Adverse effects of heat stress during summer on broiler chickens production and antioxidant mitigating effects

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Abstract

Broiler chicken meat is a good source of protein consumed universally, and is one of the most commonly farmed species in world. In addition to providing food, poultry non-edible byproducts also have value. A major advantage of broiler chicken production is their short production cycle, which results in a greater rate of production in comparison to other species. However, as with any production system, there are constraints in broiler production with one of the most pressing being energy requirements to keep the birds warm as chicks and cool later in the growth cycle, as a result of the cost needing mechanical heating and cooling. While this is feasible in more advanced economies, this is not readily affordable in developing economies. As a result, farmers rely on natural ventilation to cool the rearing houses, which generally becoming excessively warm with the resultant heat stress on the birds. Since little can be done without resorting to mechanical ventilation and cooling, exploring the use of other means to reduce heat stress is needed. For this review, we cover the various factors that induce heat stress, the physiological and behavioral responses of broiler chickens to heat stress. We also look at mitigating the adverse effect of heat stress through the use of antioxidants which possess either an anti-stress and/or antioxidant effects.

Keywords Heat stress, Oxidative stress, Global warming, Broiler chickens, Welfare

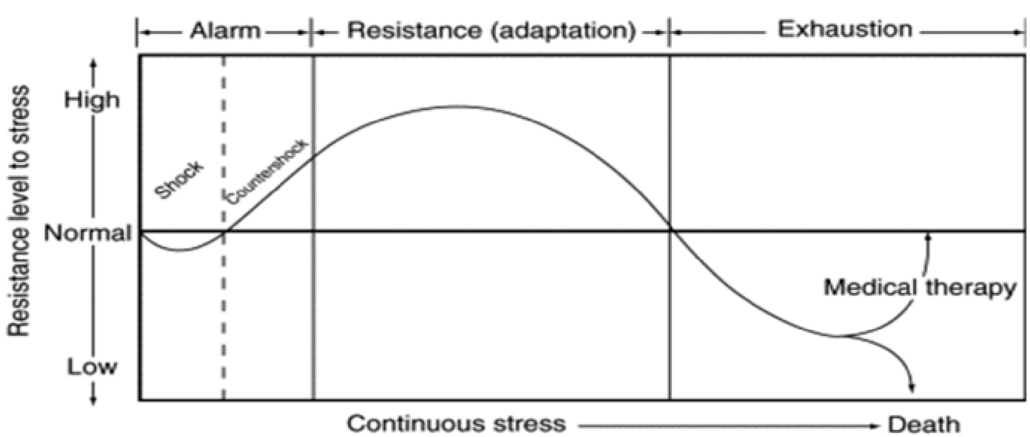
Introduction

Stressors refer to any factor that threatens the health of the body or has an adverse effect on its functioning, such as cellular injury, disease, or anxiety. Stress is a consequence of the physiological and adverse effects of the environment or management system, which induces several changes in the physiology or behavior of an animal, which in the latter case; if unchecked, leads to pathophysiology and malfunctioning (Aluwong et al. 2017; Gogoi et al. 2021). Thus, stress assists the animal to cope with its environment, i.e., physiological stress.

The general adaptation syndrome is a non-specific one-way physiological response of the body to all types of endogenous and exogenous stressors (Sumanu et al. 2019; Kim et al. 2021).

The general adaptation syndrome has three phases, namely alarm, resistance, and exhaustion (Gaidica and Dantzer 2020). The exhaustion phase signals that the animal has given all it had and is no longer able to fight; not only the stressor, but also opportunistic infections, and it will succumb in death (Fig. 1).

- Alarm phase (primary response): This phase involves the neuroendocrine system activation and stress hormone production (corticosterone). Corticotropic releasing hormone (CRH) is produced by the hypothalamus, which stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH). This further stimulates the rapid release of the stress hormone corticosterone from the adrenal gland (Getabalew et al. 2020), and corticosterone in turn increases the conversion of noradrenaline to adrenaline by stimulating the enzyme Phenylethanolamine *N*-methyltransferase (PNMT) in the adrenal medulla (Baffy 2020).
- Resistance phase (secondary response): This phase involves the effects of corticosterone on the body/organ systems. It encompasses the physiological and biochemical effects induced via the stress hormones, as they induce alterations in hematology and blood chemistry (Turk et al. 2017). During this process, glycogenolysis and gluconeogenesis occur in the liver to increase the level of glucose for the muscle and brain uptake, due to an increase in energy demand (Gaidica and Dantzer 2020). While both, corticosterone and adrenalin, can increase the production of glucose, the effect induced by corticosterone is longer lasting due to it having a longer half-life than adrenalin.
- Exhaustion phase (tertiary response): This phase involves the consequences of the various physiological changes (Haque et al. 2019). That is, the observable changes associated with stress. When the animal fails to cope with the said stressor, it will subsequently lead to decreased performance and furthermore, high morbidity and mortality rate. To avoid the adverse effects of stress on the normal physiology of the birds, early intervention is needed.



(Source: Baffy 2020)

Fig. 1. General adaptation syndrome of animals to stress showing the alarm phase which is the first response, the resistance phase which is an adaptive response and the exhaustion phase which may result in death due to continuous exposure to the stressor

Thus, if stress is left to run its course in livestock production such as poultry, it will reduce their ability to combat diseases and to gain live weight (Minka and Ayo 2013). Stress evokes harmful responses that interfere with the immunity and general health resulting in immunosuppression (Makeri et al. 2017). Of the different stressors to poultry production, environmental stress due to high ambient temperatures has been reported to be a major problem especially during the hot summer season (Beltran et al. 2021). The advent of climate change due to global warming can only be expected to make the situation worse, prompting an aggressive approach in adoption of stress mitigation strategies to sustain productivity and safeguard food security (Beltran et al. 2021).

Broiler chickens production during the hot summer season

Broiler chickens are Gallinaceous fowls that were domesticated and bred specially for the production of meat (Al-Zghoul et al. 2019; Darmani et al. 2019). They are subspecies of the red jungle fowl (*Gallus gallus*) and are hybrid of layers (Naidoo et al. 2007; Alemneh and Getabalew 2019; Dong et al. 2019). They have yellowish skin with white feathers (which are used for ornamentation or further processed into fertilizers or animal food). Under wild conditions, the birds would take 20 months to reach their adult weight. However, through very efficient selective breeding programmes, current meat strains of broiler chickens usually attain slaughter weight at about 5 weeks of age (Hassan et al. 2019; Arrazola and Torrey 2021), and grow much faster than the layers or dual-purpose breeds (Awad et al. 2020).

Today, these new breeds of chickens can be farmed in different ways, namely:

- Extensive system in which broiler chickens are not confined; that is, they are free to feed on their own. Here, the broilers are exposed to various disease conditions, effective monitoring and control is required (Mutibvu et al. 2017).
- Semi-intensive system in which broiler chickens are allowed to move out in search of feed within a confined environment. The broilers are also exposed to various disease conditions; hence, effective monitoring and control is advocated (Davoodi and Ehsani 2020).
- Intensive system in which broiler chickens are confined in deep litter and/or battery cages within an environment that is efficiently controlled and spacious, feed and water are provided ad libitum (Amao et al. 2019). This system is recommended for large-scale broiler production.

Nowadays, the production of chicken meat in the tropics, sub-tropics, and temperate regions is now reliant on keeping heavy chicken breeds, which are sold as live birds, or as fresh or frozen meat (Mohammed et al. 2018; Sumanu et al. 2019, 2021a). Chicken meat is accepted universally with no cultural or religious prohibitions attached to its consumption. The advantages of broiler chickens production globally are high turnover, ease of management, its wide acceptance for consumption, and fast returns on investment. Broiler chicken meat contains high-quality proteins with low level of fat (Bai et al. 2018). Broiler chicken meat is relatively less expensive, and its production is therefore profitable. The populace also prefers it because, being white meat, it is deemed healthier compared to red meat (Moataz et al. 2018; Wilson et al. 2018). Broiler chicken production was reported to have risen to 92.7 million tones globally in 2018 and is forecast to reach 100 million tones by the end of 2021 (Sokale et al. 2019; Olmez et al. 2021). A major benefit of rearing poultry is the relatively low production cost per unit and short production cycles which allow for multiple production cycles in a year (Vesco et al. 2017). However, these benefits are only realized when intensive farming is practiced, together with optimal management systems. The efficient and systematic management programme adopted by the farmer is very vital for the successful production of broiler chickens (Ibrahim et al. 2019; Sokale et al. 2019; Getabalew et al. 2020). Proper planning is key before the arrival of the chicks at the broiler house. The broiler production cycles are reliant on the purchase of day old chicks from hatcheries, which are from breeder farms; commercial farming systems rear them in their thousands in deep litter houses. The rearing of the chickens for about 5 weeks is dependent on the provision of feed, water, and optimum environmental conditions (Gatrell et al. 2018; Sumanu et al. 2019). At week five, broiler chickens attain a reasonable market weight of 2 kg on average and are marketed; and the cycle repeats for about 8 to 10 times annually in the tropics. Efficient biosecurity measures and management practice reduce the prevalence of most common diseases of poultry and subsequent mortality, which enhances productivity (Biswas et al. 2019).

While broiler farming has these benefits, broiler production in the rural areas faces the following challenges:

- Shortage of feed: Unavailability of specific feed for the breed of chickens or lack of funds to purchase the said feed are major problems faced by the farmers in the rural communities. For instance, in the case of broiler production, high energy feed is needed to support the rapid growth rate, thus low energy feed will impair their growth rate (Aluwong et al. 2013).
- Predators: Most poultry farms in the rural areas are often faced with the issues of reptiles, rodents, and the likes moving around the localities. This often limits the feeding pattern of the chickens as they serve as a form of stressors. Also, death may occur in the farm due to the bites obtained from the poisonous reptiles (Olawumi et al. 2019).
- Diseases: Outbreaks of mainly viral, parasitic, and bacterial diseases often limit the production of broiler chickens in rural areas. Increase in morbidity rate hampers the growth rate of broiler chickens and their general performance. Mortality may be at the high side in the farm due to diseases (Sumanu et al. 2021a).
- Lack of veterinary services: The services of a veterinarian cannot be underestimated in poultry farming. Veterinarians are responsible for the welfare of the chickens in the farm as they often advise the farmers appropriately concerning any disease condition or routine management. Therefore, the absence of their services on a farm can greatly affect the productivity of the chickens thereby limiting food availability and profitability (Olawumi et al. 2019).
- Poor housing: This is a common problem faced by poultry production in the rural areas as most farmers seldom take the welfare of the chickens into consideration (Hafez et al. 2019). Most rural farmers raise their chickens in pens with roof leakages, cracked walls, no footbaths, etc. These factors are responsible for limiting the productivity of the chickens thereby leading to food shortage for human consumption.

Other concerns are the processing of carcasses and potential contamination during processing with negative outcomes on human health. An integrated system of production was advocated in contemporary poultry industry, which takes animal health and product safety into consideration (Olawumi et al. 2019).

To mitigate the above challenges, the following factors have been shown to enhance productivity and safety:

- Housing conditions: Good housing condition increases the welfare and productivity of broiler chickens as they will often attain market weight within the production cycle (Sumanu et al. 2021a; Arrazola and Torrey 2021).
- Biosecurity: This measure enhances the performance of broiler chickens as it prevents the introduction of disease conditions and predators within the pen (Mohammed et al. 2018; Sumanu et al. 2021a).
- Improved diet: Diet with the required nutrients for broiler chickens production promotes the growth rate of the chickens evident as quick attainment of market weight (Aluwong et al. 2013; Sumanu et al. 2021a).
- Innovative processing and packaging: Adequate processing and packaging of broiler chickens that have attained market weight improves profitability. This further enhances production cycles (Kikusato et al. 2021).

While global warming can impact on all the conditions mentioned above, its effect on the optimal housing is of the biggest concern, as smaller change in temperature can have a major impact on animals' ability to be kept adequately cool in the later weeks of production, as per their thermoneutral zone (Sumanu et al. 2021b).

Thermoneutral zone of broiler chickens

Thermoneutral zone (TNZ) is defined as the ambient temperature range at which regulatory changes in the production of metabolic heat and evaporative heat loss are balanced (Egbuniwe et al. 2018). The TNZ for poultry in the tropics is reported to be 18–24 °C while it is 12–26 °C in temperate regions (Aluwong et al. 2017). The optimum temperature range for poultry production is 12–26 °C (Ravikumar et al. 2016). In South Africa, the TNZ for poultry production was reported at 18–24 °C for the KwaZulu-Natal area of South Africa (Mutibvu et al. 2017), and probably represents conditions in other parts of the country with extreme climatic conditions. In contrast, for Cape Town, it is 12–26 °C as it is a temperate (with moderate climatic conditions) region in the country. The diurnal ambient temperature often fluctuates in the tropics; exceeding the TNZ which results in heat stress in broiler chickens (Aluwong et al. 2017). Ambient temperatures that exceed TNZ of broiler chickens may elicit adverse effects on their health and energy balance, regardless of the age (Sinkalu and Ayo 2018). Increased temperature affects reproductive potentials, production, health status, and immune responses in broiler chickens.

Methods of maintaining constant ambient temperature in the poultry house

Adequate housing is paramount for broiler chicken production. The house must be well-equipped for factors like temperature, light, air, and moisture to be properly controlled. For efficient environmental control, heaters, exhaust fans, thermostats, air inlet, and evaporative cooling system are required (Schauberger et al. 2020). Appropriate temperatures should be maintained all through the production cycle in the pen; temperate regions require more insulation while the tropical and sub-tropical regions require efficient air speed (Oke et al. 2021; Sumanu et al. 2021b). It is expedient that broiler chicks are maintained in brooding temperature of about 31–32 °C for the first 14 days of life, but as they grow older, they require cooler temperature within the range of 12–26 °C for optimum growth (Egbuniwe et al. 2015). Adult broiler chickens often express changes in their behavior like congregating, eating more feed, and drinking less water when exposed to cooler temperatures and the reverse occurs when exposed to hot temperatures in order to keep warm when the temperature is not too favorable.

Poultry house ventilation

Poultry house ventilation provides fresh air that is important in sustaining life. It is essential in reducing high temperature, air contamination, and humidity to the bearable minimum/optimum level. Ventilated air loses excessive heat, odor, dust, and moisture from the poultry house; it also dissipates disease organisms that are airborne (Chirarattananon et al. 2012). Proper ventilation is a great challenge in poultry housing due to the variations in temperature, season, humidity, time of the day, age of the chickens, and wind (Samuel et al. 2013). The principle of ventilation is that, air composition changes if the air in an enclosed space is not replaced. As the air in the poultry house is exchanged by the ventilation system, oxygen needed for the sustenance of life is brought in while odors and harmful gases are removed.

Ventilation system

Ventilation system can be divided into two major types: natural ventilation system and mechanical ventilation system.

Natural ventilation system: The essential requirements for this system of ventilation is that, there must be adequate fresh air supply and distribution in the poultry house brought about, by wind direction and speeds, the geographical features of the site and orientation of poultry house in respect of the more predominant wind patterns. This ventilation can be maintained by placing air vents close to the eave of the poultry building. Curtains can also be used to maintain optimum ventilation because an equal opening often runs the length of the poultry building when curtains are lowered. The ventilation system requires some modifications between the winter and summer periods in order to keep the chickens in a comfortable state (Chirarattananon et al. 2012):

- Winter ventilation: This system is a bit complex than that for the summer months as the poultry house needs to be tightly closed to obtain maximum energy conservation and comfort, which results in humidity, odors, gases, etc. being trapped in tight enclosures which must be continually dealt with for optimum health status of the chickens (Bhadauria et al. 2016). This type of ventilation requires the removal of excessive moisture that is build up in the poultry house as compared to the summer ventilation wherein the removal of heat is required. During winter, there is less carbon dioxide and ammonia build up in the poultry house when compared with the summer season.
- Summer ventilation: During summer, natural ventilation system is required especially in poultry houses where side curtains are used, as the curtains are often raised up for optimum flow of natural air into the building whereas in winter, the curtains are mostly dropped (Xuan et al. 2012). Also, air vents are left opened to allow the influx of natural air into the building, whereas it is left covered during the winter season. Here, the removal of excessive heat is paramount due to the hot season as compared to winter ventilation where moisture is mostly at the extreme. In contemporary poultry production, environmental changes impair this system’s effectiveness due to recurrent rise in temperature resulting from global warming (Bhadauria et al. 2016).

Mechanical ventilation system: In extreme climatic conditions, this system of ventilation is required to ensure proper ventilation of the house (Yahav and Hurwitz 1996). Electric fans are used as principal components in this system for the movement of air in the poultry house.

The components of this system are fans required for air movement through the poultry house, air inlet and outlet vents and lastly, and a control unit for the regulation of the fans (timers and thermostats).

- Fans: For this system of ventilation, one must consider the wide range of climatic conditions for appropriate selection of the desired fan that can cover a large area of the poultry house. Proper wiring should be done to avoid fire outbreaks or shocks from the fan which might pose great danger to the chickens and the farmers (Bhadauria et al. 2016).
- Inlets and outlets: The fan is the determinant of the rate of air exchange in the poultry house, but the adjustment, location, and design of the air inlets are primary determinants of air uniformity. The recommended air inlet velocities in a poultry house are 600–1000 feet per minute for large size chickens and 300–500 feet per minute for average size chickens (Bhadauria et al. 2016).
- Controls: Thermostats alone or in combination with timers are used to control fans. Single stage thermostats through the activation and stoppage of fan control one or more single speed fans when temperature rises and drops, respectively (Schauberger et al. 2020). A double-throw switch thermostat also controls two-speed fans; it changes automatically from a high to low speed as the temperature increase or decrease, respectively. Therefore, when maximum ventilation is required to expel excessive heat in the poultry house, timers interconnected with thermostats are needed.

Heat stress and its adverse effects on broiler chicken production

Heat stress is caused by either high ambient temperatures (AT), lack of ventilation, and high relative humidity (RH) or a combination of these factors. In the tropics, heat stress is caused by a combination of high RH and AT (Minka and Ayo 2013). In the sub-tropical and arid regions, as expected, heat stress is more than the temperate regions, unless the broiler chickens are reared intensively with automated regulation of microclimatic conditions (Aluwong et al. 2017). In most rural areas in South Africa, broiler chickens are subjected to the adverse effects of heat stress by being raised under an extensive or free-range management system, which exposes them to significantly high AT during the hot season of the year (Mutibvu et al. 2017). The effects of high environmental parameters on broiler chickens do not only depend on the microclimate but also on the intensity of their stocking density (Bhadauria et al. 2016). The physiological adjustments made by broiler chickens to altered environmental conditions via various mechanisms, including cardiovascular, neuro-endocrine, behavioral, and respiratory thermoregulatory responses, are overwhelmed in heat stress (Kikusato and Toyomizu 2019).

High AT is detrimental to broiler chicken production through altered normal physiological functions such as reduced feed intake which leads to reduced body weight (due to poor feed conversion ratio) and subsequently impaired health status, which may lead to morbidity and mortality (Amiri et al. 2019). Other effect includes lower reproductive performance of broiler chickens resulting in reduced egg fertility in breeder flocks (Ramiah et al. 2019); as well interference with the rate at which hormones are secreted and their clearance from the body (Nyoni et al. 2019). Hence, the need to consider heat stress mitigation when designing poultry farms in the tropics.

Thermoregulation in chickens

Thermoregulation is the process by which the body maintains homeostasis of body temperature (Minka and Ayo 2013). The various processes involved in thermoregulation in birds under conditions of high temperatures are described below:

Chemical response to heat stress

The hypothalamus is responsible for the reception and integration of signals from thermal receptors to stimulate regulation in both humans and animals (Kumari and Nath 2018). During heat stress in broiler chickens, signals are sent to the hypothalamus to release corticotropic-releasing hormone, which further stimulates the pituitary gland to release adrenocorticotropic hormone that stimulates the adrenal gland to release corticosterone into the blood stream (Gaidica and Dantzer 2020). When this hormone is released in the body system, the hypothalamus is furthermore stimulated to initiate the process of thermoregulation as a response to the increased level of corticosterone in the blood (a positive feedback mechanism) (Sugiharto et al. 2017; Xu et al. 2019). This further improves the general performance of the broiler chickens, decreasing the rate of morbidity and mortality (Wasti et al. 2020).

Evaporative cooling

With chickens not having sweat glands, they are reliant on evaporative cooling from their lungs surface and air sacs to cool themselves (Xuan et al. 2012; Campderrich et al. 2019; Vieira et al. 2019). As a process, the conversion of water to water vapor expends energy in the form of heat. Therefore, as the water vaporizes from the lungs surface of the broiler chickens heat is concurrently lost from the body (Ranjan et al. 2019).

Behavioral response to promote heat loss

- Water intake: To enhance cooling further, behavioral responses include drinking of more water and eating less to enhance evaporative cooling (Shao et al. 2019).
- Food intake: In addition to the broiler chickens drinking more water, they also eat less to lower metabolic heat production from digestive processes. The gastrointestinal tract and liver contribute to heat production as the suprahepatic rete which supplies them blood functions as heat exchanger that retains metabolic heat produced by the muscle. Thermal conduction from the vessels in the liver and warm blood supply are both responsible for transferring heat to the stomach (Law et al. 2019; Hanchai et al. 2021).
- Panting/gular flutter: This behavioral response heightens the smooth passage of air through the various systems of the body, thereby increasing evaporation cooling through the lungs, which subsequently lowers the temperature of the body (Al wakeel et al. 2019).
- Enhancing surface area: Broiler chickens exposed to heat stress usually spread out their wings to initiate effective radiation of heat from the body to the environment in order to keep the body cool. There is usually shunting of blood from the gut to the comb to reduce the rate of metabolic heat production/pick-up and increase the rate of heat loss from the body system, respectively through surface radiative cooling (Tickle and Codd 2019).

Effects of heat stress on the performance of broiler chickens

In the Southern and Northern hemispheres, heat stress season falls within the period of September to March and March to June, respectively, which is thermally stressful for broiler chicken production. The ATs during this season are usually at the upper limit, which is an indicator that the season is thermally stressful to the broiler chickens (Keshri et al. 2019; Slawinska et al. 2019). Broiler chickens are homeotherms, meaning they strive to keep their body temperature relatively constant in the face of either rising or decreasing ambient temperature; but when the rate of heat dissipation to the environment is lesser than the rate of metabolic heat production and heat gained from the environment, the body temperature rises concurrently (Yousaf et al. 2019).

The following changes have been associated with heat stress:

- Changes in performance (production efficiency): Heat stress greatly impact the feeding pattern of broiler chickens and this subsequently results into 33% decrease in body weight gain (Lara and Rostagno 2013) which further impairs the production efficiency of the chickens (Toyomizu et al. 2019; Sumanu et al. 2021b).
- Immunocompetence: The immune responses of broiler chickens are impaired during heat stress due to the presence of excessive reactive oxygen species (ROS) that cause cellular damage (Seremelis et al. 2019). The body's defence mechanisms are weakened over a period of time due to the increased level of pro-inflammatory cytokines in circulation.
- Hematology: The blood parameters of broiler chickens are negatively affected during heat stress (Karadagoglu et al. 2020). About 10 to 20% decrease in concentration of white blood cells have been reported and this affects the immunity of the chickens to a greater extent (Ogbuagu et al. 2018).
- Deoxyribonucleic acid (DNA) damage: Oxidative stress, due to the excessive production of ROS also causes oxidative DNA damage (Poetsch 2020), DNA adducts that can lead to mutation in DNA which causes genetic disorders (Sofinska et al. 2020).
- Behavioral parameters: The effect of heat stress on broiler chickens generally affects the nervous system that controls all other systems of the body. Several behavioral changes in response to heat stress occurs in broiler chickens like panting, drooping feathers, drinking more water, and feeding less. Also, fear responses are often heightened in broiler chickens exposed to heat stress (Sumanu et al. 2019).
- Sleep disorders: Heat stress creates an unfavorable condition for sleeping due to the high metabolic heat production and the lack of sweat glands to dissipate the heat by the broiler chickens (Sinkalu et al. 2016). Also, during heat stress, there is decreased secretion of melatonin, a hormone from the pineal gland responsible for the regulation of sleep.
- Bone abnormalities: Bone formation is impaired due to bone marrow degradation as corticosterone is proteolytic. It degrades organic bone matrix affecting strength, it also affects calcium and phosphate absorption, which contributes to the abnormalities (Sugiharto et al. 2017; Patael et al. 2019).

Oxidative stress and antioxidant system of the body

Despite the numerous pathological changes induced by heat stress, at the physiological level, much of the effects seen are due to oxidative stress. The disproportion between antioxidants and free radicals in the body system is known as oxidative stress. Antioxidants are molecules that prevent the oxidation of other molecules (Aluwong et al. 2017), while free radicals are molecules containing oxygen. Some free radicals are produced naturally in the presence of inflammation or exercise in the body and they contribute in keeping the body healthy. The environment also contains pollutants and radiation that might also aggravate the level of exposure to oxidative stress (Sumanu et al. 2021b). An important feature of free radicals is their instability that allows them to react easily with other molecules. Their ability to react easily creates large chain reactions in the body, which are known as oxidation reactions.

Oxidative stress induced by heat stress is responsible for the impairment of several body functions like the digestion of feed, reproduction as seen in broiler breeders, etc. which eventually result in poor meat quality, increased morbidity and mortality rate, thereby decreasing their productivity (Awad et al. 2020; Sumanu et al. 2021b). Oxidative stress could also heighten fear responses in broiler chickens due to the increased level of epinephrine in the body which is evident as long duration of tonic immobility and prolonged vigilance period in most behavioral studies (Egbuniwe et al. 2018; Sumanu et al. 2019). Reduced expression of messenger ribonucleic acid (mRNA) occurs as a result of oxidative stress due to an impairment in the process of gene replication and transcription. This further leads to a decreased level of intestinal immunity locally (such as immunoglobulins) and increased apoptosis (Lee et al. 2019). Oxidative stress resulting from excessive free radical is virtually impossible to avoid especially due to the presence of heat stress resulting from the effects of global warming (Song et al. 2019). Nevertheless, increased level of exogenous antioxidants could be helpful in preventing oxidative stress based on the equilibrium state these can provides.

Several organs and tissues of the body possess a distinct antioxidant system that respond to oxidative stress (Aluwong et al. 2013; Ogbuagu et al. 2018). This system defends cells against oxidative damage to proteins, lipids, and DNA (de Almeida et al. 2019; Attia et al. 2019; Azeez et al. 2019). The body protects itself against the adverse effects of ROS via two important mechanisms, which are regulation of membrane permeability and potential antioxidant system. Antioxidant metals such as copper, zinc, and manganese are components of superoxide dismutase (SOD) enzyme that scavenge superoxide radical, which is vital in eliciting a defensive mechanism against ROS (Lee et al. 2019). SOD is responsible for the dismutation of free radicals to hydrogen peroxide; thereafter, glutathione peroxidase and catalase split the hydrogen peroxide into molecules of water and oxygen, thereby rendering the radicals inactive (Ogbuagu et al. 2018; Sumanu et al. 2019). During heat stress, the mitochondria of skeletal muscle in broiler chickens are responsible for the production of superoxide anions as a response to oxidative stress in order to neutralize the harmful effect of the increased levels of free radicals (Egbuniwe et al. 2018). Erythrocytes also show some level of antioxidant defence, but the erythrocyte life-span decreases by 50% in the presence of oxidative stress based on the fact that the stability of the erythrocyte is reduced drastically leading to haemolysis (Ogbuagu et al. 2018; Brothers et al. 2019).

Cytokines induced antioxidant formation and their roles in the body system during heat stress

Cytokines are small proteins that are important in cell signaling (Wang et al. 2019), that are unable to cross the lipid bilayer in order to penetrate the cytoplasm of a given cell (Khan et al. 2019). They serve as immunomodulating agents and also in paracrine, autocrine and endocrine signaling. Examples of cytokines are the interleukins (IL), transforming growth factor (TGF), tumor necrosis factor (TNF), interferon (IF), lymphokines, and chemokines. A broad range of cells is responsible for the production of cytokines, including T lymphocytes, B lymphocytes, macrophages, mast cells, stromal cells, fibroblasts, and endothelial cells (Seremelis et al. 2019).

Cytokines are very vital in the immune system of the body and they elicit their effects through various site-specific receptors like interferon-alpha receptor and transforming growth factor-beta receptor (Dai et al. 2019). The balance between cell-based and humoral immune responses is effectively modulated by these cytokines; they are involved in the regulation of cell responsiveness, growth, and maturation (Saleh and Al-Zghoul 2019). Cytokines are different from hormones as some cytokines are normally circulated in picomolar concentrations, but increase a 1000-fold in the phase of an infection or trauma or any form of stress, while hormones are circulated in nanomolar concentrations (Al-Zghoul 2019). The distribution of the various cellular sources of cytokines is also a major distinguisher to the hormones which are produced by more specific tissue types considered as glands. The endothelial and epithelial cells, macrophages, and, probably, all the nucleated cells are efficient producers of TNF-α, IL-6, and IL-1, with the result that the cytokines are typically referred to as immunomodulating agents (Hu et al. 2019). The last major difference between cytokines and hormones is their localized effect. As a result, cytokines are considered paracrine or autocrine in nature; as a pyrogen, they may be endocrine, chemokines, and chemotaxins; although their effect is not necessarily limited to immunomodulation (Yang et al. 2019).

Previously, the term interleukin was used for those cytokines whose assumed targets were principally leucocytes (Humam et al. 2019). Examples of cytokines are:

- Interleukins: Majority of the interleukins are produced by leukocytes. They are responsible for immune cells activation, differentiation, maturation, proliferation, adhesion, and migration (Humam et al. 2019). Their key role during immune and inflammatory responses is to modulate growth, differentiation, and activation. ILs are made up of proteins that induce many cellular and tissue reactions through their ability to bind to receptors with high affinity on the surface of the cell. They elicit both autocrine and paracrine function (Dai et al. 2019).
- Interferon: They are proteins that play a role in natural defence as they stimulate killer immune cells to knock out an invader which could be bacteria, fungi, or virus. They are also responsible for antiviral responses. The name interferon came to being based on their ability to interfere with invading viruses and inhibit their multiplication (Humam et al. 2019). The three major types of interferons produced by the body are interferon alpha, beta, and gamma. In the phase of an ongoing infection (viral) at the cellular level, interferon-alpha and beta are both released as a sign of warning to the immune system; this further triggers the white blood cells to give off interferon-gamma to combat the infection (Khan et al. 2019).
- Monokines: They are peptides exclusively produced by monocytes and macrophages. They are responsible for the regulation of inflammatory or immune responses via the binding of target cell receptors. The target cells may be macrophages and monocytes (autocrine response), leukocytes, endothelial cells, or fibroblasts (Khan et al. 2019).
- Lymphokines: They are produced by lymphocytes, which are immune cells. They are protein mediators that are responsible for directing the immune system (Humam et al. 2019). Lymphokines function by attracting lymphocytes and macrophages to the site of infection; they are subsequently activated to mount an immune response.

Lymphokines in small concentration can be detected by the circulating lymphocytes after which the concentration gradient is moved to the required immune response site (Seremelis et al. 2019).

- Chemokines: They are responsible for chemoattraction (chemotaxis) in cells. They play a vital role in the migration of cells from blood into the tissue via venules and vice versa. The development of lymphoid organ and differentiation of T cell are regulated by chemokines. They also function as neuromodulators (Calefi et al. 2019).
- Colony stimulating factors (CSFs): They are glycoproteins that bind to the hematopoietic stem cell surface that activates the signaling pathways intracellularly thereby causing the proliferation and differentiation of the cells into white blood cells specifically. They are also responsible for the response of an individual to infection and injury (Yang et al. 2019).

Cytokines generally play a role in the pathways regulating inflammatory process:

- Pro-inflammatory cytokines: They are molecules that try to act to resolve an infection and contain inflammatory foci via the activation of systemic or local inflammatory responses. They play a vital role in inflammatory disease of non-infectious and infectious origin (Zhang et al. 2019). The excessive release of these cytokines can lead to cytokine storm in the systemic circulation which may trigger several disease conditions like multiple organ failure and subsequently death. The activities of pro-inflammatory cytokines are often inhibited by the synthesis of anti-inflammatory cytokines (He et al. 2019).
- Anti-inflammatory cytokines: These cytokines are molecules responsible for immune regulation; as they control the response of pro-inflammatory cytokines, they achieve this immune response regulation by acting in concert with cytokine inhibitors and soluble cytokine receptors that are specific (Dai et al. 2019). The release of anti-inflammatory cytokines often terminates the activities of pro-inflammatory cytokine (He et al. 2019).

Cytokines are thus, not surprisingly, involved in the innate or natural response via the direct action against several agents that invade the body or they elicit an immunomodulatory effect, via the activation of monocytes-macrophages, which eventually induce the release of more cytokines (Pitargue et al. 2019). Cytokines play a vital role directly via the different immune-modulatory mechanisms, responsible for the activation of elevated body temperature, inflammatory response, and activation of macrophages (Baxter et al. 2019). Cytokines that play a key role in innate immune responses are IL-16, IL-12, IL-6, IL-1, IFN-a, IFN-g, and TNF-a.

- The IL-12, IL-6, and IL-1 are involved with the activation of natural killer cells and macrophages. They also trigger the mechanisms involved in body temperature elevation. They reduce the replication ability of the invading pathogen via the activation of immune response (Akter et al. 2019).
- The TNF-a is involved in the activation of inflammatory response. Their effects on blood vessels are responsible for the increase in vascular permeability, which subsequently leads to fluid, plasma protein, complement, and immunoglobulin accumulation. This is a collaborative defence against infections (Zhu et al. 2019).
- The IFN can either be gamma, beta or alpha, which functions differently to inhibit the replication of viruses. They are produced mainly by macrophages and minimally by fibroblasts. They elicit an antiviral and resistance effect against viruses in the body.

This is known as the innate immune responses to viral infection in the host. The IFNs induce the secretion of certain antiviral molecule called oligoadenilate-synthetase (Cheng et al. 2019).

Also of importance is that oxidative stress is induced by several inflammatory cytokines (Humam et al. 2019) from the oxidative burst reaction. During the oxidative burst reaction, the immune system rapidly releases macrophages and neutrophils as a means of defence. Cytokines induce the release of other cytokines which leads to an elevated level of oxidative stress hence their importance in chronic inflammation and hyperthermia (IL-12, 6, 1, and IFN-a) (Song et al. 2019). During heat stress, the circulatory level of pro-inflammatory cytokines like IL-6, TNF-a, etc. are heightened in broiler chickens (Ma et al. 2019). When broiler chickens are exposed to heat stress, the microglia (cells responsible for immune defence in the central nervous system) can move from a resting state to an active state during which pro-inflammatory cytokines are not released actively (Cheng et al. 2019). However, with continuous exposure to this stressor (heat), this may further trigger the release of pro-inflammatory cytokines in the systemic circulation due to the ongoing inflammatory process that occurs with further stimulation of the microglia. Therefore, it could be denoted that heat stress triggers inflammatory processes which increase the level of circulating pro-inflammatory cytokines in the body.

Effect of heat stress on oxidative DNA damage

One of the impacts of heat stress has been DNA damage and protein degradation which causes alterations in genes and cell death (Elnesr et al. 2019). Oxidative stress, which is an imbalance between the amount of ROS and endogenous antioxidants in the body, is the major factor that induces DNA damage (Sofinska et al. 2020). ROS induce several lesions to the DNA molecules such as inter-strand and intra-strand cross-links, DNA–protein cross-links, sugar, and/or base alterations and sugar-base cyclisation, all of which further result into breaks of DNA strands (Cramer et al. 2019). Ultraviolet light and ionizing radiation are exogenous agents that induce DNA damage through oxidative stress.

Mitigation strategy against the adverse effects of heat stress on broiler chicken production

With the detrimental effects of heat stress on poultry production, mitigation is necessary. In technologically advanced poultry farming, this may be achieved by the implementation of mechanical systems, as explained above (Bhadauria et al. 2016; Xuan et al. 2012). The disadvantages of this system are for instance; high cost of equipment, high maintenance cost, constant electricity supply, and potential inability to recoup investment from sales. Due to the disadvantages mentioned above, it may not be feasible to implement mechanical systems in less developed economies; also, if a cheaper and therefore more profitable alternative system or strategy exists, even those in developed economies could also adopt it. Thus, alternate mechanisms need to be investigated. With ROS production and oxidative stress being a major factor in heat stress, mitigating these changes could result in cheaper alternate methods of managing the dangers of heat stress (Sumanu et al. 2019, 2021b).

With antioxidants being molecules that have an in-built capability of preventing or slowing down other molecules' oxidation (Yang et al. 2019), they could prove to be successful as therapeutic compounds. Antioxidants prevent the peroxidation of lipids by ROS (Aluwong et al. 2017; Ogbuagu et al. 2018; Sumanu et al. 2019). They are very effective because they easily donate their own electron to free radicals. When a given antioxidant donates an electron to a free radical, the free radical is unable to cause further harm to cells as the oxidation chain reaction is broken. Oxidation is a chemical reaction in which an electron is transferred from one substance (reducing agent) to another (oxidizing agent). Antioxidants are also currently used in dietary supplements as ingredients, and their supplementation is highly beneficial against stress-induced tissue damage (Ogbuagu et al. 2018; Sumanu et al. 2019).

Antioxidants for example, probiotic, phytonutrients, and amino acids are widely used in farms and especially in poultry production as anti-stress agents via their function in the hypothalamus–pituitary–adrenal axis, which, therefore, reduce the level of corticosterone secreted in the blood (Sumanu et al. 2019; Elghandour et al. 2020). They also induce peripheral vasodilation with resultant increase in heat loss. They serve as growth promoters via the suppression of the satiety centers in the brain to induce increased feed intake which subsequently leads to an increased body weight gain (Al-Nasrawi et al. 2020; Sumanu et al. 2021a). They improve the immune system of the broiler chickens via the activation of the body defence mechanisms for instance, the endogenous antioxidants systems such as superoxide dismutase, catalase, glutathione peroxidase, etc. which subsequently prevent outbreaks of several disease conditions (Naidoo et al. 2008; Adamu et al. 2014; Zhao et al. 2019; Sumanu et al. 2021b). These antioxidants, when adequately used, could also allow return to normal behavior via thermoregulatory measures. Previous studies have reported that antioxidant substances such as probiotics of fungi and bacterium strains, and other prebiotics like curcumin, onion, avocado, etc. and phytonutrients such as fisetin, zinc gluconate, vitamins C, A, and E are highly beneficial in attenuating the adverse effects of heat stress in broiler chickens (Egbuniwe et al. 2018; Shimao et al. 2019; Sumanu et al. 2021b).

In a study by Aluwong et al. (2017), the administration of *Saccharomyces cerevisiae* probiotic and zinc gluconate at the dose of 4.125 × 106 cfu/100 mL and 50 mg/kg, respectively to broiler chickens exposed to heat stress mitigated the adverse effect of heat stress which was evident as a decrease in cloacal temperature values during the study period. They concluded that the groups of broiler chickens treated with probiotic had better thermoregulation when compared with the zinc gluconate-administered and control groups, respectively. Wang et al. (2016) stated that the administration of *Bacillus subtilis* probiotic at a dose of 1×10^6 cfu/g to broiler chickens exposed to heat stress reduced inflammatory responses and heat stress-related behaviors. It was concluded that this strain of probiotic was potent in modifying gut microbiome with resultant decreased heat production in the broiler chickens. Sinkalu et al. (2016) reported that the administration of melatonin to broiler chickens at the dose of 0.5 mg/kg during the hot-dry season reduced fear responses in broiler chickens subjected to tonic immobility test when compared with the group that was not administered with melatonin. They concluded that the administration of melatonin to broiler chickens mitigated the deleterious effect of heat stress which was evident as an increment in boldness of the chickens. It could be speculated that as broiler chickens advance in age, there is a resultant increase in metabolic heat production, which increases their exposure to heat stress and subsequently increase fear responses. Therefore, the administration of antioxidants or anti-stress agents might be effective in reducing heat stress and subsequently fear responses which are seen as boldness and alertness in the broiler chickens based on the similarities in the path-way of fear and stress responses.

Habibian et al. (2014) stated that the administration of vitamin E at a dose of 200 mg/kg to broiler chickens exposed to thermal stress reduces the heterophil/lymphocyte ratio which was a prove that the chickens were able to strive better during heat stress condition as compared to the control group. Vitamin E, a potent fat-soluble vitamin, exhibits it antioxidant effect by preventing damages caused by free radicals during the process of oxidation in the body. It was further concluded that vitamin E administration was able to improve blood parameters of the broiler chickens. The table below summarizes the effect of other antioxidants in poultry species exposed to thermal and transportation stress (Table 1).

Table 1 Effects of supplementing poultry species diet with some antioxidants during exposure to heat and transportation stress

Antioxidants	Poultry species	Effects	References
Saccharomyces cerevisiae probiotic	Broiler chickens	Improved performance indices, carcass characteristics and small intestinal morphology.	Sumanu et al. (2021a)
		Decreased erythrocyte osmotic fragility, malondialdehyde concentration and Improved superoxide dismutase enzyme activity	Ogbuagu et al. (2018)
		Decreased fear responses, muscle tissue malondialdehyde concentrations and improved muscle tissue superoxide dismutase enzyme activity	Sumanu et al. (2019)
Betaine	Quails	Enhanced endocrine secretions and erythrocyte parameters	Egbuniwe et al. (2021)
Ascorbic acid	Broiler chickens	Increased alertness and haematological parameter	Egbuniwe et al. (2018)
Melatonin	Quails	Improved colonic temperature and erythrocyte osmotic fragility	Minka and Ayo (2013)
Fisetin	Broiler chickens	Little or no effect on cloacal temperature parameter	Sumanu et al. (2021b)
Oleuropein	Broiler chickens	Improved oxidative status and hormonal concentration	Shimao et al. (2019)

As evident from the above, the control of heat stress through non-ventilation means could be more economical and cost-effective. For instance, the use of *Saccharomyces cerevisiae* probiotic in poultry production could help in mitigating heat stress, improve immune status and also serve as a growth promoter. This agent could be cost-effective based on the fact that the broiler chickens' health status would be improved and there would be a reduced need for the use of antibiotics and anticoccidial agents, assuming efficient biosecurity measures are also in place. With an improved performance in immune status, one should also see a reduction in morbidity and mortality and possible better market weights at slaughter age (Fig. 2).

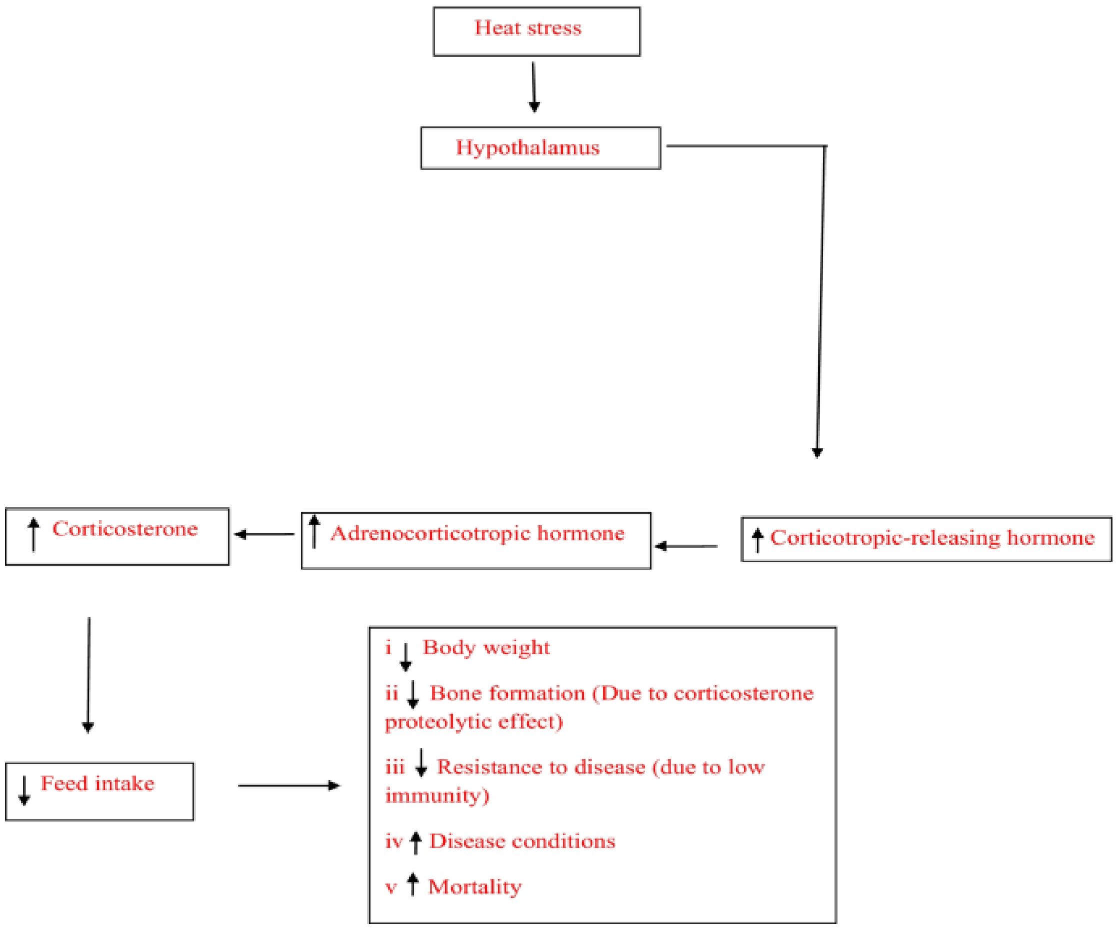


Fig. 2. Schematic diagram summarizing the adverse effect of heat stress on broiler chickens. The neuro-endocrine system responds to heat stress by stimulating the secretion of specific hormones that affect the performance parameters and welfare of the chickens

Conclusion

The target of this review is to address the adverse effects of heat stress during summer on broiler chickens production and antioxidant mitigating effects. Heat stress impairs the general performance of broiler chickens; it induces oxidative stress which elicits inflammatory responses leading to the release of inflammatory cytokines in the body. It also induces single and double stranded DNA breaks thereby resulting in oxidative DNA damage. Therefore, the use of potent antioxidants is advocated to ameliorate the adverse effects of heat stress in broiler chickens production during the hot (summer) season of the year for optimum productivity.

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Conflict of interest

The authors declare no conflict of interest.

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