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Lameness caused by *Staphylococcus aureus* in poultry: A review

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A B S T R A C T

Staphylococcus aureus is a gram-positive, facultative anaerobe coccus, which is a member of the commensal microbiota of skin and mucous membranes in humans and animals and sometimes can cause infection or disease. This bacterium produces variable toxins and enzymes including at least five types of exotoxins that leads to cell membrane damage. *Staphylococcus aureus* can cause a wide range of clinical and pathologic lesions including acute or subacute septicemia, embryo mortalities, omphalitis and yolk sac infection, arthritis and synovitis, osteomyelitis, vesicular dermatitis, gangrenous dermatitis, pododermatitis and other disorders in different avian species. *Staphylococcus aureus* infections are among the most important diseases of poultry industry, particularly, in broiler breeder flocks. Staphylococcal infections can cause large economic losses due to lameness, arthritis, poor weight gain, decreased egg production, and loss of flock uniformity. This paper reviews the characteristics of *Staphylococcus aureus* and its role in lameness and arthritis in poultry.

Keywords: *Arthritis, Lameness, Poultry, Septicemia, Staphylococcus aureus*

1 Introduction

Staphylococcus genus belongs to the Staphylococcaceae family. This family includes four genera: *Gemella*, *Macrococcus*, *Salinicoccus*, and *Staphylococcus*. The genus *Staphylococcus* is one of the gram-positive cocci, as well as aerobic and facultative anaerobic cocci (1). Currently, 45 species and 24 subspecies of *Staphylococcus* have been identified in this genus. *Staphylococci* are spore-free, spherical, gram-positive bacteria that are often clustered together in irregular clusters (2). These bacteria grow rapidly on normal culture media. They are very active in terms of metabolism and ferment many sugars, and also have the ability to produce colored substances (pigments). The color of these pigments is from white to bright yellow. Pathogenic *Staphylococci* are usually capable of hemolysis of red blood cells and can coagulate fresh plasma. The biochemical reactions of *Staphylococcus aureus* to different agents varies. These bacteria are usually coagulase-positive, catalase-positive, fermentative for glucose and mannitol, and gelatinase-positive (2). Some of these bacteria are part of the natural flora of human skin and mucus, and some

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others are capable of producing purulent lesions such as abscesses and various types of purulent infections, which sometimes lead to fatal septicemia. Staphylococcal infections are very common in birds and other animals, and the most common type of *Staphylococci*, which is often the cause of staphylococcal diseases, is *Staphylococcus aureus* (1).

2 *Staphylococcus aureus* species characteristics

The natural source for this type of bacteria is the skin and mucous membranes of humans and animals. Many staphylococcal species have adapted to certain types of animals, but *Staphylococcus aureus* exists in most terrestrial and marine organisms. Although this bacterium exists naturally in the skin and membrane, it can cause infection or disease in some cases. This organism is easily isolated from different healthy animals. This bacterium has the ability to survive in environments outside of its natural host, such as air, dust, and water, and this ability is due to the great adaptation of this bacterium to different environmental conditions and high resistance to drought conditions or osmotic pressures (1, 2).

Staphylococcus aureus produces many toxins and enzymes, including the production of at least five types of exotoxins that damage the cell membrane including alpha (α), beta (β), gamma (γ), delta (δ) and leukocidin. Also, the production of enterotoxin, which is resistant to heat and can withstand heat of 100 degrees Celsius for 30 minutes. Due to the production of coagulase by *S. aureus*, there is a possibility of plasma clotting and the appearance of fibrin, and this causes disruption in phagocytosis and digestion of bacteria by phagocytic cells, so that the bacteria will not be destroyed. In any case, the production of coagulase can be considered equal to the ability of bacteria to invade and cause disease (1, 2).

Various antimicrobial compounds can be used to treat staphylococcal infections (1). But for the treatment of staphylococcal infections, it is better to perform an antimicrobial susceptibility test before the treatment so that the appropriate drug to which the bacteria is susceptible can be used. Several methods are used to measure the susceptibility of microorganisms to antimicrobial compounds (1, 2). One of the most appropriate methods is the qualitative disk diffusion method using the standard Kirby-Bauer method (2). Considering the importance of using antimicrobial compounds in the treatment of bacterial diseases, including *Staphylococci*, we must have comprehensive information about the drug resistance pattern of *S. aureus* isolates in birds. The treatment patterns used in different places are different and are defined based on the specific conditions of each region. The origin of these differences in different places can be seen in the genetic differences of animals, genetic differences of strains and differences in other fields. According to the above, regular and consecutive research should be done in different places. In addition to *S. aureus* being a very important pathogen in birds, methicillin-resistant strains (MRSA) are resistant to beta-lactam antibiotics (3-5). This issue has caused methicillin-resistant isolates to become important pathogens in humans and animals (3, 4). Methicillin-resistant strains have been isolated in several countries today, but their distribution and importance are more debatable.

3 Clinical signs and pathology of *Staphylococcus aureus* in birds

Staphylococcus aureus can cause a wide range of pathological and clinical injuries in birds, including embryo death, omphalitis, yolk sac infection, arthritis, synovitis, septicemia, osteomyelitis, vesicular dermatitis, gangrenous dermatitis, and pododermatitis (1, 6, 7). Septicemia caused by *S. aureus* may be classified by non-specific clinical signs such as lethargy, anorexia, ruffled feathers and sudden death (1). During the initial phase of the ischemic process, the affected toes may be swollen, congested, painful, and most birds show signs of lameness (8). Arthritis and synovitis are characterized by the formation of fibrinous or serofibrinous inflammation. Synovial membrane, tendon sheaths and joint bursa are observed in staphylococcal infection in chickens (8). All joints can be involved, but it has been seen that *S. aureus* is interested in colonizing the tarsal and metatarsal joints. Following antibiotic treatment, *S. aureus* may emerge in the unstable L-form, which is difficult to treat (8).

Birds that go through the acute stage of the disease usually have swollen joints and generally do not want to walk or stand on their feet by sitting on their hock joints. The unwillingness to walk and lack of access to sufficient water and feed leads to weakness and eventually the death of the bird (1, 8).

4 Detection and isolation

Staphylococcus aureus is diagnosed by culture of suspected clinical material including joint exudates, yolk sac material and swabs from internal organs (2). The primary medium for the growth of *Staphylococci* is blood agar.

Organisms usually grow as colonies of one to three millimeters in diameter within 18 to 24 hours. Most strains of *Staphylococcus aureus* are β-hemolytic, and most other strains are non-hemolytic. Highly contaminated materials should be cultured in selected media that have an inhibitory effect on gram-negative bacteria, such as mannitol salt agar or phenylethyl alcohol agar (2). Most colonies of *S. aureus* are pigmented, while other staphylococcal colonies are gray to white. Colonies should be selected and gram-stained to observe the gram-positive cocci. Biochemical tests can differentiate *S. aureus* from other gram-positive organisms, including *Streptococcus* spp. (2).

Some staphylococcal species including *S. hyicus*, *S. intermedius*, *S. lutrae*, *S. delphini*, *S. lugdunensisis* may be coagulase positive (2). But none of the above species usually cause clinical disease in birds (9). In the diagnosis of *S. aureus*, serological tests are not common, but methods such as microplate plate agglutination and indirect immunofluorescent antibody titer method are sometimes used (1). Today, unlike in the past, many molecular methods such as PCR, Multiplex PCR, RT-PCR and other methods are used to investigate and diagnose diseases (3). The use of these types of methods has many advantages, which include speeding up time and more accuracy. Staphylococcal infections should be excluded from *Escherichia coli*, *Pasteurella multocida*, *Salmonella gallinarum*, *Mycoplasma synoviae*, reoviruses, avian adenoviruses, and any bone and joint infections or trauma (1).

5 Lameness due to *Staphylococcus aureus* infection

In the last 50 years, due to the increase in genetic selection, the growth and weight gain in broiler chickens has increased by about 300% (10). With rapid growth and maturity in the poultry skeletal system, significant development has not occurred in the birds' legs, and this problem has caused the inability to bear heavy weight and problems in the mobility system of birds (10). Also, the production programs have been intensified to achieve the maximum muscle mass in poultry, which causes a disturbance in their health status (11). Therefore, due to the reasons mentioned above, pathological injuries in the leg, such as weakness, inability to walk, deformity in the leg, infections, osteoporosis, lameness, etc., are regularly observed in poultry flocks (8). Based on an estimation made in the early 1990s, annual economic losses due to leg problems in the USA were between $80–120 million and $32–40 million in the broiler and turkey industry, respectively (8). Also, it has been estimated that each year, almost 12.5 billion birds worldwide suffer from leg problems (12).

The strength of the leg bones in birds depends on many factors, such as genetics, sex, species, age, nutrition, breeding and production conditions, the function of the endocrine system, and infectious agents, all of which can play a role in lameness in commercial poultry, individually or in cooperation with each other (13).

Infectious agents are primarily of bacterial origin, but viruses such as avian reovirus and adenoviruses sometimes lead to complications in the skeletal system of poultry. Many bacteria, such as *Enterococcus* spp., *Salmonella* spp., *E. coli*, and *S. aureus*, may also cause these complications (13-15).

The reason for infection-based lameness in poultry has yet to be fully understood. However, several investigations have indicated that microorganisms enter the bloodstream in birds, mainly via the digestive and respiratory systems (13).

Lameness occurs at different degrees, ranging from a slight walking disorder to the most severe form in which the bird cannot walk and needs help from the wings to maintain balance and walk (16, 17). In the most severe cases, the affected birds are anxious and have difficulty accessing feed and water. Skeletal abnormalities and factors related to lameness can also be practical during production, with more severe and irreversible effects in commercial flocks (16, 17).

Arthritis and subsequent lameness in birds usually occur after a septic infection or through a local joint infection caused by various bacterial agents, including *S. aureus*. Among the most important sites of lesions caused by *S. aureus* are bones, tendons, and joints. Of course, the skin, sternum bursa, yolk sac, heart, eyelids, and testicles are rarely involved. Osteomyelitis and arthritis lesions usually cause lameness in commercial poultry flocks, especially breeder and ornamental birds (1, 18). Local infections related to lameness, especially bacterial chondronecrosis (14), osteomyelitis, arthritis, and sinusitis, are common causes of lameness in young chickens (16).

In 2001, Butterworth and his colleagues used RAPD-PCR to type *S. aureus* isolated from ischemia and joint lesions in broilers (17). They proposed this method for the epidemiological studies of *S. aureus* in birds of meat-type production systems. The frequency of *S. aureus* in broiler chickens with lameness signs was expressed as 17%, which agrees with the previous investigations in Ireland (17).

In 2009, Dinev investigated the prevalence of femoral head necrosis as a cause of lameness in broiler chickens in Bulgaria and found that this type of lameness in broiler chickens was between 3-4% and 15%. The mortality due to lameness also ranged between 5-6% and 10% in affected flocks. *Escherichia coli* was present in more than 90% of the bacteriologically tested samples with femoral head necrosis associated with osteomyelitis. Based on the large-scale field observations, it was concluded that femoral head necrosis was the most frequent reason for the occurrence of lameness in broilers (14).

In 2011, Rashid et al. collected sixty 30-55 days of broilers with arthritis lesions from different flocks. After clinical and necropsy examinations, bacteriological tests were done. From 60 samples, 51 bacterial isolates were recovered, 26 of which (50.98%) were *S. aureus* and the rest of isolates were identified as *Pseudomonas aeruginosa* (27.45%), *Staphylococcus aprophyticus* (7.84%), *Escherichia coli* (7.84%), *Proteus* species (3.9%) and *Erysipelothrix rhusiopathiae* (1.9%). In the antimicrobial susceptibility test, *S. aureus* isolates were sensitive to amoxicillin but resistant to gentamicin and novobiocin. Later, Rashid and coworkers, by intravenous inoculation of *S. aureus* to 10 chickens of 35 days of age and with a dose of 10^7 cfu/ml per bird, observed arthritis, joint swelling, and inability to stand in 8 chickens (80%) (19).

The prevalence of staphylococcal infections in broiler breeder (bb) flocks was studied in the East Azerbaijan province of Iran (20). In 14 studied bb flocks, clinical signs such as lameness and arthritis, especially hock and foot joints, were observed. Six samples were selected from each flock and cultured for bacterial isolation and antimicrobial susceptibility tests. The results showed that out of 14 bb flocks, 12 (85.71%) and 2 (14.29%) were positive and negative, respectively. These findings indicated the high prevalence of staphylococcal infections in poultry. Due to its epidemiological importance, necessary measures should be taken to reduce the transmission of *S. aureus* from poultry to humans (20).

Nazia et al. (21) investigated the prevalence of septic arthritis caused by *S. aureus* in broiler and laying poultry farms in Pakistan. They collected hundreds of samples from three sample sites, including hock joint swelling / abscesses, wing / abdominal abscess / injuries, and footpad injuries / abscesses. Among 25 samples collected from one broiler farm, 69.23% from hock joint swelling/abscesses, 57.15% from wing/abdominal abscess/injuries, and 60.00% from foot pad injuries/abscesses were shown to be positive for *S. aureus*. However, from 25 samples of another broiler farm, 73.34% from hock joint swellings/abscesses/injuries, 66.67% from wing/abdominal abscess/injuries, and 75.00% from footpad injuries/abscesses were confirmed to be positive for *S. aureus*. Among 25 samples from one layer farm, 81.25% were identified as *S. aureus* from hock joint swellings/abscesses/injuries, and 71.43% from wing/abdominal abscesses/injuries were identified as *S. aureus*. In addition, among samples collected from another layer farm, 57.89% from hock joint swellings/abscesses/injuries and 75.00% from wing/abdominal abscesses/injuries were diagnosed as *S. aureus.* However, no positive samples were found in layers' foot pad injuries/abscesses. In conclusion, these researchers indicated that *S. aureus* was the cause of septic arthritis in most commercial broilers and layers, with a higher prevalence in hock joints. Moreover, the occurrence of *S. aureus* infection was slightly lower in layers (64.00%) compared to that in broilers (68.00%), with no isolation of *S. aureus* in footpad swellings/injuries (21).

Al-Rubaye and coworkers in Arkansas, USA, for the first time, identified *S. agnetis* implicated in bacterial chondronecrosis with osteomyelitis in the proximal tibia and femoral, resulting in lameness in broilers kept on the wire floor system (22). In genotyping studies, *the S. agnetis* genome was compared to that of other pathogenic *Staphylococci*, and it was found that this pathogen carried a distinct repertoire of virulence properties. Moreover, the *S. agnetis* genome contains several regions substantially different from the genomes of other pathogenic *Staphylococci*. These researchers did not determine the natural source for *S. agnetis* infection. However, they indicated that it could be due to biofilms in the drinking system (such as nipples), insect transmission, bird-to-bird contact, or vertical transmission through eggs (22).

A study in 2018 on broiler and layer flocks in India has shown that pododermatitis caused by *S. aureus* imposes excellent economic losses in the poultry industry (23). After screening 5,400 birds and taking samples from the birds' foot pads and hock joints, 119 birds were found positive for pododermatitis. The percentage of prevalence of pododermatitis caused by *S. aureus* in broiler and layer flocks was reported as 80.64% and 89.65%, respectively. Also, pododermatitis caused by *S. aureus* in native birds was 28.89%, which is considered very high. This study concluded that *S. aureus* is responsible for the outbreak of pododermatitis in most commercial broiler and layer chickens (23).

In 2019, Bagheri and coworkers took samples from birds referred to the university avian clinic and, using bacteriological standard methods, isolated 53 *S. aureus* isolates from companion and wild ornamental birds; and determined the drug resistance and RAPD-PCR patterns of all recovered isolates (18). The standard disc diffusion method was used to determine the susceptibility of the *S. aureus* isolates to 30 antimicrobial agents. Also, all *S. aureus* isolates were typed by RAPD-PCR using two pairs of 10 nucleotide primers. Antimicrobial susceptibility tests showed the highest percentage of resistance to oxacillin (58%), clindamycin (53%), and methicillin (53%). Multiple resistance was widespread among the isolates, so they were resistant to at least zero and, at most, 17 antimicrobial drugs. Also, 43 patterns of drug resistance were identified. In RAPD-PCR, five patterns (A to E) were observed among 53 *S. aureus* isolates that were tested. Among 53 isolates, 20%, 62%, 3%, 9%, %3 of the samples belonged to patterns A, B, C, D, and E, respectively. This study showed the widespread antimicrobial resistance among *S. aureus* isolates in ornamental birds, especially when the presence of MRSA isolates was noticeable. Moreover, the value of RAPD-PCR for the epidemiological differentiation of *S. aureus* in ornamental birds was confirmed (18).

In continuation of the previous research, Mohammad Alitabar (2019) searched for methicillin-resistant *S. aureus* (MRSA) isolates in joint lesions of broiler chickens in Iran (24). He also evaluated the antimicrobial susceptibility of *S. aureus* isolates recovered from lameness cases in broiler flocks. The presence of MRSA isolates was also detected by multiplex PCR. In his research, samples were taken from 47 broiler flocks with lameness signs, and finally, 10 isolates of *S. aureus* were confirmed according to standard bacteriological techniques. The antimicrobial susceptibility was performed using 30 antibacterial agents and the Kirby-Bauer disk diffusion method. Three genes of *16srRNA, mecA*, and *nuc* were detected by PCR among isolates. The antimicrobial susceptibility test showed that all isolates were resistant to oxacillin, amoxicillin, and meropenem, and 80% were resistant to cefixime, neomycin, and azithromycin. The highest sensitivity was related to ceftizoxime, ceftriaxone, cefotaxime, sulfamethoxazole+ trimethoprim, and chloramphenicol. Among the *S. aureus* isolates, the occurrence of multi-drug resistance was widespread, so they were resistant to at least 8 and, at most, 14 drugs. All study isolates were identified as *Staphylococcus* and *S. aureus* by PCR detection of *16SrRNA* and *nuc* genes, respectively. Two isolates were found to be MRSA by PCR detection of *mecA* gene. The results of this study were valuable for epidemiological monitoring and diagnosis of *S. aureus* in broiler flocks. Considering the existence of many broiler chicken farms in Iran, the presence of *S. aureus* in this type of flock, and other related issues presented above, more attention should be paid to *S. aureus* infection in poultry flocks (24).

In another study, Ekesi (2020) analyzed the genomes of bacteria isolated from the lameness outbreak in boiler farms in Arkansas, USA (25). Simon and colleagues isolated several distinct bacterial species from chondronecrosis and osteomyelitis lesions. Their results showed that the causative agents of lameness due to bacterial chondronecrosis and osteomyelitis lesions can significantly differ in specific farms. Moreover, genotyping demonstrated that the genomes of *S. aureus* in this study were significantly related to isolates obtained from European chickens (25).

Staphylococcal infections in game birds also occur frequently. In 2014, Sousa et al. studied staphylococcal infection in the nose of game birds and found that six out of 16 birds (37.5%) were infected with *Staphylococci* (26). The antimicrobial resistance of recovered *S. aureus* isolates was shown to be resistant to penicillin but sensitive to methicillin. These researchers concluded that the birds of prey may be the natural reservoirs of *S. aureus* (26).

An experimental study in China dealt with arthritis caused by *S. aureus* in broiler breeder flocks (27). *Staphylococcus aureus* was injected into the leg joints of chickens selected from broiler breeder flocks at a dose of 2.5 x 10^9 cfu/ml per bird. Most infected chickens showed signs of lameness and joint swelling in the right leg three days after inoculation, and maximum mortality was observed seven days after inoculation. The mortality rate in this study was 51.1%. These researchers stated that *S. aureus* can be continuously isolated from the blood and joint fluid of the left leg joint of infected chickens. The lesions observed in infected birds included joint swelling with caseous secretions, cartilage damage, and thickening of the synovial membrane with infiltration of inflammatory cells. The center of the lesion contained round cocci-shaped bacteria. With the severity of joint damage, the amount of intra-articular hyaluronic acid gradually decreased. Serum interleukin-6 was significantly higher compared to the control group ($P <$ 0.01) 3 days after inoculation, and its level in the serum of infected chickens increased rapidly from 0.37 µg/ml to 2.24 µg/ml one week after inoculation (27). Arthritis caused by *S. aureus* in broiler chickens usually occurs at 6-8 weeks. As reviewed by Gu et al. (2013), Most research models on arthritis caused by *S. aureus* have been developed in animals such as rabbits, mice, and swine and by intravenous inoculation with *S. aureus* (27). However, based on the experiments conducted by Gu and coworkers, the best model for inducing arthritis caused by *S. aureus* is the intra-articular injection of 2.5 x 10^9 cfu *S. aureus* per chicken. These investigators concluded that the joint cavity infection in broiler chickens is more similar to natural infection. In other words, mechanical damage to the joint leads to adhesion and bacterial invasion, primarily due to the heavy weight of broiler breeder chickens (27).

In studies conducted by several researchers, it has been reported that arachidonic acid derivatives act as potent mediators for inflammatory diseases such as septic arthritis. Meanwhile, factors such as cyclooxygenase and lipoxygenase-5 also play a role in the metabolism of this acid. In addition, reactive oxygen species and nitric oxide produced on the cell surface are the main factors in inflammatory processes such as arthritis (21, 28). Studies have shown that plant-derived flavonoids can inhibit cyclooxygenase and lipoxygenase-5, and from this point of view, inflammation is also reduced by reducing the metabolism of arachidonic acid. It is worth mentioning that the antioxidant effects of flavonoids against the production of reactive oxygen species and nitric oxide have been accurately identified. Therefore, these flavonoids can be used as suitable antioxidants for inflammations that occur sub-clinically in the flock, which are considered the starting factor of arthritis (21, 29, 30).

6 Conclusion

Iran's poultry industry is one of the largest production industries in the country. Different infectious agents are among the factors imposing economic losses on this industry. Therefore, investigating the pathology and epidemiology of infectious diseases in the poultry industry and related birds can be critical and provide helpful information about circulating pathogens to research workers in this field. *Staphylococcus aureus* is one of these infectious agents, which is very important in the poultry industry worldwide. Lameness and arthritis caused by infectious agents in poultry flocks lead to poor performance and significant economic losses due to the limited number of studies conducted on lameness cases caused by *Staphylococcus aureus* in Iranian poultry flocks. More comprehensive studies on lameness prevalence in poultry flocks, research on virulence genes of *S. aureus* involved in the development of lameness, genotyping studies, and antimicrobial susceptibility evaluation of *S. aureus* field isolates are recommended.

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Conflict of Interest

All authors declare that they have no conflicts of interest.

Author Contributions

The authors confirm contribution to the paper as follows: Conception or design of the work (SMP).

Data collection (MMT).

Drafting the article (MA, SB).

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Data Availability Statement

Data are available from the corresponding author upon reasonable request.

Ethical Considerations

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References

1. Andreasen CB. Other Bacterial Diseases (Staphylococcosis). In: Swayne DE, Boulianne M, Logue CM, McDougald LR, Nair V, Suarez D L, editors. Diseases of Poultry. 14th ed. John Wiley & Sons, Inc., NJ, USA; 2020. p. 995-1003. [DOI]
2. Quinn PJ, Markey BK, Leonard FC, Hartigan P, Fanning S, Fitzpatrick E. Veterinary Microbiology and Microbial Disease: John Wiley & Sons; 2011.
3. Lakhundi S, Zhang K. Methicillin-resistant Staphylococcus aureus: molecular characterization, evolution, and epidemiology. Clinical Microbiology Reviews. 2018;31(4):10-18. [PMID: 30209034] [PMCID: PMC6148192] [DOI]
4. Vestergaard M, Frees D, Ingmer H. Antibiotic resistance and the MRSA problem. Microbiology Spectrum. 2019;7(2):10-20. [PMID: 30900543] [DOI]
5. Silva V, Araújo S, Monteiro A, Eira J, Pereira JE, Maltez L, et al. *Staphylococcus aureus* and MRSA in livestock: antimicrobial resistance and genetic lineages. Microorganisms.

2023;11(1):124. [PMID: 36677414] [PMCID: PMC9865216] [DOI]

6. Huff G, Huff W, Rath N, Balog J. Turkey osteomyelitis complex. Poultry Science. 2000;79(7):1050-6. [PMID: 10901209] [DOI]

7. Gornatti-Churria CD, Crispo M, Shivaprasad H, Uzal FA. Gangrenous dermatitis in chickens and turkeys. Journal of Veterinary Diagnostic Investigation. 2018;30(2):188-96. [PMID: 29145799] [PMCID: PMC6505868] [DOI]

8. Szafraniec GM, Szeleszczuk P, Dolka B. Review on skeletal disorders caused by *Staphylococcus* spp. in poultry. Veterinary Quarterly. 2022;42(1):21-40. [PMID: 35076352] [PMCID: PMC8843168] [DOI]

9. Devriese LA, Vancanneyt M, Baele M, Vaneechoutte M, De Graef E, Snauwaert C, et al. *Staphylococcus pseudintermedius* sp. nov., a coagulase-positive species from animals. International Journal of Systematic and Evolutionary Microbiology. 2005;55(4):1569-73. [PMID: 16014483] [DOI]

10. Knowles TG, Kestin SC, Haslam SM, Brown SN, Green LE, Butterworth A, et al. Leg disorders in broiler chickens: prevalence, risk factors and prevention. PloS One. 2008;3(2):e1545. [PMID: 18253493] [PMCID: PMC2212134] [DOI]

11. Santos MN, Rothschild D, Widowski TM, Barbut S, Kiarie EG, Mandell I, et al. In pursuit of a better broiler: carcass traits and muscle myopathies in conventional and slower-growing strains of broiler chickens. Poultry Science. 2021;100(9):101309. [PMID: 34280646] [PMCID: PMC8318900] [DOI]

12. Nicol CJ. Welfare issues in commercial broiler production. Poultry Development Review, Roma, Italy: FAO. 2013:117-8.

13. Kierończyk B, Rawski M, Józefiak D, Świątkiewicz S. Infectious and non-infectious factors associated with leg disorders in poultry–a review. Annals of Animal Science. 2017;17(3):645-69. [DOI]

14. Dinev I. Clinical and morphological investigations on the prevalence of lameness associated with femoral head necrosis in broilers. British Poultry Science. 2009;50(3):284-90. [PMID: 19637027] [DOI]

15. Kense M, Landman WJ. *Enterococcus cecorum* infections in broiler breeders and their offspring: molecular epidemiology. Avian Pathology. 2011;40(6):603-12. [PMID: 22107095] [DOI]

16. Butterworth A. Infectious components of broiler lameness: a review. World's Poultry Science Journal. 1999;55(4):327-52. [DOI]

17. Butterworth A, Reeves N, Harbour D, Werrett G, Kestin S. Molecular typing of strains of *Staphylococcus aureus* isolated from bone and joint lesions in lame broilers by random amplification of polymorphic DNA. Poultry Science. 2001;80(9):1339-43. [PMID: 11558920] [DOI]

18. Bagheri S, Peighambari SM, Soltani M, Malekan M. RAPD-PCR and drug resistance pattern of *Staphylococcus aureus* isolates recovered from companion and wild birds. . Iranian Journal of Veterinary Medicine. 2019;13(4):355-64.

19. Rasheed B. Isolation and identification of bacteria causing arthritis in chickens. Iraqi Journal of Veterinary Sciences. 2011;25(2):93-5. [DOI]

20. Feizi A, Nazeri M, Pilevar A. Isolation of *Staphylococcus* spp. genera from broiler breeder flocks in East Azerbaijan Province of Iran: Prevalence and antimicrobial susceptibility. African Journal of Microbiology Research. 2012;6(28):5819-23. [DOI]

21. Nazia MK, Durrani N, Kamboh A, Lakho S, Rind R, Abro S, Soomro N. Prevalence of septic arthritis caused by *Staphylococcus aureus* in poultry birds at Tandojam. Pakistan Journal of Animal Health and Production. 2015;3(3):73-7. [DOI]

22. Al-Rubaye AA, Couger MB, Ojha S, Pummill JF, Koon JA, Wideman Jr RF, Rhoads DD. Genome analysis of *Staphylococcus agnetis*, an agent of lameness in broiler chickens. PloS One. 2015;10(11):e0143336. [PMID: 26606420] [PMCID: PMC4659636] [DOI]

23. Chaudhary S, Batoo AS, Hussain K, Najar AA, Upmanyu G, Agrawal K. Prevalence of pododermatitis caused by *Staphylococcus aureus* in poultry birds of Jammu. International Journal of Livestock Research. 2018;8:192-5. [DOI]

24. Mohammadali Tabar M. Detection of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates in arthritis lesions of broiler breeders: Doctor of Veterinary Medicine Thesis, University of Tehran; 2019.

25. Ekesi NS. Examining pathogenesis and preventatives in spontaneous and *Staphylococcus*-Induced bacterial chondronecrosis with osteomyelitis in broilers: Graduate Theses and Dissertations, University of Arkansas; 2020. Retrieved from https://scholarworks.uark.edu/etd/3838

26. Sousa M, Silva N, Igrejas G, Silva F, Sargo R, Alegria N, et al. Antimicrobial resistance determinants in *Staphylococcus* spp. recovered from birds of prey in Portugal. Veterinary Microbiology. 2014;171(3-4):436-40. [PMID: 24679961] [DOI]

27. Gu CQ, Hu XY, Xie CQ, Zhang WP, Wang DH, Zhou Q, Cheng GF. Observation on arthritis in broiler breeder chickens experimentally infected with Staphylococcus aureus. Pakistan Veterinary Journal. 2013;33(2):195-99.

28. Kamboh A, Zhu W-Y. Effect of increasing levels of bioflavonoids in broiler feed on plasma anti-oxidative potential, lipid metabolites, and fatty acid composition of meat. Poultry Science. 2013;92(2):454-61. [PMID: 23300313] [DOI]

29. Guardia T, Rotelli AE, Juarez AO, Pelzer LE. Anti-inflammatory properties of plant flavonoids. Effects of rutin, quercetin and hesperidin on adjuvant arthritis in rat. Il farmaco. 2001;56(9):683-7. [PMID: 11680812] [DOI]

30. Kamboh AA, Arain MA, Mughal MJ, Zaman A, Arain ZM, Soomro AH. Flavonoids: Health promoting phytochemicals for animal production-a review. Journal of Animal Health Production. 2015;3(1):6–13. [DOI]