

Impacts of synthetic androgen and estrogenic antagonist administration on growth performance, sex steroids hormones, and immune markers of male and female broilers

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ABSTRACT The influence of synthetic androgen and estrogenic antagonists (Tamoxifen) on body characteristics and immune response of male and female broilers and the correlation between sex hormone levels were estimated in our experiment. One day old chicks were sexed, and chicks of each sex were randomly distributed on three experimental treatments; the first treatment group (TAM20) chicks were supplied with estrogenic antagonist tamoxifen citrate 20 mg/kg body weight through oral administration for four times every other day from third until ninth d; Androgen treatment chicks were injected intramuscular with veterinary androgen AD GAN@ (Boldenone Undecylenate 50 mg) 1 cm/10 kg body weight at fifth and ninth day, and the third treatment

was control. Androgen treatment reported the highest feed intake with the lowest for TAM20 treatment. Concerning carcass characteristics, early androgen injection increased breast percentage significantly compared to TAM20 treatment. Androgen supplementation increased significantly comb the percentage. However, TAM20 decreased it particularly compared to control. Moreover, the percentage of comb and shanks was substantially higher for males than females. Concerning the effects of both treatments on sex hormones, androgen showed favorable effects on testosterone and estrogen compared to Tamoxifen 20 treatment. On the other hand, the administration of TAM 20 improves phagocytic activity compared to androgen administration.

Key words: androgen, TAM20, estrogen, phagocytic index, performance, carcass characteristics

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INTRODUCTION

Improving the immune response of poultry will be reflected positively on its productivity and performance. Disease, heavy vaccinations, rearing system, environmental conditions, management, and other factors act as immune stressors that affect birds' immune status, affecting growth efficiency and enteric diseases, causing significant economic shortfalls (Yang et al.,

2011; Younis et al., 2020). The effect of a gonadal steroid on the immune system varies depending on various factors such as animal species, gender, and age. The dose and hormonal administration methods, the antigen, and the host's immunocompetence may differ from immunosuppression to immunization (Ahmed and Talal, 1990; Hussein et al., 2019). Females have more robust immune responses than males (Lin et al., 1996). But this does not prove that androgens like testosterone decrease the immune system. Because of increased estrogen levels, women may have stronger immunological responses (Olsen and Kovacs, 1996) or other mechanisms based on sex-specific changes in immunological responses. Due to genetics or other factors, immune responses may differ between men and women (Ahmed and Talal, 1990).

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Tamoxifen's estrogen receptor agonist/antagonist properties are not the only ones it has (Komm and Mirkin, 2014; Younis et al., 2020); it also affects sphingolipid biosynthesis, among other things (Sharma et al., 2014). Such 'off-target' results have been shown to confer Tamoxifen's therapeutic action (Mandlekar and Kong, 2001); however, its impact on specific cell types, particularly circulating neutrophils, is still unclear (Corriden et al., 2015; Mirzaei et al., 2022). A significant immunosuppressive effect has been hypothesized based on early studies of Tamoxifen's effect on the neutrophil function that prevents transendothelial migration (de Oliveira et al., 2004; Moreland et al., 2006; Swelum et al., 2020, 2021a,b). Corriden et al. (2015) used in vitro and in vivo methods. DNA-based neutrophil extracellular traps were promoted by Tamoxifen and its effects on neutrophil chemotaxis and phagocytosis (NETs). Antimicrobial peptides, histones, and/or granule proteases coated NETs can kill bacteria and other pathogens by trapping and encasing them (Brinkmann and Zychlinsky, 2007; von Köckritz-Blickwede and Nizet, 2009). It also enhances pathogen death in vitro and MRSA clearance in vivo. Intracellular ceramide regulates neutrophil activity.

Tamoxifen, its active metabolite 4-hydroxytamoxifen, and its primary metabolite N-desmethyltamoxifen all increased NET production in freshly separated human neutrophils, according to fluorescence-based extracellular DNA detection (Corriden et al., 2015). The influence of steroidal hormones on birds' immune response is measured after ova injection (Andersson et al., 2004) or after late and long administration through either hormone implantation (Owen-Ashley et al., 2004). Our experiment studied the effect of synthetic androgen and estrogenic antagonist (Tamoxifen) administration for a short period at early ages on performance, carcass characteristics, edible and inedible organs percentages, phagocytic index, and level of sex hormones of males and females broilers chickens beside correlation coefficient between sex hormones levels and measured traits.

MATERIALS AND METHODS

Birds' Management

The Native Experimental Animal Care Committee accepted this experimental technique (DMU/VetMed-2019-/0145). This work was done at the Damamhur University poultry farm of the animal husbandry and wealth department. Two hundred twenty-five males and 225 females' one-day-old Arbor Acres chicks were obtained from a local hatchery after they were sexed. Each sex's Chicks were identified by wing bands and then randomly distributed on 3 experimental treatments (75 chicks per treatment). Each treatment included 5 replicates (15 chicks per replicate). During the first week of life, chicks of each treatment were housed collectively to can brooded well under a gas brooder and achieve 35°C under the brooder; after the first week, the chick of each replicate was housed separately on a wood shaving floor

pen 1.5 m² and supplied with 32°C brooding temperature decreased 1 oc every 2 d until 24°C.

In the first week, the light was provided for 24 h, and 5 FC was reduced to 18 h daily until the end of the experiment at 45 d. Chicks were vaccinated against Newcastle and Infectious Bronchitis at the seventh d of age through eye dropping, against Infectious Bursal Disease at 2 wk of age, and New Castle Disease again at 18 d and 30 d of age through spraying. Starter mash ration 23% CP provided for the first 3 wk of age replaced by grower crumbled ration 21% CP until the fifth week and finisher pelleted ration 19% CP until the end of the experiment. Ration stages were purchased from a local ration company. Feed and water were introduced ad libitum through manual feeders and waterers with frequent cleaning and sanitizing feeders and waterers.

Experimental Design

After sexing and wing banding of chicks, 225 of each sex were randomly distributed on three experimental treatments (75 chicks/ treatment). Chicks of the first treatment (TAM20) were supplied with tamoxifen citrate (obtained from Amriya for Pharmaceutical Industries, Alexandria, Egypt) was used as TAM citrate) as an estrogenic antagonist, 20 mg/kg body weight through oral administration of the drug after diluted with water, birds received four doses of tamoxifen citrate every other day from 3rd until 9th days according to Younis et al. (2020). Under the second treatment (Androgen), chicks were injected intramuscularly with veterinary androgen AD GAN@ (Boldenone Undecylate 50 mg) 1 cm/10 kg body weight on the fifth and ninth day to allow withdrawal time for the drug over 20 d as recommended by the manufacturer. The third treatment was the control treatment, wherever chicks of each treatment were redistributed on five replicates (15 chicks per replicate).

Growth Traits

Acute Initial and final body weights were estimated using a sensitive scale, total weight gain assessed by subtracting the initial weight from the final one, and feed intake estimated weekly by subtracting ration residues at the end of the week from ration supplied through the week to calculate net feed intake then total feed intake estimated, additionally feed conversion ratio estimated by the division of weight gain on feed intake multiplying by 100.

Carcass Characteristics

Forty carcass traits were measured at 45 d of age. Five birds per replicate were fasted for 12 h before slaughtering but still supplied with water. Birds are weighed before slaughtering and after evisceration to estimate hot carcass weight and dressing percentage by dividing carcass weight by life weight. All internal organs,

including the intestine, heart, spleen, liver, and gizzard, were weighed and calculated as a percentage of live weight after evacuated and abdominal fat. Also, comb and shanks were weighed and calculated as percentages of live weight. Carcass divided and thigh, breast (including bone and skin), neck with backbone and wings were weighed and calculated as a percentage of carcass weight.

Hormonal Assay

Blood samples were collected from the wing veins of three birds per replication at the end of the experiment. The serum was inaccessible by centrifugation at 3,000 rpm for 15 min and kept at (-20°C) until analysis. The serum testosterone and estrogen concentrations were assessed using the commercial Elisa kit (Wuhan Fine Biotech Co., Ltd, China) in an enzyme-linked immunosorbent test (ELISA) based on instructions from the manufacturer.

Phagocytic Index

Phagocytic activity was evaluated following (Jacobs, 1964) by the ability of white blood cells to engulf heat-killed organisms in a standard suspension at 37°C . The MOS chosen for such a purpose was *Staph aureus*.

Statistics

Data have been analyzed with a 2-way SAS variance analysis (Cary, 2002). Proc GLM ($P < 0.05$). The Duncan multiple range tests determined significant differences between means (Duncan, 1955) by adopting the following model:

$$Y_{ijk} = \mu + T_i + S_j + TS_{ij} + e_{ijk}$$

Where: Y_{ijk} = an observation, μ = the overall mean, T_i = effect of treatment, S_j = effect of sex, TS_{ij} = the interaction between treatment and sex and e_{ijk} = random error.

RESULTS

Performance Traits

Table 1 illustrates that neither tamoxifen nor androgen supplementation substantially influenced the body weight, total weight gain, nor feed conversion ratio compared to the control. On the contrary, feed intake was significantly highest for androgen treatments, followed by control. The lowest values were reported for TAM20 treatments ($P < 0.0001$). Males and females reported similar weight, weight gain, feed intake, and feed conversion ratio. Concerning treatment sex interaction, although there were no noteworthy differences between treatments, androgen and TAM20 treatments induced higher productive performance values for females than males, with adverse results reported for control treatments (Table 1).

Carcass Characteristics

There were no substantial differences between different treatments in carcass weight, dressing percentage, and carcass cuts percentage relative to carcass weight, except that breast percentage was meaningfully higher ($P < 0.05$) for androgen treatments than TAM20 treatments, and the 2 treatments did not differ significantly from control. Females achieved significantly higher dressing and breast percentage than males, with opposite results observed for the thigh percentage; the interaction effect had the same treatment and sex effect trend, as shown in Table 2.

The effect of treatment, sex, and their interaction on body organs is listed in Table 3. The treatment effect

Table 1. Effect of date palm pollen ethanolic extract (500 mg/kg bw/day) and/or doxorubicin (2.5 mg/kg bw/day) on body, heart, and relative heart weights myocyte cross-sectional area of control and treated rats.

Items		Initial weight	Final weight	Weight gain	Feed intake	Feed conversion
Treatment effect						
Androgen		44.5±1.17	2146.7±58.77	2102.20±58.3	3948.20±35.81 ^a	1.89±0.05
Control		45.83±1.2	2107.42±67.83	2061.58±68.03	3793.42±52.46 ^b	1.86±0.07
Tam20		45.42±0.96	2117.42±80.34	2072.00±80.32	3521.50±21.9 ^c	1.73±0.08
P-Value		NS	NS	NS	<0.0001	NS
Sex effect						
Female		46.39±0.79	2136.5±46.47	2090.11±46.61	3713.50±54.60	1.80±0.06
Male		44.06±0.94	2106.75±68.03	2062.69±67.91	3776.13±51.51	1.86±0.06
P-Value		NS	NS	NS	NS	NS
Interaction effect						
Treatment	Sex					
Androgen	Female	43.75±1.25	2179.25±111.72	2135.5±110.68	3960.75±56.95 ^a	1.87±0.1
	Male	45.00±1.83	2125.00±71.66	2080.00±71.06	3939.83±50.14 ^a	1.9±0.06
Control	Female	49.17 ± 0.83	2056.83 ± 55.5	2007.67 ± 54.77	3804.67 ± 88.74 ^b	1.91 ± 0.09
	Male	42.50 ± 1.12	2158 ± 127.05	2115.5 ± 127.27	3782.17 ± 64.68 ^b	1.82 ± 0.11
Tam20	Female	45.63 ± 1.13	2174.88 ± 80.34	2129.25 ± 80.89	3550.5 ± 29.17 ^b	1.68 ± 0.08
	Male	45.00 ± 2.04	2002.5 ± 185.13	1957.5 ± 184.03	3521.5 ± 36.08 ^b	1.85 ± 0.19
P-Value	NS	NS	NS	NS	0.02	NS

Data are expressed as mean ± SEM.

^{a,b}Means within a column followed by different superscripts are significantly different ($P < 0.05$).

Table 2. Effect of Tamoxifen and androgen supplementation on carcass characteristics of Arbor Acres chickens.

Level		Carcass wt	Dressing %	Thigh	Breast	Should	Neck
Treatment effect							
Androgen		1546.67 ± 68.95	73.89 ± 1.09	39.78 ± 0.66	38.11 ± 0.79 ^a	11.22 ± 0.32	10.78 ± 0.22
Control		1657.14 ± 93.4	76.14 ± 0.83	40.00 ± 0.62	36.86 ± 0.59 ^{ab}	12.14 ± 0.49	10.71 ± 0.18
Tam20		1511.2 ± 73.34	74.9 ± 1.02	39.90 ± 0.43	36.4 ± 0.65 ^b	11.00 ± 0.21	11.2 ± 0.29
<i>P</i> -value		NS	NS	NS	0.049	NS	NS
Sex effect							
Female		1603.17 ± 43.19	76.5 ± 0.5 ^a	39.00 ± 0.28 ^b	38.58 ± 0.48 ^a	12.25 ± 1.44	10.75 ± 0.18
Male		1528.14 ± 74.18	73.5 ± 0.86 ^b	40.64 ± 0.45 ^a	35.86 ± 0.43 ^b	11.14 ± 0.25	11.07 ± 0.22
<i>P</i> -value		NS	0.0133	0.0128	0.0002	NS	NS
Interaction effect							
Treatment	Sex						
Androgen	Female	1626.00 ± 64.48	75.5 ± 0.65	38.75 ± 0.75	39.50 ± 1.32 ^a	11.00 ± 0.41	10.75 ± 0.48 ^b
	Male	1483.2 ± 111.14	72.6 ± 1.75	40.60 ± 0.93	37.00 ± 0.71 ^{bc}	11.4 ± 0.51	10.80 ± 0.2 ^b
Control	Female	1650.00 ± 37.04	77.0 ± 1.52	39.00 ± 0.88	38.33 ± 0.33 ^{ab}	11.33 ± 0.84	11.0 ± 0.37 ^{ab}
	Male	1662.50 ± 172.7	75.5 ± 1.44	40.75 ± 0.95	35.75 ± 0.48 ^{cd}	10.75 ± 0.48	10.5 ± 0.29 ^b
Tam20	Female	1556.80 ± 91.83	77.0 ± 1.05	39.20 ± 0.37	38.00 ± 0.45 ^{ab}	10.8 ± 0.2	10.6 ± 0.24 ^b
	Male	1465.60 ± 121.3	72.8 ± 1.16	40.60 ± 0.68	34.80 ± 0.66 ^d	11.2 ± 0.37	11.8 ± 0.37 ^a
<i>P</i> -value		NS	NS	NS	0.045	NS	0.0401

Data expressed as Mean ± SEM.

^{a,b,c,d}Mean within the same column with different superscripts are meaningfully different ($P < 0.05$).

was insignificant except that the comb percentage was significantly highest ($P < 0.0001$) for androgen treatment, followed by control and TAM20 treatment. Concerning the sex effect, comb and shank percentages were higher ($P < 0.01$) for males than females, with no considerable differences for other measured body organs. Regarding the treatment of sex interaction, males under androgen treatment reported significant comb percentages followed by control. The lowest rate was for TAM20 treatment; on the contrary, the comb percentage for different therapy females was not significantly different.

Serum Testosterone

Serum testosterone in androgen-treated birds was significantly increased, followed by the control and TAM20 groups (Table 3). Testosterone levels in males were also substantially increased. Meanwhile, treatment and sex interaction substantially impacted the highest-level

testosterone hormone found in androgen-treated males, control males, and TAM20 males. The lowest level was seen in females of the three groups. Testosterone is also inversely proportional to phagocytic index, estrogen, total feed intake, weight gain, bodyweight, carcass%, dressing%, liver%, intestine%, abdominal fat%, and breast%. It is also positively proportional to total feed conversion, heart%, spleen, gizzard and gizzard fat%, shoulder %, neck& comb, and shank %, as shown in Table 5.

Serum Estrogen

Table 4 showed a considerable rise in serum estrogen levels in androgen treated group compared to both control and TAM 20 groups. In female birds, estrogen levels have significantly increased compared to males in all groups. Besides, the interaction between sex and treatment greatly influenced estrogen hormone at the most advanced level found in androgen-treated females than

Table 3. Tamoxifen and androgen supplementation impact on Edible and inedible Organs of Arbor Acres chickens.

Level		Liver %	Heart %	Spleen %	Gizzard%	Gizzard fat%	Abdominal fat%	Comb%	Shank%
Treatment effect									
Androgen		2.44 ± 0.18	0.42 ± 0.03	0.08 ± 0.02	1.46 ± 0.09	0.86 ± 0.09	1.14 ± 0.11	0.06 ± 0.01 ^a	3.67 ± 0.21
Control		2.29 ± 0.18	0.5 ± 0.03	0.08 ± 0.02	1.43 ± 0.07	0.96 ± 0.05	1.56 ± 0.18	0.04 ± 0.01 ^b	3.71 ± 0.30
Tam20		2.5 ± 0.17	0.49 ± 0.02	0.09 ± 0.05	1.57 ± 0.07	0.82 ± 0.06	1.34 ± 0.13	0.02 ± 0.01 ^c	3.8 ± 0.20
<i>P</i> -Value		NS	NS	NS	NS	NS	NS	0.0003	NS
Sex effect									
Female		2.33 ± 0.14	0.44 ± 0.03	0.06 ± 0.01	1.48 ± 0.05	0.88 ± 0.07	1.38 ± 0.15	0.02 ± 0.002 ^b	3.17 ± 0.10 ^b
Male		2.5 ± 0.14	0.49 ± 0.02	0.11 ± 0.04	1.51 ± 0.07	0.86 ± 0.04	1.29 ± 0.09	0.06 ± 0.01 ^a	4.21 ± 0.24 ^a
<i>P</i> -Value		NS	NS	NS	NS	NS	NS	<0.0001	<0.0001
Interaction effect									
Treatment	Sex								
Androgen	Female	2.75 ± 0.25 ^a	0.38 ± 0.05	0.08 ± 0.03	1.4 ± 0.07	0.83 ± 0.16	1.28 ± 0.2	0.02 ± 0.005 ^{cd}	3.0 ± 0.09 ^c
	Male	2.2 ± 0.20 ^{ab}	0.46 ± 0.02	0.08 ± 0.02	1.5 ± 0.16	0.88 ± 0.1	1.04 ± 0.1	0.09 ± 0.01 ^a	4.2 ± 0.22 ^a
Control	Female	2.0 ± 0.10 ^b	0.5 ± 0.06	0.05 ± 0.02	1.47 ± 0.03	1.03 ± 0.07	1.7 ± 0.45	0.02 ± 0.003 ^{cd}	3.0 ± 0.05 ^c
	Male	2.5 ± 0.29 ^{ab}	0.5 ± 0.04	0.1 ± 0.02	1.4 ± 0.12	0.9 ± 0.06	1.45 ± 0.09	0.06 ± 0.01 ^b	4.25 ± 0.30 ^a
Tam20	Female	2.2 ± 0.2 ^{ab}	0.46 ± 0.02	0.04 ± 0.01	1.54 ± 0.11	0.82 ± 0.11	1.28 ± 0.19	0.01 ± 0.004 ^d	3.4 ± 0.21 ^{bc}
	Male	2.8 ± 0.2 ^a	0.52 ± 0.02	0.15 ± 0.1	1.6 ± 0.1	0.82 ± 0.04	1.4 ± 0.2	0.03 ± 0.01 ^c	4.20 ± 0.40 ^a
<i>P</i> -Value		0.0272	NS	NS	NS	NS	NS	0.0045	

Data expressed as Mean ± SEM.

^{a,b,c,d}Mean within the same column with different superscripts are meaningfully different ($P < 0.05$).

Table 4. Tamoxifen and androgen supplementation impact on serum testosterone, *estrogen* level, and Phagocytic index in Arbor Acres chickens.

Level		Testosterone	Estrogen	Phagocytic index
Treat				
Androgen		1.18 ± 0.42 ^a	55.83 ± 9.44 ^a	35.5 ± 3.58 ^b
Control		0.79 ± 0.33 ^b	41.17 ± 7.4 ^b	42.33 ± 2.55 ^a
TAM20		0.61 ± 0.23 ^c	37.5 ± 2.75 ^b	47.00 ± 4.93 ^a
	<i>P</i> value	<.0001	0.0032	0.0071
Sex				
Female		0.14 ± 0.03 ^b	57.44 ± 5.7 ^a	48.67 ± 2.56 ^a
Male		1.58 ± 0.15 ^a	32.22 ± 2.56 ^b	34.56 ± 2.17 ^b
	<i>P</i> value	<.0001	<.0001	<.0001
Treat*sex				
Androgen	Female	0.25 ± 0.07 ^d	75.67 ± 5.78 ^a	42.33 ± 1.76 ^{bc}
	Male	2.11 ± 0.08 ^a	36 ± 4.36 ^{cd}	28.67 ± 3.76 ^d
Control	Female	0.07 ± 0.02 ^d	56.67 ± 4.1 ^b	46.67 ± 2.6 ^b
	Male	1.51 ± 0.1 ^b	25.67 ± 4.1 ^d	38.00 ± 2.65 ^{bc}
TAM20	Female	0.1 ± 0.01 ^d	40 ± 4.62 ^c	57.00 ± 3.46 ^a
	Male	1.13 ± 0.11 ^c	35 ± 3.21 ^{cd}	37.00 ± 3.06 ^{cd}
	<i>P</i> value	0.0004	0.0055	0.1995

Data expressed as Mean ± SEM.

^{a,b,c,d}There is a considerable difference between the mean values in the same column with different superscripts ($P < 0.05$).

control females, followed by TAM 20 females than males of both androgen and TAM 20 groups and finally control males. Estrogen is inversely proportional to testosterone, weight, dressing, heart %, gizzard%, gizzard fat %, shoulder, shank %shop, comp %, and neck %, and positively proportional to dressing %, abdominal fat %, and total feed intake as shown in Table 5.

Phagocytic Index

The rise of the phagocytic index was substantial in TAM 20 and control groups, followed by androgen-treated birds, Table 4. Moreover, the phagocytic index showed a marked increase in females associated with males of all groups. Besides, treatment and sex interaction significantly affected such index, with the highest level in TAM20 females, followed by control females. Both androgen females and control males groups were followed by TAM 20 males, and finally, androgen-treated males. The phagocytic index is inversely proportional to testosterone, total feed intake, total feed conversion, liver %, heart %, spleen %, gizzard fat%, thigh %, neck%, comb %, and shoulder %, as shown in Table 5.

DISCUSSION

The impact of early and short administration of sex hormones agonist and antagonist on broiler chickens' performance and the correlation between sex hormones level, performance, and immune response were estimated. External hormonal supplementation on performance traits was significantly affected; only feed intake increased under androgen treatments. It decreased under TAM20 treatment compared to control, although body weight and weight gain increased numerically for females and decreased for males treated with steroidal hormones.

In hens, sex steroids have had little success stimulating growth or boosting efficiency (Liebert, 2006).

Fennel and Scanes (1992) reported that the effects of androgens on the growth of white leghorn chickens were either reduced or unaffected. An anabolic effect on male and female chicks' body weight was identified when DHT was given in large quantities; however, the impact on testes growth was less pronounced (Abd El-Hack et al., 2018, 2022). Others have found that providing androgens to cockatiels slowed their growth. Exaggerated male secondary sex traits are linked to this growth (Dube and Tremblay, 1974).

A high dose of testosterone propionate (2.5 mg/wk) improved growth in female chicks receiving the injections twice weekly (Ma, 1954). Carcass characteristics did not significantly change among treatments, except that breast percentage was considerably higher in androgen treatments and lower in TAM20 treatments relative to control.

Testosterone therapy has been demonstrated to enhance growth hormone levels in the blood, resulting in increased muscular growth (Swerdloff and Wang, 1993). Comb percentages were significantly higher for androgen treatment males, control males, and TAM20 males. Adversely, different comb percentages for females of different treatments were insignificant. However, exogenous hormonal supplementation did not affect other edible and inedible organ percentages. Fennel and Scanes (1992) Androgens have stimulated male reproductive system development by facilitating the androgen receptor in the body's endocrine system. This can be seen in the growth of the testes and the hair on men's heads. Furthermore, according to testosterone propionate (TP) increased comb growth in the three experimental groups, while estradiol 3-benzoate (EB) inhibited it.

Body weight, weight gain, feed intake and conversion ratio did not change substantially by sex influence, contrary to Olawumi and Fagbuaro (2011) and Thutwa et al. (2012). The growth rate in males was significantly faster than in women, and the slaughter weights were substantially higher (Choo et al., 2014). There may be a reason for this discrepancy in the supplied hormone consequence. Observation of treatment sex interaction effect reflected better body weight and weight gain for males than females in the control treatment, which conformed with the authors' results; however, hormonal treatments inverted these results. On the contrary, reported similar feed conversion ratios.

Females had significantly higher dressing and breast percentages about the effect of sex on carcass traits. Males had a substantially higher thigh percentage. These results were at variance with Olawumi and Fagbuaro (2011) regarding dressing and breast percentage results; they reported nonsignificant differences between the 2 sexes for these traits and conformity with their thigh percentage results. Moreover, Castellini et al. (2006) showed that gender had no substantial impact on carcass traits. Nonetheless, Musa et al. (2006) reported a significant sex effect on these traits. Edible organ

Table 5. Correlation between testosterone, estrogen, phagocytic index and Edible and inedible organs, performance and carcass characteristics of Arbor Acres chickens.

	Phag	Test	Estro	W6	TFI	TWG	TFC	Life	Carc	D.P	Liv.p	IntP	H.P	Spl.P	gizP	GFP	AbFP	ThiP	Br.P	Sh.P	Ne.P	CoP	ShaP
Phag	1	-0.432	0.0105	0.170	-0.351	0.167	-0.275	-0.016	0.005	0.146	-0.040	0.143	-0.028	-0.074	0.066	-0.235	0.125	-0.024	0.006	0.194	-0.296	-0.512	-0.036
Test	-0.432	1	-0.73	-0.101	-0.479	-0.178	-0.080	-0.169	-0.177	-0.138	-0.297	-0.070	0.348	0.012	0.038	0.018	-0.015	0.062	-0.058	0.262	0.231	0.151	0.136
Estro	0.1078	0.0002	1	0.709	0.060	0.507	0.768	0.46	0.44	0.54	0.18	0.76	0.121	0.951	0.86	0.93	0.94	0.78	0.80	0.25	0.31	0.51	0.55
W6	0.010	-0.737	0.0002	1	0.718	0.0008	0.33	0.11	0.09	-0.03	0.32	0.10	-0.41	0.070	-0.05	-0.02	0.07	-0.04	0.09	-0.28	-0.04	-0.05	-0.20
TFI	0.97	0.0002	0.89	0.002	0.99	0.02	0.22	0.64	0.70	0.89	0.15	0.65	0.07	0.76	0.81	0.90	0.74	0.86	0.68	0.22	0.84	0.80	0.38
TWG	0.17	-0.10	-0.037	1	0.094	0.96	-0.86	0.93	0.92	0.64	-0.14	-0.52	-0.07	0.11	-0.36	-0.049	0.32	-0.41	0.31	-0.25	-0.14	0.048	-0.36
TFC	0.51	0.70	0.89	0.54	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0006	0.49	0.01	0.71	0.57	0.06	0.81	0.10	0.040	0.122	0.22	0.49	0.81	0.07
Life	-0.35	-0.47	0.718	0.09	1	0.07	0.34	0.21	0.21	0.14	-0.16	-0.22	-0.21	-0.19	-0.32	0.03	-0.15	-0.21	0.27	-0.17	-0.46	0.492	-0.08
Carcass	0.166	0.060	0.002	0.54	0.61	0.023	0.29	0.31	0.48	0.43	0.31	0.30	0.34	0.11	0.85	0.46	0.29	0.18	0.41	0.018	0.012	0.69	0.69
DRESSP	0.16	-0.17	0.0008	0.96	0.076	1	-0.90	0.95	0.92	0.60	-0.14	-0.49	-0.09	0.14	-0.40	-0.071	0.20	-0.45	0.31	-0.28	-0.17	0.13	-0.31
LiverP	0.51	0.50	0.99	<0.0001	0.61	<0.0001	<0.0001	<0.0001	<0.0001	0.001	0.48	0.01	0.66	0.47	0.04	0.73	0.31	0.02	0.12	0.17	0.41	0.50	0.12
IntP	-0.27	-0.08	0.33	-0.86	0.340	-0.90	1	-0.88	-0.86	-0.56	0.11	0.45	0.01	-0.22	0.32	0.09	-0.23	0.42	-0.27	0.20	0.02	0.030	0.31
H.P	0.2848	0.768	0.2222	<0.0001	0.0235	<0.0001	<0.0001	<0.0001	<0.0001	0.003	0.57	0.03	0.92	0.27	0.11	0.63	0.26	0.03	0.18	0.33	0.89	0.88	0.12
SplP	-0.016	-0.16	0.11	0.93	0.215	0.951	1	-0.88	0.97	0.54	0.02	-0.61	-0.21	0.186	-0.34	0.035	0.20	-0.36	0.35	-0.28	-0.08	0.06	-0.37
gizP	0.9407	0.4637	0.6407	<0.0001	0.2998	<0.0001	<0.0001	<0.0001	<0.0001	0.001	0.87	0.0003	0.239	0.30	0.54	0.84	0.26	0.04	0.11	0.65	0.70	0.03	0.03
GFP	0.005	-0.17	0.090	0.924	0.210	0.928	1	-0.86	0.70	0.70	-0.05	-0.67	-0.17	0.11	-0.403	0.04	0.24	-0.44	0.39	-0.39	-0.12	0.01	-0.45
AbFP	0.97	0.44	0.70	<0.0001	0.31	<0.0001	<0.0001	<0.0001	<0.0001	0.76	<0.0001	0.32	0.53	0.02	0.79	0.18	0.18	0.01	0.02	0.02	0.51	0.93	0.009
ThiP	0.14	-0.13	-0.03	0.64	0.14	0.60	0.70	-0.56	0.54	1	-0.29	-0.65	-0.006	-0.17	-0.46	0.08	0.26	-0.58	0.42	-0.62	-0.21	-0.21	-0.57
Br.P	0.5156	0.54	0.89	0.0006	0.480	0.001	0.003	0.001	<0.0001	0.09	<0.0001	0.97	0.3	0.007	0.65	0.13	0.0004	0.01	0.0001	0.22	0.22	0.0006	0.0006
ShoP	-0.04	-0.29	0.32	-0.14	-0.16	-0.14	0.11	0.02	-0.05	-0.29	1	0.13	-0.13	0.20	-0.09	0.12	0.04	0.21	-0.20	-0.06	0.25	-0.23	0.024
NeP	0.85	0.18	0.15	0.49	0.43	0.48	0.57	0.87	0.76	0.09	0.491	0.46	0.26	0.60	0.50	0.79	0.2	0.26	0.72	0.16	0.19	0.89	0.89
CoP	0.14	-0.07	0.10	-0.52	-0.22	-0.49	0.45	-0.61	-0.67	-0.65	0.13	1	0.009	-0.03	0.32	0.01	-0.05	0.34	-0.64	0.25	0.22	-0.09	0.44
ShaP	0.53	0.76	0.65	0.01	0.31	0.01	0.03	0.0003	<0.0001	<0.0001	0.49	0.95	0.85	0.08	0.92	0.79	0.06	0.0001	0.16	0.22	0.6	0.01	0.01
Phag	-0.02	0.34	-0.41	-0.07	-0.21	-0.09	0.01	-0.21	-0.17	-0.006	-0.13	0.009	1	0.23	0.13	-0.17	-0.006	-0.17	-0.10	0.09	0.07	0.17	0.33
Test	0.9	0.12	0.07	0.71	0.30	0.66	0.92	0.23	0.32	0.97	0.46	0.95	0.20	0.45	0.33	0.97	0.34	0.57	0.61	0.66	0.34	0.05	0.05
Estro	-0.07	0.01	0.07	0.11	-0.19	0.14	-0.22	0.18	0.11	-0.17	0.20	-0.03	0.23	1	0.25	-0.14	-0.12	-0.09	0.05	0.21	0.32	0.02	0.06
W6	0.74	0.95	0.76	0.57	0.34	0.47	0.27	0.30	0.53	0.34	0.26	0.85	0.20	0.16	0.42	0.51	0.61	0.74	0.22	0.07	0.87	0.71	0.71
TFI	0.06	0.038	-0.05	-0.36	-0.32	-0.40	0.32	-0.34	-0.40	-0.46	-0.09	0.32	0.13	0.25	1	0.09	-0.05	0.30	-0.160	0.48	0.29	-0.24	0.153
TWG	0.77	0.86	0.81	0.06	0.11	0.04	0.11	0.05	0.02	0.007	0.60	0.08	0.45	0.16	0.58	0.75	0.09	0.38	0.004	0.09	0.18	0.40	0.40
TFC	-0.23	0.018	-0.02	-0.04	0.037	-0.07	0.09	0.03	0.04	0.08	0.12	0.01	-0.17	-0.14	0.09	1	0.31	0.22	-0.20	-0.24	0.01	-0.16	-0.25
Life	0.29	0.93	0.90	0.81	0.8	0.7	0.63	0.8	0.7	0.6	0.5	0.9	0.33	0.4	0.58	0.07	0.21	0.26	0.18	0.93	0.37	0.16	0.16
Carcass	0.12	-0.01	0.07	0.32	-0.15	0.20	-0.23	0.20	0.24	0.26	0.04	-0.05	-0.006	-0.12	-0.05	0.31	1	0.02	-0.20	-0.08	0.16	-0.30	-0.27
DRESSP	0.577	0.945	0.740	0.107	0.465	0.319	0.264	0.266	0.180	0.136	0.790	0.790	0.97	0.51	0.7	0.07	0.87	0.2	0.62	0.35	0.09	0.12	0.12
LiverP	-0.02	0.06	-0.04	-0.41	-0.21	-0.45	0.42	-0.36	-0.4	-0.58	0.2	0.34	-0.17	-0.09	0.30	0.22	0.02	1	-0.61	0.22	0.23	0.05	0.49
IntP	0.914	0.78	0.86	0.04	0.29	0.02	0.03	0.04	0.011	0.0004	0.245	0.065	0.34	0.61	0.091	0.21	0.87	0.0002	0.21	0.20	0.75	0.003	0.003
H.P	0.006	-0.05	0.09	0.31	0.27	0.31	-0.2	0.35	0.39	0.42	-0.20	-0.64	-0.1	0.05	-0.160	-0.20	-0.2	-0.61	1	-0.031	-0.39	-0.10	-0.55
SplP	0.97	0.80	0.68	0.12	0.18	0.123	0.188	0.04	0.02	0.01	0.26	0.0001	0.57	0.74	0.38	0.25	0.0002	0.86	0.025	0.57	0.0009	0.0009	0.0009
gizP	0.19	0.26	-0.28	-0.25	-0.17	-0.28	0.20	-0.287	-0.39	-0.62	-0.06	0.25	0.09	0.21	0.48	-0.24	-0.08	0.22	-0.03	1	0.17	0.05	0.32
GFP	0.38	0.25	0.22	0.22	0.41	0.1	0.33	0.11	0.02	0.0001	0.72	0.16	0.61	0.22	0.004	0.18	0.62	0.21	0.86	0.33	0.77	0.06	0.06
AbFP	-0.29	0.23	-0.04	-0.14	-0.46	-0.17	0.02	-0.08	-0.12	-0.21	0.25	0.22	0.07	0.32	0.29	0.01	0.16	-0.39	0.17	1	-0.20	0.03	0.03
ThiP	0.18	0.31	0.84	0.49	0.01	0.41	0.89	0.65	0.51	0.22	0.16	0.22	0.66	0.07	0.09	0.93	0.35	0.20	0.33	0.33	0.27	0.85	0.85
Br.P	-0.51	0.15	-0.05	0.04	0.49	0.13	0.03	0.06	0.01	-0.21	-0.23	-0.09	0.17	0.02	-0.24	-0.16	-0.30	0.058	-0.1	0.05	-0.20	1	0.52
ShoP	0.014	0.51	0.80	0.81	0.01	0.50	0.88	0.70	0.93	0.22	0.19	0.6	0.34	0.87	0.1	0.3	0.09	0.75	0.57	0.77	0.27	0.002	0.002
NeP	-0.03	0.13	-0.20	-0.36	-0.08	-0.3	0.31	-0.3	-0.45	-0.57	0.02	0.44	0.33	0.068	0.15	-0.21	-0.27	0.49	-0.55	0.32	0.03	0.526	1
CoP	0.87	0.55	0.38	0.07	0.69	0.12	0.12	0.03	0.009	0.0006	0.89	0.01	0.05	0.71	0.40	0.16	0.12	0.003	0.0009	0.06	0.85	0.002	0.002

Data are expressed as Mean \pm SEM.

Abfp., abdominal fat; Brp., breast %; Cop., Comb %; Estro., estrogen; Gizp., gizzard %; H.p., heart %; Intp., Intestine %; Life., life weight; Liver p., liver percentage; Nep., neck %; Shop., shoulder %; Shap., shank%; Splp., Spleen %; Phag., phagocytic index; Test., Testosterone; Tfi., Total feed intake; Thp., thigh %; Twg., Total weight gain; W6., weight 6.

percentages were similar for the 2 sexes. These results agreed with [Olawumi and Fagbuaro \(2011\)](#). Concerning in edible organs percentages, comb and shank rates were significantly higher for males than females, which conforms with ([Abdelnour et al., 2020](#); [Aladaileh et al., 2020](#)).

Administration of TAM 20 to birds led to a significant decrease in both testosterone and estrogen levels. This finding is in harmony with our previous study ([Younis et al., 2020](#)), which elucidated that TAM at a dose of 10 mg/kg BW had favorable effects on the level of both estrogen and testosterone in broilers as compared to the group that established TAM at a dose of 20 mg/kg B.W. Early egg production was reported to have been boosted by TAM treatment at modest dosages in young WL hens ([Jacobs, 1964](#)). Low dosages of TAM administered to male WL chicks increased testicular and comb growth and plasma testosterone levels, coinciding with early semen production and sexual activity. Conversely, TAM exhibits both anti-estrogenic and estrogenic effects on WL male chicks, depending on the amount of TAM administered ([Rozenboim et al., 1989](#)), and does not act as a pure estrogen antagonist as has previously been assumed ([Sutherland, 1981](#)).

Our results revealed elevated serum testosterone and estrogen in androgen-treated groups. This finding is in harmony with [Alén et al. \(1985\)](#), which described an increase in the level of such 2 hormones following androgen administration in power athletes. They attributed the high estrogen level to the administered androgen as a precursor for estrogen synthesis. Our findings on the impact of sex on testosterone and estrogen hormones agree with those of a prior study ([Dewil et al., 1998](#)), with much greater estrogen levels in females and testosterone in males reporting that factor to have a considerable impact on hormone levels.

Our results revealed a significant improvement in the TAM 20 group's phagocytic index compared to the androgen-treated group. This finding agrees with a previous study ([Corriden et al., 2015](#)), which reported that Tamoxifen improves neutrophils' bactericidal activity, with high NETs production as an impossible mechanism. Such enhancement occurs mainly through the alteration of cellular ceramide concentrations. Bioactive sphingolipid Ceramide is a cell stress signal associated with neutrophil apoptosis earlier ([Scheel-Toellner et al., 2004](#); [Seumois et al., 2007](#); [Corriden et al., 2015](#)). It has been found, however, that both Tamoxifen and synthetic ceramide are potent stimulators of the new cell death pathway known as NETosis ([Wartha and Henriques-Normark, 2008](#); [El-Tarabily et al., 2021](#); [Seidavi et al., 2021](#)). Moreover, both the apoptotic and autophagic pathways can be stimulated by ceramide ([Maiuri et al., 2007](#)). It most recently was involved in the manufacturing of NET ([Remijsen et al., 2011](#); [Younis et al., 2022](#)).

Myeloid progenitors can differentiate into neutrophils with the help of androgen hormones. Testicular feminization mutation in animals and genetically engineered androgen receptor-deficient mice demonstrate

neutropenia due to the androgen insensitivity mutation ([Chuang et al., 2009](#)). Androgen-deficient prostate cancer patients and gonadectomized animals show neutropenia before androgen-replacement therapy/DHT medication is administered ([Trigunaite et al., 2013](#); [Bird et al., 2017](#)). Androgens have been shown to affect the function of neutrophils. Testosterone, for example, inhibits both the antibacterial action and the generation of pro-inflammatory cytokines by human neutrophils, while it promotes the anti-inflammatory cytokines IL-10 and TNF-alpha production ([Malkin et al., 2004](#); [Marin et al., 2010](#)). These results are in harmony with our findings, which reported reduced phagocytic activity in the androgen-treated group.

In contrast to males, our findings showed that females had much higher phagocytic activity. The X chromosome and sex hormones have been linked to disparities in immunity between men and women ([Oertelt-Prigione, 2012](#)). It is well known that a person's sex hormones can influence the activity and development of immune cells and the vulnerability of cells and tissues to harm caused by aberrant (autoimmune) processes ([Gubbels Bupp and Jorgensen, 2018](#)). These 3 hormones also influence the immune cells' reaction to estrogen, progesterone, and testosterone. Receptors for nuclear and non-nuclear hormones are involved in their actions ([Oertelt-Prigione, 2012](#)). [Gelmann \(2002\)](#) showed that the X chromosome encodes for androgen receptors, which attach to testosterone and 5-dihydrotestosterone and then transmit their nuclear action via lineage to ARE (androgen response elements) in the promoter region of vulnerable genes.

As a result of its direct and indirect actions, estrogen acts on estrogen receptors (**ER**). The E/ER complexes are linked to specific estrogen response elements (**ERE**) inside the promoter or enhancer regions of genes. At the same time, the indirect response interacts with unrelated transcription factors to alter their function ([Ho and Liao, 2002](#)). The 2 ER isoforms—ER and ER—have a few similar target genes and a few unique ones ([Stossi et al., 2004](#)) and numerous strategies to control the production of cytokines in target cells ([Oertelt-Prigione, 2012](#)). As a rule, estrogen boosts immunological responses, whereas progesterone and androgens depress them ([Younis and Ghoneim, 2022](#)). The existence or absence of an extra X chromosome is the first consideration when examining the impact of genetics on sex differences. The X chromosome, which contains roughly 1,000 genes, plays a significant role in the body's ability to fight off infection ([Fish, 2008](#)). The X chromosome has an interesting immune regulator called IL-9. A recent study found a link between the IL-9 gene polymorphism and a virus infection's sex-specific prevalence. Male children are far more often than females to contract respiratory syncytial virus (**RSV**), and the polymorphism that has been linked to an elevated risk of infection has only been found in male patients ([Schuurhof et al., 2010](#); [Fazli et al., 2015](#)).

CONCLUSIONS

This is the first study to estimate the impact of synthetic androgenic and estrogenic antagonists on the immune systems and physical traits of broiler males and females. Tamoxifen and androgen had no noticeable effect on weight gain. But androgen treatment significantly improved male-to-female secondary sexual characteristics compared to Tamoxifen with improved phagocytic index with Tamoxifen 20 supplementation. The positive effect of androgen treatment on sexual hormone levels was recorded compared to Tamoxifen 20 supplementation.

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Ethical statement: This study was declared by The experimental protocol regarding the care and handling of animals was approved by the Native Experimental Animal Care Committee and approved by the Ethics of the Institutional Committee of Animal Husbandry and Animal Wealth Development Department, Faculty of Veterinary Medicine, Damanhour University, Damanhour, Egypt (DMU/VetMed-2020-/0145). All methods were performed according to the relevant guidelines and regulations of Damanhour University in handling experimental animals.

Data availability statement: Data are available upon request.

DISCLOSURES

The authors declare no conflicts of interest.

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