

Review

An overview of *Staphylococcus epidermidis* and *Staphylococcus aureus* with a focus on developing countries

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Abstract

Most nosocomial infections by *Staphylococcus epidermidis* and *Staphylococcus aureus* have gained considerable attention due to an increase of infections caused by these strains that have been reported in recent years throughout the world.

Most notably, it is important to underline the presence of *S. epidermidis* and *S. aureus* in the human epithelia microflora and to highlight that it is impossible to eradicate them from humans.

There are various virulence factors that normally sustain the infection life cycle, such as antibiotic resistance (methicillin resistance). Furthermore, it is important to evaluate the usefulness of typing the *spa* gene from isolated strains in order to study genotypes and geographical distributions. In the present review, different cases related to patients infected by *Staphylococci* and an overview of this problem worldwide are reported.

Key words: *Staphylococcus* spp.; nosocomial infections; developing countries.

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Introduction

The human body is the habitat of large and varied populations of bacteria with properties that are at the same time potentially dangerous and helpful to human health; for this reason, in recent years, there has been a strong impulse to fully characterize the strains associated with different parts of the body under different health conditions [1]. Thus, this innocuous commensal microorganism is now globally seen as an important opportunistic pathogen related to different infections. *Staphylococcus aureus* together with *Staphylococcus epidermidis* rank first among causative agents for these kinds of commensal infections. Therefore, they became the major causes of infections of medical implants and nosocomial infections worldwide, and especially in developing countries [2].

Staphylococcus aureus spread

Staphylococcus aureus is a Gram-positive bacterium, and it is a major pathogen in humans and animals, causing a wide variety of illnesses ranging from skin and soft tissue infections to life-threatening invasive diseases. The pathogenesis of a particular *S. aureus* strain is attributed to the combined effect of

extracellular factors and toxins, together with the invasive properties of the strain such as adherence, biofilm formation, and resistance to phagocytosis.

S. aureus has long been recognized as a virulent pathogen able to cause bacteremia strongly associated with higher mortality compared to other bacterial blood stream infections [3]. The habitats of *Staphylococcus* are the nasal membranes and skin of warm-blooded animals, and they may cause a wide range of infections, such as skin infections, food poisoning, pneumonia, sepsis, osteomyelitis, and infectious endocarditis [4].

S. aureus is also an important agent of food poisoning because it can be found in water, dust, and air. In Nigeria and many other parts of the developing world, chickens live close to human dwellings and therefore play an important role in environmental contaminations; in addition, birds are vehicles for transmission of those pathogens to humans through the handling live birds or consumption of contaminated meat and other poultry products [5].

A study in Thailand showed a nasal colonization from these strains and the ease of infection transmission between hospital worker students [6]. In

recent years, methicillin-resistant *S. aureus* (MRSA) has become an increasing problem in Southeast Asia, despite improvements in healthcare and increased hospitalization rates. In China, for instance, between 2003 and 2013, *S. aureus* infections in hospitals were reported to be caused by MRSA strains in more than 60% of cases [7]. The MRSA strains are a problem worldwide, mainly in developing countries, which have special difficulties since alternative therapeutic options are either unviable or unaffordable. Moreover, in developing countries, antibiotic use is even less controlled, and many antibiotics are available without a doctor's prescription (64%) [4]. In Zimbabwe, there are studies that tried to use plant compounds instead of common drugs because they are more affordable to the population and because this new therapy could avoid the problem of multiple-resistant drugs [8].

Staphylococcus epidermidis spread

Staphylococcus epidermidis is isolated prevalently from human epithelia and colonizes predominantly the axillae, head, and nares [9]. *S. epidermidis* belongs to the group of coagulase-negative staphylococci (CoNS), which is discriminated from coagulase-positive staphylococci such as *S. aureus* by its lack of the enzyme coagulase [10].

Indeed, this pathogen is part of the human epithelia microflora and for this reason has a benign relationship with the host, but *S. epidermidis* has emerged as a pathogen causing different infections. Particularly, *S. epidermidis* represents the most frequent causative agent involved with infections involving any kind of medical devices, such as peripheral or central intravenous catheters [11]. Specifically, catheter-related infections are associated with increased mortality and contribute to an increased length of hospital stay and higher healthcare costs, which are problematic in limited-resource settings such as South Africa [12,13]. In three different hospitals Iran, nasal swabs were collected from 163 healthcare workers; 96 were cultured and resulted positive for *S. epidermidis* [14]. Similar results were reported in a study performed between 2000 and 2009 in a hospital in Kenya, where in blood samples collected from neonates, *S. epidermidis* accounted for 33% of the isolated strains [15]. Furthermore, a study carried out in Brazil showed that 2.7% of *S. epidermidis* strains were isolated from hospital healthcare wastes, indicating a potential risk of spread outside the hospital setting [16].

Spa typing

S. aureus encodes various virulence factors including the surface Ig-binding protein A (*spa*), whose function is to capture IgG molecules in the inverted orientation and therefore avoid phagocytosis of bacterial cells by the host immune system [13,12].

Typing the highly variable X region of the *spa* gene is one of the most common methods for *S. aureus* genotyping. *Spa* typing also facilitates communication and data comparison between national and international clinical laboratories; therefore, this gene contributes to understanding the diversity, carriage, and transmission of *S. aureus* strains in different populations [17]. Various studies reported different data; in a study carried out in Ghana, this strain was detected in patients affected by Buruli ulcer lesions who tested positive for *S. aureus* of 13 *spa*-types. A total of 26% of the study participants carried the same *S. aureus* genotype in their anterior nares and wounds; 16% were colonized with isolates belonging to two different genotypes at the same time, and 26% of patients were colonized with different *S. aureus* types over time [18].

Antibiotic resistance

It has been reported by the World Health Organization (WHO) that in some African regions, 80% of *Staphylococcus aureus* infections are methicillin resistant, meaning that treatment based on standard antibiotics is not effective. Methicillin resistance is an independent risk factor for mortality in *S. aureus* bacteremia [19]. A number of South African studies have characterized the contribution of *S. aureus* to bacteremia in children; for instance, a study performed on hospitalized children in Cape Town, where the proportion of MRSA has been increasing over the last few years, showed that 11.6% of bacteremia was due to *S. aureus* [20]. Infectious diseases are still the leading causes of death in children in developing countries, with neonates bearing the highest burden. In Africa alone, infectious diseases account for over 76% of deaths among children, and an estimated 36% of neonatal deaths worldwide are directly attributable to severe infections [21]. In these studies, *S. aureus* MRSA was reported to be the pathogen responsible for 3% to 63% of deaths [22].

Conclusions

This review aimed to underline the important problem of infections due to pathogens that are normally part of the human microflora, which is

emerging in all countries with a higher prevalence in developing countries.

Eradication of staphylococci might be difficult because the absence of these bacteria would be counterproductive, as they may be replaced by more harmful microorganisms; it is necessary to find a balance with these bacteria.

Specific antibiotic-resistant genes are widespread in staphylococcal infections, and this is a problem since methicillin is an antibiotic of first choice against these types of infections. Among hospital isolates of *S. epidermidis*, methicillin-resistant strains represent between 75% and 90% of cases, which is even higher than the rate reported for *S. aureus* (40%–60%).

Furthermore, the best way to deal with *S. epidermidis* and *S. aureus* infections is based on prevention, which includes appropriate sterilization of medical equipment, patients' body areas, and healthcare personnel potentially in contact with indwelling medical devices during surgery and life routines during hospital admission [23].

Addendum

We dedicate this work to Prof. Cappuccinelli, a major contributor to this and other infectious disease research projects in the field of human microbiology and neglected tropical diseases. Throughout the years, he has transmitted to our team both the method and passion for scientific research.

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