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Staphylococcus aureus, an important pathogen of public health and economic importance: A comprehensive review

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Abstract

Staphylococcus aureus belongs to the genus *Staphylococcus* and the family *Staphylococcaceae*. It is a non-motile, fermentative, and non-spore-forming bacterium that is facultative anaerobic. They develop quite large yellow or white colonies on nutrient rich agar media and are typically found in clusters that resemble a bunch of grapes when observed under a light microscope after Gram staining. *Staphylococcus aureus* is a desiccation and high osmotic condition tolerant bacteria that may thrive in potentially dry and stressful conditions. Human nares are the principal niche and greatest reservoir of *Staphylococcus aureus*; cows may be the second largest. The virulence factors produced by *Staphylococcus aureus* are essential for successful human and animal infection. It is one of the most significant bacteria in veterinary medicine, and it is widely known as a major cause of intramammary infections. *Staphylococcus aureus* is a common human pathogen that can cause a wide range of clinical infections, from minor skin infections to life-threatening infections. *Staphylococcus aureus* is a highly adaptable bacterium that develops resistance to the majority of antibiotics on the market. Drug resistance in *Staphylococcus aureus* has gradually risen over the last few decades as the pathogen have evolved and antibiotics have been abused. The treatment is ineffective; instead, control and prevention of *Staphylococcus aureus* should be prioritized. Eliminating conditions that expose the teat ends to bacteria and reducing the probability of cow-to-cow transmission are the most effective ways to prevent new infection and control *Staphylococcus aureus* in dairy animals. Contact precautions and adequate infection control techniques are used to prevent the spread of *Staphylococcus aureus* infection in humans.

Keywords: Animals, Drug Resistance, Epidemiology, Humans, Pathogenicity, Staphylococcus aureus, Public health

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1. INTRODUCTION

Staphylococcus aureus is a major pathogen that causes disease in humans as well as well animals including the birds [1]. The bacterium colonizes the skin and mucous membranes of the anterior nostrils, the gastrointestinal tract, the perineum, the urogenital tract, and the pharynx, among other places [2]. It is also found in the environment and in a variety of foods of animal origin [3,4]. It is a non-motile, non-spore-forming, facultative anaerobic bacterium that is catalase and coagulase positive biochemically [5]. *Staphylococcus aureus* is a desiccation-tolerant bacterium that may thrive in potentially dry and stressful conditions [6].

Staphylococcus aureus is responsible for a wide range of diseases both in humans as well as in animals [1, 5]. It is most typically documented in animals as the cause of mastitis in dairy cows and bumble foot in poultry [7]. Exudative dermatitis (greasy pig disease) is caused by *Staphylococcus aureus* in pigs [8]. Infections caused by *Staphylococcus aureus* in humans can range from minor skin infections to life-threatening conditions, such endocarditis, meningitis, pneumonia, osteomylitis, gastroenteritis, septicemia, and toxic shock syndrome [1,9]. The impact of *Staphylococcus aureus* on public health is linked to the animals and products used in food production. Food derived from animals can be contaminated with one or more staphylococcal enterotoxins, which can cause disease in humans [10].

Staphylococcus aureus is a highly adaptive organism that develops resistance to most antibiotics available [11]. Drug resistance in *Staphylococcus aureus* has gradually risen over the last few decades as the pathogen have evolved and antibiotics have been misused [12]. *Staphylococcus aureus* acquired determinants by horizontal gene transfer of mobile genetic elements, which led to the development of resistance to various antibiotics [13]. Resistance can also develop as a result of drug binding site alterations on molecular targets, as well as increased development of endogenous efflux pumps [14]. Therefore, the aim of this book chapter is to review *Staphylococcus aureus* as a major pathogen of medical and veterinary importance.

2. GENERAL DESCRIPTION OF *STAPHYLOCOCCUS AUREUS*

2.1. Taxonomy and Classification

Staphylococcus was originally thought to be a member of the *Micrococcae* family. Staphylococci are no longer closely connected to micrococci, according to molecular and phylogenetic analyses, and are consequently classified in a distinct family called *Staphylococcace*. *Staphylococcus aureus* belongs to the Staphylococcaceae family and the genus *Staphylococcus* [15,16]. Based on their ability to coagulate rabbit plasma, *Staphylococci* are split into two groups: coagulase positive *Staphylococci* and coagulase negative *Staphylococci*. Coagulase positive *Staphylococci* comprised of *Staphylococcus aureus subspp. aureus, Staphylococcus aureus subspp. anaerobius, Staphylococcus intermidius, Staphylococcus pseudintermidius, Staphylococcus delpini* (the last three species form the so-called *Staphylococcus intermidius* Group), *Staphylococcus schleiferi subspp. coagulans, Staphylococcus lutrae, Staphylococcus hycius* (coagulase variable) and *staphylococcus agnetis* (coagulase variable) and coagulase negative *Staphylococci*, among which are *Staphylococcus epidermis, Staphylococcus saprophyticus and Staphylococcus pasteuri* are important [15,17].

Coagulase positive *Staphylococci* species can cause severe infections compared with those caused by coagulase negative *Staphylococci* [18]. The pathogenicity of coagulase positive *Staphylococci* are related to the production of many virulence factors including toxins and enzymes from which coagulase

enzyme is considered as the most important one [19]. Among the coagulase-positive *Staphylococci*, *Staphylococcus aureus* is the most common [20]. The majority of coagulase negative *Staphylococci* are identified as food-associated saprophytes living in commensal relationships with humans and animals [15] and living in association with humans and animals forming a commensal relationship [21]. However, coagulase negative *Staphylococci* such as *Staphylococcus epidermidis* and *Staphylococcus haemolyticus* are reported to cause hospital associated infection and post-operative wound complications in humans [22].

2.2. General Biochemical and Cultural Characteristics

Staphylococcus aureus is a non-spore forming bacteria that is facultatively anaerobic, non-motile, fermentative [19]. Catalase and coagulase positive, oxidase negative, voges-proskauer positive, urease positive, DNase, maltose, glucose, and mannitol fermentation [23]. When examined under a light microscope after Gram staining, they are frequently found in clusters that resemble a bunch of grapes. The name '*Staphylococcus*' comes from the Greek words *Staphyle* (bunch of grapes) and *kokkos* (berry) [24]. Because colonies (often) exhibit a golden colour when growing on solid media, the term *aureus* is taken from Latin, which alludes to the color of gold [25].

On nutrient-rich agar media, *Staphylococcus aureus* develops large yellow or white colonies. Carotenoids imparted by the bacterium give the colonies their yellow color [25]. They appear as glistening, smooth, circle, elevated, translucent colonies on blood agar, often with a golden colours, and strains are frequently β-hemolytic (also known as complete hemolysis) [26]. Alpha hemolysin, beta hemolysin, gamma hemolysin, and delta hemolysin are the four hemolysins produced by *Staphylococcus aureus* [27]. The organism can grow in mannitol-salt agar medium containing 7.5 percent sodium chloride and is salt tolerant [28].

2.3. Growth and Survival

Staphylococcus aureus is a desiccation and high osmotic condition tolerant organism that can survive in potentially dry and stressful settings like the human nose and skin, as well as inanimate surfaces like clothing and surfaces [29]. This bacterium's widespread distribution can be due in part to its capacity to detect changing environmental conditions and respond appropriately by adapting to a wide range of environmental changes [30]. However, the processes underlying *Staphylococcus aureus'* physiological adaptations to a variety of unfavorable environments are still unknown [28].

Staphylococcus aureus can grow in a wide variety of temperatures (7°C-48.5°C; optimum 30-37°C) and pH (4.2-9.3; optimum 7-7.5) [29]. However, it has been shown that *Staphylococcus aureus* adapts, survives and even multiplies at low temperatures and high sodium chloride (NaCl) concentrations [31]. *Staphylococcus aureus* is resistant to high osmolarity, detergents, and alcohol due of its strongly cross-linked peptidoglycan, and is easily killed after pasteurization or cooking [32,33].

3. PATHOGENICITY OF STAPHYLOCOCCUS AUREUS

3.1. Virulence factors

The virulence factors produced by *Staphylococcus aureus* are essential for successful human and animal infection. To increase adherence to host extracellular matrix components, harm host cells, and resist the immune system, a diverse spectrum of secreted and cell surface-associated virulence factors can be produced [34]. Cell-surface-associated (adherence) and secreted (exotoxins) factors are the two primary groups of virulence factors [35]. Staphylococcal infections are not caused by a single virulence factor, with the exception of toxin-mediated illnesses such as toxic shock syndrome [36].

Cell surface factors are microbial surface components that recognize adhesive matrix molecules such as Staphylococcal protein A (SpA) (binds to IgG,

disrupting the host immune system's phagocytic activity), fibronectin-binding proteins (FnbpA and FnbpB) (adhesion to fibronectin and plasma clots), collagen-binding protein (adhesion to collagen tissue and cartilage), and clump (mediate clumping and adherence to fibrinogen in the presence of fibronectin). Capsular polysaccharides (which inhibit neutrophil phagocytosis) and staphyloxanthine are the other cell surface components (resistance to phagocytosis based on neutrophil reactive oxidants) [35,37].

Superantigens, cytolytic toxins, and different exotoxins are examples of secreted virulence factors. Superantigens are staphylococcal enterotoxins and toxic shock syndrome toxins that produce large T-cell and antibody-presenting cell activation [38]. ß-hemolysin and α-hemolysins are cytolytic toxins that cause erythrocyte, monocyte, and platelet lysis, while Panton valentine leukocidin causes leukocyte lysis [35]. Secreted exoproteins are exotoxins and enzymes, including nucleases, proteases, lipases, hyaluronidase and collagenase. Possibly they convert local host tissue into nutrients for bacterial growth [39].

3.2. Mechanism of pathogenicity

The pathogenesis of *Staphylococcus aureus* intramammary infection in cattle includes numerous stages: bacterial entry and attachment to the mammary epithelium, interaction with the host immune system, evasion of the host immune system, bacterial survival, and tissue invasion. After *Staphylococcus aureus* has entered the teat canal, the development of intramammary infection is influenced by a number of factors, including the initial bacterial count, the strain's virulence, and the host's immunity. Successful colonization is influenced by predisposing factors such as the pathogen's and hosts genetic backgrounds [40].

Toxins produced by *Staphylococcus aureus* disrupt cell membranes and can damage milk-producing tissues directly. The bacteria damages the tissues of the teats and glandular cisterns within the quarter at first, resulting in scar tissue formation. The bacteria then go up the duct system and into the milk-secreting cells (alveoli), where they produce profound pockets of infection. Abscesses occur, protecting the bacteria from spreading but allowing them to elude detection by the immune system and continue to infect the body. Antibiotics are unable to reach the bacteria because of the abscesses, which is the primary cause of therapy failure [41].

The production of biofilms is another significant method that *Staphylococcus aureus* maintains an infection [42]. Biofilms are multi-bacterial communities encased in a matrix made up primarily of polysaccharides, extracellular DNA, and proteins. Adhesion, maturation/ proliferation, and separation are the three primary steps of its production. Biofilm development during infection serves primarily to protect bacteria from phagocyte attacks [43]. Antimicrobial peptides (AMPs) and antibiotics can be impervious to the biofilm matrix. Some, on the other hand, can easily enter, which is likely due to the AMPs' or antibiotics chemical characteristics [44].

4. DRUG RESISTANCE OF *STAPHYLOCOCCUS AUREUS*

Antibiotic resistance is becoming a greater danger to worldwide public health [45]. The epidemiological and clinical significance of *Staphylococcus* species is based on their capacity to overcome antibiotic actions, not just their distribution and pathogenicity [46]. *Staphylococcus aureus* notorious for its capacity to become resistant to antibiotics, and its development of multi-drug resistance is a global problem [47].

Beta-lactam resistance

Beta-lactam antibiotics have previously demonstrated significant activity against *Staphylococcus aureus*, making them the drug of choice for the treatment of Staphylococcal infections due to their good safety profiles [48]. However, immediately after the antibiotic was introduced in the early 1940s, penicillin-resistant forms of *Staphylococcus aureus* evolved [49]. The expression of an enzyme (β -lactamase) that can hydrolyze the β -lactam and the acquisition of a gene encoding a modified Penicillin-binding protein (PBP) that is intrinsically resistant to inhibition by β-lactam

antibiotics are the two main mechanisms for *Staphylococc*i resistance to beta-lactam antibiotics [50].

Staphylococcus aureus' penicillin resistance is caused by the expression of a β -lactamase enzyme, which hydrolyzes the crucial β-lactam bond and eliminates the drug's antibacterial effect [14]. The acquisition of a gene that encodes a homologue of penicillin binding protein 2a (PBP2a) is the molecular foundation of resistance to methicillin and oxacillin [51]. PBP2a is encoded by the *mec*A gene, which is found in a unique section of DNA known as the staphylococcal chromosomal cassette (SCC) [52]. PBP2a stays active in the presence of β-lactam antibiotic doses that block most endogenous penicillin binding protein enzymes, allowing growth in the presence of β-lactam inhibitors by replacing their activities in cell wall formation [53].

Vancomycin resistance

Vancomycin resistance is linked to van genes which code for different resistance phenotypes and which have the same name as the corresponding genes [54]. Vancomycin resistance is divided into several gene clusters based on the DNA sequence of the ligase van gene homologues, which encode the key enzyme for the synthesis of D-alanyl D-lactate or D-alanyl D-serine (D-Ala D-Ser). At least 11 van gene clusters that confer vancomycin resistance and respond to the *van*A, *van*B, *van*D, *van*F, *van*I, *van*M, *van*C, *van*E, *van*G, *van*L and *van*N phenotypes have been described [55]. The genes encoding D-alanyl D-lactate ligases, such as *van*A, *van*B, *van*D, *van*F, *van*I, and *van*M, often lead to high levels of vancomycin resistance, while the genes encoding D-alanyl D-serine ligases, including *van*C, *van*E, vanG, vanL, and *van*N generally result in low resistance [56].

Aminoglycoside resistance

Aminoglycosides are antibiotics that are useful in the treatment of staphylococcal infections [57,58]. Changes in the position of the drug's ribosome binding site, decreased drug permeability, and drug inactivation by enzymes are the three mechanisms of resistance to aminoglycosides. In *Staphylococc*i species, enzymatic inactivation by aminoglycoside-modifying enzymes (AMEs) is a major mechanism of resistance. These enzymes are divided into three different categories based on their modifying effect: aminoglycoside acetyltransferases (AACs), aminoglycoside phosphotransferases (APHs) and aminoglycoside nucleotidyltransferases (ANTs). Three enzymes, AAC(6')-APH (2"), APH(3')-III and ANT(4)-I, are encoded by *aac(6')-aph(2"), aph(3')-IIIa, ant(4')-Ia* genes, respectively. These are the most common modifying enzymes among *Staphylococcus* species and are clinically important [59,60].

Macrolides and Lincosamides Resistance

Macrolides (e.g., erythromycin, azithromycin, spiramycin) and lincosamides (e.g., clindamycin, lincomycin) are two types of antibiotics that have similar inhibitory effects on bacterial protein synthesis despite their chemical differences. They're frequently used to treat staphylococcal infections [61,62]. The inhibition of protein synthesis is a major mechanism of resistance to macrolide and lincosamide antibiotics in *Staphylococcus aureus.* This can be mediated by several mechanisms: (a) Modification of the ribosomal binding site (by methylation or mutation in the 23S rRNA gene) encoded by the *erm* genes (*erm*A, *erm*B, *erm*C, *erm*Y, and *erm*F), (b) active efflux mediated by *msr*A/B genes, and (c) inactivation of antibiotics [63]. In addition, the inactivation of lincosamide drugs is mediated by the activation of a lincosamide nucleotide transferase, which is encoded by the *lnu*A gene [64,65].

Tetracycline Resistance

Tetracyclines are broad-spectrum antibiotics used to treat and prevent bacterial infections in humans and animals, as well as as growth promoters in livestock [66]. In *Staphylococcus aureus*, there are relative mechanisms of tetracycline resistance, which are encoded by chromosomal or transposonal t*etM* or *tetO* determinants [67,68]. Tetracycline-resistant *Staphylococcus aureus* strains with only the *tetK* gene are sensitive to minocycline. The strains with the *tet*M gene are resistant to all antibiotics of the doxycycline group [69].

5. STAPHYLOCOCCUS AUREUS ASSOCIATED INFECTIONS

5.1. In Animals

Staphylococcus aureus is one of the most significant bacterium in veterinary medicine, and it is widely known as a major cause of intramammary infections in dairy cows [70,71]. In cattle, it produces from small abscesses to severe mastitis and toxic shock syndrome [71]. It is a contagious bacterium that causes both clinical and subclinical mastitis in dairy herds, and it frequently leads to persistent and chronic infection with a low cure rate after antibiotic therapy [40,72]. *Staphlococcus aureus* are more likely to occur in animals that have been inadequately handled and treated with antibiotics regularly [73].

Staphylococcus aureus is a prominent cause of mastitis and septicemia in small ruminants, which can be of thromboembolic origin [71,74]. These infections can also arise as a result of parasite infestation, where normal skin flora *Staphylococcus aureus* can penetrate and cause fatal toxemia or a chronic condition with organ spread and abscess formation in lambs [75]. Staphylococcal infection in goats can occur as a result of parapox virus infection [18].

In poultry, *Staphylococcus aureus* is one of the main causes of bacterial infections [76]. It is often associated with bumble foot, omphalitis (yolk sac infection), arthritis, tenosynovitis (inflammation of the tendon sheath), necrotic dermatitis, necrotic skin lesions or abscesses, and osteomyelitis [77]. *Staphylococcus aureus* does not cause many diseases in pigs; *Staphylococcus hycius* is the most common cause of the skin infections in pigs [18]. However, exudative dermatitis (greasy pig disease) is known to be caused by *Staphylococcus aureus* species [8].

5.2. In Humans

Staphylococcus aureus is a common human pathogen that causes a range of illnesses. Bacteremia, infectious endocarditis, osteoarticular, skin, as well as other infections, pleuropulmonary infections, and breast infections [78]. Folliculitis, impetigo, abscess, cellulitis, and toxic epidermal necrolysis are all skin infections caused by *Staphylococcus aureus*, and staphylococcal skin infections are very contagious [79].

Toxins produced by some strains of *Staphylococcus aureus* can induce Staphylococcal food poisoning, toxic shock syndrome, or scalded skin syndrome [80]. SFP (staphylococcal food poisoning) is an intoxication caused by the intake of foods containing enough preformed enterotoxins (one or more). Staphylococcal food poisoning symptoms include nausea, intense vomiting, stomach cramping, with or without diarrhea, and they appear quickly (2-8 hours) [81]. Toxic shock syndrome is characterized by a quick onset of severe symptoms such as fever, rash, dangerously low blood pressure, and multiorgan failure [79].

6. EPIDEMIOLOGY OF STAPHYLOCOCCUS AUREUS

6.1. Reservoir

Human nostrils are the principal niche and greatest reservoir of *Staphylococcus aureus*. This facultative pathogen infects every third individual on average [82]. Although human nares are the greatest reservoir, cows may be the second largest [83]. Milking animals' skin, mucous membranes, teats, and udders are essential reservoirs [84]. Infected udders and teat skin, on the other hand, are the principal reservoirs in a dairy herd [83]. Purchased animals infected with *Staphylococcus aureus* and chronically infected animals are a major source of new *Staphylococcus* infections on a farm [84].

6.2. Transmission

Cow-to-cow transmission of *Staphylococcus aureus* occurs when milk from an infected cow comes into contact with the teat end of an uninfected cow during milking. Infected animals excrete bacteria in their milk, and can also be transmitted through contact with contaminated milking machines, farmers' hands, or contaminated bedding [85, 86]. These harmful bacteria can also be transferred by flies and the cloths used to clean udders during milking practice [85]. Other environmental transmission routes are less

frequent; although *Staphylococcus aureus* can survive in the environment for some time, it requires animal colonization to ensure its survival [41].

In Humans, staphylococcal food poisoning is an intoxication that is caused by the ingestion of food containing pre-formed *Staphylococcus* enterotoxins [87]. Some strains of *Staphylococcus aureus* produce enterotoxins in food, frequently as a result of the food not being kept hot or cold enough [88]. Food handlers with enterotoxin-producing *Staphylococcus aureus* in their noses or on their hands are thought to be the most common source of food contamination through direct contact or respiratory secretions [87]. Equipment and environment surfaces, on the other hand, might be sources of contamination [89].

7. DIAGNOSIS OF *STAPHYLOCOCCUS AUREUS*

A culture of the afflicted area is the primary test for diagnosing a *Staphlycoccus* infection. Clinical specimens are generally cultured on blood agar to isolate *Staphylococci*. After 24-48 hours at 37°C, *Staphylococcus aureus* produces creamy to off-white or yellow, smooth, round colonies with a narrow zone of full hemolysis and a broad zone of incomplete hemolysis [90,91]. Hemolysin is an exoenzyme and one of *Staphylococcus aureus'* key virulence factors that causes the erythrocyte membrane to be destroyed, resulting in the creation of a totally transparent hemolytic ring on blood agar plates [92].

Staphylococcus aureus is a Gram-positive bacterium that is cocci-shaped and tends to cluster in what is described as grape-like clusters [93]. The oozing sign, a pink oozing component of *Staphylococcus aureus*, is sometimes seen surrounding clustered gram-positive cocci. This is a quick and straightforward way to distinguish it from other Staphylococci species [94].

The catalase test examines if the organism generates catalase, an enzyme that converts hydrogen peroxide (H_2O_2) to water and oxygen. Catalase-positive organisms produce oxygen bubbles that are visible to the naked eye when combined with 3% H_2O_2, but catalase-negative organisms do not. The catalase test is used to differentiate between *Streptococci* (catalase-negative) and *Staphylococci* (catalase-positive). Because erythrocytes have catalase activity, it is better to test colonies for catalase production in non-blood media [19,95].

For the isolation and identification of *Staphylococcus aureus* from clinical and non-clinical materials, mannitol salt agar (MSA) is utilized as a selective and differential medium. Peptones and beef extract give nitrogen, vitamins, minerals, and amino acids, all of which are necessary for growth. Other bacterial organisms are partially or completely inhibited by the 7.5% sodium chloride concentration, which also provides critical electrolytes for transport and osmotic balance. Mannitol, a fermentable carbohydrate that produces acid when fermented and identified by the phenol red indicator, aids in the identification of Staphylococcal species. Yellow colonies and a yellow medium are produced by *Staphylococcus aureus* [19,23].

DNase (deoxyribonuclease) is a DNA-degrading enzyme. The enzyme DNase can be produced by *Staphylococcus aureus*. DNase agar has a DNA content of 0.2%. The plate is inoculated and incubated to detect DNase production. After the plate has grown, it is saturated with 1-N hydrochloric acid (HCl). DNase-positive cultures have a clear zone surrounding the streak where the bacterial DNase breaks down the DNA in the agar [96,97].

Coagulase is an exoenzyme that causes clots by inducing fibrin from blood plasma to be deposited on bacterial cells. Non-pathogenic *Staphylococci* do not produce coagulase, but pathogenic strains do. Coagulase is produced in two forms by *Staphylococcus aureus* (bound coagulase and free coagulase). A slide coagulase test can identify bound coagulase, also known as clumping factor, whereas a tube coagulase test may detect free coagulase. The tube coagulase test is the gold standard for routine *Staphylococcus aureus* detection [19,98].

Quantitative real-time PCR was used to detect *Staphylococci* or their toxin genes in a quantitative manner (qRT-PCR). There are commercial fast assay kits for detecting *Staphylococcus aureus* 23S rRNA. There is also a commercial array chip called ‘Staphychips' that may be used to identify five different *Staphylococci* in an array format [99].

8. PUBLIC HEALTH AND ECONOMIC IMPORTANCE OF *STAPHYLOCOCCUS AUREUS*

Staphylococcus aureus is a major public health concern around the world, and Methicillin-resistant *Staphylococcus aureus* (MRSA) has grown in relevance in hospitals (nosocomial infections), the community, and even cattle husbandry [87]. Invasive Methicillin-Susceptible *Staphylococcus aureus* (MSSA) infections are also associated with a high rate of morbidity and mortality. Invasive MSSA, for example, exceeded MRSA across all demographic groupings and epidemiological classes. Furthermore, invasive MSSA infections accounted for the majority of cases, hospitalizations, and deaths associated with invasive *Staphylococcus aureus* infections, implying that invasive MSSA infections represent a serious public health concern in the United States [100].

Microbial food poisoning has resulted in substantial morbidity and mortality in both developed and developing countries. Staphylococcal food poisoning is one of the most common causes of foodborne disease outbreaks worldwide [101]. Ingestion of foods contaminated with preformed Staphylococcal enterotoxins (SEs) causes staphylococcal food poisoning (SFP), which is one of the most common foodborne diseases and a major concern in public health programs around the world [102]. *Staphylococcus aureus* is a major cause of foodborne illness in the United States, causing an estimated 241,000 illnesses each year [103]. In developing countries, foodborne disease surveillance systems are inadequate, making it difficult to assess the true scope of the problem. As a result, the incidence of staphylococci-related foodborne diseases is thought to be much higher than reported, with many cases going unreported [104].

The disease has a sudden onset. Hyper salivation, nausea, vomiting, and stomach cramps with or without diarrhea are some of the symptoms. Physical examination may reveal indications of dehydration and hypotension if there has been severe fluid loss [87]. The most common symptoms are abdominal pains, nausea, and vomiting [105]. It is usually self-limiting and resolves within 24-48 hours of onset, but it can be dangerous in infants, the elderly and immunocompromised patients [81]. In addition to food-borne illnesses, *Staphylococcus aureus* can cause respiratory infections, skin inflammation, wound sepsis, and toxic shock syndrome [106].

Bovine mastitis, a major infectious condition that has an impact on the profitability of milk production, is the fundamental reason for *Staphylococcus aureus'* economic importance [86]. Mastitis has both direct and indirect costs. Veterinary costs, discarded milk (during treatment), and reduced milk supply and quality are all direct costs. Indirect expenses, sometimes known as hidden costs, are those that are not necessarily visible to the milk producer. These include a higher risk of complications, decreased fertility (due to extra services per conception and consequently longer calving intervals), a higher risk of culling, and, on rare occasions, fatality [107]. Mastitis can cause economic losses in dairy sheep and goats, much as it can in dairy cows, and economic losses in poultry can be caused by lower weight gain, decreased egg production, lameness, mortality, and conviction at slaughter [108].

Frequent samples should be collected from regional hospitals in developing or other countries every three months so as to monitor epidemiological samples in human population. In this case a social health protection could be established following measures and actions that are described in next section with proper monitoring schemes, geographic information utilities, digital drawings.

9. TREATMENT, PREVENTION AND CONTROL

Antibiotics have had minimal success in treating *Staphylococcus aureus* mastitis and no effective vaccination exists [109,110]. Because treatment is ineffective, controlling and preventing *Staphylococcus aureus* mastitis should be the priority [111]. However, nano-drugs have recently been employed as a surrogate to address the multi-drug resistance and intracellular persistence of *Staphylococcus aureus*, which has been linked to subclinical and recurrent bovine mastitis infection. As a result, these novel nano-carriers provide a new

technique for dealing with *Staphylococcus aureus* mastitis [112].

In humans, β-lactamase-producing strains of Staphylococcus aureus have been treated with β-lactam clavulanic acid (such as co-amoxiclav). Oxacillin, cloxacillin, and nafcillin can be used to treat methicillin-sensitive β-lactamase-producing strains; however, vancomycin, teicoplanin, and mupirocin are used to treat methicillin-resistant infections [113,114]. In patients who are allergic to vancomycin, trimethoprim-sulfamethoxazole may be used [115].

In dairy farms, the most effective way to prevent new infection and control *Staphylococcus aureus* mastitis is to eliminate conditions that expose the teat ends to bacteria and reduce the possibility of cow-to-cow transmission. Hygiene measures (dipping the teats in an antiseptic solution before and after milking, proper cleaning and maintenance of the milking equipment, milkers should always wear gloves and change them frequently), Eliminating conditions that expose the teat ends to bacteria and reducing the probability of cow-to-cow transmission are the most effective ways to prevent new infection and control *Staphylococcus aureus* mastitis in dairy farms.

Hygiene precautions (dipping the teats in an antiseptic solution before and after milking, proper cleaning and maintenance of the milking equipment, milkers should always wear gloves and change them frequently), Early detection and treatment of *Staphylococcus aureus*-infected animals, separate milking of those infected with *Staphylococcus aureus*, culling of chronically infected animals, and dry cow therapy with long-acting antibiotics to reduce an existing infection and prevent new intramammary infections are all important mechanisms for controlling and preventing *Staphylococcus aureus* mastitis [111, 116].

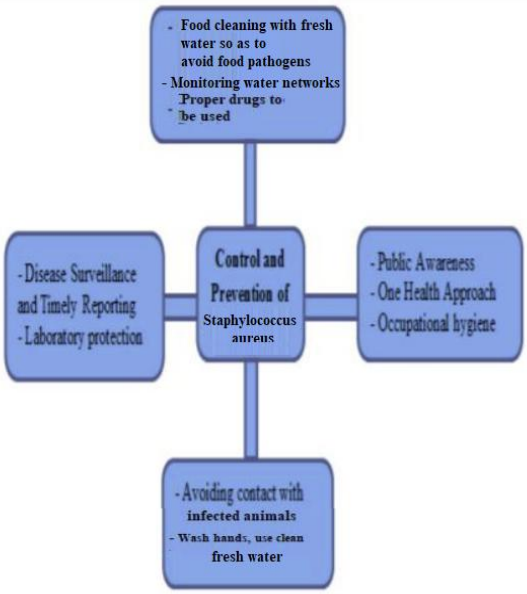

Figure 1. Measures and actions that should be followed so as to avoid associated epidiomological risks due to staphylococcus aureus.

The relative measures and actions that should be followed properly so as to avoid food pathogens and water pathogens due to staphylococcus aureus are presented in figure 1. Proper monitoring schemes are needed for good water quality in water supply networks. Special care in good use of fresh water for food cleaning and food security from particular contaminants is needed in case of nutrition's programs and diets that should be followed for human populations [122, 123, 124, 125]. Also proper designs are needed in terms of monitoring and safety of particular facilities for proper use of water networks and associated facilities for good use of hydraulic pipe networks following proper monitoring schemes, digital drawings, geographic information utilities, project management web utilities - ICTs, IoTs, taking right measures in emergencies [124, 125, 126, 127, 128, 129, 130, 131, 132].

In humans, controlling the spread of *S. aureus* infection relies on the adoption of adequate infection control techniques and contact precautions [117]. To suppress pathogen growth or eliminate the pathogen and minimize toxin production, public education on hand cleaning, and using gloves when preparing food and keeping food at the proper

temperature is needed [118]. Both at home and in human and animal health care, good cleanliness is an important general preventive and control measure. The use of conventional (systemic) antibiotics as a preventive measure against nosocomial infections caused by *S. aureus* has been suggested. However, there is no evidence that these antibiotics are effective as preventive medicines against *S. aureus* infection [119,120].

4. CONCLUSIONS AND RECOMMENDATIONS

Staphylococcus aureus causes wide array of diseases both in human and animals including the birds. Human nares are the principal niche and greatest reservoir of *Staphylococcus aureus* and cows can also be reservoirs.. *Staphylococcus aureus* is one of the most significant bacteria in veterinary medicine, *Staphylococcus aureus* is a major public health concern around the world, causing staphylococcus food poisoning. *Staphylococcus aureus* strains are resistant to β-lactam antibiotics, and others mediated by various genetic and enzymatic mechanisms. The economic importance of *Staphylococcus aureus* is associated with bovine mastitis that has an impact on the profitability of milk production. Based on the above, the following recommendations were forwarded:

- ✓ Cleanliness and hand washing is an important general preventive and control measure.
- ✓ Training on proper milking hygiene, hygiene of the cow and barn area should be given to all actors involved in milk production by concerned body.
- ✓ Close monitoring and rational use of antibiotics must be practiced to prevent antibiotic resistance from the pathogen.

Moreover, proper monitoring schemes, epidemiological studies, measures, actions should take place realizing robust designs that are needed in terms of avoiding pollutants to human, animal populations for the health and safety at receptors. Also right measures should be taken in emergencies so as to mitigate associated risks.

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AUTHOR'S CONTRIBUTION

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

CONFLICT OF INTEREST

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

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