Research Article

Sero-Biochemical and Cardiac Morphological Alterations in Broiler Chicken Triggered by Dietary Dexamethasone

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Abstract | Glucocorticoid hormone is vital for the development of the fetal heart, but overexposure can harm adult cardiovascular health. Dexamethasone (DEX) is a widely administered synthetic glucocorticoid. The focus of this study was determining how DEX affects serum biochemistry (cholesterol and triglycerides), morphology, and morphometry of broiler hearts. Eighty one-day-old chicks (DOCs) were randomly categorized into four groups i.e., one control group and three trial groups (i.e., E1, E2, and E3). The control group was given commercial broiler feed and the trial groups were given commercial broiler feed containing DEX at the rate of 3, 5, and 7 mg/kg respectively for 28 days. On days 7, 14, 21, and 28 of the trial, blood and heart samples were collected. The serum cholesterol and triglycerides levels were determined. The heart specimens were prepared for histomorphological examination after the gross morphologic and morphometric (weight, length, and width) examination. Results indicated that the DEX treated broilers had significantly higher serum cholesterol and triglyceride levels than the control broilers. In the gross morphologic and morphometric examination, the DEX supplemented groups showed varying degrees of congestion and significant decrease in all parameters of heart. The histomorphological examination showed myofibrillar degeneration and vacuolation in the DEX groups with an extensive degree at days 21 and 28 of the trial. It can be concluded that the DEX treatment affect the serum biochemical markers as well as the morphologic and morphometric parameters of the broiler heart.

Keywords | Dexamethasone, Broiler, Heart, Biochemistry, Morphometry

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INTRODUCTION

The demand for meat and meat products has been increased dramatically with population growth (Hamid et al., 2017). Poultry meat is regarded as one of the main sources of animal protein all over the world. Over the last few decades, the broiler market has expanded, consolidated, and globalized to fulfill the soaring protein demand in countries ranging from low to high income. However, the enhancement of the growth performance of broilers has always been a top priority for increasing meat production. Therefore, different drugs like glucocorticoid (GC), growth promoters (GPs) are added to broiler feed for maximizing the genetic potentiality, decreasing feed conversion ratio,

promoting survival rate and decreasing fatality in birds (Mostafa et al., 2016).

Glucocorticoids, both natural and synthetic, are steroid hormones. The GCs exert their effects by the glucocorticoid receptor (GR) almost in all organs of the body, including the brain, heart, lung, and kidney (Ackermann et al., 2010). Despite their therapeutic roles, prolonged consumption of GCs at high doses causes some detrimental effects like hepatic and cardiovascular disorders, hypertension, dyslipidemia, diabetes mellitus, etc. (Duma et al., 2006). Dexamethasone (DEX) is a familiar synthetic derivative of GC that is prescribed for its anti-inflammatory and immunosuppressant properties (Biagiotti et al., 2011). GCs like DEX are also unlawfully used as GPs, to improve the quality and quantity of meat (Capolongo et al., 2007). They are frequently used at low dosages to increase feed intake, ameliorate weight gain, decrease feed conversion ratio and nitrogen retention and increase water retention and fat content (Odore et al., 2007). Steroid drugs bind to both GRs and mineralocorticoid receptors (MRs) in cardiomyocytes, which has role in cardiovascular diseases (Richardson et al., 2016). GCs induce hypercholesterolemia and controversially, hypertriglyceridemia which are also a potent risk factor for cardiovascular diseases (Félix-Redondo et al., 2013; Dolatabadi and Mahboubi, 2015). It was reported that hypercholesterolemia and hypertriglyceridemia are associated with myocardial infarction and other cardiac diseases (Langsted et al., 2011).

DEX use is supposed to improve body weight in broilers, but it does not really improve (Afrose et al., 2018). DEX significantly reduced organ weight (Mosier et al., 1982; Rademaker and de Vries, 2009). It also reduced body mass gain and muscular development which indicates increased protein catabolism (Song et al., 2011). DEX treatment leads to hypertrophy in heart, with thickening in the left ventricular wall, elongation of cardiomyocytes, and increased diameter with pronounced interstitial fibrosis (Kamphuis et al., 2007). It also caused degeneration in the myofibrils of broiler heart and increases the distance between the intercalated discs which indicates that the junctions between two myocytes become larger (De Vries et al., 2002). Reduced cardiac mass with cardiomyocyte hypertrophy, which indicate a lowering in the number of cardiomyocytes at adult age, and a severely reduced life expectancy (De Vries et al., 2006).

The role of dietary DEX in regulating serum cholesterol and triglyceride in broiler is still obscure. Few studies were previously conducted to elucidate the effects of DEX on blood profile (Afrose et al., 2018), morphology, and biochemical adaptations in the liver (Sultana et al., 2020a), and morphometry and biometry of immune organs (Sultana et al., 2020b) in broilers. Therefore, the present study extended those observations to determine the effects of different doses of dietary GC, DEX on the serum cholesterol and triglyceride levels, morphology, and morphometry of the broiler heart.

MATERIALS AND METHODS

Ethical approval

The experimental design was accomplished following the institutional rules for the care and use of animals and obtained an authorization by the Animal Welfare and Experimentation Ethics Committee, BAU, Bangladesh approval [AWEEC/BAU/2021(3)].

Animal model

Eighty clinically healthy one-day-old broiler chicks of both sexes (Cobb-500 strain) were used for this study which were obtained from a local commercial hatchery provided (Provita Hatchery Ltd., Bangladesh). To relieve transportation-induced stress, the day-old chicks (DOCs) were given fresh, cool drinking water with vitamin C supplement when they arrived at the research shed.

Housing management

The DOCs were indiscriminately allotted to four groups (n=20 for each group). They were housed in separate cages and designated as control group (C), trial group-1 (E1), trial group-2 (E2), and trial group-3 (E3). The birds were reared on a deep litter system of housing using sawdust with the provision of artificial light. The shed was well ventilated and thermostatically controlled to maintain an initial temperature of 35°C for the first three days. Then the temperature was reduced by 2-3°C per day and kept stable after reaching 21°C. The relative humidity of the shed was maintained at 50-60 % throughout the trial.

Feeding management

The chicks were fed commercial broiler-type feed obtained from a recognized poultry feed provider (Nourish Poultry and Hatchery Ltd., Bangladesh). The purchased feed was free from any kind of hazardous materials that may tamper with the actual results. The birds were fed starter feed for the first two weeks and then shifted to grower feed for the rest of the trial period. The birds of the trial groups were additionally supplied with dietary glucocorticoid, Dexamethasone (Decason®, BP 0.5 mg, Opsonin Ltd.) in three different doses, 3mg/kg ration in group E1, 5mg/kg ration in group E2, and 7mg/kg ration in group E3. The feed and water were supplied to each bird with a separate feeder and drinker. The feed intake was constantly monitored to make sure that the broilers of the trial groups are receiving the designed rate of DEX with their diet. The total duration of the trial was 28 days.

Sample collection

On days 7, 14, 21, and 28, blood samples were collected from the cranial part of the thoracoabdominal cavity of five birds per group. For obtaining heart samples, the broilers were sacrificed by the manual cervical dislocation method. Then the birds were dissected and heart samples were obtained carefully from the cranial part of the thoracoabdominal cavity of five birds per group. The obtained samples were then washed with physiological saline (0.9%) to remove the blood and preserved in formalin solution (10%) after recording the gross morphological data.

Serum biochemical analysis

Collected blood samples were kept undisturbed in an acclivous position for clotting in sterile glass tubes. Then the glass tubes were placed in the refrigerator at 4°C for 12 hours and the serum was separated by centrifuging at 1500 rpm for 10 minutes. The amount of cholesterol and triglyceride (mg/dL) was then measured by spectrophotometer using a Human type Humalyzer 2000 analyzer (Wiesbaden, Germany). Cholesterol-LQ (CHOD-POD) and Triglycerides-LQ (GPO-POD) enzymatic-colorimetric reagent kits (CHEMELEX, S.A., Barcelona, Spain) were used to determine serum cholesterol and triglyceride respectively.

Measurement of cholesterol

Cholesterol was determined according to Naito, (1984). A reagent, composed of cholesterol esterase (1000U/L), cholesterol oxidase (300U/L), peroxidase (650U/L), 4-aminophenazone (0.4mmol/L) to 100 ml cholesterol buffer solution, was used in this process (assay conditions of the spectrophotometer: wavelength- 505 nm, light path for cuvette – 1 cm, and temperature- 37°C). Then three mixtures were prepared in separate cuvettes as blank (1 ml enzyme solution), standard (Sd) solution (1 ml reagent solution and 10 µL cholesterol aqueous primary standard (200 mg/dL), and test sample (1 ml reagent solution and 10 µL serum sample) and incubated at 37°C for five minutes. The absorbance reading of the spectrophotometer was set to zero using distilled water. The absorbance value of the samples (AbS) and standard (AbSd) were then recorded against the blank (AbB). The concentration of the cholesterol (mg/dL) in the sample was calculated using the following formula- [(AbS – AbB) / (AbSd – AbB)] × Sd concentration.

Measurement of triglyceride

Triglyceride was determined according to Kaplan, (1984). A single, ready to use reagent was used in this process which was composed of p-chlorophenol (2 mmol/L), lipoprotein lipase (150000 U/L), glycerol kinase (500 U/L), glycerol-3-oxidase (3500 U/L), peroxidase (440 U/L), 4-aminophenazone (0.1 mmol/L) and adenosine triphosphate (0.1 mmol/L). The assay conditions of the spectrophotometer were set as 505 nm wavelength, 1 cm light path for the cuvette, and 37°C temperature. Then three mixtures were prepared in separate cuvettes as blank (1 ml reagent solution), standard (1 ml reagent solution and 10 µL aqueous primary standard of TGs (200 mg/dL), and test sample (1 ml reagent solution and 10 µL serum sample) and incubated at 37°C for five minutes. The absorbance reading of the spectrophotometer was set to zero using distilled water. The absorbance values of the samples (AbS) and standard (AbSd) were then recorded against the blank (AbB) and the concentration of the TG (mg/dL) in the sample was calculated from the absorbance values using the formula previously mentioned.

Gross morphology and morphometry examination

The color of the hearts was visually inspected. The gross lesions were carefully recorded. Then the weight was measured in gram (gm) using a high precision balance (FGH Series, AND Company Ltd, Korea) and recorded. The length and width of the heart were measured in centimeter (cm) by a graded scale.

Histomorphological examination

The obtained tissue samples were processed and stained (hematoxylin and eosin; H & E) following standard procedure (Sultana et al., 2020b). All the stained tissue sections were examined under light microscope (Leica DMR; Leica Microsystems, Wetzlar, Germany) blinded to the treatment at 40X and 100X magnifications, and the lesions were recorded.

Following the histomorphological examination, photomicrographs were taken using a photomicroscope (Model: CX41U-LH50HG, Olympus Corporation, Tokyo, Japan) for better representation of the histological findings.

Statistical analyses

Statistical analysis was conducted using the Statistical Package for Social Science (IBM SPSS Statistics 22). The Shapiro-Wilk test was used to test the normal distribution of the data before statistical analysis was performed. Data were then analyzed by one-way ANOVA and subsequent post hoc Duncan's multiple range test. Probability values of less than 0.05 ($P < 0.05$) were considered significant. Data were expressed as means ± SEM (standard error of the mean).

RESULTS

Serum biochemical parameters

Serum cholesterol and triglyceride levels at different days of the experiment were shown in Figures 1A and 1B respectively. Serum cholesterol levels were significantly ($P<0.05$)

Table 1: Gross morphometric data of heart of control and dexamethasone treated broilers.

Parameters	Groups	Days			
		7	14	21	28
Weight	C	1.14±0.03^{ab}	2.57±0.17^{a}	4.23±0.35^{a}	6.25±0.21a
	E1	1.05±0.06^{b}	1.79±0.04^{b}	1.83±0.04^{d}	2.66±0.02^{c}
	E2	1.22±0.03^{a}	2.05±0.21^{b}	2.15±0.07^{c}	3.65±0.06^{b}
	E3	1.14±0.07^{ab}	2.63±0.20^{a}	2.59±0.17 ^{b}	2.72±0.10^{c}
Length	C	1.94±0.02^{a}	2.40±0.04	3.01±0.10^{a}	3.25±0.04a
	E1	1.95±0.04^{a}	2.36±0.05	2.26±0.02^{c}	2.38±0.09^{c}
	E2	1.90±0.04^{a}	2.38±0.08	2.31±0.05^{c}	2.67±0.09^{b}
	E3	1.76±002^{b}	2.55±0.16	2.51±0.06^{b}	2.44±0.05^{c}
Width	C	0.96±0.02^{b}	1.50±0.06^{a}	1.74±0.06^{a}	2.09±0.03^{a}
	E1	1.08±0.04^{a}	1.14±0.05^{b}	1.16±0.03^{c}	1.74±0.02^{b}
	E2	1.04±0.02^{a}	1.26±0.09^{b}	1.41±0.04^{b}	2.14±0.17^{a}
	E3	1.04±0.02^{a}	1.47±0.07^{a}	1.42±0.05^{b}	1.74±0.05^{b}

Data were expressed as mean ± SEM and differences among the groups of birds were compared using one-way ANOVA with post-hoc Duncan's multiple range test. Values within the same column with different alphabetic superscripts are significantly ($p<0.05$) different from each other.

higher in all the DEX treated groups when compared to the control group except for group E2 on day 7 and E1 on day 21 respectively. Cholesterol level was significantly ($P<0.05$) less in group E2 on day 7. On the contrary, group E1 showed only a numerical decrease from the control group on day 21. Significant ($P<0.05$) inter-group variations were also found between the DEX treated groups. Similarly, serum triglyceride levels significantly ($P<0.05$) increased in the DEX groups when compared to the control group except for group E1, E2 on day 7, and E3 on day 28. Triglyceride levels numerically increased in group E1, E2 on day 7 when compared to the control but decreased in group E3 on day 28 which were statistically non-significant ($P>0.05$). There were also significant ($P<0.05$) variations between the treatment groups.

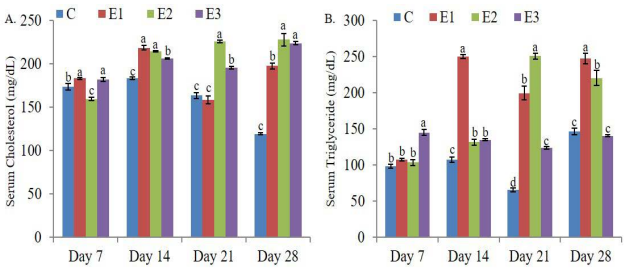

Figure 1: Dynamics of cholesterol (A) and triglyceride (B) in serum of broiler at different age and DEX treatment. Data were expressed as mean ± standard error of mean (SEM) and differences among the groups of birds were compared using one-way ANOVA with post-hoc Duncan's multiple range test. Columns with different alphabetic superscripts are significantly ($p<0.05$) different from each other.

Gross anatomical and morphometric parameters

The heart of the control group revealed normal appearance with uniform greyish pale pink color, triangular shape and yellowish-white coronary fat near the base. However, the heart of the DEX treated groups revealed some noticeable morphological alterations. In group E1, the heart appeared somewhat elongated in shape. Group E2 and E3 exhibited dark reddish discoloration of the heart with mild to moderate degree of congestion in the heart wall. The amount of coronary fat was found less in the DEX treated groups when compared to the control group (Figure 2).

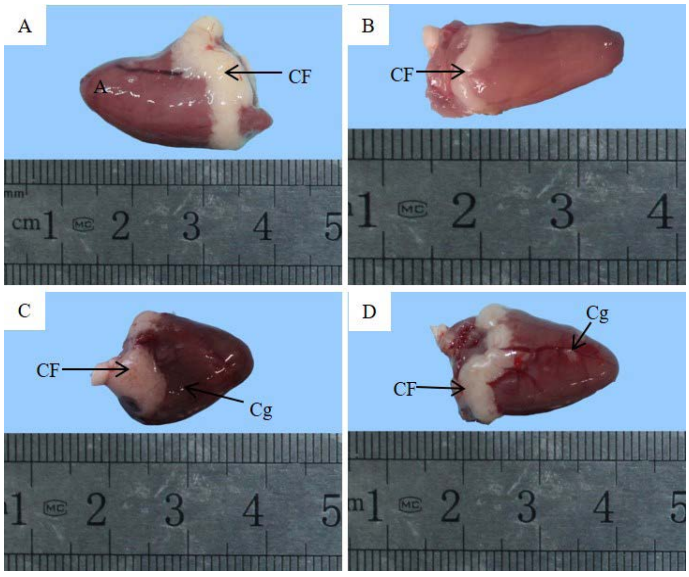

Figure 2: Gross view of hearts of 21 day old broilers. A- Control group; B- Experimental group-1; C- Experimental group-2; D- Experimental group-3. CF- Coronary fat, Cg- Congestion.

The gross morphometric parameters of the heart at different days of the experiment were shown in Table 1. Significant (P<0.05) differences in all the morphometric parameters were evident at different days of the experiment. No significant (P<0.05) difference in heart weight between the control and treatment groups was found on day 7. However, there was a significant (P<0.05) difference between group E1 and E2 on day 7. Weight of heart was significantly (P<0.05) decreased in the DEX treated groups when compared to the control group on 14, 21, and 28 days of the experiment. There were also significant (P<0.05) variations between the treatment groups. However, the lowest heart weight was found in group E1 on different days of the experiment. No significant (P<0.05) difference in heart length was found between the control and treatment groups on day 14 but it was decreased significantly (P<0.05) in the treated groups on days 21 and 28 when compared to the control group. Significant (P<0.05) inter-group variations between the treatment groups were also found on 21 and 28 days of the experiment. The width of the heart was numerically increased in the DEX treated groups on day 7 but decreased significantly (P<0.05) on days 14, 21, and 28 when compared to the control. However, both the length and width of the heart were found lowest in the E1 group on 14, 21, and 28 days of the experiment.

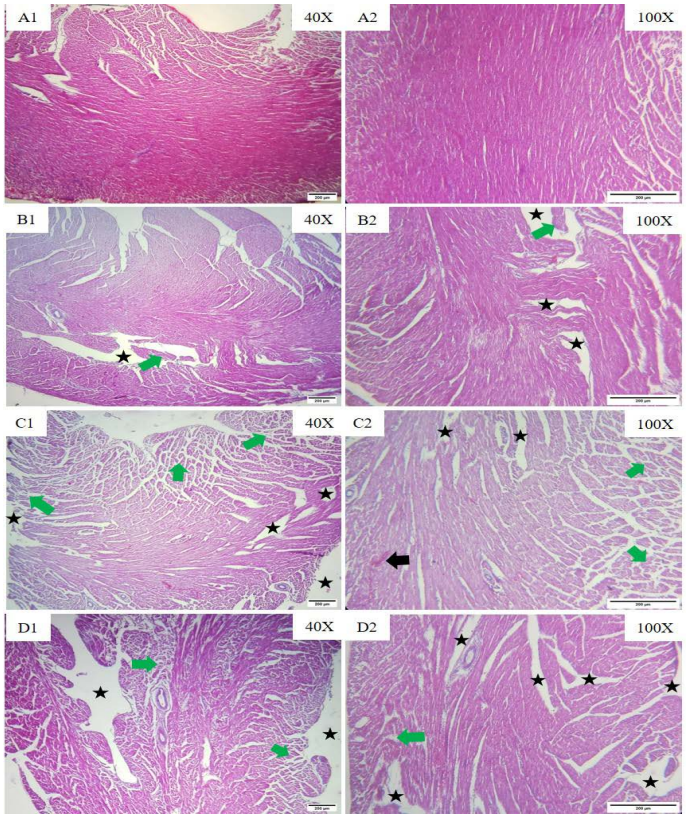

Figure 3: Representative photomicrographs of transverse section (H & E stained) of heart from 7 days old broiler of group C (A1, A2), E1 (B1, B2), E2 (C1, C2) and E3 (D1, D2). Green arrow- Myofibrillar degeneration, Black arrow- Congestion, Asterisks- Vacuolation of myofibers.

Histopathological profile of heart

In the control group at all days, the heart revealed normal histological architectures. The thick wall of the heart was primarily composed of cardiac muscle cells. The innermost layer was the endocardium which was formed from a continuous endothelial layer. The middle layer was the myocardium which was composed of bundles of cardiac muscle cells. The myocardium was covered externally by the epicardium (Figures 3-6).

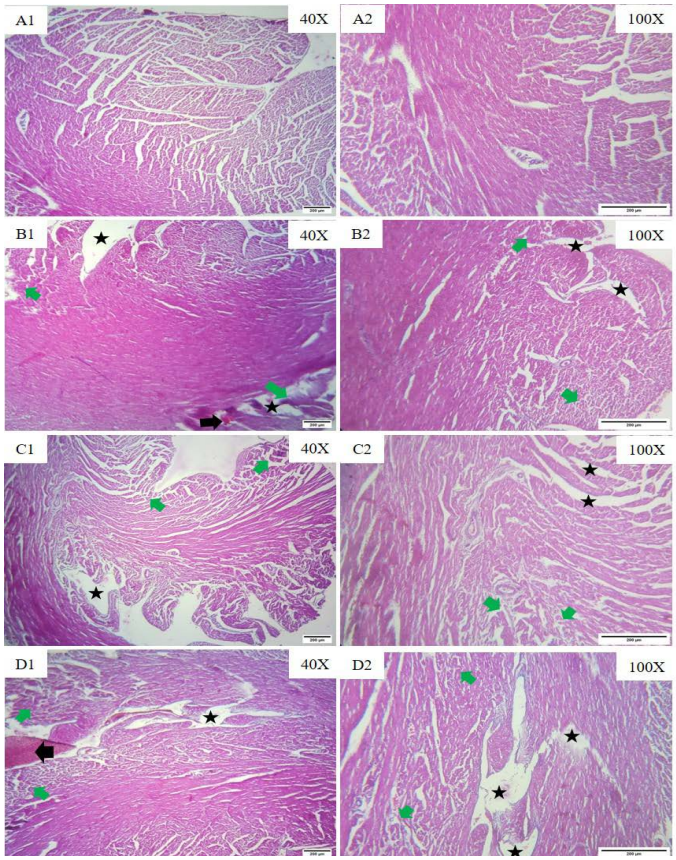

Figure 4: Representative photomicrographs of transverse section (H & E stained) of heart from 14 days old broiler of group C (A1, A2), E1 (B1, B2), E2 (C1, C2) and E3 (D1, D2). Green arrow- Myofibrillar degeneration, Black arrow- Congestion, Asterisks- Vacuolation of myofibers.

However, mild to extensive histological alterations were found in the DEX treated groups on different days of the experiment which were presented in Figures 3-6. Varying degrees of myofibrillar degeneration was seen in the hearts of the DEX treated groups along with vacuolation of myofibers. The degenerative area and vacuolation were found more extensively in the DEX treated groups on days 21 and 28 (Figure 5 and 6). A very mild degree of congestion was seen in the myocardial layer of the heart in group E2 on day 7 and groups E2 and E3 on day 21. Severe congestion in the myocardial layer was seen in the E3 group on day 14 (Figure 3, 4, and 5).

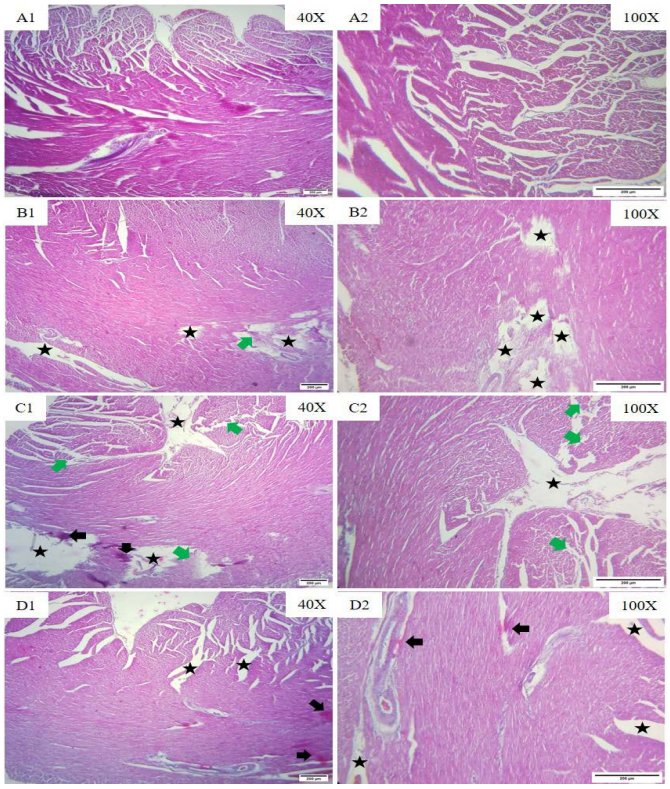

Figure 5: Representative photomicrographs of transverse section (H & E stained) of heart from 21 days old broiler of group C (A1, A2), E1 (B1, B2), E2 (C1, C2) and E3 (D1, D2). Green arrow- Myofibrillar degeneration, Black arrow- Congestion, Asterisks- Vacuolation of myofibers.

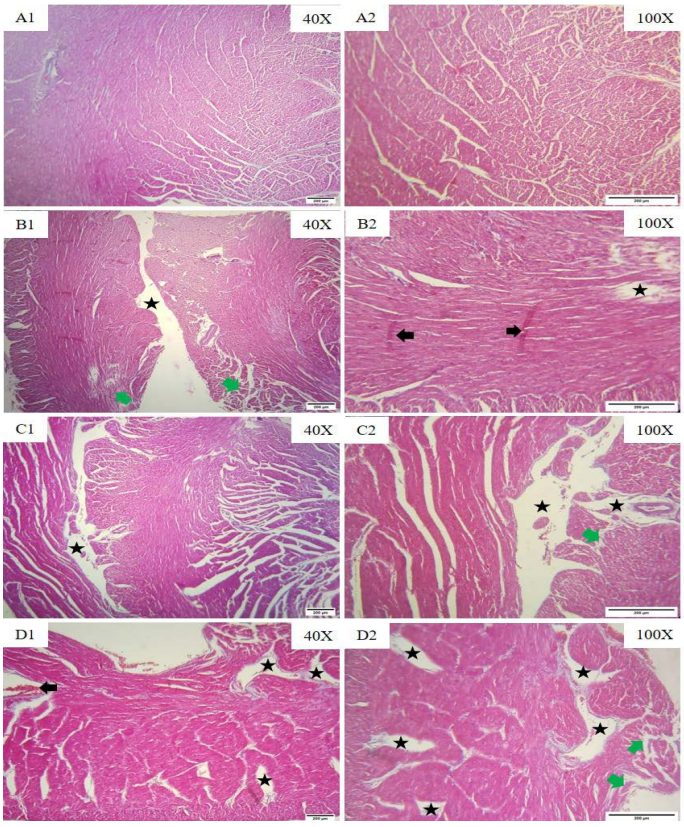

Figure 6: Representative photomicrographs of transverse section (H & E stained) of heart from 28 days old broiler of group C (A1, A2), E1 (B1, B2), E2 (C1, C2) and E3 (D1, D2). Green arrow- Myofibrillar degeneration, Black arrow- Congestion, Asterisks- Vacuolation of myofibers.

DISCUSSION

In comparison to most organs, the heart is functionally active prior to hatch. To evaluate the time-dependent impacts of DEX treatment, growth and development of myocardium should be taken into consideration. GCs play a role in both structural and functional maturation of the fetal heart although excessive exposure to GC is detrimental to adult cardiovascular health (Rog-Zielinska et al., 2015). The time and dose-dependent effects of GC on broiler hearts are not well documented. The current study aimed to investigate the effects of different doses of dietary GC, DEX on the serum cholesterol and triglyceride level, gross morphology, and the histomorphology of the broiler heart.

Serum biochemical parameters

The current study showed that serum cholesterol and triglyceride levels significantly increased in the DEX treated birds. This finding matches the result of previous research on the influence of DEX on the lipid profile of male rats and broilers (Dolatabadi and Mahboubi, 2015; Eid et al., 2003). Another study on the effect of low dose DEX on the biochemical properties highlighted that DEX significantly increased cholesterol levels without possessing a major impact on triglyceride (Wang et al., 2012).

The low lipoprotein lipase activity in the liver may be responsible for the low degradation of cholesterol and triglyceride (Kumar et al., 2011). The increased lipid content makes the body vulnerable to the free radicals or reactive oxygen species generated by GC induced stress (Eid et al., 2003). This increased levels of serum cholesterol and triglyceride are associated with myocardial infarction and cardiac diseases (Langsted et al., 2011). The elevated cholesterol levels were also shown to be strongly associated with increased ischemic heart disease mortality (Lewington et al., 2007). Triglyceride alone is also an independent risk factor for coronary heart disease (Cullen, 2000). This increased triglyceride level contribute to coronary heart disease by a direct atherogenic effect of triglyceride-rich lipoproteins as triglyceride level often reflects an increase in very low-density lipoprotein (Grundy and Vega, 1992). The triglyceride-rich lipoproteins penetrate the arterial wall which leads to the accumulation of cholesterol in the intimal space which ultimately causes atherosclerosis (Nordestgaard, 2018). The triglyceride also accumulates in the heart muscle and causes lipotoxic cardiomyopathy and cardiac steatosis (Zhang & Ren, 2011). Thus the high concentration of serum triglyceride leads to an increased risk of cardiac failure (Varbo and Nordestgaard, 2018). There-

fore, the findings of this study clearly imply that prolonged DEX treatment might be responsible, at least partially, for cardiac abnormalities in broiler.

Gross anatomical and morphometric parameters

The heart of the control groups on different days revealed normal gross morphology and morphometry (Getty, 1975). On the contrary, significant alterations in gross morphologic and morphometric parameters were seen in the DEX treated birds hearts. The amount of coronary fat was lesser in the DEX treated groups. This mismatches the previous findings where there was an augmentation of hepatic lipidosis and fat deposition in the visceral organs of the DEX exposed broilers (Cai et al., 2009). Heart weight was also decreased significantly in the treated groups when compared to the control. This finding is in accordance with previous research where a significant reduction of heart weight in response to DEX treatment was reported (Mosier et al., 1982; Rademaker and de Vries, 2009). The weight of the heart increases with body weight after birth due to an increase in volume and size of cardiomyocyte (Smolich et al., 1989). So, the decrease in weight might be due to muscular atrophy as DEX treatment restricts muscular growth by enhancing protein catabolism in the body (Song et al., 2011). These findings also justify the significant decrease in the length and width of heart in the DEX treated birds although GC treatment was reported to have a growth-promoting effect on the heart and causes cardiac enlargement (Kurowski et al., 1984).

Histopathological profile of heart

In the histomorphological examination, the heart of the control groups revealed normal histological architecture (Eurell, 2006). On the other hand, histopathological investigation of the hearts of treated groups showed some noticeable alterations in their histological architecture. These definite histopathologic abnormalities indicated that postnatal GC therapy in therapeutic or overdoses permanently affects myocyte growth. The histopathological include degeneration of myofibrils in the treated birds which is in accordance with previous research on alterations in the heart of adult rats after neonatal DEX therapy (De Vries et al., 2002). As, the incessant proliferation of cardiomyocytes during early life is suppressed due to DEX treatment, resulting in a reduced number of cardiomyocytes (Bal et al., 2009). It was found that glucocorticoids play a direct role in myofibrillar maturation and organization in subsequent in vitro studies on isolated fetal cardiomyocytes (Rog-Zielinska et al., 2015). DEX treatment also increases the length and diameter of cardiomyocytes (Kamphuis et al., 2007). However, growth and development of cardiomyocyte is suppressed by GC exposure after birth (Rudolph, 2000). Vacuolization of myofibers was also seen on different days of the experiment which were more extensive on days 21 and 28. This is a novel finding to the best of our knowledge as there was no previous report of such histopathological alterations.

The goal of this study was to investigate the effects of different doses of dietary DEX on serum biochemical markers, gross and histological characteristics of the broiler heart. All the results obtained in this study, clearly indicate that dietary DEX alters serum biochemical markers as well as gross and histological characteristics of the heart which may lead to cardiac dysfunction, heart failure, and ultimately death of broilers. However, further study is recommended to see the expression pattern of GRs in the cardiomyocytes.

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CONFLICT OF INTEREST

There is no known conflict of interest that may influence the work reported in this paper.

NOVELTY STATEMENT

To the best of our knowledge, this study is the first to evaluate the dose and time-dependent effects of dietary dexamethasone on the sero-biochemical markers and the heart of broilers.

AUTHOR CONTRIBUTIONS

NS conceptualized and supervised the experiment. RI performed the experiment and data analyses. NS and RI drafted the manuscript. AHNAK critically revised the manuscript.

REFERENCES

Ackermann D, Gresko N, Carrel M, Loffing-Cueni D, Habermehl D, Gomez-Sanchez C, Rossier BC, Loffing J (2010). In vivo nuclear translocation of mineralocorticoid and glucocorticoid receptors in rat kidney: differential effect of corticosteroids along the distal tubule. Am. J. Physiol. Renal Physiol. 299(6): F1473-1485. https://doi.org/10.1152/ajprenal.00437.2010

Afrose M, Sultana N, Islam MR (2018). Physiological

responses of corticosteroid, dexamethasone in broiler chicken. Int. J. Sci. Res. 7(12): 1459-1463. https://www.semanticscholar.org/paper/Physiological-Responses-of-Corticosteroid-%2C-in-Afrose-Sultana/b5a850750a0c441469c0ac56b02a88ac739ffcbe.

Bal MP, de Vries WB, Steendijk P, Homoet-van der Kraak P, van der Leij FR, Baan JA, van Oosterhout MF, van Bel F (2009). Histopathological changes of the heart after neonatal dexamethasone treatment: studies in 4-, 8-, and 50-week-old rats. Pediatr. Res. 66(1): 74-79. https://doi.org/10.1203/PDR.0b013e3181a283a0

Biagiotti S, Paoletti MF, Fraternale A, Rossi L, Magnani M (2011). Drug delivery by red blood cells. IUBMB life. 63(8): 621-631. https://doi.org/10.1002/iub.478

Cai Y, Song Z, Zhang X, Wang X, Jiao H, Lin H (2009). Increased de novo lipogenesis in liver contributes to the augmented fat deposition in dexamethasone exposed broiler chickens (Gallus gallus domesticus). Comp. Biochem. Physiol. Part - C: Toxicol. Pharmacol. 150(2): 164-169. https://doi.org/10.1016/j.cbpc.2009.04.005

Capolongo F, Tapparo M, Merlanti R, Ravarotto L, Tealdo E, Gallina G, Montesissa C, Dacasto M (2007). Illicit treatments in cattle and urinary 6beta-hydroxycortisol/cortisol ratio. Anal. Chim. Acta. 586(1-2): 228-232. https://doi.org/10.1016/j.aca.2006.09.033

Cullen P (2000). Evidence that triglycerides are an independent coronary heart disease risk factor. Am. J. Cardiol. 86(9): 943-949. https://doi.org/10.1016/S0002-9149(00)01127-9

De Vries WB, van der Leij FR, Bakker JM, Kamphuis PJ, van Oosterhout MF, Schipper ME, Smid GB, Bartelds B, van Bel F (2002). Alterations in adult rat heart after neonatal dexamethasone therapy. Pediatr. Res. 52(6): 900-906. https://doi.org/10.1203/00006450-200212000-00015

De Vries WB, Bal MP, Homoet-van der Kraak P, Kamphuis PJ, van der Leij FR, Baan J, Steendijk P, de Weger RA, van Bel F, van Oosterhout MF (2006). Suppression of physiological cardiomyocyte proliferation in the rat pup after neonatal glucocorticosteroid treatment. Basic Res. Cardiol. 101(1): 36-42. https://doi.org/10.1007/s00395-005-0557-0

Dolatabadi AA, Mahboubi M (2015). A study of the influence of dexamethasone on lipid profile and enzyme lactate dehydrogenase. J. Med. Life. 8(3): 72-76. PMCID: PMC5348935

Duma D, Jewell CM, Cidlowski JA (2006). Multiple glucocorticoid receptor isoforms and mechanisms of post-translational modification. J. Steroid Biochem. Mol. Biol. 102(1-5): 11-21. https://doi.org/10.1016/j.jsbmb.2006.09.009

Eid YZ, Ohtsuka A, Hayashi K (2003). Tea polyphenols reduce glucocorticoid-induced growth inhibition and oxidative stress in broiler chickens, Br. Poult. Sci. 44(1): 127-132. http://dx.doi.org/10.1080/0007166031000085427

Eurell JA, Frappier BL (2006). Dellmann's textbook of veterinary histology. Blackwell Publishing, 2121 State Avenue, Ames, Iowa 50014, USA, Edition 6th, pp: 129-130.

Félix-Redondo FJ, Grau M, Fernández-Bergés D (2013). Cholesterol and cardiovascular disease in the elderly. Facts and gaps. Aging Dis. 4(3):154-169. PMCID: PMC3660125

Getty R. Sisson, Grossman (1975). The Anatomy of the Domestic Animals. 5th Ed, Volume 2: 1968.

Grundy SM, Vega GL (1992). Two different views of the relationship of hypertriglyceridemia to coronary heart disease: implications for treatment. Arch. Intern. Med. 152(1): 28-34. https://doi.org/10.1001/archinte.1992.00400130054004.

Hamid MA, Rahman MA, Ahmed S, Hossain KM (2017). "Status of poultry industry in Bangladesh and the role of private sector for its development." Asian J. Poult. Sci. 11(1): 1-13. https://doi.org/10.3923/ajpsaj.2017.1.13.

Kamphuis PJ, De Vries WB, Bakker JM, Kavelaars A, Van Dijk JE, Schipper ME, Van Oosterhout MF, Croiset G, Heijnen CJ, Van Bel F, Wiegant VM (2007). Reduced life expectancy in rats after neonatal dexamethasone treatment. Pediatr. Res. 61(1): 72-76. https://doi.org/10.1203/01.pdr.0000249980.95264.dd

Kaplan A (1984). Triglycerides. Clin. Chem. The C.V. Mosby Co. St Louis. Toronto. Princeton. 437 and Lipids 1194-1206.

Kumar VS, Inamdar MN, Viswanatha GL (2011). Protective effect of lemongrass oil against dexamethasone induced hyperlipidemia in rats: possible role of decreased lecithin cholesterol acetyl transferase activity. Asian Pac. J. Trop. Med. 4(8): 658-660. https://doi.org/10.1016/S1995-7645(11)60167-3.

Kurowski TT, Chatterton Jr RT, Hickson RC (1984). Glucocorticoid-induced cardiac hypertrophy: additive effects of exercise. J. Appli. Physiol. 57(2): 514-519. https://doi.org/10.1152/jappl.1984.57.2.514.

Langsted A, Freiberg JJ, Tybjaerg-Hansen A, Schnohr P, Jensen GB, Nordestgaard BG (2011). Nonfasting cholesterol and triglycerides and association with risk of myocardial infarction and total mortality: the Copenhagen City Heart Study with 31 years of follow-up. J. Intern. Med. 270(1): 65-75. https://doi.org/10.1111/j.1365-2796.2010.02333.x

Lewington SG, Whitlock R, Clarke P, Sherliker J, Emberson J, Halsey N, Qizilbash R, Peto, Collins R (2007). Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55000 vascular deaths. Lancet 370(9602): 1829-1839. https://doi.org/10.1016/S0140-6736(07)61778-4.

Mosier Jr HD, Dearden LC, Jansons RA, Roberts RC, Biggd CS (1982). Disproportionate growth of organs and body weight following glucocorticoid treatment of the rat fetus. Dev. Pharmacol. Therap. 4(1-2): 89-105. https://doi.org/10.1159/000457394.

Mostafa M, El-Faham A, Ahmed A (2016). Research Article Effect of Different Sources of Growth Promoter Supplementation in Diet on Performance, Carcass Traits and Blood Constituents of Broiler Chicks. Asian J. Anim. Vet. Adv. 11(2): 106-113. https://doi.org/10.3923/ajava.2016.106.113.

Naito HK (1984). Cholesterol. Kaplan A. et al., Clin.Chem. The C.V. Mosby Co. St Louis. Toronto. Princeton. 1194-11206 and 437.

Nordestgaard BG (2016). Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease: new insights from epidemiology, genetics, and biology. Circ. Res. 118(4): 547–563. https://doi.org/10.1161/CIRCRESAHA.115.306249.

Odore R, Badino P, Barbero R, Cuniberti B, Pagliasso S, Girardi C, Re G (2007). Regulation of tissue β-adrenergic, glucocorticoid and androgen receptors induced by repeated exposure to growth promoters in male veal calves. Res. Vet. Sci. 83(2): 227-233. https://doi.org/10.1016/j.rvsc.2006.12.011

Rademaker KJ, de Vries WB (2009). "Long-term effects of neonatal hydrocortisone treatment for chronic lung disease on the developing brain and heart." Semin. Fetal Neonatal Med. 14(3): 171-177. https://doi.org/10.1016/j.

siny.2008.11.004.

Richardson RV, Batchen EJ, Denvir MA, Gray GA, Chapman KE (2016). Cardiac GR and MR: from development to pathology. Trends Endocrinol. Metab. 27(1): 35-43. https://doi.org/10.1016/j.tem.2015.10.001.

Rog-Zielinska EA, Craig MA, Manning JR, Richardson RV, Gowans GJ, Dunbar DR, Gharbi K, Kenyon CJ, Holmes MC, Hardie DG, Smith GL (2015). Glucocorticoids promote structural and functional maturation of foetal cardiomyocytes: a role for PGC-1 α. Cell Death Differ. 22(7): 1106-1116. https://doi.org/10.1038/cdd.2014.181.

Rudolph AM (2000). Myocardial growth before and after birth: clinical implications. Acta Paediatr. 89(2): 129–133. https://doi.org/10.1111/j.1651-2227.2000.tb01201.x

Smolich JJ, Walker AM, Campbell GR, Adamson TM (1989). Left and right ventricular morphometry in fetal, neonatal, and adult sheep. Am. J. Physiol. 257(1): 1–9. https://doi.org/10.1152/ajpheart.1989.257.1.H1

Song ZG, Zhang XH, Zhu LX, Jiao HC, Lin H (2011). Dexamethasone alters the expression of genes related to the growth of skeletal muscle in chickens (Gallus gallus domesticus). J. Mol. Endocrinol. 46(3): 217-225. https://doi.org/10.1530/JME-10-0162.

Sultana N, Afrose M, Rafiq K (2020a). Effects of steroid growth promoter on morphological and biochemical adaptations in liver of broiler. Vet. World 13(11): 2330-2337. https://doi.org/10.14202/vetworld.2020.2330-2337.

Sultana N, Amin T, Afrose M, Rony SA, Rafiq K (2020b). Effects of dexamethasone on the morphometry and biometry of immune organs of broiler chicken. Int. J. Morph. 38(4): 1031-1038. https://doi.org/10.4067/S0717-95022020000401032.

Varbo A, Nordestgaard BG (2018). Nonfasting triglycerides, low-density lipoprotein cholesterol, and heart failure risk: two cohort studies of 113 554 individuals. Arterioscler. Thromb. Vasc. biol. 38(2): 464-472. https://doi.org/10.1161/ATVBAHA.117.310269.

Wang X, Magkos F, Patterson BW, Reeds DN, Kampelman J, Mittendorfer B (2012). Low-dose dexamethasone administration for 3 weeks favorably affects plasma HDL concentration and composition but does not affect very low-density lipoprotein kinetics. Eur. J. Endocrinol. 167(2): 217-23. https://doi.org/10.1530/EJE-12-0180.

Zhang Y, Ren J (2011). Role of cardiac steatosis and lipotoxicity in obesity cardiomyopathy. Hypertension 572): 148-150. https://doi.org/10.1161/HYPERTENSIONAHA.110.164178.