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## Spread of livestock-associated methicillin-resistant *Staphylococcus aureus* in poultry and its risks to public health: A comprehensive review

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### Abstract

The livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) strains are prevalent in the poultry farming environment and are a common component of the bacterial microbiota on the skin and mucous membranes of healthy animals. The origin and spread of LA-MRSA are attributed to the use of antibiotics in animals, and close contact between people and different animal species increases the risk of animal exposure to humans. The epidemiology of LA-MRSA in poultry significantly changed when ST398 and ST9 were found in food-producing animals. The significance of LA-MRSA and zoonotic risk associated with handling and processing foods of avian origin is highlighted by the LA-MRSA strain's ability to infect chickens. People who work with poultry are more prone to contract LA-MRSA than the general population. There is scientific consensus that individuals who have close contact with chickens can become colonized and subsequently infected with LA-MRSA; these individuals could include breeders, medical professionals, or personnel at chicken slaughterhouses. The prevention of LA-MRSA infections and diseases of poultry origin requires taking precautions against contamination across the entire chicken production chain.

**Keywords:** Antibiotic, LA-MRSA, Chicken, Poultry, Public health.

### Introduction

The indiscriminate use of antibiotics in poultry has a tendency to hasten the emergence of commensal microbes with antimicrobial resistance (AMR) (Widodo *et al.*, 2023). The presence of antibiotic residues in meat and eggs raises concerns for human health in addition to issues related to the evolution of AMR in bacteria from poultry agriculture (Witoko *et al.*, 2019; Wibisono *et al.*, 2021). Additionally, AMR in

poultry pathogens frequently results in financial losses due to the prescription of ineffective antibiotics and the burden of disease in untreated poultry (Khairullah *et al.*, 2020a; Abreu *et al.*, 2023). Due to the development of livestock practices in the majority of developing countries, the extent of antibiotic use will quickly increase in the upcoming years (Widodo *et al.*, 2022; Millannia *et al.*, 2023). A lot of the information and presumptions regarding the incidence and development

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of AMR in animal production systems are based on organisms like *Staphylococcus aureus*, which are more typical in poultry as commensals (Igbinosa et al., 2023).

Methicillin-resistant strains of *S. aureus* (MRSA) can emerge because *S. aureus* can adapt swiftly even when exposed to only a few antibiotics (Khairullah et al., 2022). MRSA strains are intrinsically resistant to methicillin and other  $\beta$ -lactam antibiotics because they possess contain *mec* genes (such as *mecA* or its *mecC* homologue) which are harbored on a mobile genetic element called Staphylococcal chromosomal cassette *mec* (SCC*mec*) (Rahmaniar et al., 2020; Ramandinianto et al., 2020). MRSA has developed into a hazard to public health because of its ability to spread globally and cause infections in livestock (LA-MRSA), the general public (CA-MRSA), and hospitals (HA-MRSA) (Khairullah et al., 2020b). Multiple nations throughout the world have documented MRSA infections in poultry, highlighting the rising rates of antibiotic resistance, particularly in recently isolated strains (Hossain et al., 2022; Lee et al., 2022; Igbinosa et al., 2023).

The LA-MRSA strains are common in the environment of poultry farming and are a part of the typical bacterial microbiota on the skin and mucous membranes of healthy animals, including chickens and pigeons (El-Ghany, 2021). Chicken skin, feathers, respiratory tracts, and digestive tracts can all yield LA-MRSA isolates, much like in people and other animals (Bernier-Lachance et al., 2020). Concerns about the spread of LA-MRSA from poultry farms to meat intended need for human consumption have been raised as LA-MRSA strains have been identified in chicken meat from a number of different geographical locations (Dhup et al., 2015). However, human LA-MRSA strains have also been recovered from poultry, demonstrating poor hygienic and sanitary practices during the processing or slaughter of chicken (Schouls et al., 2022).

The need for high-quality feeds and increased food safety has resulted in a rise in interest in LA-MRSA in animals used for food production, such as poultry (Dweba et al., 2018). Due to increased demand, the production, processing, and distribution of chicken meat products are intensified, which increases the risk of LA-MRSA transmission and its subsequent spread across the entire meat production chain (Sadiq et al., 2020). Different forms of poultry meat, including chicken, turkey, and duck, exhibit LA-MRSA infection, but chicken meat is thought to be the main LA-MRSA reservoir (Kasela et al., 2023).

The hazards to human health make the expansion of LA-MRSA on poultry farms a serious concern (Cuny et al., 2015). The main dangers are related to the LA-MRSA strain's ability to produce *Staphylococcal* enterotoxin, which can result in *Staphylococcus* foodborne disease

(Mekhloufi et al., 2021). Cross-contamination, eating undercooked meat, and handling raw meat can all result in LA-MRSA infection (Plaza-Rodríguez et al., 2019; Khairullah et al., 2019) The purpose of writing this review is to explain the epidemiology, transmission, risk factors, public health impact, and control of LA-MRSA spread in poultry.

#### **Livestock-associated methicillin-resistant *S. aureus* (LA-MRSA)**

The MRSA strain was first identified as a nosocomial pathogen (HA-MRSA), usually in hospital settings. However, in recent years, reports have indicated the acquisition and circulation of MRSA in community settings (CA-MRSA) and agricultural settings (LA-MRSA) (Kalligeros et al., 2019; Tyasningsih et al., 2022). MRSA is a significant pathogen connected to the management of livestock and has been linked to a variety of illnesses such as localized skin infections, and systemic illnesses (toxic shock syndrome), amongst others (Hosain et al., 2021; Khairullah et al., 2023a). The emergence of the LA-MRSA strain has become a significant public health issue (Anjum et al., 2019; Yunita et al., 2020).

Based on the inclusion of a low-affinity penicillin-binding protein (PBP) of subclass B1, known as PBP2a or PBP2', LA-MRSA strains have been identified by their phenotypic  $\beta$ -lactam resistance (Fergestad et al., 2020). The intrinsic resistance of MRSA to  $\beta$ -lactam antibiotics is due to the presence of an altered PBP-encoding gene called *mec* (such as *mecA* and *mecC*). The *mec* gene is harbored on a region of the LA-MRSA bacterial chromosome called *Staphylococcal* cassette chromosome *mec* (SCC*mec*) (Masaisa et al., 2018; Ou et al., 2020).

The PBP 2a (PBP 2a), which is an important enzyme for the formation of peptidoglycan in bacterial cell walls, is encoded by the *mec* gene (Wacnik et al., 2022). When compared to other PBP, PBP 2a has a reduced affinity for binding to  $\beta$ -lactams and other antibiotics produced from penicillin, therefore it can still catalyze the manufacture of bacterial cell walls in the presence of various antibiotics (Young et al., 2022). As a result, LA-MRSA strains that produce PBP 2a can proliferate in the presence of numerous drugs and are resistant to a variety of antibiotics (Ghahremani et al., 2018). The majority of LA-MRSA strains are resistant to cephalosporins, nafcillin, methicillin, and oxacillin (Gajdacs, 2019).

LA-MRSA isolates with clonal complex 398 (CC398) are hardly ever discovered to possess the enterotoxin gene, and its absence in cases of food poisoning has not yet been recorded (Lienen et al., 2021). The immune evasion gene cluster (IEC), which is located on prophage and is typical of *S. aureus* in humans, can be recovered by LA-MRSA CC398; however, this may change with time as some kinds of IEC can carry the *sea* gene (Khairullah et al., 2023b). A recent study found that only one isolate of the LA-MRSA CC398 strain

reporting 19% of infections in humans carried the *sea* gene (Hansen *et al.*, 2020). There haven't been any LA-MRSA CC398 isolates discovered in pigs yet, although one strain with *sea* genes has been discovered among the LA-MRSA CC398 isolates reported in horses (Butaye *et al.*, 2016). The presence of LA-MRSA CC398 in milk tanks shows LA-MRSA colonization in udders and produces cases of subclinical mastitis in dairy cows (Titouche *et al.*, 2022). In the meantime, domestic and commercial rabbits have also been found to carry LA-MRSA CC398 (Moreno-Grúa *et al.*, 2018).

#### **LA-MRSA in poultry**

LA-MRSA has spread to different animal groups, seemingly through distinct pathways (Silva *et al.*, 2022). The use of antibiotics in animals is a cause of the emergence and spread of LA-MRSA, and close contact between people and various animal species raises the possibility of animal exposure to humans (Dorado-García *et al.*, 2013; Hamad *et al.*, 2023). The LA-MRSA strain in chicken was first isolated from a case of arthritis in South Korea, and since then, more germs have been discovered in both live poultry and food products with poultry origins (Kitai *et al.*, 2005). LA-MRSA has been found in poultry, which has drawn attention to the rising antibiotic resistance rates, particularly in recently discovered strains (Ježak and Kozajda, 2022). Animal meat of all kinds, including raw and frozen chicken and turkey, is contaminated with LA-MRSA (Parvin *et al.*, 2021). However, chicken flesh is thought to be a significant LA-MRSA reservoir (Hado and Assafi, 2021).

Several LA-MRSA experiments in poultry have been conducted, and two reports describe the isolation of LA-MRSA from both healthy and ill hens; however, there are few data on prevalence and incidence (Boumar-Kechih *et al.*, 2018; Musawa *et al.*, 2020). According to three recent research, ST398 was isolated from healthy chickens in two of them, while human common epidemic (CC5) clones were found to predominate in another study that used defined isolates from diseased chickens (Nemati *et al.*, 2008; El-Adawy *et al.*, 2016; Rahimi and Karimi, 2016). The zoonotic potential of LA-MRSA ST398 is supported by reports of colonization in people who frequently come into contact with poultry, placing them at high risk of getting the bacteria and raising concerns about food safety (Köck *et al.*, 2013). The ST398 LA-MRSA genome has undergone a thorough analysis, which has also shown the presence of several integrative conjugate elements, cellular genetic elements that confer antibiotic resistance, the absence of a restriction system, and type I modifications that can facilitate horizontal gene transfer (Zeggay *et al.*, 2023).

#### **Epidemiology**

Following the advent of ST398 and ST9 discovered in food-producing animals, the epidemiology of LA-MRSA in poultry substantially changed. As a result, numerous investigations have been carried

out to identify and characterize LA-MRSA isolates in chicken meat. In Germany, samples of excrement from turkey farms produced the majority of LA-MRSA strains (40%), whereas samples from broiler farms produced the least (25%) (Geenen *et al.*, 2013). On 18 of the 20 turkey farms inspected, LA-MRSA-contaminated dust was discovered, but only on 3 of the 50 chicken farms (Richter *et al.*, 2012). In addition to soil contamination, aerosols can potentially contribute to the spread of LA-MRSA (Feld *et al.*, 2018). In one investigation, the air from downwind pens on two out of five turkey farms was found to have LA-MRSA, but not the air from two broiler farms (Frieze *et al.*, 2013). To test this theory, additional research is required to ascertain the true frequency of LA-MRSA in poultry, to better understand the dynamics of this pathogen's transmission, and to assess the interactions between LA-MRSA and its hosts.

According to a recent meta-analysis of research, the prevalence of LA-MRSA in animals was estimated to be 4.1% in pigs, 2.5% in chickens, 5% in turkeys, and 2.6% in cattle, Turkey is the meat that is most frequently contaminated with LA-MRSA (Chen and Wu, 2021). LA-MRSA strains are found in human-eating chicken, turkey, and poultry meat, showing that LA-MRSA can spread across the supply chain (da Silva *et al.*, 2020). Additionally, LA-MRSA strains have been found in a variety of food products, such as raw and cooked beef, as well as poultry from Egypt, Tunisia, and Morocco (Benrabia *et al.*, 2020). In Egypt, 38% of retail raw chicken samples tested *mecA* PCR positive and 1.2% of raw chicken samples in Tunisia tested positive for LA-MRSA (Al-Ashmawy *et al.*, 2016; Said *et al.*, 2016). Mulders *et al.* (2010) found that there was a daily increase in bacterial contamination on the slaughter line and that poultry butchers' hands and the surrounding environment contained LA-MRSA. As a result, during the slaughter process, cross-infection between carcasses is possible, and LA-MRSA contamination of the environment and handlers' hands is also possible.

Poor hygiene from LA-MRSA-infected handlers who come into touch with carcasses or meat can contaminate food (Pérez-Boto *et al.*, 2023). It was discovered in the noses of broiler butchers in the Netherlands, Korea, and in the palms of chicken butchers in Egypt (Ribeiro *et al.*, 2018). LA-MRSA of poultry origin has also been reported in people (Crespo-Piazuelo and Lawlor, 2021). The LA-MRSA ST5 strain found in humans is unrelated to the type spa t002 LA-MRSA strain recovered from Turkey in the original manufacturing chain, which may have been of avian origin (Pantosti, 2012). Further research is necessary to address the significance of ST t002 in poultry and poultry meat (Nworie *et al.*, 2017). A meta-analysis study found that LA-MRSA was more common in poultry in North America (1%), Asia (2%), Europe (15%), Africa (16%), and South America (27%) (Olaru *et al.*, 2023).

The majority of these LA-MRSA isolates were identified using ST398. The prevalence of LA-MRSA has been reported in several European countries to range from 0% to 16% in broiler chickens and from 0% to 37% in chicken meat products (Sharma *et al.*, 2016). In Hong Kong, 6.8% of the 455 chicken meat samples purchased from retail establishments had LA-MRSA; the majority of these isolates belonged to ST9, whereas only one isolate was found to belong to ST398 (Boost *et al.*, 2013). In a Canadian investigation, 3 (1.2%) of the 250 chicken meat samples examined were positive for LA-MRSA. The most frequent source of HA-MRSA infection in Canada, epidemic Canadian MRSA-2 (CMRSA-2), often known as USA100, was identified in these three instances (Christianson *et al.*, 2007). Three of the 76 retail chicken samples in Detroit tested positive for LA-MRSA, all of which were identified as LA-MRSA ST8 (Bhargava *et al.*, 2011).

#### **Transmission**

LA-MRSA spreads quickly between people, animals, and the environment (Tuominen *et al.*, 2022). This strain can be spread via direct contact between animals and people as well as through contaminated surfaces, food, drink, and air (Astrup *et al.*, 2021; Waruwu *et al.*, 2023). A zoonotic risk from LA-MRSA linked to livestock exists for people, particularly farmers who work with cattle. There are possible horizontal transmission channels between humans and animals (Xing *et al.*, 2022).

The fact that the LA-MRSA strain can infect poultry highlights its significance and the zoonotic risk associated with handling and processing foods of avian origin (Belhout *et al.*, 2022). This bacterium strain becomes contaminated during food processing because of poor hygiene procedures involving chicken meat (Sudarmadi *et al.*, 2020). However, other factors that contribute to food contamination with LA-MRSA include poor food handler technique, poor meat storage, poor cooking, and poor food preparation using contaminated water (Kadariya *et al.*, 2014). Unless properly handled and butchered, poultry meat can get contaminated with LA-MRSA (Thwala *et al.*, 2021). *Staphylococcus aureus* has demonstrated a negative impact on the quality and output of chicken meat, in contrast to other forms of bacteria, particularly the LA-MRSA strain (Wu *et al.*, 2018).

Consuming tainted meat or coming into close touch with live chickens or their droppings are two ways that people can contract LA-MRSA from poultry (Gržinić *et al.*, 2023). In a study conducted in Algeria, LA-MRSA and *S. aureus* isolated from poultry were found to be more resistant to  $\beta$ -lactam antibiotics, particularly penicillin and oxacillin, than those from cattle (Vanderhaeghen *et al.*, 2010). According to the study, treating the spread of LA-MRSA from poultry to humans is more challenging than treating the spread of LA-MRSA from cows to humans (Dong *et al.*, 2021). In poultry farms, chicken excrement can also be a source of LA-MRSA infection (Tao *et al.*, 2021).

In hospitals, LA-MRSA-infected patients who have recovered can be a significant source of MRSA transmission for healthy people, such as healthcare professionals; as a result, these patients can spread the infection to those who aren't affected (Shoib *et al.*, 2023). Additionally, after touching contaminated animals, tools, or products, there is a chance that LA-MRSA will be transmitted from infected humans to animals or from infected animals to humans (Murra *et al.*, 2019; Tyasningsih *et al.*, 2019).

#### **Risk factors**

Compared to the general population, people who work with poultry are more likely to be infected with LA-MRSA (Zomer *et al.*, 2017). Farmers have an LA-MRSA prevalence of 18.2%, veterinarians have a prevalence of 9.4%, poultry slaughterhouse employees have a prevalence of 2.6%, and butchers have an LA-MRSA prevalence of 5.7% (Chen and Wu, 2021). The intensity of everyday exposure to livestock is the primary cause of the high frequency of MRSA among poultry farmers (Geenen *et al.*, 2013). According to Van Cleef *et al.* (2014), up to 98% of farmers who spent 10 hours a day working in chicken coops had LA-MRSA colonization.

According to Mulders *et al.* (2010), standard stunning procedures and hanger work in broiler slaughterhouses increase workers' risk of MRSA exposure by 20.3%. This occurs as a result of extensive contact with animals. According to the study, using conventional stunning techniques can result in an increase in dust that is contaminated with LA-MRSA because of the excessive flapping of dying chickens' wings, and dust has been identified as a route for the transfer of LA-MRSA from animals to people (Bernier-Lachance *et al.*, 2020). Dust has been defined as a route for the transfer of LA-MRSA from animals to humans.

One of the established factors contributing to the growth of resistant bacteria is the use of antibiotics, particularly in the context of chicken production (Kousar *et al.*, 2021). Antibiotic resistance can become more common when taken at sub-therapeutic levels (Yanestria *et al.*, 2022). According to Mancuso *et al.* (2021), the usage of tetracyclines, aminoglycosides, and macrolides led to LA-MRSA becoming more resistant to these antibiotics and causing adaptation. These resistance genes can be horizontally passed through animal digestion and eventually turn into environmental pollutants (Dameanti *et al.*, 2023). LA-MRSA can then spread from animals to people through cross-contamination (Aires-de-Sousa, 2017).

Residents who live close to poultry farming areas (an average distance of 2,500 to 4,500 meters) are 15% more likely to contract LA-MRSA infection, according to a population-based study by Friese *et al.* (2013) done in Denmark. Even though there was no direct contact with poultry, the study by Zomer *et al.* (2017) revealed that LA-MRSA colonization increased among those

who lived 500–1,000 m away from chicken farms. Exposure to an LA-MRSA-contaminated environment, such as using poultry feces, results in LA-MRSA colonization (Hamza *et al.*, 2020).

Moving chickens between cages can increase the danger of LA-MRSA spreading from poultry to people (Bernier-Lachance *et al.*, 2020). Despite routine cleaning of the containers, the study by Mulders *et al.* (2010) showed that MRSA could still be transmitted from chicken transport containers to abattoir personnel. This is consistent with research done by Ribeiro *et al.* (2018), which found that the rate of LA-MRSA transmission is four times higher on chicken farms that acquire chickens from LA-MRSA-free farms than it is on chicken farms that receive chickens from LA-MRSA-identified farms.

The presence of LA-MRSA contamination in chicken-derived food products is another risk factor for the spread of the pathogen from poultry to humans (Musawa *et al.*, 2020). The contamination of raw chicken meat was reported to be 65% by Kitai *et al.* (2005), 7.7% by Weese *et al.* (2010), and 11.9% by de Boer *et al.* (2009). Chicken meat contaminated with *S. aureus* bacteria which are known to be prevalent bacterial agents that cause skin illnesses in animals can happen during the slaughter of fowl colonized by LA-MRSA (Rortana *et al.*, 2021). According to Kluytmans (2010), the risk of LA-MRSA transmission through food items of animal origin relies on how well hygiene and sanitation are practiced, how much LA-MRSA is present in the product, and the capacity of the LA-MRSA strain to colonize people.

#### **Public health impact**

There is scientific agreement that people who come into direct touch with chickens can become colonized and subsequently infected with LA-MRSA; the person being discussed is a breeder, a doctor, or a worker at a chicken slaughterhouse (Crespo-Piazuelo and Lawlor, 2021). The poultry slaughterhouse employees showed very high rates of LA-MRSA transmission, especially those hanging broilers in slaughterhouses, demonstrating a direct correlation between the spread of animal and human diseases from LA-MRSA CC398 (Ivbule *et al.*, 2017). The method of stunning selected also influences the risk of LA-MRSA transfer to personnel, with traditional electrical stunning posing a higher risk than CO<sub>2</sub> stunning (Crombé *et al.*, 2013). Environmental LA-MRSA contamination in poultry farming contributes to the spread of LA-MRSA to farmers and members of their households (Tao *et al.*, 2021). Particularly among poultry producers who are highly exposed and have frequent contact with animals, nasal LA-MRSA colonization appears to be influenced by exposure to LA-MRSA CC398 in cage air (Cuny *et al.*, 2019).

The LA-MRSA ascribed to CC398 is most likely methicillin-resistant *S. aureus* (Kittler *et al.*, 2019). While the acquisition of tetracycline and methicillin

resistance by these bacteria was the result of human-to-farm transmission, it may have also resulted in decreased colonization and transmission potential in humans (Mehndiratta and Bhalla, 2014). Recently, it was established that LA-MRSA CC398 developed in the late 1990s and diverged into genotypes that were unique to particular herds, remaining largely constant over time (Effelsberg *et al.*, 2019). However, LA-MRSA CC398 was discovered to have a greater capacity to acquire mobile genetic elements (Laumay *et al.*, 2021). It has been demonstrated by Kraushaar *et al.* (2017) that the LA-MRSA strain CC398 is capable of virulence-associated lysogenic conversion *in vitro*, which can result in the emergence of novel pathotypes. The LA-MRSA CC398 strain, which has the *pvl* virulence factor, is particularly concerning *in vivo*; initial reports of hospitalization and fatalities have been made (Boswihi *et al.*, 2020). Intriguingly, LA-MRSA clone CC398 (ST1232), single locus variant ST398 has been linked to two human cases in Tokyo, Japan, in patients who had no interaction with poultry or people who worked or lived with poultry (Nakaminami *et al.*, 2020).

Long recognized as a risk factor for LA-MRSA infection are patients having surgery (Fraser *et al.*, 2010). Longitudinal research of high-risk occupational groups is necessary to determine the actual incidence of LA-MRSA infection as a result of occupational exposure, but such a study is not yet available (Golob *et al.*, 2022). Additionally, persistence and recolonization make it more difficult to create effective prevention techniques to reduce the risk of LA-MRSA infection in people who come into contact with poultry at work (Benrabia *et al.*, 2020). A 2-year study that routinely screened veterinarians for LA-MRSA colonization discovered that 44% of them were LA-MRSA carriers at one or more measurement time periods, with 13% being persistently infected with the same strain (Van Cleef *et al.*, 2016). The use of topical mupirocin nasal spray or ointment together with body washes containing chlorhexidine, polyhexanide, or octenidine is a common component of decolonization techniques (Hoang *et al.*, 2021). Mupirocin is effective against about 95% of LA-MRSA in poultry; however, there are no comparable data evaluating the efficiency of chlorhexidine, octenidine, or polyhexanide *in vitro* (George *et al.*, 2017).

#### **Control**

Making measures to prevent contamination along the entire chicken production chain is necessary for the prevention of LA-MRSA infection and diseases of poultry origin. Strategies to reduce the introduction and spread of LA-MRSA in primary production include the identification of contamination sources, management approaches that restrict animal exposure to pathogens, and the use of hygienic practices like cleaning and disinfecting, including all ventilation systems, before stocking chickens in empty pens (Ribeiro *et al.*, 2018).

At several stages of the chicken production chain, hazard analysis and critical control point systems, good manufacturing practices, and sanitation guidelines outlined in the Code of Hygienic Practice for Meat are all regularly monitored, as is the prevalence of LA-MRSA (Sadiq *et al.*, 2020). The development of LA-MRSA microbiological standards in poultry can aid in the evaluation of the microbiological safety and quality of chicken meat meant for human consumption (Silva *et al.*, 2021).

The use of masks can be beneficial for avoiding the spread of LA-MRSA from people to poultry, lowering the danger of secondary transmission to the environment, and giving personal protection against LA-MRSA (Nadimpalli *et al.*, 2018). LA-MRSA transmission from stable dust to humans can be successfully reduced by up to 37% using a respirator mask of type P2 (3M 8822) (Angen *et al.*, 2019). Farmers should constantly wash their hands with antiseptic after handling poultry, replace their gloves whenever a cage is changed, and keep the tools they use to handle chicken flesh clean in order to prevent the spread of LA-MRSA between them and the animals (Dweba *et al.*, 2018). According to Geenen *et al.* (2013), broiler farms should have amenities like changing rooms or sterilization rooms to prevent the spread of LA-MRSA to the home environment.

In the livestock industry, it should be against the law to use antibiotics without a veterinarian's supervision and prescription (Effendi *et al.*, 2018; Patel *et al.*, 2020; Putra *et al.*, 2023). Prior to distribution, routine testing for antibiotic residues in food products of animal origin must be done (Ghimpețeanu *et al.*, 2022; Baéza *et al.*, 2022). Antibiotic use can be decreased by using supplements, prebiotics, probiotics, and synbiotics (Newman and Arshad, 2020; Afnani *et al.*, 2022). According to Kwoji *et al.* (2019), decreased use of antibiotics resulted in an MRSA burden in chickens. The significance of LA-MRSA colonization and infection screening in farmers and their families is to stop and lessen the prevalence of LA-MRSA transmission in hospitals and healthcare facilities (Monaco *et al.*, 2013). Enhancing biosecurity and implementing LA-MRSA testing when purchasing fresh poultry will stop LA-MRSA from getting into the coop (Nhung *et al.*, 2017; Liebhart *et al.*, 2023). Three skin samples and environmental samples should be collected from newly obtained chickens for MRSA testing (Tao *et al.*, 2021). A recommendation is made to cull any poultry that has been identified as having LA-MRSA (Abdullahi *et al.*, 2023).

### Conclusion

The risks to human health make the spread of LA-MRSA on poultry farms a significant issue. Establishing microbiological guidelines for LA-MRSA in poultry can be useful in determining the microbiological safety and quality of chicken meat intended for human consumption.

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#### Author's contributions

ARK, KHPR, SCR, and IBM drafted the manuscript. MHE, OSMS, and DAA revised and edited the manuscripts. MKJK, IF, and KAF took part in preparing and critically checking the manuscript. RR, AH, AW, and SMY edited the references. All authors read and approved the final manuscript.

#### Conflict of interest

The authors declare that there is no conflict of interest.

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#### Data availability

All references are open access, so data can be obtained from the online web.

### References

- Abdullahi, I.N., Lozano, C., Saidenberg, A.B.S., Latorre-Fernández, J., Zarazaga, M. and Torres, C. 2023. Comparative review of the nasal carriage and genetic characteristics of *Staphylococcus aureus* in healthy livestock: Insight into zoonotic and anthroponotic clones. *Infect. Genet. Evol.* 109(1), 105408.
- Abreu, R., Semedo-Lemsaddek, T., Cunha, E., Tavares, L. and Oliveira, M. 2023. Antimicrobial drug resistance in poultry production: current status and innovative strategies for bacterial control. *Microorganisms* 11(4), 953.
- Afnani, D.A., Fatih, N., Effendi, M.H., Tyasningsih, W., Kairullah, A.R., Kurniawan, S.C., Silaen, O.S.M., Ramandianto, S.C., Widodo, A., Hendriana, K. and Riwu, K.H.P. 2022. Profile of multidrug resistance and methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from cats in Surabaya, Indonesia. *Biodiversitas* 23(11), 5703–5709.
- Aires-de-Sousa, M. 2017. Methicillin-resistant *Staphylococcus aureus* among animals: current overview. *Clin. Microbiol. Infect.* 23(6), 373–380.
- Al-Ashmawy, M.A., Sallam, K.I., Abd-Elghany, S.M., Elhadidy, M. and Tamura, T. 2016. Prevalence, molecular characterization, and antimicrobial susceptibility of methicillin-resistant *Staphylococcus aureus* isolated from milk and dairy products. *Foodborne Pathog. Dis.* 13(3), 156–162.
- Angen, Ø., Skade, L., Urth, T.R., Andersson, M., Bækbo, P. and Larsen, A.R. 2019. Controlling transmission of MRSA to Humans during short-term visits to swine farms using dust masks. *Front. Microbiol.* 9(1), 3361.
- Anjum, M.F., Marco-Jimenez, F., Duncan, D., Marín, C., Smith, R.P. and Evans, S.J. 2019. Livestock-

- associated methicillin-resistant *Staphylococcus aureus* from animals and animal products in the UK. *Front. Microbiol.* 10(1), 2136.
- Astrup, L.B., Hansen, J.E. and Pedersen, K. 2021. Occurrence and survival of livestock-associated MRSA in pig manure and on agriculture fields. *Antibiotics (Basel)* 10(4), 448.
- Baéza, E., Guillier, L. and Petracci, M. 2022. Review: production factors affecting poultry carcass and meat quality attributes. *Animal* 16(Suppl 1), 100331.
- Belhout, C., Elgroud, R. and Butaye, P. 2022. Methicillin-resistant *Staphylococcus aureus* (MRSA) and other methicillin-resistant staphylococci and mammaliococcus (MRNaS) associated with animals and food products in Arab Countries: a review. *Vet. Sci.* 9(7), 317.
- Benrabia, I., Hamdi, T.M., Shehata, A.A., Neubauer, H. and Wareth, G. 2020. Methicillin-resistant *Staphylococcus aureus* (MRSA) in poultry species in Algeria: long-term study on prevalence and antimicrobial resistance. *Vet. Sci.* 7(2), 54.
- Bernier-Lachance, J., Arsenault, J., Usongo, V., Parent, É., Labrie, J., Jacques, M., Malouin, F. and Archambault, M. 2020. Prevalence and characteristics of livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) isolated from chicken meat in the province of Quebec, Canada. *PLoS One* 15(1), e0227183.
- Bhargava, K., Wang, X., Donabedian, S., Zervos, M., de Rocha, L. and Zhang, Y. 2011. Methicillin-resistant *Staphylococcus aureus* in retail meat, Detroit, Michigan, USA. *Emerg. Infect. Dis.* 17(6), 1135–1137.
- Boost, M.V., Wong, A., Ho, J. and O'Donoghue, M. 2013. Isolation of methicillin-resistant *Staphylococcus aureus* (MRSA) from retail meats in Hong Kong. *Foodborne Pathog. Dis.* 10(8), 705–710.
- Boswihi, S.S., Udo, E.E., Mathew, B., Noronha, B., Verghese, T. and Tappa, S.B. 2020. Livestock-associated methicillin-resistant *Staphylococcus aureus* in patients admitted to Kuwait Hospitals in 2016–2017. *Front. Microbiol.* 10(1), 2912.
- Bounar-Kechih, S., Hamdi, M.T., Aggad, H., Meguenni, N. and Cantekin, Z. 2018. Carriage methicillin-resistant *Staphylococcus aureus* in poultry and cattle in Northern Algeria. *Vet. Med. Int.* 2018(1), 4636121.
- Butaye, P., Argudín, M.A. and Smith, T.C. 2016. Livestock-associated MRSA and its current evolution. *Curr. Clin. Micro. Rpt.* 3(1), 19–31.
- Chen, C. and Wu, F. 2021. Livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) colonisation and infection among livestock workers and veterinarians: a systematic review and meta-analysis. *Occup. Environ. Med.* 78(1), 530–540.
- Christianson, S., Golding, G.R., Campbell, J. and Mulvey, M.R. 2007. Comparative genomics of Canadian epidemic lineages of methicillin-resistant *Staphylococcus aureus*. *J. Clin. Microbiol.* 45(6), 1904–1911.
- Crespo-Piazuelo, D. and Lawlor, P.G. 2021. Livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) prevalence in humans in close contact with animals and measures to reduce on-farm colonisation. *Ir. Vet. J.* 74(1), 21.
- Crombé, F., Argudín, M.A., Vanderhaeghen, W., Hermans, K., Haesebrouck, F. and Butaye, P. 2013. Transmission dynamics of methicillin-resistant *Staphylococcus aureus* in Pigs. *Front. Microbiol.* 4(1), 57.
- Cuny, C., Layer, F., Hansen, S., Werner, G. and Witte, W. 2019. Nasal colonization of humans with occupational exposure to raw meat and to raw meat products with methicillin-susceptible and methicillin-resistant *Staphylococcus aureus*. *Toxins (Basel)* 11(4), 190.
- Cuny, C., Wieler, L.H. and Witte, W. 2015. Livestock-associated MRSA: the impact on humans. *Antibiotics (Basel)* 4(4), 521–543.
- da Silva, A.C., Rodrigues, M.X. and Silva, N.C.C. 2020. Methicillin-resistant *Staphylococcus aureus* in food and the prevalence in Brazil: a review. *Braz. J. Microbiol.* 51(1), 347–356.
- Dameanti, F.N.A.P., Yanestria, S.M., Widodo, A., Effendi, M.H., Plumeriastuti, H., Tyasningsih, W., Sutrisno, R. and Akramsyah, M.A. 2023. Incidence of *Escherichia coli* producing extended-spectrum beta-lactamase (ESBL) in wastewater of dairy farms in East Java, Indonesia. *Biodiversitas* 24(2), 1143–1150.
- de Boer, E., Zwartkruis-Nahuis, J.T., Wit, B., Huijsdens, X.W., de Neeling, A.J., Bosch, T., van Oosterom, R.A., Vila, A. and Heuvelink, A.E. 2009. Prevalence of methicillin-resistant *Staphylococcus aureus* in meat. *Int. J. Food Microbiol.* 134(1–2), 52–56.
- Dhup, V., Kearns, A.M., Pichon, B. and Foster, H.A. 2015. First report of identification of livestock-associated MRSA ST9 in retail meat in England. *Epidemiol. Infect.* 143(14), 2989–2992.
- Dong, Q., Liu, Y., Li, W., Liu, Y. and Ye, X. 2021. Cross-species transmission risk of livestock-associated MRSA: a systematic review and Bayesian meta-analysis of global data. *Prev. Vet. Med.* 194(1), 105429.
- Dorado-García, A., Bos, M.E., Graveland, H., Van Cleef, B.A.G.L., Verstappen, K.M., Kluytmans, J.A.J.W., Wagenaar, J.A. and Heederik, D.J. 2013. Risk factors for persistence of livestock-associated MRSA and environmental exposure in veal calf farmers and their family members: an observational longitudinal study. *BMJ Open* 3(9), e003272.

- Dweba, C.C., Zishiri, O.T. and El Zowalaty, M.E. 2018. Methicillin-resistant *Staphylococcus aureus*: livestock-associated, antimicrobial, and heavy metal resistance. *Infect. Drug Resist.* 11(1), 2497–2509.
- Effelsberg, N., Udarcsev, S., Müller, H., Kobusch, I., Linnemann, S., Boelhaue, M., Köck, R. and Mellmann, A. 2019. Genotypic characterization of livestock-associated methicillin-resistant *Staphylococcus aureus* isolates of clonal complex 398 in Pigsty visitors: transient carriage or persistence? *J. Clin. Microbiol.* 58(1), e01276–19.
- Effendi, M.H., Oktavianto, A. and Hastutiek, P. 2018. Tetracycline Resistance Gene In Streptococcus agalactiae Isolated From Bovine Subclinical Mastitis In Surabaya, Indonesia. *Philip. J. Vet. Med.* 55(SI), 115–120.
- El-Adawy, H., Ahmed, M., Hotzel, H., Monecke, S., Schulz, J., Hartung, J., Ehrlich, R., Neubauer, H. and Hafez, H.M. 2016. Characterization of methicillin-resistant *Staphylococcus aureus* isolated from healthy turkeys and broilers using DNA Microarrays. *Front. Microbiol.* 7(1), 2019.
- El-Ghany, W.A.A. 2021. *Staphylococcus aureus* in poultry, with special emphasis on methicillin-resistant strain infection: a comprehensive review from one health perspective. *Int. J. One Health* 7(2), 257–267.
- Feld, L., Bay, H., Angen, Ø., Larsen, A.R. and Madsen, A.M. 2018. Survival of LA-MRSA in dust from swine farms. *Ann. Work Expo. Health* 62(2), 147–156.
- Fergestad, M.E., Stamsås, G.A., Angeles, D.M., Salehian, Z., Wasteson, Y. and Kjos, M. 2020. Penicillin-binding protein PBP2a provides variable levels of protection toward different  $\beta$ -lactams in *Staphylococcus aureus* RN4220. *Microbiologyopen* 9(8), e1057.
- Fraser, S., Brady, R.R., Graham, C., Paterson-Brown, S. and Gibb, A.P. 2010. Methicillin-resistant *Staphylococcus aureus* in surgical patients: identification of high-risk populations for the development of targeted screening programmes. *Ann. R. Coll. Surg. Engl.* 92(4), 311–315.
- Friese, A., Schulz, J., Zimmermann, K., Tenhagen, B.A., Fetsch, A., Hartung, J. and Rösler, U. 2013. Occurrence of livestock-associated methicillin-resistant *Staphylococcus aureus* in Turkey and broiler barns and contamination of air and soil surfaces in their vicinity. *Appl. Environ. Microbiol.* 79(8), 2759–2766.
- Gajdács, M. 2019. The continuing threat of methicillin-resistant *Staphylococcus aureus*. *Antibiotics (Basel)* 8(2), 52.
- Geenen, P.L., Graat, E.A., Haenen, A., Hengeveld, P.D., Van Hoek, A.H., Huijsdens, X.W., Kappert, C.C., Lammers, G.A., Van Duijkeren, E. and Van De Giessen, A.W. 2013. Prevalence of livestock-associated MRSA on Dutch broiler farms and in people living and/or working on these farms. *Epidemiol. Infect.* 141(5), 1099–1108.
- Ghimpețeanu, O.M., Pogurschi, E.N., Popa, D.C., Dragomir, N., Drăgotoiu, T., Mihai, O.D. and Petcu, C.D. 2022. Antibiotic use in livestock and residues in food-a public health threat: a review. *Foods* 11(10), 1430.
- Ghahremani, M., Jazani, N.H. and Sharifi, Y. 2018. Emergence of vancomycin-intermediate and -resistant *Staphylococcus aureus* among methicillin-resistant *S. aureus* isolated from clinical specimens in the northwest of Iran. *J. Glob. Antimicrob. Resist.* 14(1), 4–9.
- Goerge, T., Lorenz, M.B., van Alen, S., Hübner, N.O., Becker, K. and Köck, R. 2017. MRSA colonization and infection among persons with occupational livestock exposure in Europe: prevalence, preventive options and evidence. *Vet. Microbiol.* 200(1), 6–12.
- Golob, M., Pate, M., Kušar, D., Zajc, U., Papić, B., Očepek, M., Zdovc, I. and Avberšek, J. 2022. Antimicrobial resistance and molecular characterization of methicillin-resistant *Staphylococcus aureus* from two pig farms: longitudinal study of LA-MRSA. *Antibiotics (Basel)* 11(11), 1532.
- Gržinić, G., Piotrowicz-Cieślak, A., Klimkowicz-Pawlas, A., Górny, R.L., Ławniczek-Walczuk, A., Piechowicz, L., Olkowska, E., Potrykus, M., Tankiewicz, M., Krupka, M., Siebielec, G. and Wolska, L. 2023. Intensive poultry farming: a review of the impact on the environment and human health. *Sci. Total Environ.* 858(Pt 3), 160014.
- Hado, H.A. and Assafi, M.S. 2021. Molecular fingerprinting of methicillin resistant *Staphylococcus aureus* strains isolated from human and poultry in Duhok, Iraq. *Iraqi J. Vet. Sci.* 35(1), 99–103.
- Hamad, G., Amer, A., Kirrella, G., Mehany, T., Elfayoumy, R.A., Elsabagh, R., Elghazaly, E.M., Esatbeyoglu, T., Taha, A. and Zeitoun, A. 2023. Evaluation of the prevalence of *Staphylococcus aureus* in chicken fillets and its bio-control using different seaweed extracts. *Foods* 12(1), 20.
- Hamza, D.A., Abd-Elsalam, R.M., Nader, S.M., Elhariri, M., Elhelw, R. and El-Mahallawy, H.S. 2020. Pathways of methicillin-resistant *Staphylococcus aureus* in animal model: new insights regarding public health. *Infect. Drug Resist.* 13(1), 1593–1600.
- Hansen, J.E., Stegger, M., Pedersen, K., Sieber, R.N., Larsen, J., Larsen, G., Lilje, B., Chriél, M., Andersen, P.S. and Larsen, A.R. 2020. Spread of LA-MRSA CC398 in Danish mink (*Neovison vison*) and mink farm workers. *Vet. Microbiol.* 245(1), 108705.



- Hoang, T.P.N., Ghorri, M.U. and Conway, B.R. 2021. Topical antiseptic formulations for skin and soft tissue infections. *Pharmaceutics* 13(4), 558.
- Hosain, M.Z., Kabir, S.M.L. and Kamal, M.M. 2021. Antimicrobial uses for livestock production in developing countries. *Vet. World* 14(1), 210–221.
- Hossain, M.J., Sohidullah, M., Alam, M.A., Al Mamun, M.S., Badr, Y., Altaib, H. and Rahman, M. 2022. Molecular detection of methicillin resistant *Staphylococcus aureus* (MRSA) in poultry in Bangladesh: having public health significance. *Eur. J. Vet. Med.* 2(6), 17–21.
- Igbinsola, E.O., Beshiru, A., Igbinsola, I.H., Ogojire, A.G., Ekundayo, T.C. and Okoh, A.I. 2023. Prevalence, multiple antibiotic resistance and virulence profile of methicillin-resistant *Staphylococcus aureus* (MRSA) in retail poultry meat from Edo, Nigeria. *Front. Cell. Infect. Microbiol.* 13(1), 1122059.
- Ivbule, M., Miklaševičs, E., Čupāne, L., Bērziņa, L., Bālinš, A. and Valdovska, A. 2017. Presence of methicillin-resistant *Staphylococcus aureus* in Slaughterhouse environment, pigs, carcasses, and workers. *J. Vet. Res.* 61(3), 267–277.
- Ježak, K. and Kozajda, A. 2022. Occurrence and spread of antibiotic-resistant bacteria on animal farms and in their vicinity in Poland and Ukraine—review. *Environ. Sci. Pollut. Res.* 29(7), 9533–9539.
- Kadariya, J., Smith, T.C. and Thapaliya, D. 2014. *Staphylococcus aureus* and *Staphylococcal* food-borne disease: an ongoing challenge in public health. *Biomed. Res. Int.* 2014(1), 827965.
- Kalligeros, M., Shehadeh, F., Karageorgos, S.A., Zacharioudakis, I.M. and Mylonakis, E. 2019. MRSA colonization and acquisition in the burn unit: a systematic review and meta-analysis. *Burns* 45(7), 1528–1536.
- Kasela, M., Ossowski, M., Dzikon, E., Ignatiuk, K., Wlazlo, L. and Malm, A. 2023. The epidemiology of animal-associated methicillin-resistant *Staphylococcus aureus*. *Antibiotics* 12(6), 1079.
- Khairullah, A.R., Kurniawan, S.C., Effendi, M.H., Sudjarwo, S.A., Ramandinianto, S.C., Widodo, A., Riwu, K.H.P., Silaen, O.S.M. and Rehman, S. 2023a. A review of new emerging livestock-associated methicillin-resistant *Staphylococcus aureus* from pig farms. *Vet. World* 16(1), 46–58.
- Khairullah, A.R., Kurniawan, S.C., Silaen, O.S.M., Effendi, M.H., Sudjarwo, S.A., Ramandinianto, S.C., Gololodo, M.A., Widodo, A., Riwu, K.H.P., Kurniawati, D.A. and Rehman, S. 2023b. Methicillin resistant *Staphylococcus aureus* (MRSA) isolation and *mecA* gene detection from milk and farmer hand Swab in Tulungagung, Indonesia. *Trop. Anim. Sci. J.* 46(2), 231–238.
- Khairullah, A.R., Raharjo, D., Rahmahani, J., Suwarno, S., Tyasningsih, W. and Harijani, N. 2019. Antibiotics resistant at *Staphylococcus aureus* and *Streptococcus* sp isolated from bovine mastitis in Karangploso, East Java, Indonesia. *Indian J. Forensic Med. Toxicol.* 13(4), 439.
- Khairullah, A.R., Ramandinianto, S.C. and Effendi, M.H. 2020a. A Review of Livestock-Associated Methicillin-Resistant *Staphylococcus aureus* (LA-MRSA) on Bovine Mastitis. *Syst. Rev. Pharm.* 11(7), 172–183.
- Khairullah, A.R., Rehman, S., Sudjarwo, S.A., Effendi, M.H., Ramandinianto, S.C., Gololodo, M.A., Widodo, A., Riwu, K.H.P. and Kurniawati, D.A. 2022. Detection of *mecA* gene and methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from milk and risk factors from farms in Probolinggo, Indonesia. *F1000Res.* 11(1), 722.
- Khairullah, A.R., Sudjarwo, S.A., Effendi, M.H., Harijani, N., Tyasningsih, W., Rahmahani, J., Permatasari, D.A., Ramandinianto, S.C., Widodo, A. and Riwu, K.H.P. 2020b. A review of methicillin-resistant *Staphylococcus aureus* (MRSA) on Milk and milk products: public health importance. *Syst. Rev. Pharm.* 11(8), 59–69.
- Kitai, S., Shimizu, A., Kawano, J., Sato, E., Nakano, C., Uji, T. and Kitagawa, H. 2005. Characterization of methicillin-resistant *Staphylococcus aureus* isolated from retail raw chicken meat in Japan. *J. Vet. Med. Sci.* 67(1), 107–110.
- Kittler, S., Seinige, D., Meemken, D., Müller, A., Wendlandt, S., Ehrlich, R., Monecke, S. and Kehrenberg, C. 2019. Characteristics of methicillin-resistant *Staphylococcus aureus* from broiler farms in Germany are rather lineage- than source-specific. *Poult. Sci.* 98(12), 6903–6913.
- Kluytmans, J.A. 2010. Methicillin-resistant *Staphylococcus aureus* in food products: cause for concern or case for complacency? *Clin. Microbiol. Infect.* 16(1), 11–15.
- Köck, R., Schaumburg, F., Mellmann, A., Köksal, M., Jurke, A., Becker, K. and Friedrich, A.W. 2013. Livestock-associated methicillin-resistant *Staphylococcus aureus* (MRSA) as causes of human infection and colonization in Germany. *PLoS One* 8(1), e55040.
- Kousar, S., Rehman, N., Javed, A., Hussain, A., Naem, M., Masood, S., Ali, H.A., Manzoor, A., Khan, A.A., Akrem, A., Iqbal, F., Zulfiqar, A., Jamshaid, M.B., Waqas, M., Waseem, A. and Saeed, M.Q. 2021. Intensive poultry farming practices influence antibiotic resistance profiles in *Pseudomonas aeruginosa* inhabiting nearby soils. *Infect. Drug Resist.* 14(1), 4511–4516.
- Kraushaar, B., Hammerl, J.A., Kienöl, M., Heinig, M.L., Sperling, N., Thanh, M.D., Reetz, J., Jäckel, C., Fetsch, A. and Hertwig, S. 2017. Acquisition of virulence factors in livestock-associated MRSA: lysogenic conversion of CC398 strains by virulence gene-containing phages. *Sci. Rep.* 7(1), 2004.

- Kwoji, I.D., Jauro, S., Musa, J.A., Lekko, Y.M., Salihu, S.I. and Danchuwa, H.A. 2019. Phenotypic detection of methicillin-resistant *Staphylococcus aureus* in village chickens from poultry markets in Maiduguri, Nigeria. *J. Adv. Vet. Anim. Res.* 6(2), 163–167.
- Laumay, F., Benchetrit, H., Corvaglia, A.R., van der Mee-Marquet, N. and François, P. 2021. The *Staphylococcus aureus* CC398 Lineage: an evolution driven by the acquisition of prophages and other mobile genetic elements. *Genes (Basel)* 12(11), 1752.
- Lee, G.Y., Lee, S.I., Kim, S.D., Park, J.H., Kim, G.B. and Yang, S.J. 2022. Clonal distribution and antimicrobial resistance of methicillin-susceptible and -resistant *Staphylococcus aureus* strains isolated from broiler farms, slaughterhouses, and retail chicken meat. *Poult. Sci.* 101(10), 102070.
- Liebhart, D., Bilic, I., Grafl, B., Hess, C. and Hess, M. 2023. Diagnosing infectious diseases in poultry requires a holistic approach: a review. *Poultry* 2(2), 252–280.
- Lienen, T., Schnitt, A., Hammerl, J.A., Maurischat, S. and Tenhagen, B.A. 2021. Genomic distinctions of LA-MRSA ST398 on dairy farms from different German federal states with a low risk of severe human infections. *Front. Microbiol.* 11(1), 575321.
- Mancuso, G., Midiri, A., Gerace, E. and Biondo, C. 2021. Bacterial antibiotic resistance: the most critical pathogens. *Pathogens* 10(10), 1310.
- Masaisa, F., Kayigi, E., Seni, J., Bwanga, F. and Muvunyi, C.M. 2018. Antibiotic resistance patterns and molecular characterization of methicillin-resistant *Staphylococcus aureus* in clinical settings in Rwanda. *Am. J. Trop. Med. Hyg.* 99(5), 1239–1245.
- Mehndiratta, P.L. and Bhalla, P. 2014. Use of antibiotics in animal agriculture and emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) clones: need to assess the impact on public health. *Indian J. Med. Res.* 140(3), 339–344.
- Mekhloufi, O.A., Chieffi, D., Hammoudi, A., Bensefia, S.A., Fanelli, F. and Fusco, V. 2021. Prevalence, enterotoxigenic potential and antimicrobial resistance of *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from Algerian ready to eat foods. *Toxins (Basel)* 13(12), 835.
- Millannia, S.K., Khairullah, A.R., Effendi, M.H., Utama, S., Kurniawan, S.C., Afnani, D.A., Silaen, O.S.M., Ramadhani, S., Ramandinianto, S.C., Waruwu, Y.K.K., Widodo, A., Putra, G.D.S., Farizqi, M.T.I. and Riwu, K.H.P. 2023. Phenotypic detection strategies of multidrug-resistant *Staphylococcus aureus* isolated from cat nasal swab in Madiun city, Indonesia. *Biodiversitas* 24(2), 940–946.
- Monaco, M., Pedroni, P., Sanchini, A., Bonomini, A., Indelicato, A. and Pantosti, A. 2013. Livestock-associated methicillin-resistant *Staphylococcus aureus* responsible for human colonization and infection in an area of Italy with high density of pig farming. *BMC Infect. Dis.* 13(1), 258.
- Moreno-Grúa, E., Pérez-Fuentes, S., Muñoz-Silvestre, A., Viana, D., Fernández-Ros, A.B., Sanz-Tejero, C., Corpa, J.M. and Selva, L. 2018. Characterization of livestock-associated methicillin-resistant *Staphylococcus aureus* Isolates obtained from commercial rabbitries located in the Iberian Peninsula. *Front. Microbiol.* 9(1), 1812.
- Mulders, M.N., Haenen, A.P., Geenen, P.L., Vesseur, P.C., Poldervaart, E.S., Bosch, T., Huijsdens, X.W., Hengeveld, P.D., Dam-Deisz, W.D., Graat, E.A., Mevius, D., Voss, A. and Van De Giessen, A.W. 2010. Prevalence of livestock-associated MRSA in broiler flocks and risk factors for slaughterhouse personnel in The Netherlands. *Epidemiol. Infect.* 138(5), 743–755.
- Murra, M., Mortensen, K.L. and Wang, M. 2019. Livestock-associated methicillin-resistant *Staphylococcus aureus* (clonal complex 398) causing bacteremia and epidural abscess. *Int. J. Infect. Dis.* 81(1), 107–109.
- Musawa, I.A., Yakubu, Y., Garba, B., Ballah, F.M., Jibril, H.A., Bello, A.S., Sani, M.G. and Farida, A. 2020. Dressed chicken as potential vehicle for spread of methicillin-resistant *Staphylococcus aureus* in Sokoto, Nigeria. *Future Sci. OA* 6(10), FSO619.
- Nadimpalli, M.L., Stewart, J.R., Pierce, E., Pisanic, N., Love, D.C., Hall, D., Larsen, J., Carroll, K.C., Tekle, T., Perl, T.M. and Heaney, C.D. 2018. Face mask use and persistence of livestock-associated *Staphylococcus aureus* nasal carriage among industrial hog operation workers and household contacts, USA. *Environ. Health Perspect.* 126(12), 127005.
- Nakaminami, H., Hirai, Y., Nishimura, H., Takadama, S. and Noguchi, N. 2020. Arthritis caused by MRSA CC398 in a patient without animal contact, Japan. *Emerg. Infect. Dis.* 26(4), 795–797.
- Nemati, M., Hermans, K., Lipinska, U., Denis, O., Deplano, A., Struelens, M., Devriese, L.A., Pasmans, F. and Haesebrouck, F. 2008. Antimicrobial resistance of old and recent *Staphylococcus aureus* isolates from poultry: first detection of livestock-associated methicillin-resistant strain ST398. *Antimicrob. Agents Chemother.* 52(10), 3817–3819.
- Newman, A.M. and Arshad, M. 2020. The role of probiotics, prebiotics and synbiotics in combating multidrug-resistant organisms. *Clin. Ther.* 42(9), 1637–1648.
- Nhung, N.T., Chansiripornchai, N. and Carrique-Mas, J.J. 2017. Antimicrobial resistance in bacterial

- poultry pathogens: a review. *Front. Vet. Sci.* 4(1), 126.
- Nworie, A., Onyema, A.S., Okekpa, S.I., Elom, M.O., Umoh, N.O., Usanga, V.U., Ibiam, G.A., Ukwah, B.N., Nwadi, L.C., Ezeruigbo, C., Olayinka, B.O., Ehinmidu, J.O., Onaolapo, J.A., Hanson, B.M., Wardyn, S.E. and Smith, T.C. 2017. A novel methicillin-resistant *Staphylococcus aureus* t11469 and a poultry endemic strain t002 (ST5) are present in chicken in Ebonyi State, Nigeria. *Biomed. Res. Int.* 2017(1), 2936461.
- Olaru, I.D., Walther, B. and Schaumburg, F. 2023. Zoonotic sources and the spread of antimicrobial resistance from the perspective of low and middle-income countries. *Infect. Dis. Poverty* 12(1), 59.
- Ou, C., Shang, D., Yang, J., Chen, B., Chang, J., Jin, F. and Shi, C. 2020. Prevalence of multidrug-resistant *Staphylococcus aureus* isolates with strong biofilm formation ability among animal-based food in Shanghai. *Food Control* 112(1), 107106.
- Pantosti, A. 2012. Methicillin-resistant *Staphylococcus aureus* associated with animals and its relevance to human health. *Front. Microbiol.* 3(1), 127.
- Parvin, M.S., Ali, M.Y., Talukder, S., Nahar, A., Chowdhury, E.H., Rahman, M.T. and Islam, M.T. 2021. Prevalence and multidrug resistance pattern of methicillin resistant *S. aureus* isolated from frozen chicken meat in Bangladesh. *Microorganisms* 9(3), 636.
- Patel, S.J., Wellington, M., Shah, R.M. and Ferreira, M.J. 2020. Antibiotic Stewardship in food-producing animals: challenges, progress, and opportunities. *Clin. Ther.* 42(9), 1649–1658.
- Pérez-Boto, D., D'Arrigo, M., García-Lafuente, A., Bravo, D., Pérez-Baltar, A., Gaya, P., Medina, M. and Arqués, J.L. 2023. *Staphylococcus aureus* in the processing environment of cured meat products. *Foods* 12(11), 2161.
- Plaza-Rodríguez, C., Kaesbohrer, A. and Tenhagen, B.A. 2019. Probabilistic model for the estimation of the consumer exposure to methicillin-resistant *Staphylococcus aureus* due to cross-contamination and recontamination. *Microbiologyopen* 8(11), e900.
- Putra, G.D.S., Khairullah, A.R., Effendi, M.H., Lazuardi, M., Kurniawan, S.C., Afnani, D.A., Silaen, O.S.M., Waruwu, Y.K.K., Millannia, S.K., Widodo, A., Ramadhani, S., Farizqi, M.T.I. and Riwu, K.H.P. 2023. Detection of multidrug-resistant (MDR) *Staphylococcus aureus* isolated from dairies milk in Medowo Village of Kediri District, Indonesia. *Biodiversitas* 24(1), 423–430.
- Rahimi, F. and Karimi, S. 2016. Characteristics of methicillin resistant *Staphylococcus aureus* strains isolated from Poultry in Iran. *Arch. Clin. Infect. Dis.* 10(4), e30885.
- Rahmaniar, R.P., Yunita, M.N., Effendi, M.H. and Yanestria, S.M. 2020. Encoding gene for methicillin resistant *Staphylococcus aureus* (MRSA) isolated from Nasal Swab of Dogs. *Indian Vet. J.* 97(2), 37–40.
- Ramandinianto, S.C., Khairullah, A.R., Effendi, M.H. and Hestiana, E.P. 2020. Profile of multidrug resistance (MDR) and methicillin resistant *Staphylococcus aureus* (MRSA) on dairy farms in East Java Province, Indonesia. *Indian J. Forensic Med. Toxicol.* 14(4), 3439–3445.
- Ribeiro, C.M., Stefani, L.M., Lucheis, S.B., Okano, W., Cruz, J.C.M., Souza, G.V., Casagrande, T.A.C., Bastos, P.A.S., Pinheiro, R.R., Arruda, M.M. and Afreixo, V. 2018. Methicillin-resistant *Staphylococcus aureus* in poultry and poultry meat: a meta-analysis. *J. Food Prot.* 81(7), 1055–1062.
- Richter, A., Sting, R., Popp, C., Rau, J., Tenhagen, B.A., Guerra, B., Hafez, H.M. and Fetsch, A. 2012. Prevalence of types of methicillin-resistant *Staphylococcus aureus* in turkey flocks and personnel attending the animals. *Epidemiol. Infect.* 140(12), 2223–2232.
- Rortana, C., Nguyen-Viet, H., Tum, S., Unger, F., Boqvist, S., Dang-Xuan, S., Koam, S., Grace, D., Osbjør, K., Heng, T., Sarim, S., Phirum, O., Sophia, R. and Lindahl, J.F. 2021. Prevalence of *Salmonella spp.* and *Staphylococcus aureus* in chicken meat and pork from Cambodian markets. *Pathogens* 10(5), 556.
- Sadiq, A., Samad, M., Saddam, Basharat, N., Ali, S., Roohullah, Saad, Z., Khan, A.N., Ahmad, Y., Khan, A. and Khan, J. 2020. Methicillin-resistant *Staphylococcus aureus* (MRSA) in slaughter houses and meat shops in capital territory of Pakistan during 2018–2019. *Front. Microbiol.* 11(1), 577707.
- Said, M.B., Abbassi, M.S., Bianchini, V., Sghaier, S., Cremonesi, P., Romano, A., Gualdi, V., Hassen, A. and Luini, M.V. 2016. Genetic characterization and antimicrobial resistance of *Staphylococcus aureus* isolated from bovine milk in Tunisia. *Lett. Appl. Microbiol.* 63(6), 473–481.
- Schouls, L.M., Veldman, K., Brouwer, M.S.M., Dierikx, C., Witteveen, S., van Santen-Verheuevel, M., Hendrickx, A.P.A., Landman, F., Hengeveld, P., Wullings, B., Rapallini, M., Wit, B. and van Duijkeren E. 2022. *cfp* and *fexA* genes in methicillin-resistant *Staphylococcus aureus* from humans and livestock in The Netherlands. *Commun. Med.* 2(1), 135.
- Sharma, M., Nunez-Garcia, J., Kearns, A.M., Doumith, M., Butaye, P.R., Argudín, M.A., Lahuerta-Marin, A., Pichon, B., AbuOun, M., Rogers, J., Ellis, R.J., Teale, C. and Anjum, M.F. 2016. Livestock-associated methicillin resistant *Staphylococcus aureus* (LA-MRSA) clonal complex (CC) 398 isolated from UK animals belong to European Lineages. *Front. Microbiol.* 7(1), 1741.
- Shoib, M., Aqib, A.I., Muzammil, I., Majeed, N., Bhutta, Z.A., Kulyar, M.F., Fatima, M., Zaheer,

- C.F., Muneer, A., Murtaza, M., Kashif, M., Shafqat, F. and Pu, W. 2023. MRSA compendium of epidemiology, transmission, pathophysiology, treatment, and prevention within one health framework. *Front. Microbiol.* 13(1), 1067284.
- Silva, V., Monteiro, A., Pereira, J.E., Maltez, L., Igrejas, G. and Poeta, P. 2022. MRSA in humans, pets and livestock in Portugal: Where we came from and where we are going. *Pathogens* 11(10), 1110.
- Silva, V., Vieira-Pinto, M., Saraiva, C., Manageiro, V., Reis, L., Ferreira, E., Caniça, M., Capelo, J.L., Igrejas, G. and Poeta, P. 2021. Prevalence and characteristics of multidrug-resistant livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) CC398 isolated from quails (*Coturnix coturnix japonica*) slaughtered for human consumption. *Animals (Basel)* 11(7), 2038.
- Sudarmadi, A.A.M., Prajitno, S. and Widodo, A.D.W. 2020. Antibiotic resistance in *Escherichia coli* and *Staphylococcus aureus* from retail chicken meat in Surabaya, Indonesia. *Biomol. Health Sci. J.* 3(2), 109–113.
- Tao, C.W., Chen, J.S., Hsu, B.M., Koner, S., Hung, T.C., Wu, H.M. and Rathod, J. 2021. Molecular evaluation of traditional chicken farm-associated bioaerosols for methicillin-resistant *Staphylococcus aureus* shedding. *Antibiotics* 10(8), 917.
- Thwala, T., Madoroba, E., Basson, A. and Butaye, P. 2021. Prevalence and characteristics of *Staphylococcus aureus* associated with meat and meat products in African Countries: a review. *Antibiotics* 10(9), 1108.
- Titouche, Y., Akkou, M., Houali, K., Auvray, F. and Hennekinne, J.A. 2022. Role of milk and milk products in the spread of methicillin-resistant *Staphylococcus aureus* in the dairy production chain. *J. Food Sci.* 87(9), 3699–3723.
- Tuominen, K.S., Lewerin, S.S., Jacobson, M. and Rosendal, T. 2022. Modelling environmentally mediated spread of livestock-associated methicillin-resistant *Staphylococcus aureus* in a pig herd. *Animal* 16(2), 100450.
- Tyasningsih, W., Effendi, M.H., Budiarto, B. and Syahputra, I.R. 2019. Antibiotic Resistance to *Staphylococcus aureus* and Methicillin Resistant *Staphylococcus aureus* (MRSA) Isolated from Dairy Farms in Surabaya, Indonesia. *Indian Vet. J.* 96(11): 27–31.
- Tyasningsih, W., Ramandinianto, S.C., Ansharieta, R., Witaningrum, A.M., Permatasari, D.A., Wardhana, D.K., Effendi, M.H. and Ugbo, E.N. 2022. Prevalence and antibiotic resistance of *Staphylococcus aureus* and *Escherichia coli* isolated from raw milk in East Java, Indonesia. *Vet. World* 15(8), 2021–2028.
- Van Cleef, B.A., Van Benthem, B.H., Verkade, E.J., Van Rijen, M.M., Kluytmans, M.F., Graveland, H., Bosch, T., Verstappen, K.M., Wagenaar, J.A., Heederik, D. and Kluytmans, J.A. 2016. Health and health-related quality of life in pig farmers carrying livestock-associated methicillin-resistant *Staphylococcus aureus*. *Epidemiol. Infect.* 144(8), 1774–1783.
- van Cleef, B.A., van Benthem, B.H., Verkade, E.J., van Rijen, M., Kluytmans-van den Bergh, M.F., Schouls, L.M., Duim, B., Wagenaar, J.A., Graveland, H., Bos, M.E., Heederik, D. and Kluytmans, J.A. 2014. Dynamics of methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *Staphylococcus aureus* carriage in pig farmers: a prospective cohort study. *Clin. Microbiol. Infect.* 20(10), O764–O771.
- Vanderhaeghen, W., Hermans, K., Haesebrouck, F. and Butaye, P. 2010. Methicillin-resistant *Staphylococcus aureus* (MRSA) in food production animals. *Epidemiol. Infect.* 138(5), 606–625.
- Wacnik, K., Rao, V.A., Chen, X., Lafage, L., Pazos, M., Booth, S., Vollmer, W., Hobbs, J.K., Lewis, R.J. and Foster, S.J. 2022. Penicillin-binding protein 1 (PBP1) of *Staphylococcus aureus* has multiple essential functions in cell division. *mBio* 13(4), e0066922.
- Waruwu, Y.K.K., Khairullah, A.R., Effendi, M.H., Lukiswanto, B.S., Afnani, D.A., Kurniawan, S.C., Silaen, O.S.M., Riwu, K.H.P., Widodo, A. and Ramandinianto, S.C. 2023. Detection of methicillin-resistant *Staphylococcus aureus* and multidrug resistance isolated from cats in animal clinic at Sidoarjo District, East Java, Indonesia. *Biodiversitas* 24(1), 106–111.
- Weese, J.S., Avery, B.P. and Reid-Smith, R.J. 2010. Detection and quantification of methicillin-resistant *Staphylococcus aureus* (MRSA) clones in retail meat products. *Lett. Appl. Microbiol.* 51(3), 338–342.
- Wibisono, F.J., Sumiarto, B., Untari, T., Effendi, M.H., Permatasari, D.A. and Witaningrum, A.M. 2021. Molecular identification of CTX gene of extended spectrum beta-lactamases (ESBL) producing *Escherichia coli* on layer chicken in Blitar, Indonesia. *J. Anim. Plant Sci.* 31(4), 954–959.
- Widodo, A., Lamid, M., Effendi, M.H., Khairullah, A.R., Riwu, K.H.P., Yustinasari, L.R., Kurniawan, S.C., Ansori, A.N.M., Silaen, O.S.M. and Dameanti, F.N.A.E.P. 2022. Antibiotic sensitivity profile of multidrug-resistant (MDR) *Escherichia coli* isolated from dairy cow's milk in Probolinggo, Indonesia. *Biodiversitas* 23(10), 4971–4976.
- Widodo, A., Lamid, M., Effendi, M.H., Tyasningsih, W., Wurlina, W., Al-Arif, M.A., Raharjo, D., Soeharsono, S., Khairullah, A.F., Riwu, K.H.P., Yustinasari, L.R., Kurniawan, S.C., Silaen, O.S.M., Benjamin, M.I. and Afnani, D.A. 2023. Potential hazards of multidrug resistance *Escherichia coli* collected from wastewater on dairy farms in East Java, Indonesia. *Biodiversitas* 24(3), 1900–1907.

- Witoko, M.C., Suardana, I.W. and Rudyanto, M.D. 2019. Detection of antibiotic residues in chicken eggs at the chicken egg farmers and egg distributors on trading business in denpasar municipality. *J. Vet. Anim. Sci.* 2(2), 72–78.
- Wu, S., Huang, J., Wu, Q., Zhang, J., Zhang, F., Yang, X., Wu, H., Zeng, H., Chen, M., Ding, Y., Wang, J., Lei, T., Zhang, S. and Xue, L. 2018. *Staphylococcus aureus* isolated from retail meat and meat products in China: incidence, antibiotic resistance and genetic diversity. *Front. Microbiol.* 9(1), 2767.
- Xing, L., Chen, Y., Ling, X., Wu, D., Sun, L., Lin, J. and Chen, Y. 2022. Genomic characterization of livestock-associated methicillin-resistant *Staphylococcus aureus* ST7 isolates from a case of human bacteremia in China. *Infect. Drug Resist.* 15(1), 7449–7457.
- Yanestria, S.M., Dameanti, F.N.A.E.P., Musayannah, B.G., Pratama, J.W.A., Witaningrum, A.M., Effendi, M.H. and Ugbo, E.N. 2022. Antibiotic resistance pattern of extended-spectrum  $\beta$ -lactamase (ESBL) producing *Escherichia coli* isolated from broiler farm environment in Pasuruan district, Indonesia. *Biodiversitas* 23(9), 4460–4465.
- Young, M., Walsh, D.J., Masters, E., Gondil, V.S., Laskey, E., Klaczko, M., Awad, H., McGrath, J., Schwarz, E.M., Melander, C. and Dunman, P.M. 2022. Identification of *Staphylococcus aureus* penicillin binding protein 4 (PBP4) inhibitors. *Antibiotics* 11(10), 1351.
- Yunita, M.N., Effendi, M.H., Rahmانيar, R.P., Arifah, S. and Yanestria, S.M. 2020. Identification of *spa* gene for strain typing of methicillin resistant *Staphylococcus aureus* (MRSA) isolated from nasal swab of dogs. *Biochem. Cell. Arch.* 20(Suppl 1), 2999–3004.
- Zeggay, A., Atchou, A., Valot, B., Hocquet, D., Bertrand, X. and Bouiller, K. 2023. Genome analysis of methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* ST398 strains isolated from patients with invasive infection. *Microorganisms* 11(6), 1446.
- Zomer, T.P., Wielders, C.C., Veenman, C., Hengeveld, P., van der Hoek, W., de Greeff, S.C., Smit, L.A., Heederik, D.J., Yzermans, C.J., Bosch, T., Maassen, C.B. and van Duijkeren, E. 2017. MRSA in persons not living or working on a farm in a livestock-dense area: prevalence and risk factors. *J. Antimicrob. Chemother.* 72, 893–899.