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Staphylococcus aureus from a Commensal to Zoonotic Pathogen: A Critical Appraisal

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Abstract

Staphylococcus aureus, the principal etiologic agent of staphylococcosis, is a facultative anaerobe, Gram-positive, catalase-positive, and non-motile bacterium that causes disease in humans and animals. The bacterium can produce disease in immunocompetent as well as in immunocompromised subjects. The nasal cavity, and skin of humans and animals serve as the natural ecological niches of *S. aureus*. Morphologically, the bacterium appears as grape- like structures under the microscope. Under favourable conditions, the organisms can cause illness in humans and form biofilms that protect bacteria from harsh environment. The exotoxins like toxic shock syndrome type-1, exfoliative toxin, hemolysin, leukocidin protein, and enterotoxins are well-known factors produced by bacteria responsible for causing various diseases in susceptible hosts. The furuncle, carbuncle, impetigo, and abscess are various skin infections caused by *S. aureus*. Besides, it also causes multiple systemic infections, such as pyomyositis, osteomyelitis, septic arthritis, toxic shock syndrome, and scalded skin syndrome. *Staphylococcus aureus* is a significant cause of foodborne poising in humans, and mastitis in dairy animals. The organism can easily be identified by Grams' staining and culturing on selective media. Beta-lactam drugs, vancomycin, doxycycline, clindamycin, and linezolid can be used to treat diseases. However, due to the ability of bacteria to resist many new-ageantibiotics, it is considered an emerging public health issue worldwide. Practicing personal hygiene, food safety, and farm-to-fork hygieneisessential for preventing and controlling diseases.

Keywords

Commensal, Epidemiology, Public health, *Staphylococcus aureus*, Zoonotic pathogen

1. Introduction

Staphylococcus aureus is gram-positive, non-motile, catalase-positive cocci found as a grape-like cluster under the microscope [1]. Staphylococci are widespread in the environment and are mainly found as a commensal microflora on mammals' and birds' skin and the mucous membranes, especially the nasal cavity, in 20-40% of the general population [2]. Being an opportunistic pathogen, it can cause mild to severe life-threatening diseases under favour-

ablecircumstances, such as viral infection and immunocompromised patients [3]. *Staphylococcus aureus* is well known amphizoonotic bacterium, which can spread from animals to humans and vice versa [4]. Of several known species, *S. aureus*, *S. epidermidis,* and *S. saprophyticus* are the most common disease-causing species. Most commonly, it is responsible for causing food-borne infections. The bacterium is transmitted by ingesting the contaminated food or by direct infection from contaminated handlers or materials [5]. The bacterium produces performed heat-stable toxins in food called staphylococcal enterotoxin, leading to food poisoning. Staphylococcal food poisoning is recognized worldwide as the most prevalent foodborne intoxication [6]. The mechanism of action of toxins is damaging the intestinal line of the intestine and causing gastroenteritis. A decrease in the absorption of fluid leads to electrolyte shift and, ultimately, diarrhoea [7]. Another pathogenic factor of *S. aureus* is exopolysaccharide (EPS). The EPS on the bacteria forms the biofilms. EPS helps escape the host's immune system by interfering with the penetration of the cell wall and also protection from some antibiotics [8]. The other toxic factor produced by bacteria is toxic shock syndrome toxin-1 (TSST-1), a superantigen (sAg). The diseaseis characterized by rash, fever, and hypotension. Leukocidin and haemolysin, another set of exotoxins, makepores on blood cells and cause lysis of the red blood cells, respectively. Several pathogenic factors are secreted and excreted by this bacterium, and now it has acquired the highest level of antibiotic resistance, such as MDR and XDR [9]. *Staphylococcus aureus* has long been recognized as one of the most important bacteria that cause disease in humans. Therefore, this communication aims to present a critical review on the journey of *Staphylococcus aureus* from a commensal to zoonotic pathogen of medical and veterinary importance.

2. Classification of *Staphylococcus* species

Taxonomically, staphylococci bacteria belong to the family *Staphylococcaceae* [10]. They are small gram-positive, non-spore-forming, non-motile, facultative anaerobes. Morphologically, cocci are arranged in characteristic grape-like clusters with a diameter of approximately 0.5 to 1.5 μm [11, 12]. The genera under the family *Staphylococcaceae* are *Staphylococcus*, *Stomatococcus*, *Micrococcus*, and *Planococcus*. Genus *Staphylococcus* is divided into more than 47 species and 23 subspecies [10].

One of the unique characteristics of the genus *Staphylococcus* is its ability to produce a coagulase enzyme that can cause blood coagulation (blood clotting). Depending on their ability to produce coagulase, *Staphylococcusis*-classified into coagulase-positive (CPS) and coagulase-negative *Staphylococcus* (CNS). Seven species are currently recognized as coagulase-positive: *S.aureus*, *S. delphini*, *S.hyicus*, *S.intermedius*, *S. lutrae*, *S. pseudintermedius*, and *S. schleiferi* subsp. *oagulans* [2]. Under the CPS category, *S. aureus* is the most importantspecies to cause food-borneinfection in humans. The majority of the CNS species are found as food-associated saprophytes [10]. and live in association with humans and animals forming a commensal relationship [13]. For instance, *S. carnosus* and *S. xylosus*, CNS species, are beneficial infood processing industriesand used for fermentation and good sensory flavour. On the other hand, CNS, such as *S. epidermidis* and *S. haemolyticus* are reported to cause hospital-associated infection and post-operative wound complications in humans [14].

2.1 Historical background of *Staphylococcus aureus*

Staphylococcus aureus was first discovered in the late 1880s [10]. Before the discovery of penicillin in 1940, this bacterium was responsible for causing very high mortality, around 80% [14]. In 1880, a Scottish surgeon named Alexander Ogston first reported the typical occurrence of the cocci in grape-like clusters in pus and cultures. He coined the name of the bacteria as *Staphylococcus,* which comes from the Greek word "*Staphyle*"; meaning a bunch of grapes, and "*Kokkos,*" which means a berry [15]. Later in 1884, German physician Friedrich Julius Rosenbach was able to grow *Staphylococcus* in pure culture and categorized them according to the production of colour by different species. He named the colonies showing a golden appearance due to some pigmentation as *Staphylococcus aureus*, which originated from the word "*aurum,*" meaning gold [16]. The property of coagulation of human plasma by *S. aureus* was initially documented in 1903.

2.2 Characteristics of *Staphylococcus aureus*

Morphology

Staphylococcus aureus is a spherical gram-positive bacterium that appears in pairs, short chains, or bunched, grape-like clusters on microscopic examination [11]. It forms glistening, smooth, raised, and circular colonies on a solid medium. On non-selective media, the colony can reach up to the dimensions of about 4-6 mm in diameter [15]. Colony on agar may show different colours due to the production of pigments. Variations may be found within the colony, ranging from orange to greyish or greyish-white in colour [16, 17].

Growth and survival characteristics of Staphylococcus aureus

Staphylococci can grow and survive under adverse environmental conditions [18]. For example, bacterium displays remarkable salt tolerance. Hence, bacteria cancolonize environments with low water content and high salinity and establish a monopoly, as many other micro-organisms do not survive [11]. Mannitol salt Agar, a selective media for *Staphylococcus*, is based on the principle of high tolerance. Besides it, Baired parker agar is also used as primary media to grow and differentiate the *S. aureus* from others [19]. Staphylococci are usually readily killed at cooking and pasteurization temperatures but can survive frozen storage. Staphylococcal enterotoxins (SEs) are, however, extremely heat stable [11, 18]. The strains of *S. aureus* are quite immune to desiccation and high osmotic conditions. It has also been established that staphylococci can persist for extended periods under numerous nutrient-limiting environments [20]. These properties facilitate their survival and the ability to outcompete other microbes within the environment or foods [18].

Virulence factors

The bacterium has more than 50 virulence factors with a wide array of biological activities. They consist of toxins (α, β, δ-toxin, P-V leukocidin, enterotoxin, exfoliative toxin, toxic shock syndrome toxin), immune-modulatory factors or antigens (capsule, adhesins), and exoenzymes (coagulase, lipase, hyaluronidase, staphylokinase, nuclease) [2]. They are responsible for various toxin-mediated and suppurative diseases [17]. These virulence factors directly or indirectly help the bacteria to attach, invade and cause disease in susceptible humans and animals. Broadly, these virulence factors can be divided into two main categories, i.e., cell-surface associated (surface proteins) and secreted proteins (exotoxins) [7]. Except for toxin-mediated diseases, such as food-borne intoxication, toxic shock syndrome, etc., staphylococcal infections are not caused by a single virulence factor. The different virulence factors play a different role in the pathogenesis of other staphylococcal diseases [17].

The main known virulence factors and their function are as follows.

Cell surface proteins: These are proteins covalently attached to the peptidoglycan on the surface of the cell wall and play a vital role in the pathogenesis of staphylococcal infections. They are commonly known as cell wall–anchored (CWA) proteins. There are over 20 surface proteins anchored to *S. aureus;* however, the number may vary with species. The important ones are as follows:

Staphylococcal protein A: It is a 42-kilo Dalton-sized protein encoded by the *Spa* (staphylococcal protein A) gene. The protein A binds to Immunoglobulin G (IgG), thus inhibiting the phagocytosis activity of the host immune system against bacterial invasion.

Collagen-binding protein: This protein helps the bacteria to adhere tothe collagen part of the host cells. This is a 135-kDa protein encoded by the *cna* (collagen adhesin) gene.

Fibrinogen-binding protein A (clumping factor A or ClfA): Bacteria bind to platelets by binding plasma proteins. It particularly mediates clumping and adherence with fibrinogen in the presence of fibronectin, thus causing clumping of the platelets.

Secreted Factors/proteins: The virulence of *S. aureus* also relies on the secretion of many different proteins. Broadly, these factors could be of two types, i.e., exotoxins and exoenzymes, with several other classes under each category. Exotoxins may include cytotoxins, staphylococcal superantigens, cytotoxic enzymes, and exoenzymes consisting of several cofactors and enzymes. Examples of staphylococcal superantigens are staphylococcal enterotoxins (SEA, SEB), T and B cell superantigens, and the toxic shock syndrome toxin, which are exotoxins secreted by some *S. aureus.* In general, they modulate T cell proliferation and interfere with the function of T cells, esp. CD4 T cells. This leads to a high release of interleukins and tumor-necrotic factors. Cytolytic toxins include *a*- and ß-hemolysin and exfoliative toxins, which induce the lysis of blood cellsand the formation of blisters and superficial desquamation in a susceptible host, respectively. Panton-Valentine leukocidin, PVL, is another cytotoxin that induces lysis of the leukocytes. Nuclease, lipase, proteases, etc., are exoenzymes that cleave and inactivates different biological molecule of a defense system. Bacteria use hyaluronidase to destroy the host tissue andhelp the infection spread to the neighbouring tissues. ß lactamase is an enzyme that inactivates the ß-lactam group of antimicrobials, thus establishing antibiotic resistance. Another important exoenzyme is coagulase which has taxonomical significance too. The ability of *S. aureus* to induce coagulase-mediated coagulation of plasma is one of the critical criteria used in modern medical microbiology for species classification as “coagulase-positive” and “coagulase-negative” species. These factors might have different functions and substrates to act on, but ultimately, they function to break down bacterial and host molecules for nutrient acquisition, bacterial survival, and dissemination.

Antimicrobial Resistance

Antimicrobial resistance is an emerging global public health threat [21]. Resistance to commonly available antimicrobials has become a severe problem in many parts of the world, bringing the ineffectiveness of available

treatment options for common infections in some settings [22, 23]. Many antimicrobials meant for human medicine, are being used in food-producing animals, specifically in developing countries. This may play a significant role in the spread of AMR bacteria. Persons with invasive medical devices (such as peripheral and central venous catheters) or compromised immune systems are particularly vulnerable to *S. aureus* infection.

Antimicrobial resitance *S. aureus* (SA) is the pathogen of most significant concern worldwide because of its intrinsic virulence and ability to cause a diverse array of life-threatening infections [24]. *S. aureus* can compromise effective opsonization by antibodies using a polysaccharide microcapsule and surface proteins like (Staphylococcus protein A (SpA). Besides, bacteria reside in the abscess that limiting access to the antimicrobial [25]. Phagocytosed bacteria can survive within the PMNs by producing enzymes such as catalase, superoxide dismutase, etc.

More than 90% of *S. aureus* strains acquired resistance by modifying and expressing penicillin-binding proteins (PBP) and inactivating the drug by β-lactamase synthesis. Bacteria develop resistance to β-lactam antibiotics, such as penicillin and methicillin, due to the production of enzymes called β-lactamase which hydrolyzes the amide bond of β-lactam antibiotics. These strains are commonly known as methicillin-resistant *S.aureus* (MRSA), which was first described in England in 1961. MRSA is the primary cause of nosocomial infection in humans, also called hospital-acquired acquired MRSA. Glycopeptides, vancomycin, and teicoplanin are commonly used antibiotics to treat MRSA. Unfortunately, the recent variants of MRSA have become resistant to vancomycin. Rare strains called vancomycin-intermediate *S.aureus* (VISA), with reduced sensitivity to vancomycin, have also emerged. Their emergence has ushered in a new era of uncertainty in human health care. In addition to hospital-acquired acquired MRSA, community-acquired and livestock-acquired MRSA has become a major concern [25]. Evidence suggests that domestic animals, including food animals, can serve as reservoirs and shedders of MRSA, and the transmission between host species may be possible [26].

3. Epidemiology

Host Range

Staphylococcus species are ubiquitous organisms distributed all over the world [12]. The natural ecological niches of *S. aureus* are the nasal cavity, and skin of humans, and warm-blooded animals [1]. It colonizes the upper respiratory, urogenital tracts, and gastrointestinal tracts of about 20% to 30% of humans [10]. They inhabit the distal nasal passages, external nares, mucous membranes, teats, udder, and skin, especially near mucocutaneous borders such as the perineum, external genitalia of milking animals [27]. They act as the most crucial reservoir and source of contamination [28]. The infection due *to S. aureus* has been described in humans as well as many species of animals including the poultry [4].

Transmission

The animals, which are natural colonizers of *Staphylococcus* specieson their bodies act as the primary reservoir of *S. aureus* and, under appropriate circumstances, can transmit bacteria to susceptible hosts [8]. Besides, animals with sub-clinical inflammatory infections are another potent reservoir and source of disease in the dairy environment [1]. The transmission can be direct or indirect. Example of indirect transmission includes contaminated milking environments like milking buckets, poor drainage condition, and personnel hygiene. Milkers' hand, flies, and towels used during milking are very common objects which can spread these pathogenic bacteria to clean udders from infected ones during milking practice [29].

Staphylococcus aureus is opportunistic commensal bacteria that generally live on or inside the host without causing disease [12]. However, under a suitable environment, it emerges as pathogenic bacteria capable of causing many types of local or systemic suppurative infection. Besides bacteria, its toxins also cause diseases. Food-borne intoxication is caused by ingesting enough doses of enterotoxins produced in food by some strains of *S. aureus* [30]. The food kept or stored at a temperature from 45°Fto 140°F is more susceptible to toxin production.Staphylococcal enterotoxins are quite stable in the environment. Although cooking can kill the vegetative form of bacteria, the toxin remains active at cooking temperature easily. Toxins can remain stable at 100^{o}C boiling for a few minutes. However, sick animals, equipment, and environmental surfaces can also be sources of contamination with *S. aureus* [31].

Risk factors

Animal-related factors:

Older animals are more prone to mammary gland infection due to dilated teats and lower immune response. Old animals are more susceptible, almost double, to the risk of getting mastitis than young animals [3]. On the other hand, some studies did not find age as a risk factor for mastitis [32]. Lactating animals are more likely to get infected with bacteria due to the high contact time with different equipment and animal handler. Some studies re-

ported a higher prevalence of subclinical or clinical mastitis during early lactation. It could be due to the rapid changes in the physiology of postpartum tissues of the mammary gland, which may cause constant stress and decreased immune status [3]. The milk-yielding animals are more prone to mastitis. The pressure produced by the overproduction of milk and the constant loss of micronutrients via milk may predispose animals to intramammary infections [32]. The higher parity of animals was found to be more susceptible to mastitis infection [3]. This could be justifiable with the carry-over of infection from one parity to the next [33]. Moreover, higher parity yields stress on the udder, causing the broadening of the teat canal due to the pressure on the teat sphincter resulting in an increased chance of microbe entry and hence more susceptibility to infection.

Environment-related factors:

Staphylococcus aureus infection rate is positively correlated with the lack of cleanliness and hygiene in the milking area [5]. The unhygienic conditions at farms and other risk factors may significantly increase the severity of the disease along with animal-related factors such as age, parity, etc. [1]. Poor management strategiesmay help spread *S. aureus* from one animal/farm to other animals/farms [34]. Cows reared in the intensive system are found to be more prone to mastitis. As a vector, it has been found that ticks may also spread the pathogen from one animal to others. Many studies have reported a higher prevalence of mastitis in tick-infested dairy animals [13]. The knuckling method of the milking, dirty hand of milkers, towels, milking buckets etc, are also the primary route of disease transmission [35].

3.1 Pathogenesis of *Staphylococcus aureus*

A surface protein enables the bacteria to form a biofilm which ultimately helps the bacteria inthe colonization of host tissues. Once colonized, the bacteria secret or excrete various virulence factors like leukocidin, kinases, and hyaluronidase, which promote bacterial invasion and spread in host tissues [5]. Bacterial capsule and surface proteins inhibit phagocytic engulfment by macrophages. However, if phagocytized, carotenoids and catalase enzymes help the bacteria to survive in phagocytes. Bacteria escape the host's defense mechanism by adopting immunological disguises using a few virulence factors such as Protein A and coagulase. Moreover, they damage host cell membranes through bacterial hemolysins, leukotoxin, and leucocidin [30]. The bacteria also produce the exotoxins called toxicshock syndrometoxin (TSST), leukocidin toxin, exfoliatintoxin, hemolysin, and enterotoxins, which can damage host cells or tissues and can cause diseases [1]. Inherent and acquired genes for resistance to multiple antimicrobial agents are another mechanism of survival used by some strains of *S. aureus* [36, 37].

3.2 Staphylococcus aureus infections

In humans

Staphylococcus aureus causes a diverse array of diseases in humans [19]. The infections range from local mild skin infections to life-threatening systemic diseases, such as bacteremia, endocarditis, lung infection, breast infection, osteomyelitis, and toxic shock syndrome [11, 13]. Skin infections due to *S. aureus* include folliculitis, impetigo, abscess, cellulitis, and toxic epidermal necrolysis. All Staphylococcal skin infections are contagious [9]. The diseases can be severe in older people and immune-compromised adults. Mortality rates due to bacteremia may vary from 2.5% to 40% depending on the patient's age, clinical manifestation, and immune status [38].

Some strains of *S. aureus* produce toxins that can cause food poisoning, toxic shock syndrome, or scalded skin syndrome [5]. In the case of food poisoning, there is rapid onset of symptoms, i.e., within 3-5 hours following the ingestion of preformed toxin in contaminated food [30]. Common symptoms of staphylococcal food poisoning include nausea, vomiting, abdominal cramps, and diarrhea [1]. The disease may become severe in immune-compromised elders; however, in young individuals, it only causes headaches, muscle pain, and occasionally changes in blood pressure and pulse rate [23]. Toxic shock syndrome is a rapidly progressive disease with severe symptoms, including increased temperature, rash, hypotension, and multi-organ failure [31].

In animals

Bovine mastitis is a widespread livestock production-related disease. *Staphylococcus aureus* is the major pathogen causing clinical and subclinical mastitis in dairy and other farm animals [3]. The subclinical form is 15-40 times more prevalent than clinical mastitis [3]. Tong and co-workers [13] reported that *S. aureus* causes clinical, mainly gangrenous mastitis and subclinical mastitis in small ruminants. Like humans, *S. aureus* infections may vary from simple abscesses to severe systemic mastitis, inflammations of different organs, and toxic shock syndrome in cattle. It can cause dermatitis, furunculosis, gastroenteritis, osteomyelitis, meningitis, lung infection, heart infection, and wound infections [19]. In birds, *S. aureus* is often associated with bumble foot, omphalitis (yolk sac infection), arthritis, tenosynovitis (inflammation of tendon sheath), necrotic dermatitis, necrotic skin lesions or abscesses and

osteomyelitis [30]. *Staphylococcus aureus* can cause exudative dermatitis (greasy pig disease) in pigs [26]. It is the most critical fish pathogen, and its prevalence has been observed in seafood and different species of fish [39].

The bacterium produces toxins that cause damage to cell membranes and milk-producing tissue. Firstly, *S. aureus* affects the tissue lining of the teats and glands of one-quarter of the udder, spreading to the adjacent quarters and eventually forming scar tissue. The bacteria further spread into the duct system and establish deep-seated pockets of infection in the alveoli. This is followed by the formation of abscesses, which, although preventing the bacteria from spreading, however, helping the bacteria to hide from the host's defense mechanism. The abscesses hinder the availability of the antimicrobial agent to reach the target, i.e., bacteria, hence, affecting the efficacy of treatment [3, 30].

3.3 Public health and economic importance of *Staphylococcus aureus*

Public health significance

Staphylococcus aureus is a significant pathogen of public health concern worldwide [1, 12]. It is a major cause of foodborne infections globally [6]. Antimicrobial-resistant *S. aureus,* such as MRSA and VRSA, have emerged as a great challenge, especially in hospitals (nosocomial infection) [37]. In this context, Iyer and co-workers [21] reported that MRSA was responsible for nosocomial infections in Saudi Arabia.

The situation worsens with the rise of antimicrobial-resistant *S. aureus* in community settings and livestock farms [31]. MRSA is regarded as a newly emerging zoonotic agent. Being able to transmit in both directions, i.e., from humans to animals and from animal to humans when in close contact, MRSA infection is called amphixenosis. Therefore, people living in areas with a higher livestock density (pigs, cattle, and veal calves) are at a higher risk of being colonized by livestock acquired-MRSA.

Staphylococcal food poisoning is one of the most common foodborne diseases (FBD) and is a significant threat to public health [12, 9]. Globally, one-third of the population is affected by FBD every year. As a significant contributor to FBD, *S. aureus* causes an estimated 241,000 illnesses annually in the United States [23, 40]. In developing countries, the surveillance system of FBD hardly exists, and it is, therefore, difficult to estimate the actual magnitude of the problem [41]. The organism can cause various non-food-related suppurative inflammatory conditions almost related to all organs, such as lungs, skin, heart, bones, brain, etc. [5].

The economic significance

Staphylococcus aureus is an important pathogen of economic importance [12]. Bovine mastitis significantly impacts the economy because it directly or indirectly affects milk production [3]. *Staphylococcus aureus* plays a significant role in the pathogenesis of bovine mastitis [3]. The direct effect on the economy is due to health disorders of the mammary gland, decreased milk yield, loss of milk quality (impaired nutritive value of milk), etc., and indirect effects are due to fertility disorders, systemic diseases resulting in treatment cost, and ultimately production costs [19]. Clinical mastitis may often cause serious damage to the udder along with systemic disorders, even leading to the culling of affected animals [3]. Due to the difficulty in detection, subclinical mastitis is more common and difficult to control. Bacteria spread widely among dairy herdsand become endemic in particular settings. This results in reduced milk quality and yield, thusa reduction in the farmer's income. Like dairy cows, ovine and caprine mastitis can cause economic losses due to decreased milk production, milk quality, increased mortality, and treatment costs. In poultry, *S. aureus* infection causes economic losses that may be due to reduced weight gain, decreased egg production, lameness, mortality, and condemnation at slaughter [3, 26].

3.4 Treatment

The treatment of patients/sick animals depends on the history of the case, age and immune status of patients, pathogenesis, the origin of infection, and types of *S. aureus* [1]. The most common antimicrobials used to treat staphylococcal infections are β-lactam antimicrobials [30], which include penicillin, tetracycline, streptomycin, novobiocin, sulfonamides, lincomycin, linezolid, and spectinomycin. The extensive and off-label use of antibiotics generates selective pressures to drive the emergence of resistant strains. With the emergence of penicillin-resistant *staphylococcus*, semisynthetic penicillin (methicillin) was introduced for treatment in 1959. Methicillin-resistant S. aureus (MRSA) strains rapidly emerged within one year of usage. *MecA* and *Mec*C genes are primarily responsible for developing resistance against methicillin in *S. aureus* [30]. Vancomycin, a tricyclic glycopeptide antibiotic, is usually effective for MRSA. However, recently some isolates of *S. aureus* were found to carry the gene '*vanA,'* which is responsible for resistance to vancomycin [42]. The infections can also be treated alone or in combination therapy usingerythromycin, sulfa drugs, minocycline, or rifampin [43].

3.5 Prevention and Control

The ubiquitous nature of the bacteria makes it difficult to prevent the occurrence of staphylococcal infections [44]. Good hygienic practices are the most effective and recommended method to avoid the occurrence and transmission of disease. These may include personnel hygiene, proper farm management, milk hygiene, regular cleanliness and sanitation of equipment and environments, etc. [5].

Control of the disease can be done by eliminating the conditions that expose cow teats to the bacteria and reducing the possibility of spread from cow to cow [3]. Hygienic procedures should be followed during the milking of animals. Milking of *S. aureus-infected* cows should be done separately in the last, i.e., after finishing milking of healthy animals. Antimicrobial sensitivity tests should be performed before prescribing antibiotics to infected cows. Education of animal owners and handlers regarding the usage of antibiotics, completion of the treatment procedure, and following the rules of the withdrawal period is very crucial. Cow therapy is vital for controlling *S. Aureus* spread on a farm [33].

The animal origin foods should be handled, stored, transported, and used carefully; the medical checking of the employee should be undertaken, and training should be given to food handlers [28]. As *S. aureus* has zoonotic importance, proper care should be taken at all the steps of production and supply chains of milk and milk products as well as during the handling of patients at hospitals [1]. Proper use of antimicrobials for both humans and animals-may help to control the spread of drug-resistant *S. aureus* [1].

4. Conclusion and Recommendations

Staphylococcus aureus is the non-motile, gram-positive, facultative anaerobe responsible for causing FBD and several local and systemic suppurative inflammatory conditions in humans and animals. As a commensal organism, it naturally colonizes the nose, pharynx, genitalia, other soft tissues, and skin of animals and humans. However, it emerges as an opportunistic pathogen under favorable conditions such as concurrent infection, immunocompromised individuals, poor nutrition, etc. Poor sanitation and animal farm management may cause clinical or subclinical mastitis, ultimately affecting humans by causing food-borne intoxication. Milk and other dairy products can easily be contaminated by performed toxin which causes food poisoning. Scalded skin syndrome and toxic shock syndrome are also a severe disease caused by *S. aureus*. *S. aureus* can produce more than 50 virulence factors with various biological activities. The presence of a capsule, the ability to make biofilm, secretion of bound coagulase, protein A, several enzymes and toxins, etc., all together facilitate the pathogenesis of bacteria. Microscopy, culture, biochemical tests, and serological tests are standard methods for diagnosis. Treatment is always challenging due to AMR *S. aureus*.

Therefore, based on the above conclusion, the following recommendation is forwarded: -

- Implementation of food safety and hygiene is of utmost importance.
- Keeping personal hygiene during the handling of food is imperative.
- Storage of food at the proper place and temperature; and cooking at the appropriate temperature are also necessary.
- Creating awareness regarding the transmission route and bacteria's zoonotic importance is highly recommended.
- One Health approach is essential to sustain good health for all.

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Authors' contribution

All the authors contributed equally. They read the final version and approved it for publication.

Conflict of interest

The authors declare that they do not have a conflict of interest.

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