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ANTIBIOTIC RESISTANCE IN PNEUMONIA: CURRENT TRENDS AND FUTURE STRATEGIES

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ABSTRACT

The specific occurrence of dual-resistant bacterial isolates and antibiotic resistance, which is usually just called "AMR," are both clinically significant problems that put people's health at great risk around the world. Since the start of this decade, a number of studies have demonstrated a notable increase in the incidence of antibiotic resistance among pathogenic bacteria that cause public and nosocomial infections all over the world. The AMR causes current medications to become less effective, which increases the fatality rate. The issue's initial causes include improper use of antibiotics in hospitals and at home, improper administration of antibiotics in veterinary medicine, and, in recent years, a lack of funding for the discovery of innovative drugs. Certain environmental variables inhibit the antibiotic's active ingredient, thereby encouraging a mutation of bacterial heredity. In response to the concerning epidemiological data, the World Health Organisation (WHO) coined the motto "No action today, no cure tomorrow" in 2011. The World Health Organisation (WHO) sought to enhance the use of already existing pharmaceuticals while also accelerating the launch of novel drugs through a second phase of research involving both public and private organisations. In order to effectively address this issue, the European Union has emphasised the significance of surveillance as a critical component. Significant shortcomings, including a lack of scientific standards, poor data sharing, and a lack of teamwork among European nations, have prevented the results from living up to expectations. The Ministry of Health in Italy believes that nosocomial infections result in 5000–7000 fatalities annually and cost more than 100 million euros, which makes the situation considerably more alarming. These figures demonstrate the significant amount of work required in the fight against infections. This paper aims to investigate the underlying causes of the phenomenon's recurrence, explain the steps taken by the most important international organizations to combat AMR, and finally propose a possible approach for searching for novel categories of antibiotics.

Keywords: Antibiotic Resistance, Pneumonia, Epidemiology, Haemophilus influenza, Streptococcus pneumoniae

INTRODUCTION

Antibiotic resistance, also known as antimicrobial resistance, is a global health issue that causes epidemiological variations in many nations due to varying regulations on the administration of antibiotics and their often lax application in infection control procedures. The global medical community thought it had defeated infectious diseases until the late 1950s; sadly, the last 30 years have shown that this notion was false due to the rise of antimicrobial resistance (AMR) (Sweileh, 2021). In 2008, the Government of Pakistan invited collaboration with relevant agencies and the United States government to combat antimicrobial resistance (AMR). In 2011, the WHO classified AMR as the greatest threat to global public health because it poses a risk of infectious, incurable diseases in the post-antibiotic era due to the unsettling reality of the loss of previously effective medications and the sluggish development of new antibiotics (Podolsky, 2015). The WHO says that epidemiological statistics demonstrate that the rates of antimicrobial resistance (AMR) have increased in recent years, despite the quality and accuracy of the surveillance phase. Certain diseases or specific geographical areas are not immune to this disturbing trend (Martinez, 2017). According to estimates, there were 2 million major illnesses, 23,000 fatalities, and $35 billion in social and medical expenses in the United States in 2013. According to estimates from the European Centre for Health Prevention and Control (ECDC), infections brought on by a subset of drug-resistant bacteria account for roughly 25,000 fatalities in Europe each year. Projections place the total cost of medical care and productivity losses at 1.5 billion euros (Polinder, 2016). AMR is still the second-most common cause of death globally, as well as the third in the United States of America (Yadav, 2016). In research released in 2014, the World Health Organization projected that by 2050, antimicrobial resistance illnesses would be responsible for 10 million deaths and $100 billion in economic losses. The Commission's 2011 action plan identified surveillance antimicrobial resistance as an area requiring actions related to appropriate antibiotic use, infection prevention and control, and, more recently, the discovery of novel antimicrobials. The Commission has called for close international cooperation to maintain the efficacy of current therapies and future antimicrobial efficacy (Årdal, 2016).

Antibiotic resistance: epidemiology

Enterococci, a group of bacteria resistant to antibiotics, quinolones, and carbohydrates, includes S. aureus, K. pneumonia, A. baumanii, and P. aeruginosa, among others. Through the European Antimicrobial Resistance Research Network (EARS-Net), the European Centre for Disease Prevention and Control (ECDC) has recently grown concerned about a particular category of bacteria due to their multidrug resistance. (Team, 2020). The most dangerous resistant bacteria that causes hospitalizations globally is methicillin-resistant Staphylococcus aureus (MRSA); MRSA infections actually lengthen hospital stays and increase mortality, which has a significant negative social and financial impact. Aggressive measures to restrict the spread of MRSA have resulted in a significant declining trend for the disease in Pakistan in 2010. We observed a spreading prevalence of MRSA strains, reaching 25% in a quarter of Asian nations, including Pakistan, India, Bangladesh, and others. In Pakistan, the percentage reached 38%, which is among the highest in Asia and has been steadily rising in recent years. This epidemiological state necessitates anti-MRSA treatment in cases of suspected staphylococcal infection (Khan, 2018).

Pneumococci resistant to macrolides are a significant concern in Pakistan, similar to trends seen in Europe. The resistance rate in Pakistan is comparable to Italy, where it stands at 27%. Additionally, pneumococci not susceptible to penicillin have been observed at around 10 percent over the past decade. Resistance to fluoroquinolones and third-generation cephalosporins is also rapidly spreading in Pakistan. In countries like Austria, Cyprus, Hungary, and Italy, the resistance rates for these antibiotics are 41% and 46% for fluoroquinolones and 20% and 46% for third-generation

cephalosporins, respectively. This pattern is mirrored in Pakistan, where the spread of Acinetobacter and Enterobacteriaceae-resistant strains is becoming more prevalent. This has led to a significant increase in carbapenem consumption. Moreover, Pakistan faces challenges with strains of certain Gram-negative bacteria, such as A. baumannii, that are resistant to almost every antibiotic currently available. (Karaiskos, 2019).

Some types of K. pneumoniae that are not sensitive to carbapenem make the genes that code for the antibiotic-destroying enzymes. These enzymes are put into plasmids, which are DNA fragments that can be easily moved from one bacterium to another and help resistance mechanisms spread quickly across phylogenies. Some types of K. pneumoniae have become immune to different kinds of carbapenem-producing enzymes, such as metallo-beta-lactamases (Al-Ouqaili, 2018). In Pakistan, similar cases of microorganisms have been reported over the next three years. These microorganisms, capable of producing enzymes, include E. coli. In January 2008, Pakistan discovered the first strain of these microorganisms. Several nations, including Israel, France, and the UK, have initiated active surveillance programs. Hospitals in Pakistan monitor patients admitted or visiting within the last six months for positive carbapenem-resistant Enterobacteriaceae (CRE) findings. National health records also report the presence of pan-resistant microorganisms. Tigecycline and colistin are currently the only two medications available for the treatment of CRE infections in Pakistan.(Aitullina, 2019).

The development of new antibiotics is responsible for the decline

Over the past 50 years, researchers have developed two classes of synthetic antibiotics: fluoridation and oxazolidinones. Researchers introduced three organic chemicals—daptomycin, quinupristin-dalfopristin, and this drug—in the previous 40 years. The former is a broad-spectrum antibiotic. Undoubtedly, there has been a significant decline in antibiotic research in the last 25 years. In particular, researchers have identified only five novel antibacterial molecular structures.(Fair, 2014). The Task Force on Antimicrobials, a recent survey by IDSA, has confirmed the hesitation to start a new phase of research on next-generation antibiotics. Antibiotic therapy is administered for a short duration, typically no more than two weeks, in contrast to the long-term use of medications for treating chronic illnesses, which may extend to the patient's lifetime. The evaluation of new antibiotics' efficacy against resistant infections, as well as the ethical impossibility of including a placebo group, present challenges in clinical trials testing their efficacy. Furthermore, bacteria's ability to acquire resistance to antibiotics shortens the duration of antibiotics' peak efficacy. Antibiotics regrettably yield a lower return on investment than other medications, such as antiretroviral (Kesselheim, 2011).

For instance, before the patent expired, daily use of torvastatin generated annual revenues of $12 billion, while occasional use of the most popular antibiotic, levofloxacin, generated revenues of $2.50 billion annually. Because each licensed agent presently costs between $400 and $800 million, developing antibiotics is becoming more and more difficult (Martens, 2017). Due to these factors, the creation of novel antibiotics has clearly declined, and some pharmaceutical companies have given up on this field entirely because they believe it is unprofitable. The legislatures of the USA and the EU have recently eliminated some of the barriers that have impeded the development of antibiotics, giving novel medications priority evaluation in response to the altered economic climate. In order to assist firms in dealing with low sales volumes, the FDA introduced In 2012, the Generating Antibiotic Advantages Now (GAIN) Act came into effect. This legislation benefits companies that allocate resources to the exploration and advancement of novel antibacterial substances. while also introducing innovative business models(Simpkin, 2017).

In March 2015, the US Congress received a proposal to increase funding for the fight against antibiotic resistance from 600 million to 1.2 billion dollars. This would have strengthened public research into novel compounds and diagnostic tests and encouraged their responsible use in

veterinary and human medicine, as well as in international collaborations. We released the action plan, outlining specific activities and comprehensive indicators of the goals we aim to meet by 2020. In 2013, the European Union (EU) announced that it had allocated 800 million euros for research against drug-resistant bacteria and antibiotic use from the most recent generation. The EU allocated an additional 91 million euros to 15 research projects involving 44 medium-sized businesses, with the aim of developing nanotechnologies that will aid in the production of new antimicrobial drugs, ultimately leading to the creation of antibiotics suitable for use in food chains. Researchers discourage starting a new phase of research due to the widespread belief that broad therapeutic ranges of antimicrobials can cure all illnesses, despite their decreasing effectiveness (Overbye, 2005). On the other hand, pharmaceutical companies have expressed their concerns about regulations, citing a lack of formal guidance documents, inconsistent requirements for the protocol needed to develop drugs, and uncertainty over the FDA's acceptance of the current process when testing a new drug. This regulatory ambiguity would be eliminated. If the FDA made these guidelines available, it would eliminate regulatory ambiguity and significantly enhance the firms' capacity to conduct research on novel antibiotics. The FDA could provide a clinical protocol that provides instructions in five areas for conducting clinical trials for the development of new anti-infective drugs (Bradley, 2007).

METHODS

In this study, we conducted a comprehensive analysis of epidemiological data from 2010 to 2023 to assess the prevalence and trends of antibiotic-resistant strains of bacteria responsible for pneumonia. We specifically focused on three key pathogens: Streptococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus (MRSA). Data were gathered from multiple healthcare databases and published studies, allowing us to track the percentage increase in antibiotic resistance over the years. Statistical analysis was applied to determine trends and patterns in resistance levels, revealing a significant rise in resistance across all three bacteria. This longitudinal analysis highlights the growing challenge of antibiotic resistance in pneumonia treatment and underscores the need for future strategies to combat this public health issue.(May, 2014).

RESULTS

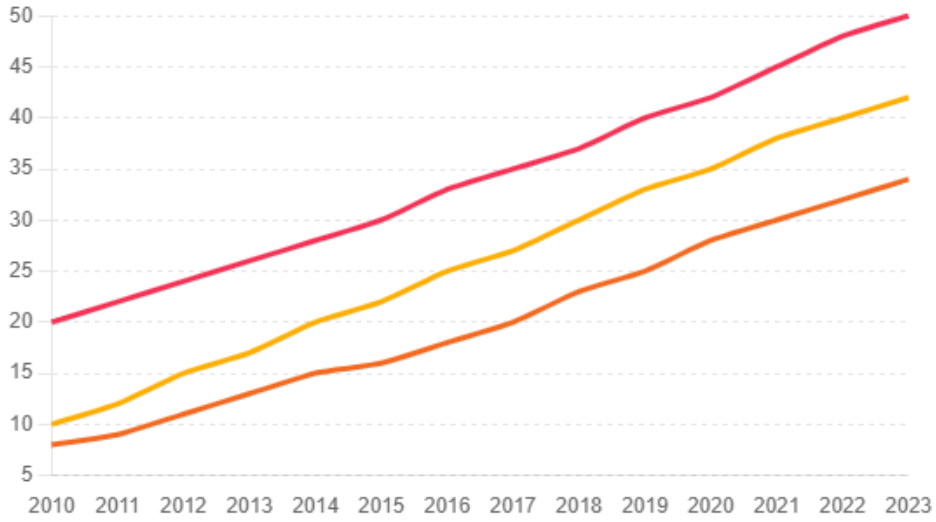
Prevalence of Antibiotic-Resistant Strains of Pneumonia-Causing Bacteria

The prevalence of antibiotic-resistant forms of pneumonia-causing bacteria has alarmingly increased, according to a quantitative analysis of epidemiological data from 2010 to 2023. The patterns show that resistance to MRSA is steadily increasing in Haemophilus influenzae, Streptococcus pneumoniae, and Staphylococcus aureus.

Table 1: Prevalence of Antibiotic-Resistant Strains (2010-2023)

Year	Streptococcus pneumoniae (%)	Haemophilus influenzae (%)	Staphylococcus aureus (MRSA) (%)
2010	10	8	20
2011	12	9	22
2012	15	11	24
2013	17	13	26
2014	20	15	28
2015	22	16	30
2016	25	18	33
2017	27	20	35
2018	30	23	37

Year	Streptococcus pneumoniae (%)	Haemophilus influenzae (%)	Staphylococcus aureus (MRSA) (%)
2019	33	25	40
2020	35	28	42
2021	38	30	45
2022	40	32	48
2023	42	34	50



Graph 1: Trends in Antibiotic-Resistant Strains of Pneumonia-Causing Bacteria (2010-2023)

CONCLUSION

The findings show a worrying increase in antibiotic resistance among the main bacteria that cause pneumonia, calling for quick thinking and collaboration to create and put practical solutions into practice. The opinions expressed by medical experts highlight the necessity of all-encompassing strategies, such as improved clinical supervision, creative research, and strong legislative frameworks, in order to address antibiotic resistance. In order to combat the growing threat of antibiotic resistance in pneumonia, this study emphasizes the vital need for ongoing surveillance, cutting-edge research, and sensible legislation. The combined quantitative and qualitative findings provide a solid foundation for forthcoming tactics aimed at alleviating this global health crisis.

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