Control)- AMR Report (see Table 1). However, resistant microbes will not remain confined to specific geographical regions. Therefore, combating AMR will require cooperation both internationally and within the WHO European Region. (ECDC & WHO, 2023).

Table 1: Percentage of isolates with resistance phenotype by bacterial species and antimicrobial group/agent in Türkiye. Along with the countries with the highest AMR percentage in the region*

Bacterial species	Antimicrobial group/agent	Percentage of isolates with resistance phenotype (%)	Countries with the highest AMR percentage in the WHO European Region
E.coli	Aminopenicillin resistance	≥ 50%	
	Third-generation cephalosporin resistance	≥ 50%	**≥ 50% in four (9%) countries (North Macedonia, Russia, Türkiye and Ukraine)
	Carbapenem resistance	≥ 1%	**≥ 1% in eight (18%) countries (Belarus, Cyprus, Georgia, Greece, Russia, Serbia, Türkiye and Ukraine)
	Fluoroquinolone resistance	≥ 50%	**≥ 50% in four (9%) countries (Cyprus, North Macedonia, Russia and Türkiye)
	Aminoglycoside resistance	10% to 25%	
	Combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides	10% to 25%	

Table 1 continued.

K.pneumoniae	Third-generation cephalosporin resistance	≥ 50%	**≥ 50% in 19 (42%) countries (including Türkiye)
	Carbapenem resistance	25% to 50%	≥ 50% in eight (%18) countries (Belarus, Georgia, Greece,Moldova, Romania, Russia, Serbia and Ukraine)
	Fluoroquinolone resistance	≥ 50%	
	Aminoglycoside resistance	25% to 50%	
	Combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides	25% to 50%	
P.aeruginosa	Piperacillin-tazobactam resistance	25% to 50%	
	Ceftazidime resistance	25% to 50%	
	Carbapenem resistance	25% to 50%	≥ 50% in six (14%) countries (Belarus, Georgia, Moldova, Russia, Serbia and Ukraine).
	Fluoroquinolone resistance	25% to 50%	
	Aminoglycoside resistance	10% to 25%	
	Combined resistance to ≥ 3 antimicrobial groups (among piperacillin-tazobactam, ceftazidime, carbapenems, fluoroquinolones and aminoglycosides)	25% to 50%	
Acinetobacter spp.	Carbapenem resistance	≥ 50%	**≥ 50% in twenty-five (56%) countries (including Türkiye)
	Fluoroquinolone resistance	≥ 50%	
	Aminoglycoside resistance	≥ 50%	
	Combined resistance to carbapenems, fluoroquinolones and aminoglycosides	≥ 50%	
S.aureus	Methicillin-resistant Staphylococcus aureus (MRSA)	25% to 50%	**≥ 25% in thirteen (30%) countries (including Türkiye)
S.pneumoniae	Penicillin non-wild-type	≥ 50%	**≥ 25% in five (12%) countries (Belarus, France, Romania, Serbia and Türkiye)
	Macrolide resistance	25% to 50%	
	Combined penicillin non-wild-type and resistance to macrolides	25% to 50%	
E.faecalis	High-level gentamicin resistance	10% to 25%	
E.faecium	Vancomycin resistance	10% to 25%	≥ 50% in five (11%) countries

* 2023 ECDC-WHO AMR Report - According to WHO European Region Figures. (ECDC & WHO, 2023)
** If it includes Türkiye, it is marked in the table.
AMR: Antimicrobial Resistance, ECDC: European Centre for Disease Prevention and Control, WHO: World Health Organization.

Resistance to anti-tuberculosis drugs

Among the leading causes of death due to a single infectious agent, COVID-19 ranks first, followed by tuberculosis. Approximately over 1.5 million people lost their lives to tuberculosis in 2020 (Global Tuberculosis Report, 2020). Rifampicin resistance, one of the most significant treatment failures, accounts for approximately 25% of AMR-related deaths. Drug-resistant tuberculosis is evaluated for prevalence and trends at national, regional, and international levels by the WHO-hosted Global Project on Anti-TB Drug Resistance Surveillance, which has been in place since 1994 (Global Tuberculosis Programme, 2024). In Türkiye, the 'Tuberculosis Laboratory Surveillance Network (TULSA)' project, which monitors the status of TB drug resistance, was initiated in 2011. The data obtained were recognized by the WHO as part of regional drug resistance surveillance and were first included in the WHO's annual TB report in 2012. The scope of TULSA has been expanded every year and, since 2016, it has been extended to cover all of Türkiye. In 2018, the culture rate for pulmonary TB across the country was raised to 86.8%, and the Drug Susceptibility Testing rate for culture-positive cases was increased to 95.8%. In addition to providing national-level TB drug resistance data, TULSA has improved TB laboratory practices and established a mechanism for the continuous collection of laboratory-based surveillance data in Türkiye. (Antituberculosis Drug Resistance Laboratory Surveillance Network (TULSA), 2024). According to 2022 Estimates of TB burden, the incidence of MDR/RR-TB (multidrug-resistant/rifampicin-resistant tuberculosis) in Türkiye is 350 (260-440), and the rate is 0.41 (0.31-0.51) per 100,000 population. This rate is 5.2 (4.7-5.7) globally and 7.2 (5.4-9) for the WHO European Region (Global Tuberculosis Programme, 2024). Globally, addressing the deficiencies in the detection of drug-resistant tuberculosis, researching new diagnostic methods, improving laboratory capacities, and investing in surveillance implementation have become more important than ever (Dean et al., 2022).

Antifungal Resistance

The rising resistance of Aspergillus spp. to triazoles is an increasing public health concern. The first case of azole-resistant Aspergillus fumigatus (ARAF) was reported in the Netherlands in the 1980s. In recent years, increasing rates of azole resistance have been reported on all continents except Antarctica. Data from the SCARE-Network, a multicenter study consisting of 19 European and 4 non-European centers, found an overall ARAF prevalence of 3.2% (range 0 to 26%) between 2009 and 2011. The Netherlands have reported one of the highest ARAF-prevalence in Europe, with 8–15% between 2013 and 2018. In Denmark and Italy, resistance rates in clinical isolates and samples were 6.1% and 6.25%, respectively. ARAF prevalence of 9.3% was observed in environmental isolates in Colombia, while it is suggested to be 17.1% in African continent (Bosetti & Neofytos, 2023). In a multicenter study conducted in Türkiye, the prevalence of ARAF in environmental isolates was found as 1.3% and in clinical isolates at 3.3% (Ener et al., 2022). On the other hand, managing resistance in Aspergillus fumigatus acquired through environmental exposure presents significant challenges. This environmental pathogen has experienced increased exposure to these azole-based fungicides owing to their use in agriculture for controlling plant pathogenic moulds, especially Fusarium and A. flavus. The most commonly used type of fungicides in agriculture are azole drugs. Due to frequent exposure, A. fumigatus has developed cross-resistance to medical azoles. Additionally, bird species that move between different environments and are highly susceptible to aspergillosis can cause the spread of resistant Aspergillus isolates (Picot et al., 2022). A recent study showed that as the residue levels of azole fungicides in soil increased, the prevalence of azole-resistant A. Fumigatus also increased (Cao et al., 2021). Therefore, the rise in azole resistance should be monitored, and its use should be regulated within a One Health approach.

Resistance to Antiparasitic Drugs

A significant portion of animal-based foods consumed worldwide is produced in countries where parasitic diseases are prevalent. The amount of drugs used in these countries may vary according to national regulations. Food and live animals carrying resistant pathogens circulate globally, increasing the associated risks. (Picot et al., 2022) Drug resistance levels are rising in protozoan parasites (such as Plasmodium, Giardia, Leishmania, Trypanosoma, and helminths). One of the reasons why progress in eliminating malaria has stalled is the resistance of Plasmodium species to drugs. Additionally, the effectiveness of albendazole and mebendazole-the most widely used anthelmintics in both veterinary and human medicine-has declined due to improper use. (Picot et al., 2022; Tinkler, 2020). In a 2021 document, WOAH encourages the prudent use of several classes of anthelmintic chemicals available for parasite control in food-producing ruminants such as sheep, goats and cattle (Responsible and Prudent Use of Anthelmintic Chemicals to Help Control Anthelmintic Resistance in Grazing Livestock Species, 2021). Köse et al. discovered resistance to albendazole and several other drugs in sheep (Köse et al., 2007). Additionally, Çırak et al. revealed resistance to macrocyclic lactones in horses, while Önder et al. identified Haemonchus contortus with approximately 12% benzimidazole resistance in sheep (Çırak et al., 2010; Önder et al., 2015). Although anthelmintic resistance has been documented in studies from Türkiye, further research is needed. In conclusion, preventive measures should be implemented before high resistance rates and therapeutic failures emerge in parasite populations. (Picot et al., 2022).

Important antimicrobial agents in veterinary medicine

The FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and AMR was held in Oslo and Geneva in 2003-2004. According to the decisions made at the Oslo Workshop, it was determined that critically important antimicrobials in both human and veterinary medicine should be identified, and a proper balance should be established where these lists overlap. Antimicrobials used in human medicine were divided into three groups in the WHO CIA list in 2005, according to their importance for human medicine: "Critically important," "Highly important," and "Important.". The list supports the development of joint strategies with other sectors in accordance with One Health objectives and is updated as needed. (WHO Advisory Group of the Critically Important Antimicrobials for Human Medicine (AG-CIA), 2019). In 2007, the OIE List of Antimicrobial Agents of Veterinary Importance divided the drugs into 3 groups: Veterinary critically important antimicrobial agents (VCIA), Veterinary highly important antimicrobial agents (VHIA) and Veterinary important antimicrobial agents (VIA). Fluoroquinolones listed under VCIA and third- and fourth-generation cephalosporins are also considered critically important for human health.Additionally, colistin is classified under the WHO's "Highest Priority Critically Important Antimicrobials" category. Therefore, guidelines were developed for the use of these three classes of drugs. Some of these guidelines include banning their use as growth promoters, not using them as first-line treatment without medical indication, and basing their use as second-line treatment on test results (OIE List of Antimicrobial Agents of Veterinary Importance, 2021). According to a study on surveillance systems for animal diseases and AMU in Sierra Leone, 25% of livestock were found to have an infectious disease and antimicrobial drugs were used in one-quarter of the sick animals. Most of the drugs used belonged to the World Organization for Animal Health's "veterinary critically important (VCIA)" category (77%) and the WHO's "critically important" (17%) and "highly important" (60%) categories for human health. While these findings indicate significant improvement in the animal health surveillance system, they also highlight the need for better management to prevent misuse. Therefore, implementing a more stringent surveillance system in agricultural facilities will offer a better understanding of current antibiotic usage conditions. (Bangura et al., 2022). In a systematic review and meta-analysis study, Tang et al. examined the restriction of antibiotic use in food-producing animals and its relationship with the prevalence of antibiotic resistance in animals. Interventions limiting antibiotic use in animals commonly resulted in a 10 to 15% reduction in the prevalence of antibiotic resistance, varying based on factors such as antibiotic class, sample type, and assessed bacteria, with an overall range from 0 to 39% (Tang et al., 2017).

AMR and the Environment

Although the One Health approach includes human, animal, and environmental health, the environmental aspect is often overlooked. The environment has various effects on both human and animal health. Clean water and healthy soil are essential for preventing disease and its transmission. Additionally, having clean slaughterhouses, protecting the animals and plants' natural habitat, and increasing biodiversity can reduce infectious diseases. The environment can serve both as a transmission route and a source of certain bacteria. Additionally, humans and animals can be exposed to both antimicrobial drugs and antimicrobial-resistant bacteria through the environment. Therefore, the importance of the environment should not be ignored in the fight against AMR. For instance, the frequent use of antibiotics in farming to increase efficiency means that fruits and vegetables can be a source of AMR (Humboldt-Dachroeden & Mantovani, 2021a). Another important issue to consider is the use of pesticides. The combined effects of pesticides with other present contaminants can trigger cross resistance (Malagón-Rojas et al., 2020). Another environmental factor that may cause AMR is toxic metals. These metals can originate from industrial emissions, soil composition, or feed additives like copper (Aquilina et al., 2016). Furthermore, resistant bacterias can be transmitted into the food chain through fertilizers used in farming. In addition, spread of AMR in the environment can be caused by wastewater from plants and animals (Wang et al., 2018). Climate change may increase the frequency of heavy rainfall, raising the risk of water source contamination by zoonotic pathogens from animal and human waste. (Semenza & Menne, 2009). Additionally, the use of antimicrobials in animals can lead to the development of antimicrobial-resistant zoonotic bacteria (Wielinga & Schlundt, 2012). More data is needed to comprehensively evaluate all these environmental factors (Humboldt-Dachroeden & Mantovani, 2021b). In December 1998, the European Union banned the antibiotics Tylosin, Virginiamycin, Zinc Bacitrasin, and Spiramycin. To monitor the antibiotic resistance, surveillance programs were initiated in 1999. From 2006 onwards, antibiotic growth promoters were completely banned across Europe. In Türkiye, this ban started on January 21, 2006, and no antibiotic feed additives have been allowed to be imported since that date (Tuncer, 2007).

Environmental Measures in Türkiye

As part of harmonization with the European Union in 2011, the implementation of 'Good Manufacturing Practices (GMP)' was mandated for the production of veterinary medicinal products. The Ministry of Food, Agriculture, and Livestock carries out its operations in collaboration with GMP-certified veterinary medical product manufacturers and companies holding operational permits. The Ministry engages in educational and regulatory activities concerning AMR and rational antibiotic use, and develops strategies within the One Health framework. The directive addresses collaborations necessary for combating animal diseases, hygiene, controlling rabies, and promoting public health. At the 44th Congress of the Turkish Veterinary Medical Association (TVHB), a joint statement was presented with the Turkish Medical Association (TTB). This statement emphasized the significance of national and international collaboration between human and veterinary physicians in terms of legislation, education, and implementation. Moreover, the recommendations included enhancing epidemiological research on zoonotic diseases, establishing a comprehensive database, and promoting collaboration and advancements related to One Health among medical and veterinary faculties. (Hiçcan, 2017).

The economic aspect of AMR

According to the "UK Review on AMR" report published in 2016; It is estimated that if current trends continue, 10 million people will die every year in the world due to AMR by 2050, and will cost the global economy 100 trillion US dollars between 2015 and 2050 (Tackling Drug-Resistant Infections Globally: Final Report and Recommendations | AMR Review, 2016). To evaluate the loss that AMR could cause to the global economy, The World Bank used economic simulation tools in 2017 and reported 2 different scenarios corresponding to low/high AMR impacts. Simulation of the optimistic scenario with low AMR impact showed that by 2050, the global GDP would decline by 1.1% compared to a baseline scenario with no AMR effects resulting in a GDP gap of over $1 trillion per year by 2030. The high AMR impact scenario projects a 3.8% reduction in annual GDP by 2050 and a $3.4 trillion deficit each year after 2030. It is also projected that developing countries will be more severely affected than developed ones, increasing the economic gap and inequality. AMR will reduce effective treatment rates against infections in the livestock industry. Thus, there will be a decrease in the production of animal foods and an increase in the cost of protein-containing foods. According to World Bank estimates, AMR will result in an 11% loss in animal production by 2050, further worsening the global economic situation. (Drug-Resistant Infections: A Threat to Our Economic Future- Final Report, 2017; Pulingam et al., 2022)

CONCLUSION

Although antimicrobials have saved countless lives and provided many conveniences, the emergence of AMR has led to devastating consequences. Resistance rates are increasing both in the world and in Türkiye and continue to be a risk for all stakeholders of One Health. Türkiye is among the countries with the highest AMR rates in the WHO European Region. Urgent measures must be taken in this regard. Türkiye joined the GLASS-AMR program in 2022; participation in the AMC program should also be pursued by improving the existing infrastructure. All healthcare professionals should be familiar with both the WHO CIA list and the OIE classification of Antimicrobial Agents of Veterinary Importance and should be trained on rational drug use with current guidelines. In addition, One Health and AMR should be included more in the education curricula of the university and their importance should be explained. It is important to consider humans, animals, and the environment together in the fight. Progress in combating AMR—recognized by WHO as one of the top 10 global public health threats—can be achieved through a One Health approach, intersectoral cooperation, and effective policymaking.

Conflict of Interest: The authors declare no conflict of interest.

Financial Support: No financial support was received for the research and/or authorship of this article.

Author Contributions: Concept, planning, literature review, data collection, and reporting were performed by SK, AİB, AHÇ, EA, EE, and MB. Supervision, revision, and final review were conducted by EÜ, MEG, and SK.

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