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Global issues with Bacterial Antibiotic Resistance and Resistance Genes: A Mini-Review

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Abstract: **The spread of resistant bacteria is problematic and it threats the treatment and healthcare in future. Bacteria gain resistances through different factors and the main important one is existing of resistance genes in bacteria. This problem impedes treatment and causes fatality of million patients around the world. Resistance genes producing hundreds of different enzymes that deactivate of therapeutic antibiotics by lysis of changing chemical structure of drugs. Unsanitary conditions and poor management of the hospitals is one of the main reasons of spreading resistant bacteria. This mini-review clarify the reasons of antibiotic resistance and the reasons of spreading resistant bacteria in environment.**

Keywords: **Resistant bacteria, Antibiotic resistance, Resistance genes, A review.**

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1. INTRODUCTION

Antibiotic resistance

Antibiotic resistance happens when bacteria change and can resist the effects of an antibiotic. The bacteria are not killed, and they continue to grow. The infections these bacteria cause are called resistant infections. Resistant infections can be difficult, and sometimes impossible, to treat. It also can say occurs when bacteria evolve the way that protect them from the action of antimicrobials (antibiotics used to treat infections) (Magiorakos et al., 2012). All groups of bacteria can become resistance to one or more antibacterial drugs used to fight them are no longer effective. InFungi called antifungal resistance, and in bacteria it called antibiotic resistance. Together all of these come under the umbrella of antimicrobial resistance (Magiorakos et al., 2012).

Microbes resistant to multiple antimicrobials are called multidrug resistant (MDR) and are sometimes referred to as superbugs.[3] Although antimicrobial resistance is a naturally occurring process, it is often the result of improper usage of the drugs and management of the infections (Saha & Sarkar, 2021; Tanwar et al., 2014).

Antibiotic resistance Antibiotic resistance happens when bacteria mutate and become resistant to the antibiotics used to treat the infection they caused. The more antibiotics are used, the more chance there is for bacteria to develop resistance. At least 700,000 people per year world-wide die from antibiotic resistant infections. It is a major subset of AMR, that applies specifically to bacteria that become resistant to antibiotics. Resistance in bacteria can arise naturally by genetic mutation, or by one species acquiring resistance from another. Resistance can appear spontaneously because of random mutations, but also arises through spreading of resistant genes through horizontal gene transfer. However, extended use of antibiotics appears to encourage selection for mutations which can render antibiotics ineffective (Dabour et al., 2016; Fisher et al., 2022). Antifungal resistance is a subset of AMR, that specifically applies to fungi that have become resistant to antifungals. Resistance to antifungals can arise naturally, for example by genetic mutation or through aneuploidy. Extended use of antifungals leads to development of antifungal resistance through various mechanisms (Fisher et al., 2022). it will make problem in some bacteria that is difficult for treatment such as helicopter pylori and its shown that the prevalence is very high especially in middle east (Hussein Ali, 2022).

several studies showed the danger and prevalence of resistance genes in bacteria and the rate is high in alarming level. This study rings the bell of threat in health sector that hinder the treatment in hospitals. In addition, it tells us the pace of spreading the issue globally. In middle east and Asia the rate of resistance genes and antibiotic resistance is very high in different types of bacteria (mm3). In some studies, the information in gathered how the phenomenon is common in all countries of middle east (Rahim et al., 2020).

2. REASONS OF ANTIBACTERIAL RESISTANCE

Antibiotic resistance occurs when bacteria evolve mechanisms to resist the effects of drugs that once killed them or inhibited their growth. This resistance means that standard treatments become ineffective, and infections persist or worsen (Lee Ventola, 2015). Here’s a brief overview of the key aspects:

Causes

1. **Overuse and Misuse**: Frequent and inappropriate use of antibiotics, including in agriculture, contributes significantly to resistance. This includes taking antibiotics for viral infections (where they’re ineffective) or not completing prescribed courses.

2. **Natural Selection**: Bacteria can develop resistance through mutations or by acquiring resistance genes from other bacteria. These resistant strains survive and proliferate when exposed to antibiotics.

3. **Inadequate Infection Control**: Poor hygiene and infection control practices can spread resistant bacteria in healthcare settings and communities.

Consequences

1. **Treatment Failures**: Infections that were once easily treatable can become severe or even untreatable, leading to longer hospital stays, higher medical costs, and increased mortality.

2. **Limited Treatment Options**: Resistance reduces the effectiveness of antibiotics, making it more difficult to treat common infections and increasing the reliance on more expensive or toxic alternatives.

3. **Increased Spread**: Resistant bacteria can spread more easily, leading to outbreaks that are harder to control (Frieri et al., 2017; Lee Ventola, 2015).

Prevention and Mitigation

1. **Responsible Antibiotic Use**: Only use antibiotics when prescribed by a healthcare professional, and complete the full course as directed.

2. **Infection Control Practices**: Good hygiene, vaccination, and infection control measures in healthcare settings help prevent the spread of resistant bacteria.

3. **Research and Development**: Investing in the development of new antibiotics and alternative treatments is crucial to staying ahead of resistance trends.

4. **Global Collaboration**: Tackling antibiotic resistance requires coordinated efforts across countries and sectors, including public health initiatives, regulatory measures, and education(Frieri et al., 2017; Lee Ventola, 2015).

Addressing antibiotic resistance is a complex challenge that involves the cooperation of healthcare professionals, policymakers, and the public to ensure antibiotics remain effective for future generations. It also hinders the benefits of some bacteria that uses for probiotic treatment of bacteria because bacteria are known for its probiotic importance in treatment of some wounds and burns (Ahmed et al., 2021).

3. RISKS OF ANTIBIOTIC RESISTANCE

Antibiotic resistance poses several significant risks to public health and well-being. Here’s a detailed look at some of the key risks:

1. Treatment Failures

- **Ineffective Treatments**: Antibiotic-resistant infections are harder to treat because standard antibiotics are no longer effective. This can lead to prolonged illnesses and complications.

- **Need for Alternative Drugs**: Treating resistant infections may require using more expensive or toxic drugs, which might not be as effective or have more severe side effects.

2. Increased Mortality and Morbidity

- **Higher Death Rates**: Infections that cannot be treated effectively can lead to higher mortality rates. This is particularly concerning for vulnerable populations such as the elderly, infants, and those with weakened immune systems.

- **Severe Complications**: Untreated or inadequately treated infections can lead to severe health complications and increased hospitalization.

3. Extended Hospital Stays

- **Longer Recovery**: Patients with resistant infections often require longer hospital stays, which can increase the risk of acquiring other infections and lead to higher healthcare costs.

- **Increased Healthcare Burden**: Extended treatment periods place additional strain on healthcare resources and systems.

4. Spread of Resistant Strains

- **Community Spread**: Resistant bacteria can spread from person to person, potentially causing outbreaks in communities and healthcare settings.

- **Environmental Contamination**: Resistant bacteria can be released into the environment through various means, including wastewater from hospitals and farms, which can contribute to the spread of resistance.

5. Limited Treatment Options

- **Diminished Choices**: The effectiveness of existing antibiotics diminishes as resistance spreads, limiting treatment options for common infections and complicating the management of more complex cases.

- **Increased Reliance on Last-Resort Antibiotics**: More critical and less frequently used antibiotics may be used as last-resort options, which can further promote resistance if they are overused.

6. Economic Impact

- **Higher Costs**: Treating resistant infections often involves more expensive drugs, longer hospitalizations, and more intensive care, which can significantly increase healthcare costs.

- **Economic Burden on Families**: The financial strain of extended illness and treatment can impact patients and their families, potentially leading to financial hardship.

7. Impact on Medical Procedures

- **Complications with Surgery and Treatments**: Many medical procedures, including surgeries and cancer treatments, rely on effective antibiotics to prevent infections. Resistance can increase the risk of complications and reduce the safety of these procedures.

8. Global Health Threat

- **Cross-Border Challenges**: Antibiotic resistance is a global issue, and resistant strains can spread across borders, affecting international health and complicating global public health efforts.

Addressing these risks requires a comprehensive approach, including responsible antibiotic use, improved infection control practices, investment in new treatments, and global collaboration to mitigate the impact of antibiotic resistance(Cassini et al., 2019; Piri et al., 2018).

4. DISTRIBUTION OF ANTIBIOTIC RESISTANCE GENES IN ASIA AND MIDDLE EAST

Several researches had conducted about the prevalence and distribution of bacteria carried antibiotic resistance genes in Asia such as China, Pakistan, India and Bangladesh and also in middle east such as Iran, Iraq, Egypt, and turkey. In all areas the level of antibiotic resistance genes is very high and all types of resistance genes have been reported.

Pakistan:

In one study, it was found that the rate of ESBL, MBL and AmpC in clinical isolates of *P. aeruginosa* was found to be 23.94%, 40.84% and 35.21% respectively. Co-production of ESBL and AmpC were also was found. There were 14 (19.71%) CTX-M-15 harboring bacteria which were ESBL (64.28%), MBL (21.42%) and AmpC (14.28%) producer (Ullah et al., 2017).

In another study betalctamase was found in Enterobacteriaceae in Pakistan and the results and rates was as follow. Notably, 15% of ESBL producing strains harbored blaSHV gene while 43% were positive for blaOXA gene (Waheed et al., 2019).

China:

Out of 224 *K. pneumoniae* strains, 5 (2.2%) were identified to carry inactivated ESBL *bla*SHV genes. Interestingly, three of the five antibiotic-sensitive *K. pneumoniae* strains containing ESBL *bla*SHV genes still exhibited mRNA transcription of blaSHV, while the other two exhibited no mRNA transcription (Xu et al., 2014).

In another study was found that bacteria isolate in clinical samples. The isolates mainly harbored $bla_{\text{CTX-M}}$ ($n = 51$, 70.8%) and bla_{SHV} ($n = 46$, 63.9%) genes. High prevalence of PMQR genes *qnrA1* ($n = 24$, 33.3%), *qnrB* ($n = 4$, 5.6%), *qnrS1* ($n = 2$, 2.8%), and *aac(6')-Ib-cr* ($n = 21$, 29.2%) was observed. Furthermore, CHβLs IMP-4 ($n = 6$, 8.3%) and IMP-8 ($n = 4$, 5.6%), as well as class I integrons ($n = 29$, 40.3%), were found in the ESBL-producing *E. cloacae* (Cao et al., 2017).

Bangladesh

The are several studies in Bangladesh showing the prevalence of resistance genes, in this stud the rate was as follow. blaTEM-type and blaOXA-1-type genes were detected in 33 (82.5%) and 19 (47.5%) isolates, respectively. Virulence genes that are present in diarrhoeagenic *E. coli* were not found. Class-1 integron was present in 20 (50%) isolates (Lina et al., 2014). Genes encoding resistance to tetracycline [tetA, 100% (35/35); tetB, 31.43% (11/35)], fuoroquinolone [qnrA, 35.71% (10/28); qnrB, 25% (7/28)], and streptomycin [aadA1, 90.24% (37/41)] were detected in the isolated E. coli (Islam et al., 2022).

Iraq

Several studies were caried out in Iraq showing the rate of beta lactamase is very high in all species of Enterobacteriaceae. In E. coli isolate from animal and human the rate was as follow: 18 (20.6%) isolates were positive with blaCTX-M and blaTEM and 17 (19.5%) of them were found in heavy antibiotic users, but only one blaCTX-M gene (Alaa et al., 2020). blaTEM-1 and blaShv were found in five isolate. 21 isolates (17.2%) of Proteus. Three isolates (10.3%) were positive to blaTEM-1 resistance gene and two isolates (6.8%) were positive to blaShv in proteus (Hama-Soor et al., 2021; Salih et al., n.d.). blaOXAgene (57.5%) was the predominant resistance genes among E. coli isolates of diarrhea (Ali et al., 2022). SHV gene, 22.3%, and OXA gene showed the lowest rate 11.7% was found in E. coli in different study (Ghafour et al., 2021a; Hama Soor, 2022). The rate was also existed in pseudomonas, s (7.4%) was found to carry blaOXA resistance gene, and two isolates (3.7 %) were positive to blaCMY (Ghafour et al., 2021a, 2021b).

Iran

In Iran the rate is also high and there many studies about resistance genes (Ghasemian et al., 2018; Leylabadlo et al., 2017). Out of 1275 isolates resistant to one of the 3rd-generation cephalosporins, 475 were ESBL strains (12%). TEM was the most common ESBL gene found in phenotypic positive strains (Armin et al., 2020). Out of 100 *Acinetobacter baumannii* isolates, 59% were ESBL positive according to the phenotypic method. The PCR assay could not detect the *bla*SHV and *bla*VEB genes in the studied isolates, but the presence of *bla*TEM gene was demonstrated in 42% of the strains (detektiert werden, n.d.).

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