



Chronic Heat Stress Effect on Metabolic Parameters of Poultry: A Meta-Analysis

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Abstract

Many scientific researchers reported the significant effect of heat stress (HS) on commercial poultry production. Bird metabolism and blood parameters change during acute and chronic heat stress status. This article reviewed and analyzed the broiler blood parameters under normal thermal and cyclic-chronic heat stress conditions. All the reviewed reports were achieved from Elsevier, PubMed, Web of Science, and Google Scholar those were in English up to January 27, 2022. Outcomes of blood cholesterol (Chol), triglyceride (Tri), glucose (Glu), corticosterone (Cortico), uric acid (UA), sodium (Na⁺), Potassium (K⁺), and triiodothyronine (T3) were calculated by standardized mean difference (SMD) with 95% confidence interval (CI). Articles with common metabolite differentiated between 4 or 7 studies with 94-662 chicks in each of them. Chronic HS had no significant effect on blood concentrations of Cortico (5 studies: SMD=1.8153 95% CI=-2.9524; 6.5830), Tri (studies=7 SMD=0.4559 95% CI=-0.2923; 1.2040), Uric (studies=5 SMD= 0.9590 95% CI= -0.3338; 2.2518), T3 (studies=4 SMD= -9.006 95% CI= -46.1608; 28.1487), K⁺ (studies=4 SMD= -6.675 95% CI= -20.1400; 6.7898) , but significantly increased Glu (studies=8 SMD= 0.3064 95% CI= 0.0027; 0.6100), Chol (studies=6 SMD= 0.7655 95% CI= 0.2653; 1.2658) and decreased Na⁺ (studies=4 SMD= -1.723 95% CI= -3.1536; -0.2925) levels. Statistically significant effects of chronic heat stress reflexed as a decrease in serum sodium, increase in cholesterol, and glucose level. But there was no significant difference between triglyceride, corticosterone, uric acid, potassium, and triiodothyronine in the heat stress and normal temperature group. Based on our meta-analysis, high blood glucose, high Cholesterol, and losing electrolyte balance are major problems in chickens during cyclic-chronic heat stress acclimatizing programs.

Introduction

Strategies in poultry breeding programs aim to increase feed efficiency, growth rate, and body weight (BW); decrease abdominal fat and production costs, and modulate the biochemical and physiological parameters (Mohammadabadi *et al.*, 2010; Mohammadi Far *et al.*, 2014; Mohammadifar and Mohammadabadi, 2017). Stresses are disturbance agents of homeostasis, and mental and physical illness is a common result of them. The Hypothalamic-pituitary-adrenal axis (HPA) and adrenergic pathways are the main processors of stress, and their activation in stressful conditions results in increasing corticosteroid level, body reserve

depletion, and decline in immune response and productive performance (Nakagawa *et al.*, 2016; Nakagawa *et al.*, 2020).

Heat stress leads to reactive oxygen species (ROS) formation and consequently stimulates the peroxidation of lipid sources. Descriptive changes in the metabolic profile of chickens are a decrease in plasma triglyceride, total cholesterol, uric acid, and thyroid hormone levels and an increase in plasma glucose and corticosterone levels (Lin *et al.*, 2006; Bahry *et al.*, 2017).

During heat stress, the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system (ANS) are overactivated which resulted in alteration of the biochemical and physiological

parameters. Increased plasma corticosterone, decreased triglyceride and cholesterol, and some metabolic changes have been reported in heat stressed chickens (Ito *et al.*, 2015; Chowdhury *et al.*, 2017). These changes are the result of body strategies and the biological mechanisms that led to acclimatization or mortality in commercial poultry. This adaptation to heat stress conditions depended on age and heat stress duration. A previous meta-analysis has proved a significant effect of HS on feed intake, body weight gain, and feed conversion rate compared to the control group (Liu *et al.*, 2020). These significant changes in performance indexes are results of changes in the metabolic profile of chickens (Lin *et al.*, 2006; Bahry *et al.*, 2017). Based on the above literature the purpose of this research was to investigate and meta-analysis of blood metabolite changes in chronic heat stressed chickens of different ages.

Materials and Methods

Elsevier, pub med, web of science, and google scholar scientific websites and research engines were used for English scientific publications containing keywords such as heat stress, chick, bird and hot weather, poultry, metabolite, and serum up to November 27, 2021. Keywords were surveyed in titles and abstracts of identified articles. If the title and abstract would not able to show sufficient information to select or dismiss the study for analysis, the study was reviewed in the whole text. Researches in meat-type and egg-type chickens with control and cyclic-chronic heat stress treatments were chosen that have reported one of the metabolic parameters.

Data collection

Chosen article with potential criteria was reviewed and data was gathered in Excel sheets. Every sheet had the year of publication, authors name, chick breed, chicken number and age, temperature for the HS group and control group, heat stress duration, and blood metabolites.

Statistical Analysis

R free software (Team, 2013) was used for statistical analysis. standardized mean difference (SMD) (Cumpston *et al.*, 2019) with a 95% confidence interval (CI) was applied to calculate the difference between parameters means of heat stress and control groups. Heterogeneity among studies was examined by Cochran's Q statistic and I2 test (Higgins *et al.*, 2003; Cumpston *et al.*, 2019). Significant heterogeneity was observed if the P-value < 0.05 (Q statistic) and/or I2 > 50, and after that, the random-effect model was used, otherwise, the fixed-effect model was used. Significant heterogeneity observed if P-value < 0.05 (Q statistic) and/or I2 > 50.

The random effects model for each parameter, displayed by $\hat{\theta}_j = \bar{\theta} + u_j + e_j$, where, $\hat{\theta}_j$ is the parameter estimate in study j, $\bar{\theta}$ is the weighted mean of the parameter in the population, u_j is the between-study component of the deviance from the mean, with $u_j \sim N(0, \tau^2)$, where τ^2 is the amount of heterogeneity among studies, while e_j is the within-study component of the deviation from the mean in study j, with $e_j \sim N(0, \sigma^2)$. For computing the common effect on the estimates of the parameters over every study, that is necessary to weight the individual values.

Table 1. Characteristics of included articles

Article	Strain	No chicks in each group	Chicken age/experiment duration (day)	Control temperature	Heat stress temperature/daily duration (h)
Azad <i>et al.</i> 2010	Ross	6	14.14	31	38.8
Roushdy <i>et al.</i> 2018	Ross/Cobb	45	22.20	22	40.6
Alhenaky <i>et al.</i> 2017	Hubbard	24	27.10	25	38.4
Song <i>et al.</i> 2012a	Layer	8	168.7	20	38.6
Sun <i>et al.</i> , 2015	Ross	9	35.7	22	38.10
Wang <i>et al.</i> 2018	Layer	30	14.27	30	39.8
Beckford <i>et al.</i> 2020	Ross708	4	31.8	23	39.8
Sugiharto <i>et al.</i> 2017	Lohman	5	22.13	28	39.5
Barrett <i>et al.</i> 2019	Layer	201	168.28	20	39.8
Quinteiro-Filho <i>et al.</i> 2012	Ross	90	35.7	26	39.10
Garriga <i>et al.</i> 2006	Ross	13	28.14	26	39.8
Al Wakeel <i>et al.</i> 2017	Ross	3	21.14	28	39.6
Erfani <i>et al.</i> 2021	Ross	20	28.14	25	40.8
Yin <i>et al.</i> 2021	Arbor	6	21.21	28	40.2
Hamidi <i>et al.</i> 2021	Ross	8	21.21	28	39.10
El-Naggar <i>et al.</i> 2019	Ross/Cubb	24	21.14	28	40.5

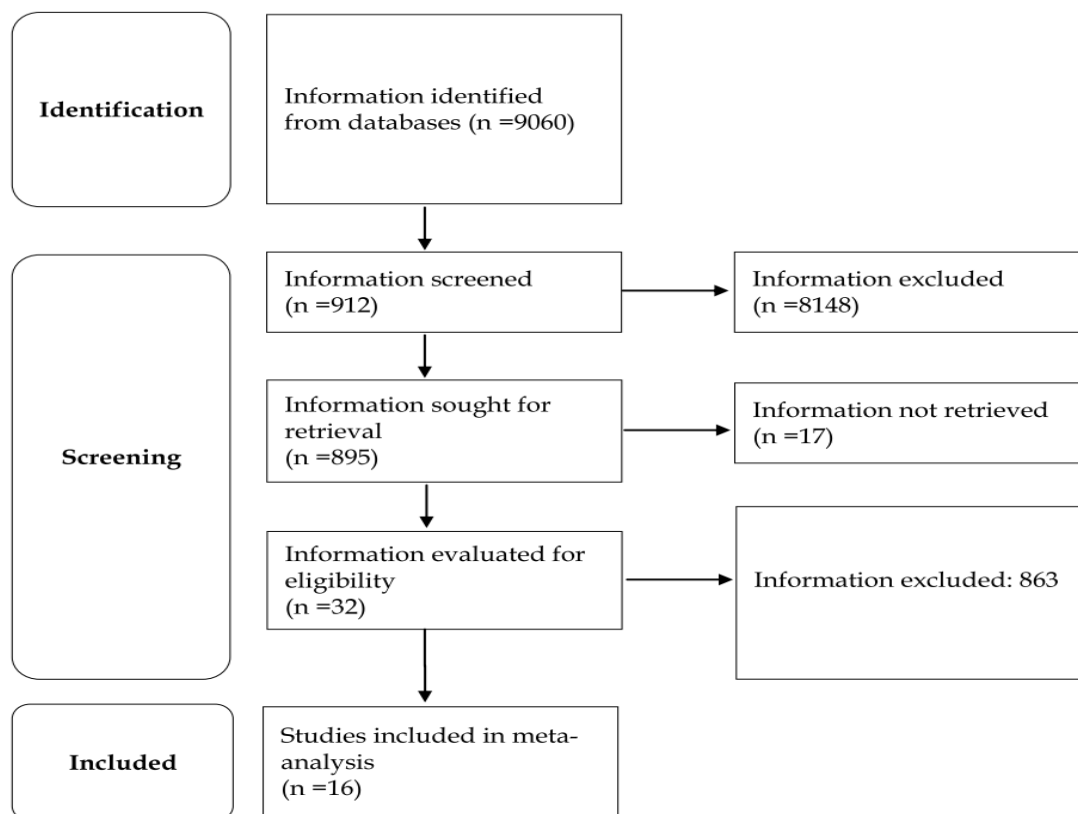


Figure 1. Illustrated flowchart of the number of retrieved and reviewed studies.

Study reviewing method

The results of searching by keywords in electronic databases were a total of 9060 scientific articles. After excluding studies without a control group and metabolite keywords remained a total of 912 articles. Among them, only *Gallus Gallus Domesticus* containing the article with chronic heat stress condition was selected and a total of 16 eligible articles (Table 1 and Figure 1) including all of the criteria was obtained (Garriga *et al.*, 2006; Azad *et al.*, 2010; Quinteiro-Filho *et al.*, 2012; Song *et al.*, 2012a; Sun *et al.*, 2015; Al Wakeel *et al.*, 2017; Alhenaky *et al.*, 2017; Sugiharto *et al.*, 2017; Roushdy *et al.*, 2018; Wang *et al.*, 2018; Barrett *et al.*, 2019; El-Naggar *et al.*, 2019; Beckford *et al.*, 2020; Erfani *et al.*, 2021; Hamidi *et al.*, 2021; Yin *et al.*, 2021).

Heat stress and control temperature characteristics

Heat stress condition induction was 38-40 °C between 13-35 days of age and duration of 7-28 days in different studies. Daily Heat stress exposition cycle was 4-10 hours. The control group was reared under 26-30 °C based on the age of the chicken.

Results

Cholesterol

A total of six evaluations from four studies (Sugiharto *et al.*, 2017; Roushdy *et al.*, 2018; El-Naggar *et al.*, 2019; Yin *et al.*, 2021) explained Chol between HS and Control group. Significant heterogeneity was observed, by that means the random-effect model was applied ($I^2 = 62\%$, $P = 0.02$). According to Figure 2, Chol was significantly elevated in the chickens exposed to HS compared with the control group (SMD= 0.7655 95% CI= 0.2653; 1.2658).

Glucose

A total of eight evaluations from eight studies (Garriga *et al.*, 2006; Azad *et al.*, 2010; Song *et al.*, 2012a; Sun *et al.*, 2015; Sugiharto *et al.*, 2017; Wang *et al.*, 2018; Beckford *et al.*, 2020; Erfani *et al.*, 2021) reported Glu between HS and control group. Significant heterogeneity was not found by the common-effect model was applied ($I^2 = 31\%$, $P = 0.18$). According to Figure 3, Glu was significantly increased in the chickens exposed to HS compared with the control group (SMD= 0.3064 95% CI= 0.0027; 0.6100).

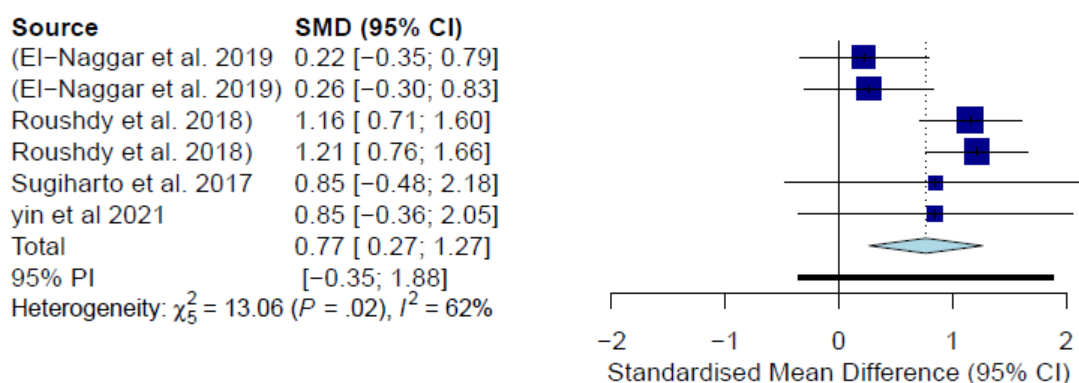


Figure 2. The blobbogram of blood Chol concentration between the chickens exposed to heat stress and thermoneutral conditions. Chol was significantly increased in the chickens exposed to HS compared with the normal control (SMD= 0.7655 95% CI= 0.2653; 1.2658).

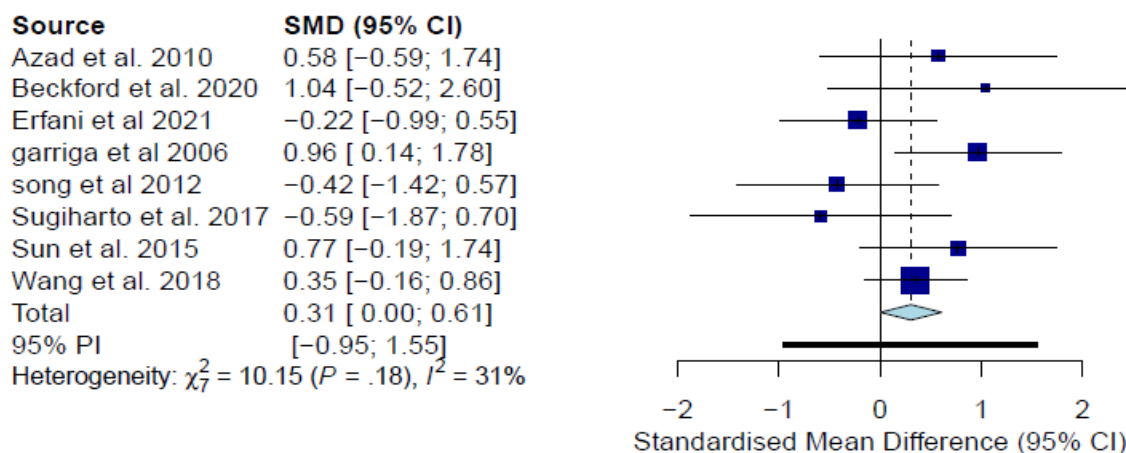


Figure 3. The blobbogram of blood Glu concentration between the chickens exposed to heat stress and thermoneutral conditions. Glu was significantly increased in the chickens exposed to HS compared with the normal control (SMD= 0.3064 95% CI= 0.0027; 0.6100).

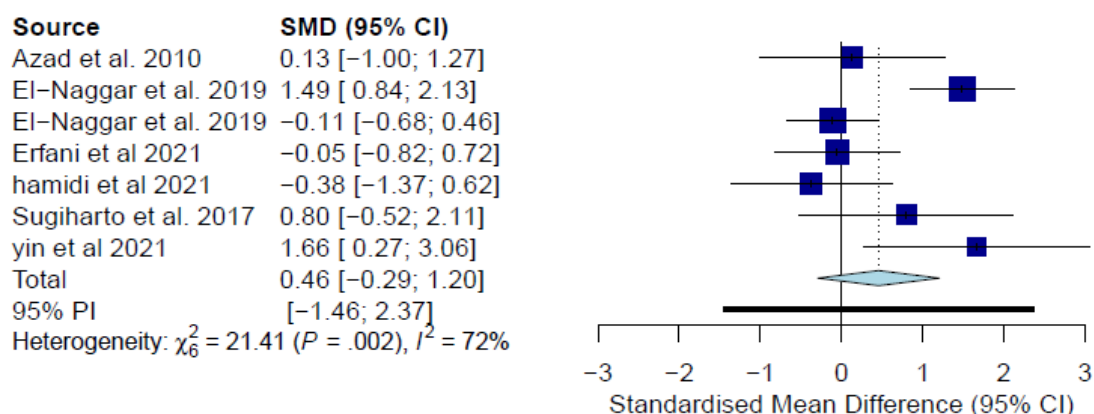


Figure 4. The blobbogram of blood triglyceride concentration between the chickens exposed to heat stress and thermoneutral conditions. No significant difference was observed between groups. (SMD=0.4559 95% CI=-0.2923; 1.2040).

Triglyceride

A total of seven evaluations from six studies (Azad *et al.*, 2010; Sugiharto *et al.*, 2017; El-Naggar *et al.*, 2019; Erfani *et al.*, 2021; Hamidi *et al.*, 2021; Yin *et al.*, 2021) reported Tri between HS and Control group. Significant heterogeneity was observed, by that means the random-effect model was applied ($I^2 = 72\%$, $P = 0.0015$). According to Figure 4, there was no significant difference between groups. (SMD=0.4559 95% CI=-0.2923; 1.2040).

Source	SMD (95% CI)
Azad et al. 2010	1.51 [0.16; 2.86]
Roushdy et al. 2018	0.07 [-0.34; 0.49]
Roushdy et al. 2018	0.07 [-0.34; 0.49]
Sugiharto et al. 2017	1.69 [0.13; 3.26]
Sun et al. 2015	2.35 [1.08; 3.62]
Total	0.96 [-0.33; 2.25]
95% PI	[-2.28; 4.20]
Heterogeneity: $\chi^2_4 = 18.44$ ($P = .001$), $I^2 = 78\%$	

Uric acid

A total of five evaluations from four studies (Azad *et al.*, 2010; Sun *et al.*, 2015; Sugiharto *et al.*, 2017; Roushdy *et al.*, 2018) reported UA between HS and control group. Significant heterogeneity was observed, by that means the random-effect model was applied ($I^2 = 78.3\%$, $P = 0.186$). According to Figure 5, there was no significant difference between groups (SMD= 0.9590 95% CI= -0.3338; 2.2518).

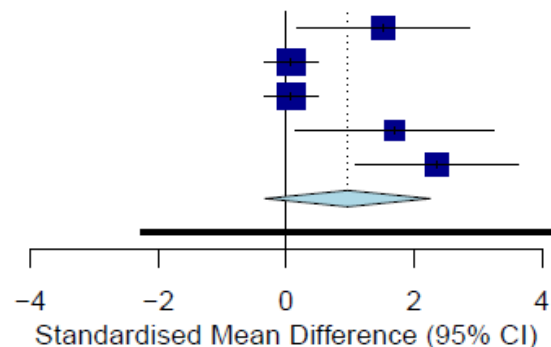


Figure 5. The blobbogram of blood uric acid concentration between the chickens exposed to heat stress and thermoneutral conditions. No significant difference was observed between groups. (SMD= 0.9590 95% CI= -0.3338; 2.2518).

Corticosterone

A total of five evaluations from five studies (Garriga *et al.*, 2006; Quinteiro-Filho *et al.*, 2012; Sun *et al.*, 2015; Alhenaky *et al.*, 2017; Beckford *et al.*, 2020) reported Cortico between HS and control group.

Source	SMD (95% CI)
Alhenaky et al. 2017	0.58 [0.00; 1.16]
Beckford et al. 2020	11.76 [3.55; 19.96]
garriga et al 2006	1.72 [0.80; 2.65]
Quinteiro-Filho et al. 2012	0.15 [-0.15; 0.44]
Sun et al. 2015	0.22 [-0.71; 1.15]
Total	1.82 [-2.95; 6.58]
95% PI	[-11.61; 15.24]
Heterogeneity: $\chi^2_4 = 18.50$ ($P < .001$), $I^2 = 78\%$	

Significant heterogeneity was observed, by that means the random-effect model was applied ($I^2 = 78.4\%$, $P = 0.001$). According to Figure 6, no significant difference between groups was observed (SMD=1.8153 95% CI=-2.9524; 6.5830).

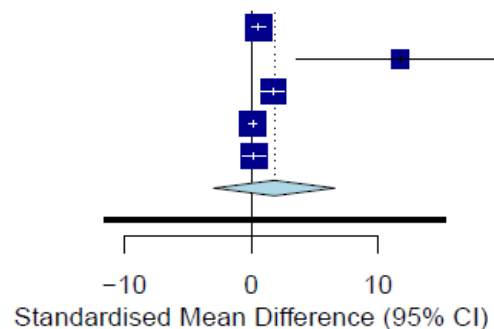


Figure 6. The blobbogram of blood corticosterone concentration between the chickens exposed to heat stress and thermoneutral conditions. No significant difference was observed between groups. (SMD=1.8153 95% CI=-2.9524; 6.5830).

Triiodothyronine

A total of four evaluations from four studies (Garriga *et al.*, 2006; Song *et al.*, 2012a; Al Wakeel *et al.*, 2017; Erfani *et al.*, 2021) reported T3 between HS and control group. Significant heterogeneity was observed, by that means the random-effect model was applied ($I^2 = 96.5\%$, $P = 0.0001$). According to Figure

7, there was no significant difference between groups (SMD= -9.006 95% CI= -46.1608; 28.1487).

Sodium

A total of four evaluations from three studies (Azad *et al.*, 2010; Roushdy *et al.*, 2018; Barrett *et al.*, 2019) reported Na⁺ between HS and Control group.

Significant heterogeneity was observed, thereby the random-effect model was applied ($I^2= 91.5\%$, $P= 0.0001$). According to Figure 8, Na^+ was

significantly decreased in the chickens exposed to HS compared with the control group (SMD= -1.723 95% CI= -3.1536; -0.2925).

Source	SMD (95% CI)
garriga et al 2006	-1.95 [-2.90; -0.99]
Al.Wakeel et al 2020	-26.86 [-34.82; -18.90]
Erfani et al 2021	0.52 [-0.26; 1.31]
Total (fixed effect)	-0.62 [-1.22; -0.01]
Total (random effects)	-9.01 [-46.16; 28.15]
95% PI	[-224.87; 206.86]
Heterogeneity: $\chi^2_2 = 57.21$ ($P < .001$), $I^2 = 97\%$	

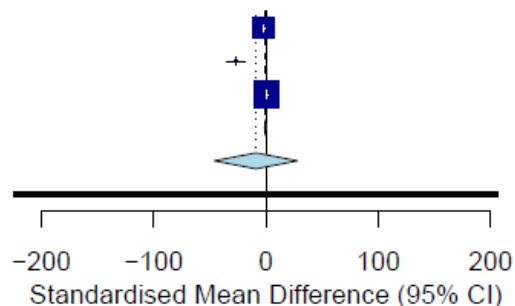


Figure 7. The blobbogram of blood triiodothyronine concentration between the chickens exposed to heat stress and thermoneutral conditions. No significant difference was observed between groups. (SMD= -9.006 95% CI= -46.1608; 28.1487).

Source	SMD (95% CI)
Azad et al. 2010	-1.50 [-2.85; -0.16]
Barrett et al. 2019	-1.06 [-1.26; -0.85]
Roushdy et al. 2018	-3.01 [-3.62; -2.40]
Roushdy et al. 2018	-1.35 [-1.81; -0.89]
Total	-1.72 [-3.15; -0.29]
95% PI	[-5.74; 2.29]
Heterogeneity: $\chi^2_3 = 35.48$ ($P < .001$), $I^2 = 92\%$	

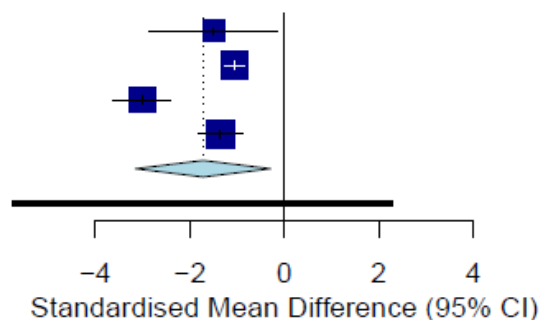


Figure 8. The blobbogram of sodium between the chickens exposed to heat stress and thermoneutral conditions. Na^+ was significantly decreased in the chickens exposed to HS compared with the normal control (SMD= -1.723 95% CI= -3.1536; -0.2925).

Potassium

A total of four evaluations from three studies (Azad *et al.*, 2010; Roushdy *et al.*, 2018; Beckford *et al.*, 2020) reported K^+ between HS and control group. Significant heterogeneity was observed, thereby the

random-effect model was applied ($I^2=93\%$, $P=0.0001$). According to Figure 9, there was no significant difference between groups (SMD= -6.675 95% CI= -20.1400; 6.7898).

Source	SMD (95% CI)
Azad et al. 2010	-2.95 [-4.78; -1.12]
Beckford et al. 2020	-24.75 [-41.83; -7.67]
Roushdy et al. 2018	-6.01 [-7.00; -5.02]
Roushdy et al. 2018	-2.50 [-3.05; -1.94]
Total	-6.68 [-20.14; 6.79]
95% PI	[-46.47; 33.12]
Heterogeneity: $\chi^2_3 = 43.06$ ($P < .001$), $I^2 = 93\%$	

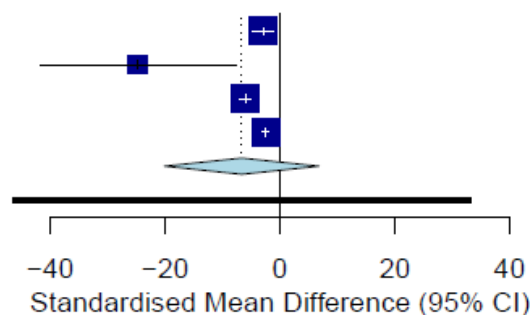


Figure 9. The blobbogram of blood potassium concentration between the chickens exposed to heat stress and thermoneutral conditions. no significant difference was observed between groups. (SMD= -6.675 95% CI= -20.1400; 6.7898).

Discussion

Based on the literature review, there was a significant difference in blood metabolites level between heat stressed and control groups, but results of recent the meta-analysis of 16 studies only showed a significant effect of chronic heat stress on Na⁺, Chol, and, Glu but not on UA, Cortico, Tri, K⁺, T3 levels.

Negative influences of high ambient temperature on the performance of broilers were noted and a significant reduction of feed intake, live weight gain, and feed efficiency was observed. Overactivity of neuroendocrine circuits such as sympathetic pathways and adrenal glands are responsible for the physiological and biochemical parameters alteration. The results of this activation are changes in the metabolic profile of chickens, as indicated in the form of declined plasma triglyceride, total cholesterol, thyroid hormones, and uric acid levels and elevated blood corticosterone and glucose levels (Lin *et al.*, 2006; Bahry *et al.*, 2017).

There are different experiments on the HPA axis activation during heat stress conditions. For example, heat stress induction in 14-day-old male layer chicks, 35 °C environmental temperature for 1 or 48 hours, had no significant effect on the plasma corticosterone level compared to those normal temperature chicks (Chowdhury *et al.*, 2012). Also, broilers of 6-week-age treated with chronic-cyclical heat stress condition had no significant change in their blood corticosterone levels (Sun *et al.*, 2015). Conversely, 2-5 hours of heat stress induction in 14-day-old chicks elevated significantly plasma corticosterone levels in the 5th hour of heat stress exposure (Ito *et al.*, 2015). By reviewing these reported differences in the blood corticosterone level during heat stress conditions, it would be able to tell that the level of blood corticosterone changes are transitory and probably come back to its previous level either immediately or need a longer time based on the strain, sex, age, heat stress duration, and experimental conditions. In addition, glucocorticoid secretion has a diurnal rhythm.

Heat stress decreases blood T3 levels (Wan *et al.*, 2017). Thyroid hormones enhance oxidative metabolism and respiratory rate by increasing the mitochondrial cytochrome content and cellular mitochondrial content. 35-day-old chickens exhibited a significant decrease in their plasma T3 level under a six-hours-heat stress experiment versus the control group. In contrast, the plasma T4 level was significantly elevated in the sixth-hour-heat exposure group (Lin *et al.*, 2006). A significant decrease of T3 levels following 12-hour cyclical heat stress in 21-35 days of growing period and the T4 level significantly increase has been reported (Piestun *et al.*, 2008). Deiodinase enzymes converted T4 to T3 and one of the reasons for declining blood T3 levels during heat stress is temperately deiodinase inactivation and

might be solved in cyclic-heat stress conditions (Jastrebski *et al.*, 2017).

Lipid metabolism in poultry is influenced by Heat stress. Triglycerides are important in the metabolism of lipids that are consumed in the body and compensates for reduced energy intake. Therefore, temporarily decrease in serum triglyceride could occur during high ambient temperature status. But in chronic-cyclic-heat stress chicks blood glucose, triglyceride, and cholesterol levels elevated (Sun *et al.*, 2015).

Blood uric acid concentration during chronic-cyclical heat stress in broilers of 35-42 days of age (Sun *et al.*, 2015) and 24-week-old hens significantly increased (Song *et al.*, 2012b), but it was not significantly different between heat-stressed and control group during 6-hour acute heat stress exposure (Lin *et al.*, 2006). Similarly, heat stress treatment did not significantly change blood uric acid in 7-day-old chicks (Moraes *et al.*, 2004). Inversely blood uric acid level of 14-day-old chicks showed a significant decrease, when exposed to 48 hours of high-temperature challenge (Chowdhury *et al.*, 2012). Protein digestion and amino acid deamination lead to the formation of uric acid that it is the main mechanism of birds for eliminating the waste products of nitrogen. Two days of consistent heat stress in chicken led to more protein and amino acids breaking down the elevation of blood uric acid level (Chowdhury *et al.*, 2012)..

Sodium and potassium are the most important osmoles of blood and are necessary for cation-anion balance. Sodium and potassium are important ions of the outer and inner cells respectively. Chronic heat stress showed a decreasing and increasing effect on blood sodium and glucose level respectively. Lower blood sodium and higher glucose level as a consequence of chronic heat stress led to water imbalance in the body, and more blood osmotic pressure and these might be related to morbidity and mortality. The previous meta-analysis reported lower body weight and more significant mortality in chronic heat stress conditions (Liu *et al.*, 2020). Significant loss of Na⁺ and K⁺ at heat stress exposed-chicken has been reported previously and electrolyte supplements can help birds to alleviate this imbalance (Sahin *et al.*, 2003; Sahin *et al.*, 2009).

Conclusion

The restriction of the recent study was few studies that were included in this analysis. Based on our meta-analysis, high blood glucose, high Cholesterol, and losing electrolyte balance are major problems in chickens during cyclic-chronic heat stress acclimatizing programs. Continuing a higher performance and preventing morbidity and mortality depended on preserving body electrolyte balance. Investigation of molecular and cellular mechanisms of

electrolyte and metabolite during cyclic-chronic heat stress exposure would be able to help and solve this problem.

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