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The Currents and Future Prospect of *Staphylococcus aureus* in Causing Antimicrobial Resistance

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Abstract

Staphylococcus aureus is bacterial pathogen, which is known to colonize and infect both humans and animals and to contaminate food as well. The pathogenicity of *Staphylococcus aureus* is related to the expression of a large number of virulence factors that promote adhesion and evasion of the host immunologic responses. The evolution of *Staphylococcus aureus* in the antibiotic era has revealed the emergence of virulent strains, many of which include acquisition of antimicrobial resistant to methicillin. The high burden of methicillin resistance *Staphylococcus aureus* has been first reported in healthcare facilities, second in community, and last in livestock settings worldwide. Methicillin resistance *Staphylococcus aureus* strains may spread in all geographic regions between different ecological niches resulting in major healthcare costs and relevant economic losses in the food animal industry.

Introduction

Antimicrobial resistance (AMR) has emerged as a global health threat [1]. It causes treatment failures and leads to increased morbidity, mortality, and healthcare costs [2]. If prompt action was not taken, the yearly death due to AMR could reach 10 million by 2050 [3]. The first economic report also proposed that the general impact of AMR on the health care industry would cost trillions of US dollars by 2050 [4]. Antimicrobials are used in a variety of sectors, especially in veterinary and public health for treating different animals and human diseases [5]. Additionally, it also used as growth promoter in animals [6]. However, extensive and inappropriate use of antimicrobials in animals urge AMR that threatens both human and animal health [7]. Knowledge, attitudes, and practice (KAPs) of farmers and patients have been a contributing factor for the spread and emergence of resistant microorganisms [8].

Globally, more than 50% of all medicines are prescribed, dispensed, or sold inappropriately and it is highly pronounced in resource-limited countries including Ethiopia [9]. Because, there is irrational use of antibiotics, poor infection-control policy, substandard medicines, limited knowledge regarding AMR, and misdiagnosis [10]. Annual antimicrobial usage in food animals was globally estimated at 63,000 tons in 2015, with a projected increase of about 67% by 2030 [11]. The link between antimicrobial use (AMU) in livestock and humans is due to resistant bacteria selected by the pressure of veterinary AMU being transferred to humans through exposure to animals, foods, and the environment [12]. Food-producing animals are linked to humans via the food chain and shared environment [13].

Nowadays, the growth of AMR also threatens to restrict the effectiveness of existing drugs used on farms and the treatment of veterinary bacterial pathogens [14,15]. In dairy farms antimicrobials used for the treatment of different diseases of dairy cows; for instance, *Staphylococcal* mastitis is the most common, which may contribute to increased AMR of pathogens frequently found in milk [16]. The rapid evolution and MDR of *S. aureus* strains are a result of chromosomal changes or the exchange of genetic material via plasmids and transposons, which may also be due to extensive use of antimicrobials [17]. These MDR patterns make it difficult and complicate the treatment of infections caused by resistant *S. aureus* [18].

The management practices employed for milk production are one of the factors for the dissemination of AMR bacterial strains [19]. There is also occupational contact with livestock, which is an established risk factor for exposure to Livestock-Associated Methicillin-resistant *S. aureus* (MRSA) [20]. Improper milking hygiene, especially the lack of post milking teat disinfectants, are also the major factors for the occurrence of MRSA. Some studies from Brazil showed high MRSA prevalence (12.2%) from those who lack of pre- and post-dipping procedures, using one udder towel on more than one cow, and use of gloves is inappropriate [21].

In developing nations including Ethiopia, MDR *S. aureus* is frequently isolated from animals and humans [22]. Additionally, suboptimal prescribing and inadequate public adherence to recommended behaviors such as the failure to finish prescribed antibiotic courses may result in the occurrence of AMR [9]. Some strains of *S. aureus* have developed resistance to many antibiotics, especially penicillin and all β-lactam drugs because of their ability to produce β -lactamase enzymes that will inactive many of the available antibiotic therapies for *Staphylococcal* mastitis such as methicillin and flucloxacillin [23]. Methicillin and vancomycin are the two remarkable antibiotic resistance achieved by *S. aureus*. However, antimicrobial drugs such as chloramphenicol, ciprofloxacin, novobiocin, and tetracycline were also reported to have poor effectiveness against *S. aureus* [24].

Public health significance of Staphylococcus aureus

Staphylococcus aureus is a major pathogen of public health concern and a growing burden for the healthcare system all over the globe [25]. Approximately about 30% of the human population is colonized with *S. aureus* [26]. It causes a wide range of serious diseases in humans like bacteremia, skin and soft tissue infections, and infectious endocarditis (IE), osteoarticular, pleuropulmonary, and food poisoning as well as life-threatening postsurgical infections [27].

The highest incidence rate of infection with *S. aureus* occurs at extreme life (old age), immunocompromised individuals, and acquired immunodeficiency syndrome (AIDS) or defects in neutrophil function, diabetes and loss of normal skin barriers are core predisposing factors of an individual [28]. These bacteria alone have been found to cause hospitalization rates as high as 14% and the fatality rates range from 0.03% in the general population to as high as 4.4% for highly sensitive persons [29]. For instance, the *S. aureus* bacteremia can cause mortality rates of around 20-30% [30].

The emergence of methicillin-resistant *S. aureus* (MRSA) strain has also become a pathogen of increasing importance in the hospital community and also in livestock in addition to SEs [31,32]. Specifically, the new strain of *S. aureus*, livestock-associated methicillin-resistant *S. aureus* (LA-MRSA), is recognized as an emerging novel pathogen that causes human infections [33]. Different figures were provided by various nations regarding the annual mortality rate due to AMR with 22000, 25000 and 12500 extra deaths in the United States, Europe, and France respectively [34].

The economic significance of Staphylococcus aureus

Staphylococcus aureus has major effects on the economy of the world directly or indirectly [35]. It results in huge financial losses in dairy farms associated with mortality, culling of infected dairy cows, spoiling of the milk, lower shelf life, decreased yield of milk products, cost of treatment, and decreased milk quality (change in milk composition, and palatability). There is also loss of the milk due to drug residue [36]. The infection caused by this species of bacteria is estimated to be present in up to 90% of dairy farms and is responsible for 35% of the economic losses in the dairy industry. For instance, annual losses due to *Staphylococcal* mastitis are estimated to be 35 billion US dollars in the world [37]. It also causes high hospitalization costs for drug resistance like MRSA [38]. Furthermore, this species of bacteria also cause damage to food through the production of different enterotoxins [39].

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