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Current Status and Decisions Regarding the Global Situation of Antibiotic Use and Resistance

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Abstract

The worldwide public health authorities are very concerned about antibiotic resistance. However, recent hospital and some community-based data indicated an increase in the prevalence of antibiotic resistance in emerging nations like India. The rapid rise in antibiotic resistance (ABR), coupled with the dearth of new antimicrobial medications with novel modes of action, poses a severe threat to the effectiveness of antibiotics [2]. Antimicrobials are used irrationally, which is one of the main causes of ABR. The World Health Organization has found that medications are used rationally when patients obtain the required medications, for the greatest possible efficacy, in dosages that are specific to their individual needs, for a long enough period of time, and at the least expensive cost to both the patient and society. The relatively recent development of antibiotics as therapeutic agents significantly altered the environment necessary for the evolution and spread of resistance by posing previously unheard-of selection pressures, particularly on the microbiota of humans and domestic animals, but also in heavily antibiotic-polluted environments. A wide variety of antibiotic resistance genes (ARGs) have been mobilized and horizontally transferred to many bacterial species, especially those that cause illness, as a result of this selective pressure. The final, obvious results of such accumulated evolutionary events are gradually growing challenges in the prevention and treatment of bacterial diseases. In this Review, we present our current understanding of the roles of the environment, including antibiotic pollution, in

resistance evolution, in transmission and as a mere reflection of the regional antibiotic resistance situation in the clinic. We provide a perspective on current evidence, describe risk scenarios, discuss methods for surveillance and the assessment of potential drivers, and finally identify some actions to mitigate risks.

Keywords

Antibiotic resistance, knowledge, rational use, Antibiotic Susceptibility, Medical - Patient Communication.

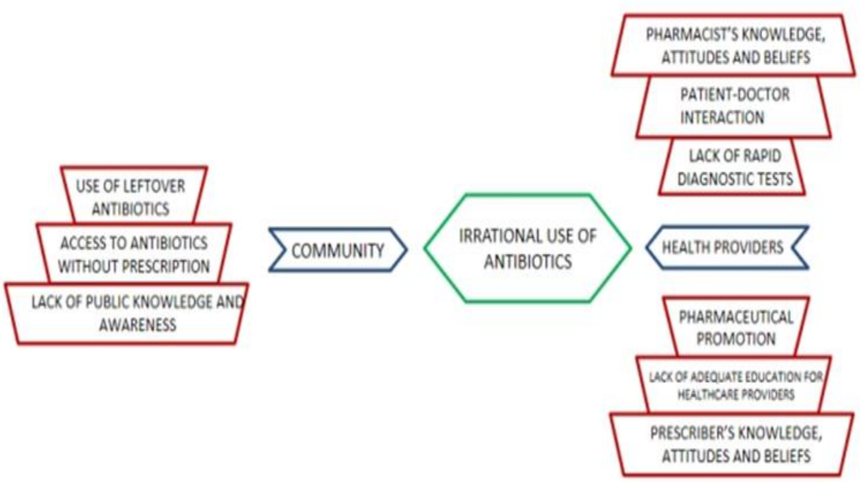
Current Global Situation of Antibiotic Use and Resistance

One of the most expensive, life-saving treatments is the use of antibiotics, which also helps patients live longer [1]. However, the rapid rise in antibiotic resistance (ABR), coupled with the dearth of new antimicrobial medications with novel modes of action, poses a severe threat to the effectiveness of antibiotics [2]. Antimicrobials are used irrationally, which is one of the main causes of ABR. The World Health Organization has found that medications are used rationally. (WHO), when patients obtain the required medications, for the greatest possible efficacy, in dosages that are specific to their individual needs, for a long enough period of time, and at the least expensive cost to both the patient and society. Irrational or unnecessary pharmaceutical use happens when a few of these conditions are not met [3]. In locations where antibiotics are used more often, antimicrobial resistance is frequently shown to be higher in cases of common infections [4,5]. While Greece and Spain witnessed an increase in antibiotic use between 2012 and 2016, Norway, Luxembourg, Finland, and Sweden saw a statistically significant drop. For widespread use in the communities, Greece ingested 36.3 specified daily doses (DDD) for every 1000 residents daily (DDD/TID) in 2016. (i.e., outside hospitals). In the Netherlands, minus or minus 10.4 DDD/TID, a third of this amount was also used. Although hospitals only use 10–20% of all antibiotics, they are used at a much deeper level than the general population. Hospitals play a significant role in the use of last-resort antibiotics like polmyxins and carbapenems [5-8]. For instance, ESAC-Net statistics indicate that hospitals employed different beta-lactam antibiotic classes, including carbapenems, more frequently than the general public [5]. The proportion of invasive Klebsiella pneumoniae that is carbapenem-resistant is directly correlated with carbapenem usage. Data showing that over a million prescriptions for carbapenem were written in Europe each year is therefore a grave cause for concern. Antibiotic resistance has detrimental implications on both health and the economy. Each year, 700,000 individuals die from diseases that are resistant to treatment. If nothing is done, this is projected to increase by about 10 million until 2050, with associated expenses reaching up to US $100 trillion globally [6]. Multiresistance is expected to cause cumulative losses of more than 2.9 trillion USD annually by 2050 [7]. Relatively low and middle-income countries (LMICs) use the most antibiotics, despite the fact that high-income countries use the most antibiotics overall [9], and they also have particular challenges in the fight against antibiotic resistance [10]. However, it should be noted that low levels of use were the starting point for the rapid increase in antibiotic consumption, and many people in LMICs continue to experience more harm from a lack of access to healthcare than from the overuse of antibiotics. Worldwide, resistance spreads quickly, and events in LMICs, such as the expansion of bacterial resistance and resistant genes, have a significant impact on all of Europe [11]. Therefore, quick international cooperation is necessary to address this growing problem.

Spread of Antimicrobial Resistance

Bacteria can acquire the genetic information encoding antibiotic resistance from other bacteria or through a de novo gene mutation. Because of the strong selection pressure brought on by the widespread use of antibiotics, bacteria carrying the resistance gene survive and grow [8]. The rapid emergence of multiresistant bacteria, which has been noted in numerous nations and for some of which there is no treatment available, is a major cause for concern. Antibiotic group combination resistance was typical in E. Extended-spectrum beta-lactamase production was triggered by E. coli and Klebsiella pneumonia (ESBL). Extended-spectrum beta-lactamase was detected in 87.4% of third-generation cephalosporin-resistant bacteria from 2017. (ESBL). There were 16.9% invasive Methicillin-resistant Staphylococcus aureus (MRSA) isolates, with significant regional variations (1.0% in Norway to 44.4% in Romania) [4]. It is crucial to pinpoint the key causes of irrational antibiotic use in Europe in order to combat the threat of ABR. In this research, we outline the main factors that contribute to irrational antibiotic use among European healthcare professionals (HCPs) and the general public (see Figure 1). Additionally, the factors shown in Figure 1, such as the lack of antibacterials (or antibiotic combinations) with new therapeutic modes of action, a lack of sewage disposal, or One Health strategy factors, such as the use of antibacterials in the environment and the animal and food industries, were outside the purview of this study, which was intended to concentrate only on human antibiotic usage. We further stress the urgent need for proactive actions from governments, academics, and medical professionals in the private and public sectors to minimize ABR through improved antimicrobial usage.

Image 1: Irrational Antibiotic Usage



We carried out an extensive review of the most recent literature utilizing the databases Cochrane, Google Scholar, PubMed, as well as several institutional websites in order to acquire a unique viewpoint on the topics that are frequently highlighted as the causes of excessive antibiotic usage from (World Health Organization). Antibiotic use, antibiotic intake, anti-bacterial agents, and antimicrobials, prescribing, prescription, unnecessary prescribing, overmedication, over prescription, excessive, pattern, medicine use, judicious, drug misuse, medicine misuse, distributing, and dispensation were all used as phrases for database-specific searches. To uncover pertinent information, we have employed a technique called snowballing, which entails searching through paper reference lists for related studies. Additionally, we selected eminent academic works from global organizations to act as European data references. The literature search revealed the prevailing theme, and the key works within the theme were analyzed, compared, and contrasted. The recurring topics that have been discussed and highlighted in the published articles are listed here.

Factors that Lead to Unreasonable Antibiotic Use in the General Population

A. Lack of Public Knowledge and Awareness

Public perceptions of attitudes about beliefs around antibiotics have a significant impact on antibiotic irrationality [12]. There is unquestionably a need to increase awareness of antibiotic use and resistance among European and other developed countries. For instance, drugs are ineffectual against viruses, and 44% of people are unsure whether antibiotics have any effect on the common cold and influenza. Both social groups and different nations exhibit notable distinctions. Low education levels and poor economic conditions are associated with higher antibiotic use (44% versus 31%) and 39% versus 32–33%, respectively [12]. However, a study from Southern Sweden found that socioeconomic factors associated with privilege were significantly associated with rising antibiotic use, especially in young children (0–6 years) [13]. In comparison to other districts, antibiotic use was higher in those with factors including a high family median income and a higher employment rate. This suggests that although if antibiotic use among children may, in some cases, increase with parental affluence, it cannot be fully explained by economic factors alone. People frequently have a poor understanding of and misconceptions about ABR. Since many individuals believe, they don't help to the spread of ABR, they are ignorant that bacteria, and not people, develop resistance to antibiotics [14]. ABR is most frequently seen in places where people don't seem to be aware of the issue. The underlying factor in this case is cultural inequalities in public perceptions, opinions, and awareness regarding antibiotic use, resistance, and self-medication [15]. 10% of patientsreported that they had received information on the proper use of antibiotics from pharmacists in the preceding 12 months, compared to 27% who said they had received it from television commercials, 26% from television news, 19% from newspapers, and 13% from the internet [12].

B. Antibiotic Dispensing Without A Prescription

The availability of antimicrobials without a prescription is in fact a driving factor for irrational antimicrobial consumption due to a likely lack of accessibility to competent diagnostics and diagnostic instruments. In the end, this contributes to the growth and spread of ABR. 93 percent of Europeans get their antibiotics on prescription, but not from any other source save a doctor. 4% of Europeans reported getting their final course of medication without a prescription, despite legal framework stating that antibiotics must only be administered with a doctor's recommendation and that over-the-counter (OTC) sales of antimicrobials are illegal in all European Union Member States (there are minor differences in a majority of people, for example, ointment or eye drops that involve antibiotics) [12]. Only 79% of respondents in Greece reported doing so. 7.5% of 1198 participants in a survey in the Portuguese Algarve region reported that getting antibiotics without a prescription was simple [17]. The way antibiotics are used is significantly influenced by the distribution technique. In a number of nations, you can get antibiotics without a prescription at your neighborhood pharmacy. UTIs account for 1-3% of all GP encounters annually, making them one of the most common acute medical conditions in the UK. The availability of antibiotics to treat small UTIs by pharmacists in one Scottish region has improved patient access to therapy and cut down on the number of appointments. Over-the-counter antibiotics are frequently administered by a pharmacist. In short therapy regimens, the bulk of these drugs are generally used as topical treatments or as ocular drops. The proliferation of ABR involves controlling the availability of licensed OTC antibiotics and monitoring their usage, however this should not be confused with the illegal supply of antibiotics available only by prescription [19]. A European study [20] found that using antibiotics without having a prescription, getting them online, or buying them abroad, is becoming a bigger issue. [21]. Another issue is the growing number of online physicians that are able to legally prescribe antibiotics without having to undergo a physical examination. Despite the fact that there is no evidence to support irrational antibiotic prescriptions being the consequence of their consultations, they may still be a contributing factor [22, 23]. It is imperative to keep in mind that inappropriate antibiotic use results from a lack of a full evaluation and any required screening before antibiotics are provided.

Knowledge, Attitudes, and Perceptions of Antibiotic Use and Resistance among Healthcare Professionals

Prescribers are ultimately responsible for choosing which kind of antibiotics to use and how much of each type to use. Their perspectives, knowledge, and experience regarding the usage of antibiotics and resistance are likely to have an effect on the prescriptions they write. It has been suggested that the attitude and knowledge of doctors affect clinical practice indicators used to evaluate the quality of antibiotic prescribing. However, data from Sweden show that the decreased percentage of antibiotic prescriptions within Sweden have not increased complications of the illnesses due to not responding with antibiotics, for example, the frequency of infections[25]. According to the results of a Spanish investigation, factors influencing general practitioners' prescription of antibiotics include lack of information about ABR, a complacent approach toward patients, and fear of infection-related problems. According to a recent systematic research, clinicians typically believed that ABR was a serious problem, even though it wasn't in their immediate area. A qualitative method from Sweden found that some physicians did not consider resistance to be a problem in their routine clinical practice. This is in contrast to the majority of clinicians who believed it to be a problem in their own practice [26, 27]. Although other doctors were aware of these issues, many didn't think it would have much of an impact on their own practice since they perceived it as an issue in other nations, various regions of the country, or hospitals. The way GPs described how they dealt with UTIs in practice was similar to how they felt about ABR [27, 28]. As well as attitudes, workload and working in emergency departments have been recognized as significant determinants of antibiotic prescribing [29].

Inadequate Training for Healthcare Providers

Inadequate teaching on antibiotic prescribing at medical school and later in the early phases of clinical practice, as well as a lack of continuing professional progress in successful employment, can all result in erroneous antibiotic prescribing. The importance of undergraduate training in ethical prescribing practices has lately been highlighted by the WHO [29, 26]. According to a recent survey on self-reported preparation among end-of-year medical graduates in 129 countries, 66.1% of students wished to get more training on prudent or broad antibiotic usage (ranging from 20.3% in Sweden to 94.3%) [30]. Compared to the first year after certification, when only 60% of junior physicians sought further training in giving antibiotics, 74% of those with more experience wanted it [31].

Advertising of Pharmaceuticals

Additionally, it is believed that pharmaceutical promotion increases the number of irrational prescriptions. Advertising cannot be misleading and must be consistent with facts about the drug that has been approved, according to regulations on pharmaceutical marketing. On the other hand, it has been asserted that, globally, even countries with adequate funds for regulatory oversight vary greatly in how well they monitor pharmaceutical advertising and uphold the law with appropriate sanctions [32]. Pharmaceutical advertising has an impact on the prescription and dispensing decisions made by healthcare providers. A 2010 systematic analysis of numerous studies indicated a link between physicians' exposure to pharmaceutical corporate information and worse prescribing quality, more frequent prescriptions, and higher pricing. However, it is important to recognize the diversity of the included studies [33]. A productive method for establishing connections that influence prescription behavior is one-on-one engagement between sales representatives and physicians. In reality, salespeople are skilled in persuading and persuasion methods. According to a recent study from Germany, specialists who met pharmaceutical sales representatives more regularly wrote more prescriptions overall than those who were visited less frequently [34]. To identify potential influencing factors, focus groups with 33 clinicians from a Spanish qualitative study looked at their prescribing practices and knowledge of antibiotics. It was established that medical professionals thought pharmaceutical advertising and promotion had a very meaningful influence on their choice to recommend an antibiotic. Some of the participants claimed.

Lack of Local Antibiotic Susceptibility Data and Rapid and Adequate Diagnostic Tests

A significant problem that contributes to improper antibiotic prescription and usage is the lack of adequate diagnostic tests to quickly identify the organism and its antimicrobial sensitivity profile, direct antibiotic prescriptions at the point of treatment, and minimize the requirement for wide spectrum antibiotics [35, 36]. Empiric prescriptions nearly often come before culture findings since conventional culture and sensitivity testing take time. Empiric prescription is the norm in all countries, although if a culture is done and after-culture data are collected, the choices of antibiotics may be narrowed. New techniques in diagnostic technology, such as nucleic acid amplification tests (NAAT), matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF), and antigen detection have made timely antibiotic optimization possible [36,37] [37,38]. However, faster diagnostics are not always followed by better antibiotic prescription. A concurrent antimicrobial stewardship programme has been shown to be crucial and to hasten the improvement of antibiotic prescription [38, 39]. Another notable issue is how poorly fast diagnostic tests perform on tests for antibiotic resistance. Even though certain methods can identify specific resistance signs, these tests are still unable to identify diseases' complete profiles of antibiotic susceptibility. The medical history of the patient, the existence of any infections nearby, and laboratory workflow should all be taken into consideration when selecting an appropriate diagnostic test. However, faster diagnosis are not always followed by better antibiotic prescription. A concurrent antimicrobial stewardship programme has been shown to be crucial and to hasten the improvement of antibiotic prescription [39]. Another notable issue is how poorly fast diagnostic tests perform on tests for antibiotic resistance. Even though certain methods can identify specific resistance signs, these tests are still unable to identify diseases' complete profiles of antibiotic susceptibility. The medical history of the patient, the existence of any infections nearby, and laboratory workflow should all be taken into consideration when selecting an appropriate diagnostic test. Medical professionals can access varying degrees of regional antibiotic sensitivity data for the most common bacteria in different European countries. Many countries only report statistics from a small number of hospitals in a specific geographical area. Since the sampling cannot be regarded as representative, regional differences within a country may not be revealed [4]. According to their prevalence in the general population, different patient categories (such as paediatric, intensive care unit, or neurosurgery cases) and illness types should be represented in the surveillance sample of patients. The Global Antibiotic Resistance Surveillance System (GLASS) [39, 40] was established by the World Health Organization (WHO) in 2015 as the first global cooperative effort to control antimicrobial resistance surveillance. By offering a systematic method for the collection, evaluation, and exchange of data on antibiotic resistance by governments all around the world, GLASS intends to document the state of existing or recently established national surveillance systems.

Medical-Patient Communication

Numerous studies have shown how crucial it is for patients and doctors to connect and communicate while administering antibiotics. In order to maintain a positive patient-physician connection, doctors exaggerated patients' expectations for antibiotics, according to a qualitative study carried out in the United Kingdom [40, 41]. A survey of 1000 GPs in the UK found that 55% of them felt under pressure to prescribe antibiotics even when they weren't sure they were necessary and that 44% admitted to writing prescriptions to get patients to leave the clinic [41, 42]. The development of ABR, the medicalization of patients' symptoms, and rising healthcare costs are just a few of the negative effects of incorrect or excessive antibacterial prescriptions and/or overprescribing [42, 43]. In primary care, RTIs in both adults and children account for the vast majority of antibiotic prescriptions with a systemic indication [43, 44]. RTIs are rarely treated with antibiotics, and 60% to 90% of recommended medications are unsuitable [44, 46] Furthermore, RTIs frequently resolve on their own, necessitating no need for antibiotics. In line with a typical antibiotic regimen, the projected time course of RTI symptoms is one week for merely an acute sore throat, one and a half weeks for a cold, and three weeks for an acute cough and bronchitis [48, 49].

Improve Knowledge of Antibiotic Resistance

In order to combat Antibiotic resistance, surveillance is essential. The absence of monitoring may lead to policies that are poorly thought out, ineffectual, and wasteful of resources. In order to inform treatment recommendations, identify intervention priorities, customize and target treatments, and track the effectiveness of interventions, it is essential to understand trends in antibiotic usage and resistance. [58, 59].

Encourage innovative approaches to creating antibiotics that are focused on public health

There is no consistent approach for establishing priorities in the funding of antibiotic research and development. There are currently not enough efficient new antibiotics, vaccines, or diagnostics being developed. Furthermore, the majority of publicly funded R&D projects in this field focus on the early stages of basic research. There is much less funding available for later stages of antibiotic research, clinical trials, and post-marketing surveillance, all of which require ongoing financial support. It takes focused research to help create new, effective treatment philosophies [45, 47]. The pharmaceutical industry has made a sizable contribution to the effort to ensure the moral and responsible use of antibiotics. Partnerships for product development (PDPs) should always include stewardship principles for any medications that result from collaboration. PDPs can address the lack of new antibiotic development while concentrating on unmet medical needs. To make it possible to quickly identify potentially infectious organisms, to assist doctors in determining whether or not to begin antibiotic therapy, and to generally improve the treatment of infectious diseases, rapid diagnostic tests that are innovative, reasonably priced, and easy to use are required. It's also crucial to find new medicines that don't encourage resistance. Preclinical research of various monoclonal antibodies indicated their potential to treat infectious diseases both in vitro and in animal models [64, 65].

Enhanced Regulations on Pharmaceutical Advertising

Governments should enforce proactive and effective regulations on pharmaceutical promotion, keeping in mind the risks that improper and excessive use of antibiotics pose to the public's health. At the absolute least, pre-vetting should be applied to all marketing for antibiotics. Pharmaceuticals containing antibiotics should only be sold by prescription, unless the healthcare system specifies the prescription order.

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