Meta-analysis of the relationship of mycotoxins with biochemical and hematological parameters in broilers

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ABSTRACT A meta-analysis was carried out to study the association of mycotoxins with hematological and biochemical profiles in broilers. Ninety-eight articles published between 1980 and 2009 were used in the database, totaling 37,371 broilers. The information was selected from the Materials and Methods and Results sections in the selected articles and then tabulated in a database. Meta-analysis followed 3 sequential analyses: graphic, correlation, and variance-covariance. Mycotoxins reduced ($P < 0.05$) the hematocrit (−5%), hemoglobin (−15%), leukocytes (−25%), heterophils (−2%), lymphocytes (−2%), uric acid (−31%), creatine kinase (−27%), creatinine (−23%), triglycerides (−39%), albumin (−17%), globulin (−1%), total cholesterol (−14%), calcium (−5%), and inorganic phosphorus (−12%). Mycotoxins also altered ($P < 0.05$) the concentrations of alkaline phosphatase, alanine aminotransferase, and aspartate aminotransferase. A quadratic effect was observed on the relationship between the concentration of aflatoxin in diets and the serum concentration of alkaline phosphatase, γ-glutamyl transferase, alanine aminotransferase, and aspartate aminotransferase. The total protein concentration in blood was 18% lower ($P < 0.05$) in broilers challenged by aflatoxins compared with that of the unchallenged ones. The inclusion of antimycotoxin additives in diets with aflatoxins altered ($P < 0.05$) some variables (uric acid, creatinine, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and γ-glutamyl transferase) in relation to the group that received diets with the mycotoxin and without the additive. The meta-analysis performed in this study allowed us to address and quantify systematically the relationship of mycotoxins with alterations in hematologic and biochemical profiles in broilers.

Key words: aflatoxin, antimycotoxin additive, blood, hemogram

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INTRODUCTION

For several decades, poultry production has intensified to meet the increased meat demand. Changes in production practices had an important effect on the evolution of health challenges. So, insofar as the production was intensified, there was an increase in animal health risks. Some of the most important health challenges are related to feed quality. The cereals that are the main components in poultry diets are subject to contamination by a diverse fungal biota. The mold contamination can directly and indirectly influence the cereal quality, negatively affecting some grain properties (Bhattacharya and Raha, 2002). In addition, under favorable environmental conditions, some specific strains of filamentous fungi produce toxic metabolites, called mycotoxins (Pitt, 2000).

Structurally, mycotoxins compose a complex group of low-molecular weight substances, naturally occurring in diverse substrates, including foods and feeds. Twenty-five percent of the world's cereal production is estimated to be contaminated by mycotoxins (CAST, 2003). Apart from this high prevalence, these substances play an important role in a range of toxic mechanisms, which includes the compromising of several important metabolic functions (Hussein and Brasel, 2001; Bhat et al., 2010).

Mycotoxicosis is an important problem in commercial poultry farming, compromising performance and interfering in biochemical and hematological profiles in challenged animals (Daghir, 2008). The study of blood variables in challenged animals can facilitate the diagnosis of mycotoxicosis. As these parameters are more sensitive than variables such as performance, this determination would indicate the intoxication in advance to other symptoms (Oğuz et al., 2000).

However, the toxicity mechanisms are specific to each mycotoxin type and the toxic effects usually vary (Bennett and Klich, 2003). In this context, the results observed in natural and experimental challenges are

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generally inconsistent and inconclusive in some aspects (Andretta et al., 2011). An alternative to this problem is the meta-analytic approach that allows integrating different variables and establishing systematic responses adjusted to the diversity of available experimental publications (Lovatto et al., 2007). Therefore, this study was performed using meta-analysis to investigate the relationship of mycotoxins with hematologic and biochemical profiles in broilers.

MATERIALS AND METHODS

Analysis Design

Indexed publications with in vivo experimental results on broilers challenged by mycotoxins were selected. The search strategy to select the publications was to consult different online data sources with key words in English. The main criteria for selecting publications were a) diets with mycotoxins, b) commercial broiler strains, and c) experimental intoxications. After the selection of the publications and the subsequent exploratory analysis, information related to the proposed theoretical model (hematologic and biochemical parameters) and other variables were tabulated to permit the descriptive analysis of studies included in the database. The data were selected from the Materials and Methods and Results sections in the articles and then tabulated in a database.

The methodology for defining dependent and independent variables and for data codification followed the propositions described in literature (Lovatto et al., 2007; Sauvant et al., 2008). Some codifications were used with qualitative grouping criteria as a resource to associate homogenous groups with some common characteristics and include them in analytical models as a variation source. In this case, the main codifications were used for mycotoxin challenge (control group, animals fed with mycotoxin-free diets; or challenge group, animals fed with diets contaminated by mycotoxins), for mycotoxin type under study (control or contaminated for specific mycotoxins, used for analysis with aflatoxins, considering animals fed with mycotoxin-free diets or groups challenged by aflatoxins), and for presence of antimycotoxin additives in diets (challenged-untreated: animals that received diets with mycotoxin but without antimycotoxin additives; or challenged-treated: animals that received diets with mycotoxins and antimycotoxin additives). The aflatoxin challenge was the subject in most treatments grouped in the mycotoxin codification (67% of the treatments). The individual effect quantification of other mycotoxins was not possible because treatments with T2 toxin (11%), fumonisins (10%), deoxynivalenol (4%), ochratoxins (6%), and zearalenone (2%) were less frequent in the database.

Other codifications were used in analyses as moderating variables, with the objective of considering the variability of compiled studies (article, inter- and intra-effects). A specific sequential number was attributed to each study inserted in the database for codification of the article effect (general). Intercodification was formed by uniting the general codification and sequential numbers to attribute a specific code to each database treatment. Intracodification, similar to the previous procedure, was attributed to groups with repeated measurements (BW, age, and mycotoxin concentration in diets).

The analyzed variables were 1) experimental characteristics (challenge period, type and concentration of mycotoxins in diets, nutritional composition of diets, age, weight, and sex of birds), 2) hematological (erythrocytes, hematocrit, hemoglobin, mean corpuscular hemoglobin, leukocytes, heterophils, lymphocytes, monocytes, eosinophils, basophils, and thrombocytes), and 3) biochemical parameters (alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, γ-glutamyl transferase, lactate dehydrogenase, glucose, creatine kinase, creatinine, uric acid, urea, triglycerides, albumin, globulin, total protein, total cholesterol, serum calcium, and serum phosphorus) of broilers.

The meta-analysis followed 3 sequential analyses: 1) graphical (to control database quality and observe biological coherence of data), 2) correlation (between the diverse variables to identify related factors), and 3) variance-covariance (to compare groups and to obtain the prediction equations). All variance-covariance analyses were performed considering the codification for general, inter- or intra-effects (Lovatto et al., 2007); the sex (males, females, and mixed groups); and the sampling time (challege period, in days, was included as a covariable). After this exploratory analysis, sex and sampling time were maintained in the models only when statistical significance ($P > 0.05$) was found for their effects. The dispersion measure used to evaluate the results was the residual SD because it better characterizes intra- and model variability. Regression equations were obtained through the variance-covariance analysis using the GLM procedure. Equations were generated considering the effects of challenge period, animal age, and aflatoxin concentration in diets. These analyses were performed for all variables influenced by aflatoxins (according to previous observation in the variance test). However, only the equations whose components presented statistical significance ($P > 0.05$) were considered in this study. All analyses were made using Minitab 15 software (Minitab Inc., State College, PA).

Description of the Database

The database occupied 1,401 lines and 189 columns on a spreadsheet composed from 98 articles published between 1980 and 2009 (mode: 2004). The most frequent periodicals in the database were *Poultry Science* (30% of the papers), *The Journal of Applied Poultry Research* (6%), *International Journal of Poultry Science*

(6%), *Ciência Rural* (5%), and *Research in Veterinary Science* (4%). Most of the experiments were conducted in American (28% of the papers) and Brazilian (19%) institutions.

The studies included in the database totaled 37,731 broilers, with an average of 253 broilers per paper (mode: 140) and 58 per treatment (mode: 30). The genetics were described in 64% of the papers (54% Ross, 17% Cobb, 11% Arbor, and 7% Hubbard). Initial average age of the broilers was 9 d (ranging from 1–43 d, mode: 1 d) and final average age was 27 d (from 7–56 d, mode: 21 d). Average experiment duration was 18 d, with the longest being 55 d. Most (61%) of the papers used male broilers, 4% used females, 16% used mixed lots, and 18% did not describe broiler sex in the study. The facilities used included boxes (57%) and cages (26%), and 17% of the authors did not present the installation type. Average temperature in experimental facilities was 25°C (ranging from 21–27°C, mode: 26°C). No information about stress caused by environmental conditions (heat, cold, or humidity) or sanitary challenge was presented in database papers.

Vaccination (for bronchitis, Marek, and Newcastle disease) was described in 9 studies under analysis. However, only data from animals vaccinated in the pretrial period were considered for analysis. Unvaccinated animals were used in 3 studies. The other papers did not describe the procedures for animal vaccination.

Corn and soybean meal were the main ingredients, used in 65% of the diets. Average mycotoxin concentrations were 0.95 mg/kg for aflatoxins (range of 0–5 mg/kg); 4.29 mg/kg for deoxynivalenol (range of 0–15 mg/kg); 2.87 mg/kg for T2 toxin (range of 0–13.5 mg/kg); 0.78 mg/kg for ochratoxins (range of 0–4.18 mg/kg); 5.05 mg/kg for zearalenone (range of 0–111 mg/kg), and 112.8 mg/kg for fumonisins (range of 0–400 mg/kg).

RESULTS AND DISCUSSION

Hematological parameters in broilers challenged by mycotoxins or aflatoxins are presented in Table 1. The mean corpuscular hemoglobin and the count of erythrocytes, monocytes, eosinophils, basophils, and thrombocytes were not affected ($P > 0.05$) by the presence of mycotoxins or aflatoxins in diets. Mycotoxins reduced ($P < 0.05$) the concentration of hematocrit by 5% and hemoglobin by 15%. Likewise, the hemoglobin and hematocrit were reduced ($P < 0.05$) by aflatoxin in 6 and 20%, respectively. Broilers challenged by mycotoxins had a lower count ($P < 0.05$) of leukocytes (−25%), heterophils (−2%), and lymphocytes (−2%). Aflatoxins also reduced ($P < 0.05$) the leukocytes (−10%), heterophils (−2%), and lymphocytes (−4%). These data support the description of some mycotoxins, particularly aflatoxins, as substances with effects on hematopoiesis and immune response (Oğuz et al., 2003). In the aflatoxin case, the production of several cells may be affected by changes in the formation of humoral substances, such as cytokines (Corrier, 1991).

Biochemical parameters in broilers challenged by mycotoxins or aflatoxins are presented in Table 2. The results suggest that some enzymes can be used for the diagnosis of mycotoxicosis. The concentration of alkaline phosphatase was 54% higher ($P < 0.05$) in broilers challenged by mycotoxins and 47% higher ($P < 0.05$) in broilers fed with diets containing aflatoxins. The serum concentration of alanine aminotransferase was 12% higher ($P < 0.05$) in broilers challenged by mycotoxins and 17% higher ($P < 0.05$) in those challenged by af-

Table 1. Hemogram obtained by meta-analysis of mycotoxin (M) and aflatoxin (Af) unchallenged (M- and Af-) or challenged (M+ and Af+) broilers

	Mycotoxin challenge[1]					Aflatoxin challenge				
Cell type	M-	M+	*P*-value	RSD[2]	Adj.[3]	Af-	Af+	*P*-value	RSD	Adj.
Red blood cells										
Erythrocytes (μm/mm^3)	2.36	2.54	NS	0.30	—	2.33	2.44	NS	0.32	—
Hematocrit (%)	31.0	29.4	**	2.4	P	33.2	31.1	***	2.5	P/S
Hemoglobin (g/dL)	9.86	8.40	**	0.70	P/S	9.26	7.38	***	0.63	P/S
Mean corpuscular hemoglobin (pg)	28.5	24.6	NS	3.3	S	26.0	25.2	NS	3.7	—
White blood cells										
Leukocyte (× 10^3/μL)	24.8	18.6	*	1.2	P/S	24.1	21.8	*	3.7	S
Heterophil (%)	34.6	33.9	*	6.2	P	37.4	36.5	*	6.3	—
Lymphocyte (%)	53.1	52.0	*	5.6	P	56.3	54.3	*	5.7	—
Monocyte (%)	3.50	4.10	NS	0.07	—	3.76	4.54	NS	0.10	P
Eosinophil (%)	1.52	2.01	NS	0.77	—	1.65	2.42	NS	0.80	—
Basophil (%)	2.41	3.46	NS	0.08	P/S	2.69	3.99	NS	0.10	S
Thrombocyte (× 10^3/μL)	23.5	26.3	NS	2.8	S	29.3	25.3	NS	2.6	S

[1]Mycotoxins: aflatoxins, deoxynivalenol, T2 toxin, ochratoxins, zearalenone, and fumonisins.

[2]Residual SD.

[3]Adjustments: P = challenge period used as a covariable (sampling time, expressed in days); S = sex (male, female, or mixed groups) used as a variable in the model. A moderating codification was used in all analyses.

*$P \leq 0.05$; **$P \leq 0.01$; and ***$P \leq 0.001$.

Table 2. Biochemical parameters obtained by meta-analysis of mycotoxin (M) and aflatoxin (Af) unchallenged (M- and Af-) or challenged (M+ and Af+) broilers

	Mycotoxin challenge[1]					Aflatoxin challenge				
Parameter	M-	M+	*P*-value	RSD[2]	Adj.[3]	Af-	Af+	*P*-value	RSD	Adj.
Hepatic parameter										
Alkaline phosphatase (U/L)	12.0	18.5	***	2.4	—	13.6	20.0	***	2.7	S
Alanine aminotransferase (U/L)	7.38	8.24	**	2.02	P	6.19	7.23	**	2.06	P
Aspartate aminotransferase (U/L)	284	329	*	25	S	284	324	*	26	—
γ-Glutamyl transferase (U/L)	16.4	17.4	NS	3.5	P/S	17.3	19.0	*	1.2	S
Lactate dehydrogenase (U/L)	397	456	NS	15	—	411	414	NS	19	—
Renal parameter										
Uric acid (mg/dL)	7.39	5.08	**	0.97	P	7.17	5.77	*	0.88	—
Urea (mg/dL)	3.83	3.94	NS	0.38	P	3.95	4.05	NS	0.37	—
Creatinine (mg/dL)	0.82	0.63	*	0.08	P/S	0.77	0.67	*	0.06	S
General parameter										
Glucose (mg/dL)	251	212	NS	19	—	239	210	*	20	P
Creatine kinase (U/L)	1,867	1,364	*	48	S	2,003	1,870	**	98	S
Triglycerides (mg/dL)	98.9	60.5	*	8.8	—	81.2	60.9	***	11.1	P
Albumin (g/dL)	1.33	1.11	**	0.10	P/S	1.34	1.07	***	0.2	P/S
Globulin (g/dL)	1.90	1.88	*	0.93	—	2.15	2.03	*	0.69	—
Total protein (g/dL)	3.09	2.60	***	0.51	P/S	3.12	2.55	**	0.20	P/S
Total cholesterol (mg/dL)	141	121	*	17	P/S	139	106	***	20	—
Serum calcium (mg/dL)	8.36	7.91	***	0.91	—	9.01	8.16	***	0.88	—
Serum phosphorus (mg/dL)	5.97	5.24	**	0.25	—	6.25	5.49	**	0.24	—

[1]Mycotoxins: aflatoxins, deoxynivalenol, T2 toxin, ochratoxins, zearalenone, and fumonisins.

[2]Residual SD.

[3]Adjustments: P = challenge period used as a covariable (sampling time, expressed in days); S = sex (male, female, or mixed groups) used as a variable in the model. A moderating codification was used in all analyses.

*$P \leq 0.05$; **$P \leq 0.01$; ***$P \leq 0.001$.

latoxins. The concentration of aspartate aminotransferase was 16% higher ($P < 0.05$) in broilers challenged by mycotoxins and 14% higher in broilers challenged by aflatoxins.

The concentration of γ-glutamyl transferase was not affected ($P > 0.05$) by the presence of mycotoxins in diets. However, the variable was 10% higher ($P < 0.05$) in animals challenged by aflatoxins, a condition that can indicate bile cholestasis and duct hyperplasia (Borsa et al., 1998). The presence of aflatoxins or mycotoxins in diets did not change ($P > 0.05$) the plasma concentration of lactate dehydrogenase in broilers.

A quadratic effect was observed on the relationship among the concentration of aflatoxin in diets and the serum concentration of alkaline phosphatase, γ-glutamyl transferase, alanine aminotransferase, and aspartate aminotransferase (Figure 1). The increase in the concentration of these enzymes is recognized as evidence of injury on the membrane integrity of liver cells.

Mycotoxins reduced ($P < 0.05$) the concentrations of uric acid (−31%), creatine kinase (−27%), and creatinine (−23%). The same variables were affected ($P < 0.05$) by the presence of aflatoxins in diets, with a reduction of 20% for uric acid, 7% for creatine kinase, and 13% for creatinine compared with those of the control groups. The concentration of urea was not affected ($P > 0.05$) by the presence of mycotoxins or aflatoxins in diets. This observation may be partially explained by the great variability among results in the database studies.

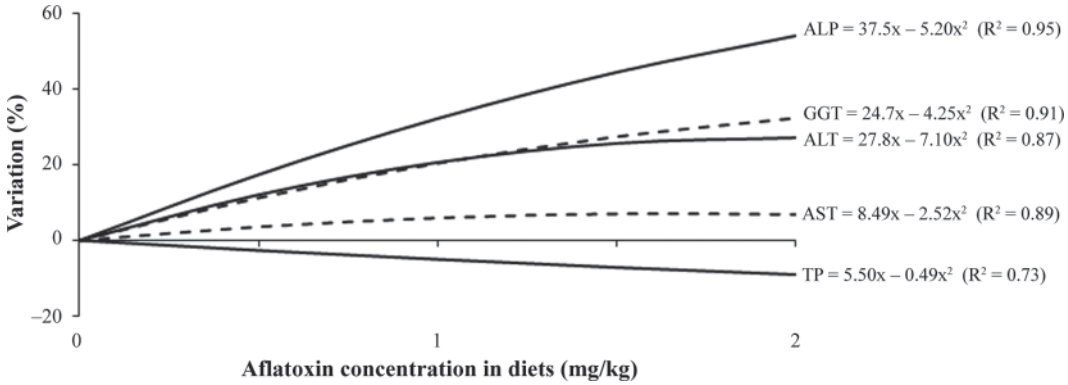

Figure 1. Variation (%) in serum alkaline phosphatase (ALP), γ-glutamyl transferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total protein (TP) as a function of the aflatoxin concentration in broiler diets.

The behavior of creatine kinase in challenged broilers is not constant. The increase in serum levels of this substance may reflect cell damage with leakage of the contents into the blood. The relationship was not observed in the present study, and this condition is probably related to the reduction in protein synthesis caused by mycotoxins. Renal toxicity may be indicated by lower levels of creatinine, as described in previous studies (Harvey et al., 1993). The decrease observed in uric acid levels can be explained by changes in the efficiency of amino acid utilization, in enzyme systems, in renal filtration, or in reabsorption rates or by unknown aspects (Swamy et al., 2002). However, in several studies of the database, the level of uric acid appeared increased as evidence of injury in hepatocytes, where the substance is produced.

The glucose concentration was not affected ($P > 0.05$) by the presence of mycotoxins in diets. However, broilers challenged by aflatoxins presented a reduction ($P < 0.05$) of 12% in the plasma concentration of glucose. Animals challenged by mycotoxins showed lower plasma levels ($P < 0.05$) of triglycerides (−39%), albumin (−17%), globulin (−1%), and total cholesterol (−14%). Aflatoxins reduced ($P < 0.05$) by 25% the concentration of triglycerides, by 20% in albumin, by 6% in globulin, and by 24% in total cholesterol.

The interference on the plasma levels of albumin may be due to damage in hepatocytes and impairment of protein synthesis in challenged broilers (Faixová et al., 2007). The transport and plasma profile of lipids may also be influenced by liver damage caused by mycotoxins, particularly aflatoxins. Thus, serum cholesterol reduction caused by aflatoxin can be related to inhibition of the biosynthesis of the compound to liver damage and changes in concentration of circulating cholesterol to the liver (Kubena et al., 1993).

Mycotoxins and aflatoxins reduced ($P < 0.05$) the serum concentration of calcium by 5 and 9%, respectively. The inorganic phosphorus concentration was 12% lower ($P < 0.05$) in groups challenged by mycotoxins and aflatoxins. Changes in serum concentrations of calcium and phosphorus during the intoxication may reflect the reduction in feed intake and also a possible impairment in the ability to absorb these nutrients in the gastrointestinal tract (Kubena et al., 1989). Hypocalcemia may also be associated with secondary deficiency of vitamin D (Sergeev et al., 1990). The reduction in plasma phosphorus levels may be related to renal disorders, like alteration on sensitivity to parathyroid hormone (Glahn et al., 1991).

The total protein concentration in blood was 14% lower ($P < 0.05$) in broilers challenged by mycotoxins and 18% lower ($P < 0.05$) in those challenged by aflatoxins. Each 1 mg/kg of aflatoxin in diets represented a reduction of 5% in the blood content of total protein (Figure 1). Besides the concentration of aflatoxins in diets, the supply period of contaminated feed has also influenced the blood concentration of total protein in broilers ($Y = 3.95 - 0.105A + 0.007A^2 - 0.012\text{P} + 0.003\text{P}^2$; $\text{R}^2 = 0.75$; where A = aflatoxin concentration in diets, expressed in mg/kg, and P = period of feeding contaminated diets, expressed in days). These changes are probably associated with the impairment of functions, such as amino acid transport and protein synthesis, usually related to aflatoxicosis (Meissonnier et al., 2005).

Mycotoxins constitute a group of substances with diverse structures. Furthermore, each mycotoxin has an action mechanism with different clinical manifestations, according to the ingested dose. However, the comparison of different mycotoxins within the same treatment (encoding for mycotoxin challenge) was performed in this study. The reason for this was the low number of database studies involving certain mycotoxins (T2 toxin, fumonisins, deoxynivalenol, ochratoxins, and zearalenone) that do not allow individual comparisons.

A similar behavior was observed for several variables in the comparisons of mycotoxins versus control or aflatoxins versus control. This relationship may reflect, in part, the higher frequency of studies involving aflatoxins in the database. So, as most studies grouped in the mycotoxin codification involved aflatoxin-chal-

Table 3. Equations obtained through variance-covariance analysis to estimate the variation (%) in biochemical and hematological parameters in broilers challenged by aflatoxins compared with controls

Parameter	Equations considering challenge period[1]	R^2	Equations considering broiler age[2]	R^2
Hematocrit	$-0.933 - (0.003 \times \text{P})$	0.65	$-2.595 + (0.089 \times \text{A})$	0.65
Hemoglobin	$-0.604 - (0.022 \times \text{P})$	0.59	—	
Alkaline phosphatase	—		$12.179 - (0.593 \times \text{A})$	0.55
Alanine aminotransferase	$6.037 + (0.035 \times \text{P})$	0.61	$3.990 - (0.175 \times \text{A})$	0.61
γ-Glutamyl transferase	—		$7.504 + (0.469 \times \text{A})$	0.60
Glucose	$-0.835 - (0.067 \times \text{P})$	0.65	—	
Triglycerides	$-4.736 - (0.143 \times \text{P})$	0.88	—	
Albumin	$-5.447 - (1.979 \times \text{P}) + (0.037 \times \text{P}^2)$	0.72	$-17.340 + (0.089 \times \text{A})$	0.67
Total protein	$-22.384 - (0.415 \times \text{P}) + (0.018 \times \text{P}^2)$	0.62	$-19.291 + (0.112 \times \text{A})$	0.68
Total cholesterol	$-5.269 - (0.468 \times \text{P})$	0.63	—	

[1]P = challenge period used as a covariable (sampling time, expressed in days).

[2]A = aflatoxin concentration in diets, expressed in mg/kg.

Table 4. Variation (%) in biochemical parameters of challenge-treated broilers (fed diets with aflatoxins and antimycotoxin additive) in relation to challenge-untreated animals (fed diets with aflatoxins and without antimycotoxin additive)

Parameter	Variation	*P*-value
Uric acid	+7.6	*
Creatinine	+9.3	*
Creatine kinase	+5.9	NS
Alkaline phosphatase	−12.0	***
Alanine aminotransferase	−8.24	**
Aspartate aminotransferase	−2.84	**
γ-Glutamyl transferase	−17.4	*

*$P \leq 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$.

lenged animals, it is probable that aflatoxin presented a greater influence on the results in relation to other mycotoxins.

Equations to estimate the variation (%) in biochemical and hematological parameters in broilers challenged by aflatoxins are presented in Table 3. For each day of aflatoxin challenge period, there is an expected 0.003% reduction in hematocrit, 0.002% in hemoglobin, 0.067% in glucose, and 0.448% in total cholesterol concentration. Likewise, the increase in one day during the challenge period represented a 0.035% increase in the concentration of alanine aminotransferase. A quadratic effect was observed on the relationship between the challenge period and the serum concentration of albumin and total protein.

Animal age was a covariable that explained the variation in hematocrit, alkaline phosphatase, alanine aminotransferase, γ-glutamyl transferase, glucose, triglycerides, albumin, and total protein levels in aflatoxin-challenged broilers. In generally, the aflatoxin effect on variables under study was greater in younger broilers. A similar relationship was observed for performance variables in a previous meta-analytical study (Andretta et al., 2011). Although these equations are empirical, the inclusion of age as a variable makes them dynamic, permitting their application in mathematical models.

The inclusion of antimycotoxin additives in diets contaminated with aflatoxins (challenge-treated group) reduced ($P < 0.05$) the plasma concentration of alkaline phosphatase by 12%, alanine aminotransferase by 8.2%, aspartate aminotransferase by 2.8%, and γ-glutamyl transferase by 17% compared with those of the group of challenge-untreated animals (Table 4). The use of antimycotoxin additives increased ($P < 0.05$) by 7.6% the concentration of uric acid and by 9.3% the serum creatinine concentration in challenge-treated broilers compared with that of challenge-untreated animals. Levels of creatine kinase did not differ ($P > 0.05$) between challenge-treated and challenge-untreated groups. The basic mechanism of protection offered by tested additives involves the adsorption of mycotoxins in the digestive tract (Huwig et al., 2001).

Mycotoxins are important due to the severe damage to animal health and profitability in the poultry industry. The meta-analysis performed in this study allowed us to address and quantify systematically the association of mycotoxins with broiler hematologic and biochemical profiles. The meta-analysis used the complementarities among previous studies to highlight gaps, hardly studied in traditional experimental designs. This study is innovative because it seeks to understand and quantify interactions among mycotoxins and other factors, such as animal age, challege period, and mycotoxin concentration in diets. The results of this study point to the possibility of exploring this relationship as a potential tool to diagnosis and to better understand the mycotoxicosis in broilers.

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