



SUDDEN DEATH SYNDROME IN BROILER CHICKENS: A REVIEW ON THE ETIOLOGY AND PREVENTION OF THE SYNDROME*

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Abstract

Sudden death syndrome (SDS) is a condition in which apparently healthy broiler chickens die suddenly. There are short convulsions and frantic wing-beating prior to death, and the weight of internal organs is the same as in healthy chickens. The exact etiology of SDS is unknown. Heart problems have been implicated as a potential cause of the disease in broiler chickens. Despite considerable research, effective methods of prevention are still being sought. Furthermore, the prophylactic measures often make production less profitable (reduced body weight gain resulting from restricted feeding) and prolong the growth period. It is necessary to continue research on SDS, in particular on stimulation of the cardiovascular system to reduce the susceptibility of broilers to sudden death syndrome under intensive production systems.

Key words: broiler chickens, sudden death syndrome, causes, diagnosis

Due to breeding progress over the last 50 years, the growth period required for broiler chickens to reach slaughter weights has been considerably shortened (Gous, 2010). On the other hand, the short growth period paralleled by rapid muscle growth prevents the complete development and normal function of the internal organs, e.g. the cardio-pulmonary system.

In modern broiler chicken production the sudden death syndrome (SDS) may be one of the main causes for mortality at the end of the fattening period but starts already in the second week of life (Julian, 2005) and causes severe economic losses (Nain et al., 2007; Olkowski et al., 2008). The incidence of SDS has increased over the last four decades, but its pathogenesis is not completely understood. By 1983, sudden death syndrome became a serious problem for broiler chicken producers in Australia (Hopkinson et al., 1984). In 1990, Jacob et al. reported 33% of all deaths to be caused by sudden death syndrome.

Sudden death syndrome occurs in well fed and apparently healthy birds (*Gallus gallus*) and is characterized by short, wing-beating convulsions, while the weight of internal organs such as the heart, liver and lungs does

not allow diagnosing the causes of death because it is the same as in healthy birds (Imaeda, 1999). As reported by Basaki et al. (2019), chickens have no discernible clinical symptoms and show no atypical behaviour until less than a minute before death. Over 70% of SDS mortality affects broiler cockerels (Olkowski and Classen, 1998). SDS occurs in 0.5–5% of broiler flocks and peaks at about 2 to 4 weeks of age (Basaki et al., 2016).

The syndrome is considered an important contributing factor in the growth of fast-growing chickens as it significantly reduces the economic efficiency of live poultry production (Ning et al., 2019). Therefore, the aim of this study is to analyse peer-reviewed articles that define sudden death syndrome in broiler chickens. The present review discusses sudden death syndrome in the context of pathogenesis and pathophysiological symptoms, followed by known prevention.

Etiology and pathogenesis of SDS

Many different factors contribute to the sudden death syndrome in broilers, including nutrition, genetic background, and environmental factors (Julian, 2005). However, the main factor causing the bird's reaction,

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namely acute cardiac arrhythmia leading to sudden death syndrome, has still not been diagnosed (Olkowski et al., 2008).

Genetic background and metabolic disorders

According to SCAHAW (2000), fast growth rates significantly increase the risk of ascites and SDS by increased oxygen demand of the broiler chickens, which intensifies the activity of the cardio-pulmonary system. Due to the intensive genetic selection for weight gain, cardiac and pulmonary growth and development is insufficient to meet the needs of fast growing chickens, which leads to the symptoms of cardiac insufficiency and thus sudden death syndrome.

According to Olkowski et al. (2008), the incidence of SDS in broiler chickens is influenced mostly by interacting genetic (Towbin, 2001) and environmental etiology factors (Prandota, 2004). In turn, Julian (2005) stated that sudden death syndrome is a metabolic disease, in which an imbalance of metabolites or electrolytes results in ventricular fibrillation and the consequent death.

In turn, Squires and Summers (1993), maintain that SDS is caused by metabolic disorders related not so much to rapid weight gain but to increased body oxygen demand, which disrupts electrolyte balance and blood pH. Acute changes in electrolytes and pH lead to SDS. Cerrone and Priori (2011) hold that genetic disorders of the cardiac ionic channels can disrupt the fine balance of ionic currents and cause arrhythmia and sudden death syndrome in the absence of structural heart defects. Safaei et al. (2021) showed that metabolic alterations related to hypoxia in the cardiac tissues of broiler chickens may have an important role in the pathogenesis of cardiac insufficiency and SDS. On the other hand, according to Kittelsen et al. (2015), congested and oedematous lungs (lung congestion), which are fairly common in broiler chickens in the growth period and diagnosed as the only pathological lesion during necropsy examination, can be classified as SDS. Birds with lung congestion had no other lesions and were presumably healthy before death, which the authors believe points to sudden death syndrome. Meshram and Bijoy (2017) state that sufficient fluid is lost from the circulatory system into the lung tissue spaces to result in peripheral circulatory failure or shock. In SDS death appears to be caused by heart damage which leads to lung oedema so that the chickens are unable to breathe.

Many authors believe that the new lines of fast-growing broiler chickens are particularly susceptible to cardiac defects. It is likely that broiler mortality due to cardiac problems is at the same time responsible for sudden death syndrome caused by acute or chronic cardiac insufficiency or cardiac arrest (Nain et al., 2007; Olkowski, 2007).

According to Gesek et al. (2016), overload of cardiac muscle, prolonged hypoxia and increasing body weight on day 38 of age are the likely reasons for the largest number of lesions and ischemic fibres, which may lead to

heart failure in broiler chickens. The authors reported that the most frequently diagnosed lesions in broiler chickens were degeneration of the fibres with vacuolation, congestion of cardiac muscle, oedema and vacuolization of the Purkinje cells. The lesions were most numerous in the septum, followed by the left and right ventricles of the heart. Ischaemic cardiomyocytes were also most numerous in the left ventricle. In their latest research, Olkowski et al. (2020) observe that broiler chickens selected for rapid growth are highly susceptible to dilated cardiomyopathy. Conformational changes of cardiac proteins and pathological changes are indicative of accumulation of damaged and aggregated proteins in the affected cardiomyocytes, which leads to pathological remodelling of the heart (mainly of the left ventricle) and contractile dysfunction

The pathogenesis of sudden death syndrome is also thought to be related to cardiac arrhythmia (Nain et al., 2007). Many recent studies have linked SDS to cardiac arrhythmia, but the mechanism of arrhythmia and the factors responsible for its consequences have not been adequately studied. The disease mainly affects broiler chickens, which are genetically determined for rapid muscle growth while being much more susceptible to arrhythmia (Olkowski et al., 2008; Gregory et al., 2014; Ning et al., 2019). In broiler chickens, Olkowski and Classen (1998) found cardiac arrhythmias as early as 7 days of age. The incidence of arrhythmias increased with age and by 42–44 days of age it affected 17% of the broiler population, mainly cockerels. According to Moghadam et al. (2005), a predisposition to cardiac problems that lead to SDS is heritable with a positive correlation with body weight and ascites.

Nutritional factors

One of the earliest studies on SDS sought the causes in the type of feed (crumbled or pelleted), attributing them to the preparation process rather than feed concentration (Proudfoot et al., 1982), the low dietary content of potassium, phosphorus, protein and energy (Hopkinson et al., 1984), or light intensity (Newberry et al., 1986).

SDS is associated with acute heart failure, which is induced, among others, by excessive dietary levels of vitamin D₃ (Nain et al., 2007). According to these authors, the high level of vitamin D₃ in feed increases the incidence of SDS in broiler chickens almost 2.5-fold from 5 weeks of growth. Probably, vitamin D₃ weakens the heart muscle and doubles the frequency of ventricular fibrillation and arrhythmia, which directly contributes to the sudden death syndrome (Walentynowicz et al., 2004). Nain et al. (2007) hold the view that the mechanism of SDS in broilers involves two interacting factors: the appearance of morphological changes that cause arrhythmia, and electrophysiological changes in cardiac tissue due to vitamin D₃ supplementation, which also cause cardiac arrhythmia. The combination of these factors, namely the high risk of cardiac electrophysiological instability coupled with morphological changes are the cause of this

disease in broilers. Also a high calcium and phosphorus content of feed, which exceeds recommended values, may considerably increase the incidence of SDS in birds, while supplementing excessive doses of vitamin D₃ additionally increases disease symptoms in broiler chickens. Because fast-growing broilers are prone to a number of leg problems, in practice vitamin D₃ is very often supplemented at the highest level. However, the increased doses of vitamin D₃ make the heart muscle more sensitive to adverse effects of stress, as a result of which even a benign and sporadically occurring arrhythmia may develop into an acute and life-threatening cardiac dysrhythmia (Rubart and Zipes, 2005; Nain et al., 2007).

Stress

Modern research also suggests that arrhythmia-inducing stress could be a major factor in SDS (Julian, 2005; Olkowski et al., 2008) and mortality later diagnosed as SDS can occur even several days after a stress-inducing episode (Olkowski et al., 2008). According to Lampert et al. (2000), stress aggravates the symptoms of sudden death syndrome, and considering that modern, commercially produced broiler chickens are exposed to different types of environmental stress (crowding, lighting, noise, production process, etc.) or metabolic stress associated with rapid weight gains, SDS and the related losses are a significant factor in profitability of broiler production. According to Olkowski (2007), stress is the most important factor of cardiac arrhythmia in broiler chickens, causing pathological changes in the heart muscle, bundle of His and Purkinje fibres of fast-growing broilers, which is conducive to chronic arrhythmia. Where electrical stability of the heart is disturbed, every case of arrhythmia may easily develop into fatal ventricular fibrillation and sudden death. Likewise, Basaki et al. (2019) hold that sudden death syndrome is directly related to the stress placed on broiler chickens and is associated with ventricular tachycardia and ventricular fibrillation; however, its pathogenesis at the molecular level is not precisely determined.

Zhang et al. (2008) demonstrated that male broiler chickens are more prone to ventricular fibrillation and have higher levels of serum enzymes such as lactate dehydrogenase and creatine kinase. The observed differences may cause the heart muscle to be more sensitive to stress-induced damage, thus leading to differences in susceptibility to the sudden death syndrome depending on sex. Many studies have shown that sudden death syndrome is much more frequently observed in male broiler chickens (Gesek et al., 2016; Tumova et al., 2019).

Despite numerous studies that have been undertaken over many years, the reasons for sudden death syndrome in broiler chickens are not completely clear. Researchers consider various genetic, developmental, physiological, nutritional and environmental factors as stimulating SDS, their interactions and their effects on the incidence of SDS.

Pathophysiological symptoms of SDS

Determining the cause of sudden death syndrome and identifying birds susceptible to the disease still encounter considerable difficulties. Blanchard et al. (2002) attempted, based on electrocardiogram and rectal temperature, to show birds in which SDS may occur. However, the applied methods failed to conclusively identify all birds that will die from sudden death syndrome with any certainty. In turn, Newberry et al. (1987) made continuous video recordings of litter-raised broiler chickens from 3 to 10 weeks of rearing. The behavioural data were collected to identify chickens in which SDS may occur within the next 12 h of life. The authors only observed that all the birds with SDS exhibited a sudden attack just before death, lasting an average of 53 s and characterized by loss of balance, wing flapping, and strong muscular contractions. There was no evidence to identify birds that will die from SDS in the future.

Pathological changes in the heart

Olkowski et al. (2008) reported that the detailed histopathological changes in the heart may be used to identify structural characteristics that predispose broilers to lethal arrhythmia responsible for sudden death syndrome.

Molecular studies

Caspase enzymes are a family of cysteine proteases involved in the initiation and execution of cell apoptosis. Some of them also regulate inflammatory processes. Caspases exist as inactive zymogens in cells and under certain conditions undergo a cascade of activation, which may lead to apoptotic death (Korzeniewska-Dyl, 2007). Normal caspase function controls physiological apoptosis in tissues and organs, for example during embryogenesis. Increased caspase activity was observed in cells damaged by myocardial infarction (Korzeniewska-Dyl, 2008). Caspase-3 activity is measured to evaluate the rate of apoptosis (Wolf and Green, 1999). According to some researchers, determining the expression of apoptosis markers, including caspase-3, could be used in the future to identify animals at high risk of sudden death syndrome caused by heart defects (Opdal and Rognum, 2004; Olkowski et al., 2008).

Dysfunction of the RYR2 gene, which controls rapid release of Ca²⁺, has also been associated with ventricular tachycardia and sudden cardiac death also in humans with structurally normal heart. Therefore, in their next study Basaki et al. (2019) endeavoured to expand existing knowledge about the molecular mechanisms predisposing broiler chickens to fatal arrhythmia and determined the occurrence of possible mutations and changes in the expression level of chicken RYR2 gene (*chRYR2*) in the left ventricle of birds that died of SDS. The authors showed a possible connection between susceptibility to cardiac arrhythmia in birds with SDS and changes in intracellular Ca²⁺ cycling machinery induced by mutations of *chRYR2*. The identification of *chRYR2* defects can be applied to select for chickens with lower susceptibility to

SDS and thus to decrease the poultry industry losses due to SDS mortality.

Biochemical studies

Imaeda (2000) observed a high level of calcium ions in the heart muscle, and increased catecholamine and adrenaline levels in birds with sudden death syndrome. Many studies confirm changes in thyroid hormone levels of chickens diagnosed with SDS (Luger et al., 2001 and 2002; Olkowski, 2007).

Some studies have also shown that an elevated blood level of lactic acid may contribute to SDS in broiler chickens (Imaeda, 2000; Boroumandnia et al., 2021) because it causes damage to the cardiovascular system (Meshram and Bijoy, 2017). The level of creatine kinase is used as an indicator for clinical diagnosis of cardiac and circulatory disturbances (Imaeda, 1999), while an increased blood level of creatine kinase is thought to be the first indicator of myocardial infarction (Adams and Apple, 2004). Increased levels of creatine kinase, observed in birds subjected to stress, are an indicator for pathological changes in the heart muscle of poultry and the increasing risk of sudden death syndrome (Olkowski, 2007). Safaei et al. (2021) investigated the metabolic and molecular alterations related to hypoxia in the myocardium of broiler chickens with SDS. The results showed the elevation of lactate level and activities of lactate dehydrogenase and creatine phosphokinase in the cardiac muscle of SDS-affected chickens. In turn, Imaeda (1999) found serum lactate dehydrogenase (LDH) and glutamic oxaloacetic transaminase (GOT) to increase in SDS broiler chickens and concluded that their levels could be used to identify birds with sudden death syndrome. Praveen Kumar et al. (2020) induced SDS through administration of lactic acid. In the blood serum of chickens that died of SDS they observed increased levels of potassium, calcium, magnesium and phosphorus, increased activity of lactate dehydrogenase and creatinine phosphokinase, and decreased levels of sodium.

Diagnosis of sudden death syndrome faces substantial difficulties. The clinical manifestations generally occur between 2 and 4 weeks of age and most often affect males. Anatomopathological and histopathological lesions observed in postmortem examination are non-specific. Also this aspect of sudden death syndrome in broiler chickens requires further research.

Prevention of SDS

Nutritional and dietary modifications

Many authors believe that physical form of the feed, nutrient content and the type of feed additives may contribute to reducing SDS mortality.

Numerous studies showed that feeding mash to broiler chickens may significantly slow the growth of birds and lower the incidence of cardiac defects compared to feeding pelleted or crumbled feed, thus reducing the risk of sudden death syndrome (Table 1). However, Scott (2002) did not find any effect of feeding mash and pelleted diets to broiler chickens on the incidence of this disease.

Olkowski et al. (2008) found that the incidence of SDS and cardiac arrhythmia decrease when broiler weight gains are controlled by feed restriction. As early as 1988, Bowes et al., who investigated the effect of restricting feed intake by 25% compared to *ad libitum* feeding on the frequency of SDS in broiler chickens, concluded that SDS mortality was 3.33% in birds fed *ad libitum* compared to 0% for birds restricted in feed intake. However, Lippens et al. (2000) subjected broiler chickens to restricted feeding in the first period of growth and only observed a tendency for lower SDS mortality. Nassef et al. (2015) studied the effect of a 20% feed restriction from 7 to 21 days of age on the frequency of SDS in broiler chickens. The authors observed a significant reduction in the incidence of SDS in the group of restricted-fed birds (0.72% SDS) compared to 2.2% SDS in chickens fed *ad libitum*. However, because restricted feeding had adverse effects on growth performance, blood parameters and income over feed cost, authors do not recommend using this method in commercial broiler production to reduce the number of diagnosed SDS deaths. Also Tumova et al. (2019) restricted the feeding of broiler chickens from 7 to 14 days of age to 80% (R80) or 65% (R65) of the *ad libitum* diet and observed a significant decrease in the incidence of SDS with decreasing feed intake. The differences were more noticeable in cockerels than in pullets, with SDS mortality of 19, 12 and 10% for *ad libitum* fed, R80 and R65 cockerels, and 12%, 9% and 3% for hens, respectively.

According to Scott (2002), limiting the nutritive value, in particular the energy level of feed improves the welfare of broiler chickens and protects them against sudden death syndrome. As reported by Karki (2011), SDS mortality in broiler chickens increases beyond 40 days of age and may average up to 9.6%, while restricted feeding and 8–10% lower dietary nutrient concentration significantly reduce mortality caused by SDS. In 1984, Mollison et al. observed that a lower dietary energy to protein ratio caused the incidence of SDS in a broiler flock to decrease. In turn, Madrigal et al. (2002) compared the effect of feeding low-energy, high-energy and high-fibre diets to broilers in the first period of growth on the incidence of sudden death syndrome but found diet type to have no influence.

Table 1. Studies investigating the effect of physical form of feed on the incidence of SDS

Physical form of feed	Major findings	References
Mash (mash feed vs. pelleted feed)	Slows down growth, reduces incidence of cardiac defects, lowers risk of SDS	Bennett et al. (2002)
Mash (mash feed vs. pelleted and crumbled feed)	Slows down growth, lowest mortality caused by SDS	Azizian and Saki (2020)
Mash (mash feed vs. pelleted feed)	0% mortality due to SDS	Kuleile et al. (2020)
Mash (mash feed vs. pelleted feed)	Lower rate of growth, lower risk of SDS	Meshram and Bijoy (2017)

Although herbs have a broad spectrum of activity, many of them have never found practical application in poultry breeding. Plant extracts contain a number of pharmacologically active substances that not only show bacteriostatic, anti-stress and antifungal activity, but also stimulate the immune, hormonal and circulatory systems (Recoquillay, 2006). The application of herb extracts to enhance cardiovascular function in poultry requires further study. Bölükbaşı et al. (2007) reported that thyme oil (200 and 300 mg/kg) reduced plasma cholesterol and triglyceride levels in laying hens. Similar studies on the feeding of thyme to broilers were also conducted by Sarica et al. (2005). Nasir and Grashorn (2010) found that fermented juice from *Echinacea purpurea* had a positive effect on the level of creatine kinase, and thus on the cardiovascular system and on reducing the risk of sudden death syndrome, and observed chicken mortality to decrease.

Shabani et al. (2013) found that supplementation of broiler chicken diets with vitamin E and selenium or B-complex vitamins or multivitamin electrolytes is relatively effective in controlling the incidence of sudden death syndrome.

As reported by Maddahian et al. (2015), probiotics reduce blood lipid metabolites, which decreases the incidence of metabolic disorders and may indirectly reduce the incidence of SDS.

According to McLennan (2001) and Mozaffarian (2008), long-chain omega-3 fatty acids EPA and DHA have protective effects on the cardiovascular system because they prevent cardiac arrhythmia in humans and animals. Therefore, Gregory et al. (2014) suggest that elevating cardiac levels of EPA and DHA in broiler chickens may prevent SDS. Fish oil is a valuable source of omega-3 fatty acids, but it has limited use in poultry nutrition due to its price and the fact that it changes the aroma of chicken meat. On the other hand, rapeseed oil is much less expensive, has no effect on meat aroma and is a rich source of α -linolenic acid, which is converted to EPA and DHA after being ingested. A 3% rapeseed oil supplement in broiler chicken diets considerably increases EPA and DHA levels in heart phospholipids, which may counteract arrhythmia, thus protecting from SDS.

Ajuyah et al. (2003) assumed that hen's diet has an effect on composition of lipids in the chick yolk sac, which are later found in phospholipids of cardiac tissue. In turn, the differences in tissue phospholipids caused by maternal diet may influence eicosanoid synthesis in cardiac tissue. The authors believe that modification of n-3 fatty acids in the maternal diet and thus of yolk fatty acids, increases the level of long-chain n-3 fatty acids in myocardial tissues, which is associated with lower eicosanoid production. This process may contribute to lower incidence of metabolic diseases (SDS) in poultry.

In a recent preliminary study, Boroumandnia et al. (2021) suggested supplementing the diet with guanidinoacetic acid (GAA) that has a direct or indirect effect on the cardiovascular system; this may, to a certain de-

gree, protect birds from lactic acidosis and thus reduce the incidence of SDS in broiler chickens. Dietary guanidinoacetic acid decreased mortality but also had a negative effect on chicken growth, which means that effective methods of SDS prevention still need to be sought.

Chicken housing conditions

According to Nain et al. (2007), rearing broiler chicks in the first week of age at 34°C, gradually decreased to 21°C on the last day of the third week and to 17°C at the end of the fifth week increases the rate of metabolic changes, which burdens the cardiovascular system of birds. As a result, rearing broilers in reduced ambient temperature considerably increases heart disturbances and mortality due to SDS. Stocking density is another factor that increases percentage mortality caused by the sudden death syndrome in winter and in summer (Imaeda, 2000). Similar results were obtained by Naeem et al. (2016), who studied the effect of stocking density of Hubbard broilers (8, 9, 10 and 12 birds/m²) exposed to elevated ambient temperature on SDS deaths. Mortality due to SDS tended to increase with increasing stocking density and was recorded as 0.0%, 3.3%, 6.7% and 10.0%, respectively.

When investigating the effect of photoperiod length on broiler chickens, Lewis et al. (2009) showed that extension of photoperiod from 2 to 10 hours was negatively correlated with SDS, while lengthening the photoperiod beyond 10 hours was positively correlated with sudden death syndrome and increased SDS mortality. Likewise, Brickett et al. (2007) reported that broiler chickens provided with a photoperiod longer than 10 hours had a higher incidence of SDS. Also Scott (2002) showed that the lighting programme has a decisive influence on sudden death syndrome in broiler chickens. However, both intermittent and constant lighting programme increase the incidence of SDS compared to the light day in which dark period is gradually extended to 16 h dark on day 11 of growth and gradually shortened to 4 h dark on day 29 of age (Scott, 2002; Hassanzadeh et al., 2019). As reported by Taati et al. (2019), melatonin secretion could be a defence mechanism against numerous types of stress and may be involved in the body's physiological adaptation to stress factors, because melatonin has a suppressive effect on the nervous system. On the other hand, as noted above, stress is one of the main stimuli activating deaths due to sudden death syndrome. The authors, based on the study of Scott (2002) concerning intermittent lighting programmes, assumed that under stress conditions increased melatonin secretion may mitigate the adverse effect of histamine on cardiac action in broiler chickens. Taati et al. (2019) demonstrated that exogenous intracerebroventricular melatonin results in sinusoidal bradycardia in broiler chickens, and therefore increased melatonin secretion could be used to alleviate the adverse effects of stress (cardiac arrhythmia) in broiler chickens, which has a direct impact on reducing the incidence of SDS.

Prevention of sudden death syndrome is difficult and is mainly based on reducing stress stimuli that affect broiler chickens through modification of flock management parameters, including dietary modifications, diversification of the lighting programme, thermal conditions, and stocking density.

Conclusions

The exact causes of SDS are still unclear, but it is likely that cardiac problems are a potential cause of this condition in broiler chickens. The methods that have been used to prevent sudden death syndrome are not completely effective. What is more, despite reducing the incidence of SDS mortality in broilers, these methods often make production less profitable due to decreased weight gains and prolonged growth periods. Further research on SDS is therefore necessary. It can be assumed that reducing the stress on the cardiovascular system should contribute to reducing the incidence of sudden death syndrome in intensive broiler production systems. However, it remains crucial to conduct research on elaborating good practices for prevention and management of broiler chickens to minimize the incidence of SDS.

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