

***Staphylococcus aureus* in poultry, with special emphasis on methicillin-resistant strain infection: A comprehensive review from one health perspective**

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Abstract

Staphylococcus aureus is a Gram-positive coccus normally present on the skin and internal organs of animals, birds, and humans. Under certain conditions, *S. aureus* could produce septicemia and affection of the skin, joints, and heart, as well as sepsis and death. The pathogenicity of *S. aureus* is associated with the presence of some virulent surface proteins and the production of some virulent toxins and enzymes. This pathogen is considered one of the most important and worldwide foodborne causes as it is incriminated in most cases of food poisoning. The hazardous use of antibiotics in the veterinary field leads to the development of multidrug-resistant *S. aureus* strains that can be transmitted to humans. The incidence of methicillin-resistant *S. aureus* (MRSA) strains has increased globally. These resistant strains have been detected in live animals, poultry, and humans. In addition, retail animal products, especially those of avian origin, are considered the main source of MRSA strains that can be easily transmitted to humans. MRSA infection is regarded as nosocomial or occupational. Humans get infected with MRSA strains through improper handling or preparation of contaminated animals or poultry carcasses or improper cooking with contaminated meat. Live birds also can transmit MRSA to close-contact workers in poultry farms. Transmission of MRSA infection in hospitals is from an infected individual to a healthy one. Prevention and control of MRSA are based on the application of hygienic measures in farms as well as proper processing, handling, and cooking of retail poultry products. The cooperation between veterinary and human practitioners is a must to avoid the possibility of zoonotic transmission. Accordingly, this review focused on the sources and transmission of MRSA infection, virulence and resistance factors, incidence and prevalence in poultry and different products, antibiotic resistance, and prevention and control strategies.

Keywords: chickens, food poisoning, humans, methicillin-resistant *Staphylococci*, zoonosis.

Introduction

Staphylococcus aureus is regarded as an opportunistic and commensal organism of animals, birds, and humans. It may reside asymptotically on the skin and in the nose of animals [1]. However, under certain circumstances, *S. aureus* causes skin and soft-tissue infection, osteomyelitis, endocarditis, sepsis, and death [2]. Like in humans and other animals, *S. aureus* could be isolated as a normal microflora from poultry skin, feathers, and respiratory and intestinal tracts [3,4]. Nevertheless, this pathogen could be associated with some disease conditions, such as dermatitis, arthritis, osteomyelitis, synovitis, tenosynovitis, femoral head necrosis, bumble-foot, and omphalitis [5]. The severity of lesions is linked to the presence of some virulence factors, such as enzymes and toxins [6].

S. aureus is recognized as the third most important worldwide cause of foodborne infections [7].

A concentration of 10^5 to 10^8 colony-forming units of *S. aureus*/g in food can cause food poisoning in humans [8]. Staphylococcal food poisoning is associated with the secretion of enterotoxins produced in the exponential phase of pathogen growth [9]. Enterotoxigenic *S. aureus* strains can contaminate food, causing foodborne poisoning and toxic shock syndrome [10,11].

Antibiotic-resistant bacteria in animals are of growing concern because of their possible role in transmission to humans as foodborne pathogens [12]. There is no doubt that the extensive usage of antimicrobials in the poultry industry enhanced the ability of *S. aureus* to acquire many resistance genes and thus become more virulent [13]. These resistance genes and the resistant bacteria could be transferred to humans through meat consumption and in sequence threaten the effectiveness of prevention and control strategies [14]. Dissemination of antimicrobial resistance among *Staphylococcus* strains is probably due to variations in DNA sequences and horizontal transfer of resistance genes [15].

Methicillin-resistant *S. aureus* (MRSA) strains have been increasingly reported as emerging pathogenic strains that cause great problems in veterinary medicine. The term "MRSA" is related to nonsusceptibility to at least one of the antimicrobials in three or

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more categories and whose resistance to oxacillin or ceftiofur predicts nonsusceptibility to most categories of β -lactam antimicrobials [16]. About 96% of *S. aureus* strains are resistant to at least one antibiotic, whereas 32% are resistant to multiple antimicrobial classes [17]. The World Health Organization (WHO) has classified MRSA strains as “high priority 2 pathogens,” due to their great threat to the health of both humans and animals. The first identification of MRSA strains was in 1961 in England, after which they have emerged worldwide [18]. Since the 1990s, MRSA has been regarded as a nosocomial or community-associated pathogen and has become a significant public health and worldwide zoonotic problem [19]. Resistant MRSA strains represent a great threat to consumer health [20-22].

In poultry, MRSA strains were isolated for the 1st time from arthritis cases in South Korea; then, different strains have been isolated from live birds and retail poultry products [23]. The presence of MRSA in live poultry has been reported and has highlighted the increase in the antibiotic resistance rate, especially in recently isolated strains [17]. Different kinds of animal meat as well as frozen and raw chickens and turkeys show the presence of MRSA [21,24]. However, chicken meat is considered an important reservoir for MRSA [25].

Therefore, this review focused on the sources and transmission of MRSA infection, virulence and resistance factors, incidence and prevalence in poultry and different products, antibiotic resistance, and prevention and control strategies.

Sources and Transmission of MRSA Infection

MRSA is rapidly disseminated among animals, humans, and the environment. It can spread through water, air, food, and contaminated surfaces and transmits through direct contact between animals and humans [26-28]. Livestock-associated MRSA poses a zoonotic risk to humans, especially close-contact workers [29]. The horizontal route of transmission among animals or humans may occur.

Avian MRSA strains can infect birds and show zoonotic importance and risk for poultry handlers and processors [30,31]. Poor hygienic practice during the processing of foodstuff as chicken meat results in contamination with bacterial toxins. However, improper handling by food handlers, improper meat storage, inadequate food cooking, and improper food preparation using contaminated water are also sources of food contamination with MRSA [32,33]. Chicken meat could be contaminated with MRSA during bird slaughtering or meat preparation [20,21]. Unlike other types of bacteria, *S. aureus*, especially MRSA strains, has shown relative resistance to the adverse effects of freezing conditions [34].

Transmission of MRSA from poultry to humans may occur through ingestion of contaminated meat or direct contact with live bird or their droppings [31]. In an Algerian study, *S. aureus* and MRSA isolated from

avian origin were more resistant to β -lactam antibiotics, especially penicillin and oxacillin, than bovine origin [35]. The study suggested transmission of MRSA from poultry to bovine and humans with great difficulties in treatment trials. Poultry litter is another source of *S. aureus* infection in poultry farms [36-38].

At healthcare units, discharge of infected patients with MRSA may be an important source of infection to healthy contact individuals, such as health workers; consequently, they may transmit the infection to noninfected persons. In addition, there is a possibility of transmission of MRSA from infected humans to animals (anthroponosis) or from infected animals to contact humans (zoonosis) after handling of animals and contaminated equipment or products [31].

Virulence and Resistance Factors

S. aureus is a Gram-positive, nonmotile, and non-spore-forming coccus. This organism can grow from 15°C to 45°C and requires higher sodium chloride concentrations (10%) [39]. However, at room temperature, *S. aureus* could multiply quickly and release toxins, producing illness.

Multidrug-resistant (MDR) *S. aureus* strains are resistant to three or more classes of antibiotics, and they show difficulties in the treatment [40]. Unfortunately, the incidence of MDR *S. aureus* strains has increased due to the hazardous use of antimicrobials in the prophylaxis and treatment of diseases in either animals or humans. Multiple cross-resistance has been detected in MRSA strains in food products of chicken and turkey origins [41]. Lately, MDR *S. aureus* isolates have been reported in food poisoning outbreaks after consumption of contaminated food products [42].

The ability of *S. aureus* strains to show multiple resistances to antibiotics might be due to the production of an exopolysaccharide barrier [43] and carriage of variable MDR genes on plasmids that could be exchanged and spread to other *Staphylococcus* species [44]. Therefore, this resistance could normally be produced by horizontal gene transfer or mutation and selection [45].

There are some important cell-surface proteins on *S. aureus* that mediate the virulence and adhesion of the organism to host cells. These proteins include an elastin-binding protein and clumping factors A and B (*clfA* and *clfB* genes) [46,47], matrix adhesion proteins, and extracellular matrix fibrinogen and collagen proteins [48]. Besides, protein A (*spa* gene) is a multifunctional surface protein located on a fragment crystallizable portion of immunoglobulin G (IgG). This protein produces immune evasion and hinders the antibody-mediated immune clearance of the pathogen, so it can act as a superantigen of B cells [48]. Accordingly, protein A antagonizes the phagocytosis of opsonized bacteria through binding with IgG [49].

Numerous genetic elements encode virulence and resistance of MRSA to antimicrobials [50].

The synthesis of penicillin-binding protein (PBP), modified PBP2a [51], PBP2' [52], or MRSA-PBP [53] is considered the most important, if not the only, means of conferring high resistance to β -lactams. Moreover, the absence of resistance to methicillin in *S. aureus* strains is frequently associated with the absence of PBP [54]. The production of PBP2a with decreasing susceptibility to β -lactam antibiotics in MRSA is encoded by the *mecA* gene [55,56], which carries insertion sites for genetic elements that facilitate the gain of resistance determinants to other antimicrobials [57]. Methicillin is penicillin-resistant to penicillinase, and *S. aureus* strains become resistant to methicillin by acquiring the *mecA* gene [58]. This gene is found in staphylococcal cassette chromosome *mec* (SCC*mec*), responsible for resistance to several antibiotics [59]. There are seven main variants of SCC*mec* (Types I-VII). MDR *S. aureus* strains associated with the *mecA* gene were detected in retail meat products [60], chicken meat and giblets [14], and ready-to-eat meat products [61]. In addition, the *mecC* gene showed verified 70% homology to the methicillin resistance *mecA* gene [62].

In Bangladesh, Islam *et al.* [63] found that more than 74% of *S. aureus* isolates collected from ready-to-eat food and processed meat products harbored enterotoxin genes with distribution percentages of 26%, 11%, 49%, and 13% for *sea*, *seb*, *sec*, and *sed* genes, respectively. *seb*, *sec*, and *see* genes can resist the hydrolysis process produced by gastric and jejunal enzymes, and they are heat stable at 100°C for 30 min [64]. This explains why food poisoning caused by *S. aureus* is a leading worldwide cause of food-borne bacterial intoxication [65].

γ -Hemolysin (*hlg* gene) is considered one of the most important virulent genes of *Staphylococcus* as it is responsible for pore formation in red blood cells after binding of acting proteins *hlgA* and *hlgB* [66]. Coagulase (*coa* gene) is another virulence marker of *Staphylococcus*. Coagulase helps in fibrin formation surrounding staphylococcal abscess, which helps in localized infection and protects bacteria from the phagocytosis process [67].

Several toxin gene groups as enterotoxins (*sea*, *seb*, *sec*, *sed*, *see*, *seg*, *seh*, and *sei*), toxic shock syndrome toxin 1 (*tst*), exfoliative toxins (*eta* and *atb*), leukocidins (*lukE-lukD* and *lukM*), Pantone-Valentine leukocidin (*lukS-lukF*), and hemolysins (*hla*, *hly*, and *hld*) were used to detect MRSA from retail chicken and turkey meat in Oklahoma [68].

Incidence and Prevalence in Poultry and Different Products

Poultry farms

Live birds are regarded as an important reservoir for pathogenic *S. aureus* strains. For example, Mamza *et al.* [69] isolated *S. aureus* strains at a rate of 52.5% from apparently healthy and diseased chickens, whereas

Suleiman *et al.* [70] found coagulase-positive *S. aureus* in 54% of apparently healthy chicken samples. In addition, Nworie *et al.* [71] showed that 76% (247 of 325) of *S. aureus* isolated from nasal and cloacal swabs of chickens were from poultry, and the prevalence rates of the organism were 6.1% and 15.3% in broilers and layers, respectively. However, *S. aureus* in 90% of nasal and cloacal swabs of broilers were detected in Egypt [72]. Two hundred and fifty broiler chicken samples, including nasal, tracheal, and cloacal swabs, hock joint, and liver, were collected from apparently healthy and diseased birds for isolation of *S. aureus* [73]. Results showed the presence of 157 *Staphylococcus* isolates with an isolation rate of 62.8%, of which 81 (55.9%) were coagulase-positive and 76 (48.4%) were coagulase-negative. Recently, Bounar-Kechih *et al.* [35] collected 8375 chicken samples (1875 from laying hens and 6500 from broiler chickens) in the northern region of Algeria between 2009 and 2014. They demonstrated that the prevalence rates of *S. aureus* were 42% and 12% in laying hens and broilers, respectively.

Based on phenotypic and genotypic characterizations of MRSA in poultry farms, live poultry are frequently carrying MRSA [74-76]. Cloacal and nasal swabs of 75 broilers and 50 laying hens were collected from poultry flocks in Belgium. Results showed detection of 15 MRSA strains from broilers, but no strain was obtained from laying hens [77]. In poultry farms in China, MRSA strains were reported with variable prevalence rates from one farm to another according to antibiotic usage load [78]. Moreover, MRSA strains were found in 11 of 250 (4.4%) pooled pharyngeal swabs of broilers in the Netherlands [79]. A cross-sectional study of Friese *et al.* [80] revealed detection of MRSA in air samples of poultry farms (7 of 9, 77.8%) and 50-54% of broiler samples and 62-77% of turkey samples. In Nigeria, Adeyeye and Adewale [30] demonstrated MRSA strains in 90 of 100 cloacal swabs of 6-week-old diarrheic broiler chickens at an incidence rate of 90%. However, the percentage carriage of MRSA in poultry was 6.1%, and all MRSA strains were MDR. A strong correlation between methicillin resistance and cross-resistance to β -lactam antimicrobials was detected in Qena Province, Egypt [81]. Besides, Abd El Tawab *et al.* [5] characterized MRSA strains in 66% of the samples from bumble-foot and skin of chickens. MRSA prevalence was 57% in laying hens and 50% in broiler chickens in Algeria [35]. Recently, Benrabia *et al.* [82] detected MRSA strains in 252 of 4248 (5.9%) nasal swabs, representing 654 breeding hens, 838 laying hens, 1614 broiler chickens, and 1142 turkeys [82].

Poultry products

Meat products may contain MRSA and play an important role in human food poisoning infection [83]. The prevalence rate of MRSA isolated

from raw retail meat products ranged from <1% in the Netherlands [84] to 11.9% in Korea [85]. The presence of MRSA in commercial raw poultry meat was recorded in 2004 in Japan, where two *mecA*-positive MRSA strains were detected in 444 raw poultry meat samples [23]. Of 150 calf/lamb meat and chicken part samples, 80 (including 26 isolates of poultry origin) were *S. aureus* strains, the overall methicillin resistance rate of *S. aureus* strains was 67.5%, and the methicillin resistance was 76.4% and 55.5% for chicken carcass and chicken giblets, respectively [86]. In the United States, of 136 poultry meat samples, 47% were contaminated with *S. aureus* and 52% of the isolates were demonstrated as MRSA [17]. However, 2 (1.2%) MRSA strains were also detected in 114 retail chilled chickens and 53 turkeys [68]. In 2012 in Qena Province, 44% (11 of 25), 52% (13 of 25), 40% (10 of 25), 24% (6 of 25), and 44% (11 of 25) of MRSA strains were identified from whole chicken carcasses, chicken portions, chicken luncheon, chicken sausages, and chicken burgers, respectively [81]. Therefore, contaminated poultry meat or products are considered one of the important sources of transmission of MRSA to humans, probably due to unhygienic poultry slaughterhouses and food preparation establishments. In England, 9 of 61 (7.3%) MRSA strains were isolated from chicken and turkey meat samples [87], whereas MRSA strains were found in 4% of 102 chicken meat samples in Denmark [88]. Lately, in Northern Algeria, the prevalence of MRSA in laying and broiler chickens in slaughterhouses was demonstrated in 23.9% and 6.4% of the samples, respectively [35]. Recent studies revealed the presence of MRSA in raw and frozen chicken meat in different countries worldwide, such as China [20], Bangladesh [89,90], Hong Kong [22], and Egypt [21,91]. Interestingly, MRSA strains were also isolated from quail meat [92-94]. Recently, Saadati *et al.* [95] found that 2 of 70 (2.86%) quail samples were MRSA strains in shopping centers of Iran.

Table eggs also are incriminated in foodborne infection with *S. aureus*. Stepień-Pyśniak *et al.* [96] isolated *S. aureus* from eggs at a rate of 45.7%, of which 2.5%, 38.7%, and 58.8% were found in the white, yolk, and on shell, respectively. Moreover, coagulase-positive *S. aureus* strains were isolated from eggs at a prevalence rate of 40% and an isolation rate of 29 (14.5%), 15 (7.5%), and 36 (18%) from shell, contents, and both shell and contents, respectively [64]. In the latest study of Kemal *et al.* [97], 93 (27.8%) *S. aureus* strains were demonstrated in 335 egg samples, with 63 (18.8%) from shell and 30 (8.9%) from contents.

Infection of humans

As a result of the spread of MRSA beyond hospital premises, the epidemiology of MRSA showed worldwide changes [98]. Nowadays, MRSA is considered a community pathogen in many parts of the world [99]. Variable incidence and prevalence of

MRSA have been reported in human clinics [100,101]. Hafiz *et al.* [102] stated that the prevalence of MRSA could be ~60%. A relatively high prevalence of MRSA infections (up to 30%) has been demonstrated in African countries, such as Nigeria, Kenya, and Cameroon, whereas it was <10% in Tunisia [103]. In Nigeria, 20.2% [104], 41.5% [105], 48.78% [106], and 50% [107] of *S. aureus* strains showed methicillin resistance among clinical patient samples. In 2001 in Algeria, the frequency of MRSA infection was 14%, but this percentage recently showed a significant increase to 40% in hospitals [108,109]. In northwest Algeria, vancomycin resistance of MRSA has been detected as 54% in poultry and 1.8% in humans [110].

The European Centre for Disease Prevention and Control [111] estimated that MRSA strains caused 17,000 blood infections and 5400 deaths in 2007 in Europe and 84,000 invasive infections and 11,000 deaths in 2011 in the United States [112]. In Hong Kong, 32% of mortality from MRSA bacteremia cases has been reported [113]. Moreover, Wu *et al.* [20] estimated that *S. aureus*, particularly MRSA, is incriminated in 241,000 foodborne illness cases each year in the United States. In China, *S. aureus* is responsible for 12.5% of foodborne bacterial outbreaks, and it is regarded as the third most frequent food poisoning pathogen after *Vibrio parahaemolyticus* (27.8%) and *Salmonella* (23.1%) [114].

The emergence of MRSA in human infections is significantly related to the high prevalence in poultry meat, which is considered a great health hazard for consumers [84]. Recently, MRSA strains have gained deep attention due to the possibility of zoonotic transmission to humans from contaminated retail meat or food chain [20,21,115]. In addition, MRSA has been identified as a key pathogen in nosocomial (hospital or community) and livestock-associated infections [116]. The molecular epidemiology of *S. aureus* and MRSA from food animals and occupationally exposed humans have been also reported [117-120]. Tested food, including poultry meat in hospitals, showed the presence of MRSA with a total prevalence of 7.62%; besides, a high prevalence of human and poultry-based biotypes was seen in hospital food samples [121]. *S. aureus*, particularly MRSA, is a leading cause of food poisoning and other illness of humans, such as postoperative wound infections, septicemia, and pneumonia [122,123]. MRSA is a major cause of global human morbidity and mortality [124,125]. In developing countries, it has been estimated that contamination of chicken meat or related products with MRSA is one of the most important causes of human digestive problems with high morbidity and mortality [22].

Infection of humans with MRSA strains may also occur through direct contact with infected live birds in farms. In Nigeria, MRSA strains were isolated from nasal swabs of 25 close-contact workers, showing symptoms of cough, and from five attendants

without signs in infected broiler chicken farm with an incidence rate of 83.3% [31], suggesting that MRSA infection in poultry may be acquired from humans and may also spread from poultry to the workers at the same farm. Another study by Nworie *et al.* [71] in the Ebonyi State of Nigeria revealed that 24% (78 of 325) of 325 *S. aureus* isolates were from the clinics, and the percentage of carriage of MRSA was 15.3% in the clinics. All MRSA strains were MDR.

Antibiotic Resistance

β -Lactam antimicrobials, including cephalosporins and carbapenems (penicillin, oxacillin, cloxacillin, methicillin, flucloxacillin, and dicloxacillin), are the most commonly used antibiotics for the treatment of *S. aureus* [126-128]. *S. aureus* strains showed developed resistance to these antibiotics due to a plasmid-encoded penicillinase/ β -lactamase [129,130]. β -Lactamase is produced by *S. aureus* strains that have the *bla* gene. This enzyme deactivates β -lactam antibiotics through cleavage with the β -lactam ring [131,132]. In a large study by Lee [30], 1913 samples of feces, feed, milk, joint, uterus, trachea, and meat were collected from cattle, poultry, and pigs in Korea from May 2001 to April 2003 to detect the zoonotic potential of MRSA. Results showed that isolation of 421 *S. aureus* strains as 28 isolates were resistant to >2 $\mu\text{g/mL}$ oxacillin. Moreover, 15 of 28 isolates were *mecA* positive. In Bangladesh, *S. aureus* strains isolated from newly hatched chicks and broiler and layer flocks [133] and frozen chicken rinse [134] showed 100% resistance to amoxicillin and ampicillin. In Upper Egypt, all *S. aureus* coagulase-positive isolates showed resistance to ampicillin, cefotaxime, and methicillin [73]. Besides, Morshdy *et al.* [135] found that *S. aureus* strains isolated from ready-to-eat food in Sharkia Province, Egypt, showed the highest resistance to both methicillin and cefotaxime (100%), followed by amoxicillin (85.18%). A recent study in India revealed that poultry litter isolates of *S. aureus* are β -lactamase producers and completely resistant to penicillin [38]. Moreover, Kemal *et al.* [97] detected high resistance to penicillin, ampicillin, and amoxicillin in *S. aureus* strains isolated from sold eggs in Eastern Ethiopia.

Resistance of *S. aureus* isolates, especially those from broiler chicken origin, to other classes of antimicrobials, such as fluoroquinolones, aminoglycosides, tetracyclines, and macrolides, has been reported [136,137]. Coagulase-positive *S. aureus* strains from live and slaughtered chickens showed 100% resistance to tetracycline, penicillin, and erythromycin [13]. In the Hail region of Saudi Arabia, *S. aureus* strains were isolated from 50 retail chicken meat samples at a percentage of 24%, of which 25% resistance to tetracycline was found [138]. MRSA strains isolated from broilers and layers of chickens between 2009 and 2014 in Northern Algeria showed cross-resistance to aminoglycosides,

fluoroquinolones, macrolides, sulfonamides, and tetracyclines [35]. However, recent studies emphasized that MRSA strains of animal origin showed more resistance to tetracycline, ciprofloxacin, and gentamicin than those isolated from human origin [127,139].

In addition, vancomycin [38,140] and inducible clindamycin [141] resistant *S. aureus* strains are increasingly demonstrated. In Northwest Algeria, vancomycin resistance has been detected in 54% of poultry and 1.8 % of human MRSA strains [110].

Prevention and Control Strategies

Sources of MRSA infections in humans and evidence to support animal-to-human transmission still need more investigations. Thus, molecular epidemiological studies concerning animal and human reservoirs, identifying the diversity of *S. aureus* and determining the antimicrobial susceptibility of *S. aureus*, are very important [142,143]. There is a great interest in detecting the diversity of MRSA in many settings. Animal-adapted clones may experience more host-adaptive evolutionary changes resulting in an epidemic spread of new and more virulent MRSA strains in the human population. Now, the most widely used molecular epidemiological techniques are *Staphylococcus* protein A gene typing and sequence types (ST). Different MRSA regional clones have been described in various countries worldwide. In Africa, existing clones of MRSA are replaced by many and new clonal identities from different countries. For instance, ST250-I [1B] was mainly associated with hospital-acquired infections in Ibadan, southwest Nigeria, and Ghana. ST8-IV [2B] was found in Cameroon, Angola, Ghana, Gabon, Nigeria, Madagascar, and South Africa, whereas ST8-II [2A] was only detected in South Africa [142]. Moreover, the small set of lineages and the clonal complex (CC) types (CC5, CC8, CC22, CC30, and CC48) are linked to most MRSA infection cases in hospitals. The whole-genome sequencing map revealed zoonotic transmission of MRSA harboring *mecC* (CC130) in both animals and humans in Europe. However, the clinical importance of *mecC*-positive MRSA is not yet clear in Africa. In addition, CC398 of MRSA of swine origin was closely related to those found in humans, different animal species, and meat products [143]. The community-associated (CC8) and hospital-associated (CC70) MRSA have been isolated from raw chicken, turkey, pork, and beef [143].

Regular monitoring of MRSA strains from poultry and livestock is necessary to understand the changes in the genetic selection and zoonotic potential of these resistant strains [94]. Monitoring of antimicrobial resistance is also essential to determine the effectiveness of new and antimicrobial generations.

To prevent MRSA infections, awareness, public health education, and good hygiene are critical, especially in veterinary medicine [144]. There is a great need for better sanitary education of food handlers

to decrease their potential role as reservoirs and shedders of MRSA. In addition, hygienic measures should be taken into consideration to ensure the safety of food products, and a proper risk assessment should be applied to further clarify the possible health hazards for consumers. Parvin *et al.* [145] recommended the proper application of good manufacturing and hygiene practices and well-designed hazard analysis of a critical control point program in slaughterhouses and processing units to avoid contamination of poultry meat with MRSA.

Raising public awareness of the proper thermal processing and cooking of eggs, especially for immunocompromised individuals, such as pregnant women, children, and the elderly, is essential [64]. In addition, increasing the awareness of safe household rearing procedures of chicken as well as storage and handling of eggs is also crucial to prevent the dissemination of foodborne pathogens through the environment and the transfer of infection to other animals and humans [64].

The emergence of antibiotic resistance due to the indiscriminate use of antibiotics in poultry and animal farms can increase the difficulties of human treatment. The higher MRSA contamination of chicken products may be associated with antibiotics in bird husbandry [84]. Thus, it is better to use some classes of antimicrobials for animal disease treatment and other classes for human treatment [146].

The control and prevention of transmission of MRSA in healthcare facilities are also serious issues [147]. Patients after surgical operations, especially those who do not respond to antibiotic treatment, should consider possible MRSA infections. Suspected cases with MRSA should be kept under isolation conditions and subjected to bacteriological examination and antibiotic susceptibility testing before therapy. Special hygienic precautions and healthcare of contact persons should be considered with confirmed cases with MRSA infections. Controlling the possibility of zoonotic transmission should be through the cooperation between veterinary and medical professionals. Owners of animals should be advised by veterinarians about the possibility and risk of acquiring MRSA infections after contact with infected animals.

The WHO has developed a global action plan on antimicrobial resistance in collaboration with the Food and Agriculture Organization of the United Nations and the World Organization for Animal Health (OIE). On May 26, 2015, the World Assembly of Delegates of the OIE recommended the following: (1) Regular updating of the OIE list of antimicrobial agents of veterinary importance. (2) Annual data collection from OIE member countries to create a global database managed in parallel with the World Animal Health Information System. (3) Improvement of veterinary legislation and education of OIE member countries to facilitate the implementation of OIE and Codex Alimentarius guidelines related to antimicrobial resistance. (4) Regular surveillance of

antimicrobial resistance with data collection on the use of antimicrobial agents in food-producing animals. (5) OIE member countries should follow the guidance of the WHO global action plan on antimicrobial resistance with the support of OIE and WHO in the spirit of the “One Health” approach. (6) Strengthening the OIE collaboration with international organizations to combat counterfeit products. (7) Improvement of the rapid diagnostic tools to explore alternatives to antimicrobial use in animals, such as vaccine development.

Conclusion

The role of slaughterhouse workers in the spread of MRSA through the contamination of meat or handling contaminated meat and related products cannot be neglected. Accordingly, strict hygienic measures should be applied during food preparation; besides, strong legislation should be followed to produce food of high keeping quality. Workers in processing plants should wear special clothes and gloves during handling and processing of carcasses. Proper storage of retail carcasses is very important. In poultry farms, close-contact workers may be at high risk of MRSA infection and could be potential sources of community outbreaks. Thus, they should be careful and take all hygienic measures and precautions during the handling of live birds. Infected poultry flocks and their litter should be hygienically disposed.

The high prevalence of MRSA is alarming due to the significant public health consequence if the infection is transmitted to humans through the food chain. Therefore, continuous surveillance and monitoring of MDR *S. aureus* isolates are required to better define bacterial resistance to antimicrobial agents. A combined approach regarding the diagnosis and treatment of MRSA infection in humans and animals must be developed. The increase in antibiotic resistance among *S. aureus* isolates in poultry and human clinical cases call for caution in using these antibiotics. In addition, the link between antibiotic usage in animals and MRSA development should be paid more attention and the scientific community should be forced to follow and search for reservoirs of these resistant organisms.

Authors' Contributions

WAA: Collected the literature, drafted and revised the manuscript, and approved the final manuscript.

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Competing Interests

The author declares that she has no competing interests.

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