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A Review of Superbug: A Global Threat in Health Care System

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Abstract

The rapid spread and dissemination of the multidrug-resistant bacteria worldwide represents a major public health problem. The development of antibiotics decreased the mortality among the human and animals leading to a better life expectancy. But the injudicious use of antimicrobials and selection pressure the microbes have developed resistance which became more prominent during last few decades. With the evolution of Methicilin-resistant *Staphylococcus aureus* (MRSA), Hospital-acquired MRSA, Community-acquired MRSA and MDR TB (Multidrug resistant tuberculosis) challenge for the clinicians have increased to a greater extent. The global emergence and dissemination of acquired carbapenemases among gram negative bacteria are considered a major public health problem. Gram-negative bacteria, most notably *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, are among the most important causes of serious hospital-acquired and community-onset bacterial infections in humans, and resistance to antimicrobial agents in these bacteria has become an increasingly relevant problem. Recent development in nanotechnology based drug delivery system may prove to be solution for combating these resistant bacteria. However policies and regulations for antibiotic use should be formulated to control the further development of resistance among the microbes. [Bangladesh Journal of Infectious Diseases 2017;4(1):25-28]

Keywords: Multidrug resistance; injudicious use; emergence; hospital acquired

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Introduction

The use of antibiotics for combating the infectious agents dated back to the era of Alexander Flemming. With the development of antibiotics to higher synthetics groups, came to fore the emergence of resistant microbes. Antibiotics are used for combating the infectious diseases but their excessive and misuse have given rise the formation of superbugs graving a major problem worldwide. Superbug is a term used to describe the newly evolved bacterial species resistant to antibiotics. This resistance to antibiotics by Super bugs causes economic losses by increasing the duration of infection, treatment cost and decreasing the success of surgical treatments due to hospital acquired infections[1]. The world is facing a growing threat from multidrug-resistant (MDR) gram negative "superbugs," such as *Pseudomonas aeruginosa, Acinetobacter baumannii* and *Klebsiella pneumoniae*[2]. This morbidity and mortality loss caused there of indirectly hampers the economic developments in countries. The previous reports say that the cost of medical sectors for treating resistant bacterial infections and MDR TB (multidrug resistant) reaches to 4 to 7 dollar billion per year[3] and 180,000 dollar in United State[4]. High antimicrobial resistance was observed against all β-lactam and non- β-lactam antibiotics by the MBL producers. In developing countries also the misuse and underuse of antimicrobials due to lack of awareness of patients, medical workers and financial problems emerged the antimicrobial resistant strains[5-6]. Due to rapid globalization of human population by travel and other factor these resistant strains spread easily between developed and developing countries making it a global problem[7-8].

Sequential Emergence of Various Superbugs

Initially Drug-resistant strains were found on Hospitals due to use of most antibiotics[9]. *Staphylococcus aureus* was the first resistant bug discovered in 1943 against Penicillin[10]. In 1967, *Streptococcus pneumoniae* and after that the *Enterococcus faecium* was found resistant to Penicillin[11]. After penicilin, methicillin was the target antibiotic and first methicilin-resistant *S. aureus* (MRSA) was found in 1961 in UK and became a major bug worldwide in 1980s[12]. After that both Hospital-acquired MRSA (HA-MRSA)[13] and Community acquired MRSA (CA-MRSA)[14] The first outbreak of CA-MRSA has occurred in the indigenous populations of Western Australia[15] and after that it emerged worldwide. Resistant gram-negative bugs emerged simultaneously with gram-positive strains. Multidrug resistance was first seen in enteric bacteria like *Escherichia coli*, *Shigella* and *Salmonella* in late 1950s-1960s[16] Extended-spectrum beta-lactamase containing bugs prevailed in Europe and then worldwide[17-18]. After that carbapenemase-producing gram-negative bugs like extensively drug-resistant *Acinetobacter spp.* and enterobacteriacae producing New-Delhi metallo-protease-1 (NDM-1) *Klebsiella pneumoniae* producing carbapenemases were emerged[19]. In 21st century many multidrug resistance bugs prevailed like *Pseudomonas aeuroginosa*, *Mycobacterium tuberculosis* strains resistant to four and more line of drugs specific for TB called as extremely drug resistant (XDR) strains[20-21] and totally drug resistant (TDR) strains[22] etc. First XDR isolate was discovered in 2001[23]. The cycle of creating new antibiotics and bacteria becoming resistant to them has contributed to the antibiotic resistance pandemic the world is currently facing. The increase in the antibiotic resistance coincided with the decline in the production of new antibiotics. Newer antibiotics are discovered to combat these resistant strains and simultaneously the bugs mutate their genes and by selection process become resistant to all drugs slowly causing challenge for physicians to treat infections[24].

Mechanisms of Antibiotic Resistance

The prolonged administration or misuse of antimicrobials resulted in selection pressure which favors the evolution of resistant strains and subsequently their transmission causes spread of the resistant strains in the environment. The long-term use of a single antibiotic has favored the development of strains resistant to both same antibiotics along with other related antibiotics[25]. The spread of resistance traits occurs among different ecological groups and taxonomical groups by the presence of mobile genetic elements like bacteriophage, plasmids, naked DNA, transposons etc[26-27]. The main resistance mechanisms to multiple antibiotics in *Acinetobacter* spp. and other superbugs can be summarily outlined as follows (i) production of hydrolyzing enzymes for like β-lactam hydrolysis by different kinds of β-lactamases (Class A to D β-lactamases), (ii) changes in penicillin-binding proteins (PBPs) that prevent the action of β-lactams, (iii) alterations in the structure and number of porin proteins that result in decreased permeability to antibiotics through the outer membrane of the bacterial cell and (iv) the activity of efflux pumps that further

decrease the concentration of antibiotics within the bacterial cell[28].

By Mutation of target sites they resist the action of fluoroquinolones and by modification of Aminoglycosides by bacterial enzymes they resist Aminoglycosides[29-30]. MDR, XTR and TDR TB microorganisms show resistance to antibiotics by spontaneous mutation in various genes[31]. Resistance to Macrolides and related antibiotics mostly occurs due to the r RNA modification responsible for their bindings with ribosomes[32].

Prevention and Control

Antimicrobial resistant bugs are the emerging present day threats. The followings are some control and preventive measures should be taken to minimize their developments, spread and to promote development of new therapeutics. Most of the infections spread and occur from the contact of infected persons and lack of hygienic practices. Proper sanitation and hygiene maintenance in food and other things can reduce the spread of superbugs.

Inappropriate use of antibiotics occurs due to unnecessary length of treatment, wrong prescription and its use without infections[33]. Both physicians and people education about it can check the development of resistant strains. Some policies and regulations should be practiced in both developing and developed countries to check the unnecessary drug promotions[34].

Antibiotics are used vividly in food animals like chicken, cattle, pigs, agricultural fields and fish farming methods. These uses establish a direct link for the appearance of resistance in humans[35]. Attempts should be taken to check the spread of antimicrobial resistances by restricting human to human transmission of resistant strains, decreasing the use of broad spectrum antimicrobial and developing new and novel antimicrobials[36]. Steps should be taken to prevent infections by inhibiting key gene products involved in the infection process[37-39].

Conclusion

Vivid research and application of Nanotechnology for identification of resistant bacteria and therapy for combating superbugs should be practiced. Ultraviolet- C irradiation is useful to reduce the load of MRSA in food and Beverage industry as well as in hospital rooms. Hydrogen peroxide vapour is also effective in Hospital wards to reduce resistant bacterial strains.

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