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The Relationship Between Friesian Calves Performance and Growth Hormone and Leptin Levels

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Abstract | Studying the possible association between the growth rate reflecting leptin (LP) and growth hormone (GH) levels, is a route for forecasting the performance of later growth and reproductive traits in Friesian calves. thirty calves (15 males, and 15 females), were categorized into three equal groups. The 1st group (n=5 males and 5 females), which recorded the lowest values from GH, and LP at weaning (105 d) considering then the average daily gain (ADG) from birth to weaning in each animal; 2nd group that had moderate values, and 3rd group that had the highest values. The results indicated that the 3rd group exhibited the 33.47% and 19.60% highest ADG, with decreased levels of GH by 14.05% and 17.96%, and elevated LP by 22.41% and 32.72% in males and females at 540 d, respectively, compared to then the 1st group, which delayed in all ages. In addition, skeletal growth (body length, height at withers, and heart girth) adhered to the same pattern. Calves in the 3rd group reached maturity earlier (about 50d and 63d) and recorded heavier body weights (about 35 kg and 55 kg) of both males and females, respectively. Also, sexual activity, semen characteristics and testosterone levels for bulls developed earlier than the 1st group. Heifers in the same group were superior in reproductive performance such as reaching puberty, and fertility compared to other groups. The 3rd group showed the highest concentrations of serum proteins, glucose, and lipid profiles. The 2nd group came next, and 1st group registered the lowest concentrations. In conclusion, data on GH and LP levels from birth to weaning could be a useful early-life selection tool for selecting high-performing individuals and predicting improved animal performance in the distant future throughout different ages (from 105 d to 540 d of age).

Keywords | Friesian, Leptin, Growth hormone, Growth performance, Reproduction

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INTRODUCTION

There is a strong relationship between the growth hormone (GH) level in the early life of a calf and its future growth rate. Oguro *et al.* (2003) stated that the secretion or deficiency of GH in cattle could be an indicator of beef or milk production potential. The GH is crucial in numerous physiological processes (Oberbauer, 2015). Numerous re-

searchers have examined the role of growth hormone (GH) in improving the growth performance of cattle. For instance, Krasnopiorova *et al.* (2012), highlighted that GH possesses extensive physiological functions, including regulating growth, lactation, mammary gland development, gluconeogenesis, lipolysis activation, and promoting amino acid uptake into muscle proteins. Similarly, Akçay *et al.* (2015) claimed that GH has a significant direct or indirect impact on tissue growth and fat metabolism, making it crucial for animal reproduction, lactation, and growth stimulation.

Leptin (LP) is secreted predominantly by the white adipose tissue (Trayhurn and Wood, 2005; Barbagallo *et al.*, 2021). Secreted constitutively, the levels of LP in serum, therefore, associate positively with the percentage of body fat mass (Fried *et al.*, 2000; Singh *et al.*, 2022). LP serves as a covert intermediary potentially connecting metabolic status with the reproductive axis (Hausman *et al.*, 2012). LP is a valuable biomolecule marker for identifying individuals with high performance, contributing to enhanced adaptability and productivity (Agarwal *et al.*, 2009). The physiological function of LP and its gene's association with various economic traits have positioned it as a prime candidate for study and enhancement in animals via appropriate breeding and management strategies (Saleem *et al.*, 2015). It has been shown to have significant roles in several other physiological processes, as shown by the widespread distribution of LP receptors in the body. These roles encompass its functions in (a) regulating appetite and body weight (Cowley *et al.*, 2001), (b) modulating immunity and inflammation (Batra *et al.*, 2010), and (c) influencing sexual development and reproduction (Ahima *et al.*, 1997; Clarke and Henry, 1999; Dardeno *et al.*, 2010; Park and Ahima, 2015).

The secretion of GH is known to be significantly impacted by body weight, with suppression shown in obesity and cachexia. Additionally, Different researchs have shown that LP levels control the release of GH. These findings reported that activity of GH is influenced by LP and were carried out in vivo on GH-deficient animal models, including pigs, rats, humans, cattle and sheep (Considine, 1997; Carro *et al.*, 1997; Carro *et al.*, 1999; Tannenbaum *et al.*, 1998; Watanobe and Habu, 2002). These results suggested that the GH axis uses LP as a metabolic signal. Since blood LP levels and LP-mRNA content in adipocytes are connected with body fat and weight (Hamilton *et al.*, 1995; Lonnqvist *et al.*, 1995; Considine *et al.*, 1996), and because GH release is significantly regulated by nutritional status and body weight (Dieguez and Casanueva, 1995), the regulatory role of leptin on GH secretion is not surprising. Houseknecht *et al.* (2000) cultured cow adipocytes using growth hormone alone and combined with dexamethasone, insulin, and insulin-like growth factor-1 (IGF-1). Carro *et al.* (1999) reported that administering 10 µg of LP intraperitoneally (i.c.v.) to hypophysectomized fasting rats resulted in a drop in somatostatin mRNA content and an increase in GHRH mRNA levels, suggesting that LP acts on the hypothalamic neurons responsible for generating somatostatin and GHRH. These results revealed that somatostatin and GHRH function as mediators of leptin-induced GH production. The growth hormone, when combined with other ingredients, attenuated the effect of insulin or dexamethasone stimulation on LP expression. However, after incubation for 24 hours, the growth hormone by itself showed no influence on LP expression from bovine adipose tissue. Additional in vivo experiments demonstrated that growth hormone inhibited LP expression (Chen *et al.*, 1998; Rauch al., 1998; Isozaki *et al.*, 1999).

Selecting calves with superior growth associations with high concentrations of GH, and LP before weaning aids in saving costs and increasing profit. Therefore, this investigation aimed to establish if the growth rate correlated with blood levels of LP and GH levels in Friesian male and female calves could predict future growth performance, reproductive success, and relevant economic characteristics.

MATERIALS AND METHODS

The current study was investigated at El-Gemmezah Experimental Station belonging to APRI, ARC, located at Gharbiya Governorate in the Nile Delta of Egypt. At 8.5 m a.s.l at a latitude of 30°48'07.1"N, and a longitude of 31°08'25.4"E.

Animals, Housing, Feeding, and Management

All calves were clinically healthy and physiologically sound. All calves were kept in fair hygienic conditions throughout the experimental period. The experimental animals were vaccinated and dewormed following the recommended regimen. They were housed tied in semi-open sheds during the experimental periods.

Calves were fed separately on colostrum during their first three days of life, receiving two meals at a rate of 10% of their body weight. The calves received individual feedings of milk at a rate of 10% of their body weight, distributed over two meals daily for six weeks. Milk allowances were gradually decreased leading up to weaning at the age of 15 weeks. Starting from the third week of age, calves had access to both calf starter and hay.

After weaning, animals were fed in separate groups in separate pens (3 pens/sex), the experimental rations were tailored according to (NRC, 2001) to promote an ADG of 1.2 kg/d. The rations consisted of a 65% concentrate feed mixture (CFM) and a 35% roughage on a DM basis. Calves in each group were fed on a ration containing green berseem (*Trifolium alexandrinum*) in winter and spring or corn silage in summer, and fall with rice straw as raghages, and a CFM. The feed amounts were adjusted every 30 days ac-

cording to live body weight. Feeds were offered individually to calves. CFM was delivered two times daily at 0800 and 1500 h, rice straw was given at 1100 h, and green berseem or corn silage was given at 0900 h. Calves were watered twice daily post-feeding in the morning and in the afternoon. Daily feed consumption was recorded for each calf.

From 105 to 540 days of age, the weight of each calf was recorded every 28 days. For female calves, weight at the first estrus, first service, at conception, and right after delivery, and for male calves, weight at maturation was detected. The ADG was determined individually by dividing the periodic weight gain by the number of days between each weighing. Following a 16-hour fast, the calves were individually weighed in the morning before being provided access to water and feed.

Table 1: Experimental groups are categorized based on their body weight gain, and concentrations of growth hormone and leptin of male and female Friesian calves.

Items	Groups		
	A	B	C
Males			
Body Wt. gain (g/day) at 105d	< 550	550-700	> 700
Growth hormone (ng/ml)	< 13	13-15	> 15
Leptin (ng/ml)	<3.5	3.5-4.0	>4.0
Females			
Body Wt. gain (g/day) at 105d	< 450	450 –650	> 650
Growth hormone (ng/ml)	< 11	11-13	> 13
Leptin (ng/ml)	<4.0	4.0-5.5	>5.5

Experimental Design

Thirty Friesian calves (15 males and 15 females) with a birth weight of 32.60 ±0.41 kg on average were selected randomly and observed from birth to weaning. At the weaning age (105 days), the average daily gain (ADG) and growth hormone (GH) and leptin (LP) levels were estimated to identify the animals with the lowest and highest estimated rates. According to the average values of GH levels reported by Trenkle (1971) and Yousef *et al.* (1969) and the average values of LP levels reported by Karaayvaz *et al.* (2022) and Eğritağ *et al.* (2022) in cattle, male and female calves were divided separately into three equal groups (5 each, Table 1) as follows : The first group (A) had the lowest GH and LP levels which, were less than 13 and 3.5 (ng/ml) in males and less than 11 and 4 (ng/ml) in females, respectively, at the same time, ADG values were less than 600 g and 450 g in the same calves. The second group (B) had moderate GH and LP values that ranged from 13–15 and 3.5–4.0 (ng/ml) in males and 11-13 and 4.0-5.5 (ng/ml) in females, respectively, at the same time, ADG values ranged from 600–700 g and 450 -650 g in the same calves. The third group had the highest GH and LP levels which, were greater than 15 and 4.0 (ng/ml) in males and greater than 13 and 5.5 (ng/ml) in females, respectively, at the same time, ADG values were less than 700 g and 650 g in the same calves.

Blood Samples and Serum Analysis

Samples of blood were taken from 15 male and 15 female Friesian calves after birth, and from weaning (105 d) until 540 d of life at 3-month intervals to determine both hormones and metabolite profiles. For male calves only, at the age of maturation, one blood sample was taken from each bull to measure testosterone concentration. Prior to morning feeding, blood samples were drawn from the jugular vein into 15 ml polypropylene tubes. Blood was allowed to clot for approximately 4 hours at room temperature. Every blood sample obtained was centrifuged for 20 min at 1,800 × *g*, and the harvested serum packed in Eppendorf tubes was frozen at – 20°C until further analysis.

The concentration of GH was measured using a commercial ELISA kit provided by the Beijing Sino-UK Institute of Biological Technology, Beijing, China, following the methodology described by Yang *et al.* (2019). Leptin concentrations in serum were determined using a solid-phase sandwich ELISA (EAI-2395, DRG Instruments GmbH, Germany). We utilized the state-of-the-art Immulite analyzer by Siemens Healthcare Diagnostics, Inc., USA, to measure serum testosterone concentrations through the highly accurate chemiluminescence method. We utilized the state-of-the-art Immulite analyzer by Siemens Healthcare Diagnostics, Inc., USA, to measure serum testosterone concentrations through the highly accurate chemiluminescence method.

Using a commercial kit (Biolabo, Glucose GOD-PAP, Cat. No. 87109), the glucose/oxidase technique was used to measure the serum glucose concentration. Using kits from Biodiognostic (CAT. No. TP 2020 and AB 1010), the colorimetric method was used to quantify the serum total protein and albumin content. The amount of globulin was calculated by deducting albumin from the total protein. The serum levels of total cholesterol and triglycerides were measured following enzymatic hydrolysis and oxidation. High-density lipoprotein cholesterol (HDLc) levels were assessed using the Cholesterol Assay E-Test Kit (Wako, Osaka, Japan), adhering to the methods outlined by Lopes-Virella *et al.* (1977). Low-density lipoprotein cholesterol (LDLc) levels were estimated using the Friedewald equation: LDLc = TC - HDLc - (TG/5), where (TG/5) denotes very low-density lipoprotein cholesterol (VLDLc).

Skeletal Growth

The skeletal growth of calves was studied using size dimensions taken at 3-month intervals from 105 to 540 d of age. Height at withers (from the upper point of the shoulder blade to the ground) was measured by a height stick. A flexible tape measured heart girth (body circumference directly posterior

to front legs). Body length (from the point of the withers to the end of the pin bone) was measured by a flexible tape.

Puberty and Sexual Performance

Until puberty (first collected ejaculate with motile sperm) and maturity, male calves were under surveillance for sexual behavior following post-weaning. Up until maturity, calves were examined every week between 0800 and 0900 h for libido. Calves were exposed to a randomly selected teaser heifer in estrus for 25 minutes to test the animals' sexual desire. All calves were released from the collection area without any restrictions to watch sexual activity toward the heifer. The following criteria were examined: first mounting without erection (stage I), first mounting with erection (stage II) and first collecting ejaculate containing motile sperm (stage III). The following sexual behavior traits were recorded; testes circumference: measured around the testes' broad point (the paired testes' greatest circumference) using a flexible tape. Reaction time is the period it takes for a bull to start mounting and ejaculating after heifers are introduced to him is measured in minutes. The latency period is the amount of time that passes between ejaculation and return activity is measured in minutes, according to Kridli and Al-Yacoub (2006).

Semen Collection and Evaluation

Utilizing an artificial vagina semen ejaculates were obtained at maturity to assess their semen traits, as stated by Almquist and Hale (1973). At the time of collection, the temperature within the artificial vagina's inner liner-rubber sleeve was set to 41–43°C. For every collection, a graduated collecting tube and a clean inner liner were used. The inner sleeve was lubricated using white sterile vaseline applied with a sterile rod.

Following collection, each ejaculate's semen was quickly transported to the laboratory, where the volume of each ejaculate was quantified using a transparent graduated plastic tube, precisely to the nearest 0.1 ml. Two successful ejaculates are collected separately to analyze the features of spermatozoa according to Salisbury *et al.* (1978). A drop of semen was examined under a low-power (×10) microscope with a heated slide set at 37°C to measure the percentage of sperm motility. Using a hemocytometer the number of spermatozoa/ml of semen was estimated. The progressive motility score was measured as a percentage (%). Total and motile sperm output, mathematically calculated.

Reproductive Characteristics of Heifers

In the groups mentioned earlier (A, B, and C), fifteen heifers were monitored for estrus to ascertain the age at their first estrus. The detection of the first estrus in heifers was conducted thrice a day at 0800, 1600, and 2100 h. All heifers underwent palpation 5 to 11 days after the pubertal estrus to verify ovulation. Heifers were artificially inseminated at the third estrus. Heifers underwent twice-daily checks (at 0800 and 2100 h) following the first artificial insemination (AI) to monitor for estrus in non-pregnant individuals. About 12 hours following the diagnosis of estrus, they were inseminated. Estrus's return following each AI was thought to be a diagnostic indication of the absence of pregnancy. Rectal palpation was used to verify the pregnancy 45 days following the date of insemination. Cases of dystocia in heifers were recorded at the time of parturition. Additionally, the body weight of newborn calves and instances of stillbirth were recorded during the 48 hours following parturition. Calving ease is categorized into two types: assisted and unassisted. Assisted calving encompasses all forms of assistance, from manual pulling to cesarean sections (Johanson and Berger, 2003).

Statistical Analysis

The statistical analyses were carried out using the GLM procedure, of SAS. Duncan's New Multiple Range Test of the same SAS program was applied to determine significant differences among all tested treatments. The model of the statistical analysis was as follows:

$$Y_{ij} = \mu + G_i + e_{ij}$$

Where;
Y_{ij} = an observation.
μ = overall means.
G_i = ADG and hormone levels at weaning levels (i = low; A: moderate; B: High, C).
e_{ij} = random error.

RESULTS AND DISCUSSION

Growth Hormone, Leptin, and Growth Performance

At the weaning age after the suckling period, male and female calves were divided into three groups as described in Table 1.

The pooled data in Table 2 displays the basis of the current study. The 3rd group (C), recorded the highest values of ADG correlated with the highest GH, and leptin levels, then came group B, whereas group A had the lowest values. At the beginning of the current study (at birth), male and female calves in all groups had similar BW. Differences among groups were significantly high (P<0.0001). The 3rd group's superiority in daily gain in either male or female calves is linked to the highest GH and leptin concentrations compared with the other groups.

Temporal changes in BW for both male and female calves groups during the entire study, are shown in Figure 1. The BW of the group C in both male and female calves rose with age and were greater (P<0.001) than that of the A and B groups, also, the male and female calves of group B were heavier (P<0.001) than the group A at 180 d (C, 192.33

and 175.65; B, 180.21 and 149.55; A, 165.33 and 149.55 kg), 360 d (C, 365.22 and 336.55; B, 365.22 and 300.00; A, 323.55 and 283.21 kg), and 540 d of age (C, 542.35 and 470.25; B, 520.33 and 435.32; A, 470.22 and 410.22 kg) for male and female calves, respectively.

Table 2: Birth weight, weaning weight, body weight gain, growth hormone, and leptin concentration from birth to 105 days of male and female Friesian calves.

Items	Groups			±MSE	P value
	A	B	C		
Males					
Birth Wt. (kg)	30.40[a]	31.60[a]	31.80[a]	0.41	0.7920
Weaning Wt. (kg) at 105d	99.80[c]	109.60[b]	118.40[a]	0.84	<0.0001
Body Wt. gain (kg)	0.661[c]	0.743[b]	0.825[a]	0.009	<0.0001
Growth hormone (ng/ml)	12.17[c]	14.33[b]	16.36[a]	0.18	<0.0001
Leptin (ng/ml)	3.23[c]	3.79[b]	4.55[a]	0.09	<0.0001
Females					
Birth Wt. (kg)	28.55[a]	29.01[a]	29.08[a]	0.44	0.9329
Weaning Wt. (kg) at 105d	90.32[c]	95.22[b]	103.20[a]	1.55	<0.0001
Body Wt. gain (kg)	0.588[c]	0.631[b]	0.706[a]	0.016	<0.0001
Growth hormone (ng/ml)	10.89[c]	12.66[b]	14.55[a]	0.15	<0.0001
Leptin (ng/ml)	4.19[c]	4.96[b]	6.18[a]	0.04	<0.0001

[a, b and c]: Means within each row with different superscripts are significantly differ ($P < 0.05$).

Temporal changes in ADG, serum GH, and leptin concentrations their relationship for both male and female calves groups during the entire study, are shown in Figure 2. Pooled data showed that the ADG of the male, and female calves followed the growth sigmoid curve. Calves commenced their life with small growth rates and elevated with advanced age. The highest average daily body weight gains were extremely noticeable (P<0.0001) in the C group (1.101 and 0.996 kg/d) compared to the other two groups (B 0.990 and 0.841; A 0.893 and 0.787 kg/d) in male and female calves, respectively.

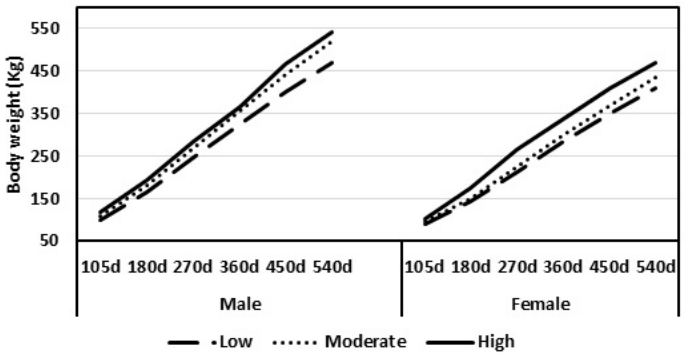

Figure 1: Live body weight (kg) post-weaning till maturity of male and female Friesian calves.

Serum leptin concentration is closely related to changes in body weights (Figure 1) and growth rates. Circulating leptin increased through the post-weaning till maturity. The lowest level of leptin was observed at the beginning of the study at weaning age (4.550, 3.790, and 3.226 ng/dl) for male calves, and (6.180, 4.955, and 4.190 ng/dl) for female calves. Serum leptin concentration rapidly increased and reached the peak at 540 d of age in the C (6.665 and 9.410 ng/dl) followed by B (6.245 and 7.935 ng/dl), but the response was delayed in the A (5.445 and 7.090 ng/dl) group for male and female calves, respectively.

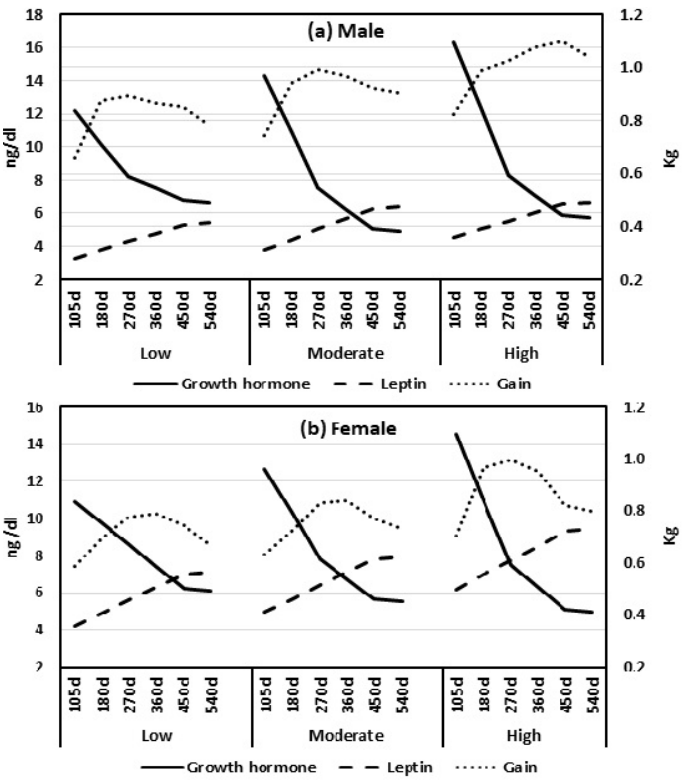

Figure 2: Relationship between body weight gain, growth hormone, and leptin from weaning to maturity of male (a) and female (b) Friesian calves.

The highest level of GH was observed at the beginning of the study, and the pre-weaning weight increases were associated with individual values (Table 1). Serum GH levels were reduced with advanced age, taking the opposite trend with both growth rates and serum leptin levels. At 540 days of age, it recorded its minimum value. It initiated at 16.362, 14.330, and 12.174 ng/dl at 105 d until it reached 5.725, 4.889, and 6.661 ng/dl at 540 d of age in male calves, whereas its levels in female calves were 14.554, 12.658, and 10.888 ng/dl at 105 d of age, and 4.979, 5.507, and 6.069 ng/dl at 540 d of age.

Skeletal Growth

Figure 3 displayed the temporal changes in skeletal growth for male and female Friesian calves in three experimental groups (A, B, and C), including body length (BL), height at withers (HW), and heart girth (HG). According to current data, skeletal growth (BL, HW, and HG) followed the same pattern as body weight and ADG (Figures 1 and 2).

The C group recorded greater (P<0.0001) values (140.80 and 124.40 cm BL; 132.80 and 129.60 cm HW; 170.60 and 162.60 cm HG) of body dimensions compared to the A and B groups, also, the B group (128.60 and 120.20 cm BL; 130.80 and 125.00 cm HW; 169.60 and 158.80 cm HG) were greater than the A group (120.80 and 118.40 cm BL; 128.00 and 125.00 cm HW; 162.20 and 155.20 cm HG) in male and female calves, respectively.

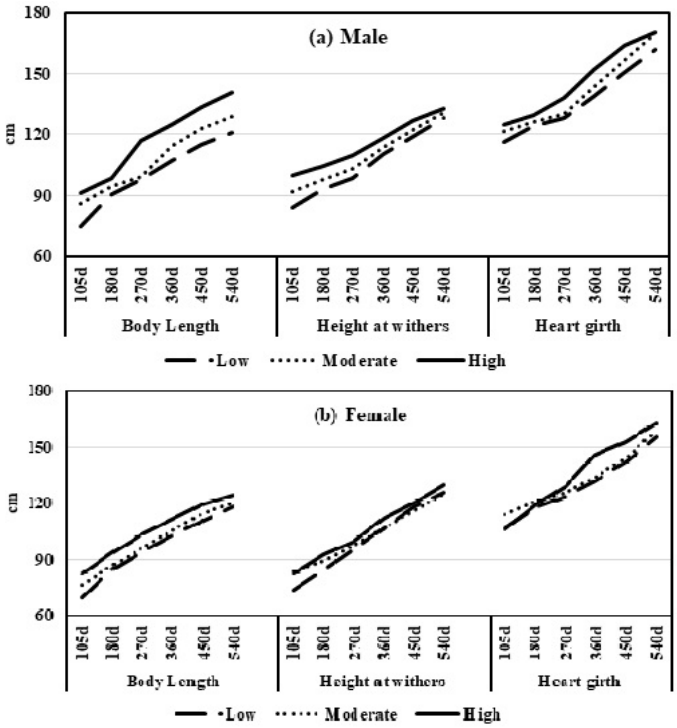

Figure 3: Live body dimensions (cm) from weaning to maturity of male (a) and female (b) Friesian calves.

Reproductive Performance of Bulls

The C-group Friesian bulls recorded significantly (P<0.0001) the earliest age with the heaviest weight at maturation followed by Friesian bulls in the B-group, whereas those in the A-group significantly showed the oldest and the lightest (Table 3). The mature bulls in the A group had lower (P<0.0001) testes circumferences than counterparts in the C and B groups; the differences between the C and B groups in testes circumference were not detected. During the maturity of bull calves, the reaction time and latency period were significantly (P<0.0001) reduced in the bulls of the C group (1.18 and 2.26 min.) followed by bulls in the B group (1.63 and 2.56 min.) compared to the bulls in the A group (2.18 and 2.98 min.), which had the longest (Table 3). It is also worth noting serum testosterone levels in mature bulls displayed an exactly similar trend (P<0.0001) as that of ADG, GH, and leptin levels (Table 3).

Some of the physical semen characteristics of the experimental mature bulls are demonstrated in Table 3. Bulls recorded the highest ADG, GH, and leptin values (group C) had significantly (P<0.0001) the greatest values of volume, sperm concentrations, total sperm output, and total motile sperm then came bulls recorded moderate ADG, GH, and leptin values (group B), however, those recorded the minimum ADG, GH, and leptin values (group A) significantly displayed the smallest. Progressive motility percentages were higher (P<0.0010) in the bulls of the C group than in the bulls of the A group; the differences between the C and B groups were not detected. Bulls in the C group were significantly (P<0.0146) abnormal sperm percentage values compared to bulls in the A group. In contrast, bulls in the B group recorded intermediate values without significance with both the C and A groups. Semen pH did not change significantly within bulls in different groups.

Table 3: Reproductive performance and semen characteristics of the experimental Friesian bulls effected by ADG, GH and leptin level.

Items	Groups			±MSE	P value
	A	B	C		
Reproductive traits					
Age at maturity (day)	467.60^{c}	447.80^{b}	418.00^{a}	3.58	<0.0001
Body weight at maturity (kg)	412.33^{c}	436.00^{b}	447.00^{a}	4.62	<0.0001
Testes circumference (cm)	31.60^{b}	34.90^{a}	36.00^{a}	0.50	<0.0001
Reaction time (min)	2.18^{c}	1.63^{b}	1.18^{a}	0.05	<0.0001
Latency period (min)	2.98^{c}	2.56^{b}	2.26^{a}	0.07	<0.0001
Testosterone level (ng/ml)	1.09^{c}	1.37^{b}	1.65^{a}	0.05	<0.0001
Semen characteristics					
Volume (ml)	2.86^{c}	3.22^{b}	3.88^{a}	0.07	<0.0001
Progressive motility (%)	62.20^{b}	70.00^{a}	78.40^{a}	1.52	0.0010
Semen pH	7.06^{a}	7.00^{a}	0.69^{a}	0.03	0.1069
Sperm concentration/ml (×10^{9})	1.04^{c}	1.28^{b}	1.62^{a}	0.02	<0.0001
Total perm output (×10^{9})	2.97^{c}	4.12^{b}	6.29^{a}	0.12	<0.0001
Motile sperm/ml (×10^{9})	0.65^{c}	0.90^{b}	1.27^{a}	0.03	<0.0001
Total motile sperm (×10^{9})	1.85^{c}	2.89^{b}	4.93^{a}	0.11	<0.0001
Abnormal sperm (%)	20.60^{b}	17.00^{ab}	14.80^{a}	1.23	0.0146

$^{a, b \text{ and } c}$: Means within each row with different superscripts are significantly differ ($P < 0.05$).

Reproductive Performance of Heifers

Heifers had the highest ADG, GH, and leptin levels (group C) attained significantly (P<0.0001) displaying 1st estrous, 1st service, conception, and parturition at the most precocious age, followed by heifers had moderate ADG, GH, and leptin levels (group B). At the same time, those had the lowest ADG, GH, and leptin levels (group A) significantly showed the oldest one (Table 4). Heifers in group C were significantly (P<0.0414) heaviest in weight at 1st estrus, weight at 1st service (P<0.0001), and weight at parturition (P<0.0057) compared to other groups (B and A). Service periods were significantly shorter (P<0.0029) with heifers in the C and B groups than the A group, which

had the longest. The number of services per conception was significantly (P<0.0217) fewer in the C group than in the A group and tended to be reduced compared to the B group. Primiparous cows in the A group were needed for assistance at calving by 20%, as the A group recorded one case of dystocia. Whereas, C and B groups of primiparous cows delivered without complications. In addition, the proportion of stillbirth cases was 0% in the C and B groups compared to 20% in the A group. Moreover, birth weight was significantly (P<0.0008) heavier in the group C (32.83 kg) than in the B and A groups (30.33 and 28.83 kg).

Table 4: Reproduction performance of the experimental Friesian heifers affected by ADG, GH and leptin level.

Traits	Groups			±MSE	P value
	A	B	C		
Age at first estrus (day)	496.67^{a}	482.17^{b}	467.67^{c}	4.18	0.0008
Weight at first estrus (kg)	385.00^{c}	408.83^{b}	425.00^{a}	4.93	0.0414
Age at first service (day)	571.17^{a}	550.17^{b}	532.67^{c}	4.13	<0.0001
Weight at first service (kg)	419.00^{c}	438.00^{b}	464.00^{a}	3.62	<0.0001
Age at conception (day)	657.33^{a}	611.00^{b}	594.00^{b}	6.67	<0.0001
Weight at conception (kg)	428.00^{b}	449.00^{ab}	483.00^{a}	4.78	0.0011
Interval service to conception	86.17^{a}	60.83^{b}	61.33^{b}	4.88	0.0029
No. of services / conception	3.33^{a}	2.83^{ab}	2.00^{b}	0.30	0.0217
Age at parturition (day)	939.00^{a}	889.33^{b}	865.33^{c}	6.73	<0.0001
Weight post-parturition (kg)	430.00^{c}	448.00^{b}	490.00^{a}	10.70	0.0057
No. of dystocia cases	1/5 (20%)	0/5 (0%)	0/5 (0%)		
Still birth of calves	1/5 (20%)	0/5 (0%)	0/5 (0%)		
Birth weight of calves	28.83^{c}	30.33^{b}	32.83^{a}	0.43	0.0008

$^{a, b \text{ and } c}$: Means within each row with different superscripts are significantly differ ($P < 0.05$).

Endocrine and Metabolic Parameters

Overall means of GH, total protein (TP), and albumin in serum were significantly influenced by ADG, and GH levels in the experimental groups (C, B, and A) either, in male or female calves (Table 5). Also, the results displayed the H and M groups had significantly higher (P<0.01) values of serum leptin, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) than values recorded in the group A; the differences between the C and B groups numerically but not significant both in male and female calves (Table 5). Moreover, serum glucose and cholesterol were higher (P<0.01) in the C group compared with those estimated in the B and A groups; the B group recorded higher values than the A group, but the differences were non-significant, either in the male or female calves. Furthermore, mean values of globulin and albumin/globulin ratio in serum did not change significantly by experimental groups. Current data support the hypothesis that growth performance including ADG and BW (growth period), age and BW at maturation, testes circumference, semen properties (for male calves), and age and BW at puberty onset, fertility, and reproductive rate (for female calves) is influenced by genetic potential for pre- (Rodríguez-Sánchez *et al*., 2015) and post-weaning (Nepomuceno *et al*., 2017) growth. The objective is to leverage the direct association between growth rate and both growth hormone and leptin levels as a bio-maker in predicting the performance of subsequent economic traits in Friesian calves.

Growth Hormone, Leptin, and Growth Performance: The results showed that the 3rd group (C) concerning average daily gain (ADG) values associated with the serum GH and leptin levels in both male and female calves was the best compared to the A and B groups (Table 2, Figures 1 and 2). A similar association between ADG, and GH levels was also reported (Mohamed *et al*., 2019) in Baladi calves. Who suggested that ADG related to GH levels in the serum of males and females through the direct effect of GH or indirect effect through activation of IGF-1 to modulate growth performance through its impacts on adipose, and muscle (Oberbauer, 2015).

Many organs and hormones control growth performance, called the somatotrophic axis. The somatotrophic axis is a crucial network of organs and hormones that collectively regulate muscle growth, adipose tissue function, reproductive processes, and various physiological functions associated with an animal's overall metabolism and growth (Renaville *et al*., 2002). This axis comprises GH, and some growth factors (Renaville *et al*., 2002). Furthermore, leptin is one of the hormones or nutritionally regulated substances that operate as messengers (positive and negative feedback controls) that may trigger anabolic and catabolic pathways in tissues (Davis *et al*., 2012).

Current results showed that serum GH levels in male and female calves diminished along with increasing age throughout the different groups of the experiment (Figure 2). This lowering of GH level with rising age may be because of many mechanisms, separately or in combination, including impaired GHRH secretion or action, diminished somatotroph numbers, or compromised function, and elevated sensitivity to the detrimental effects of feedback on insulin growth factor-1 (IGF-1) (Chapman *et al*., 1997). The current findings concur with those of Nazaimoon *et al*. (1993), who reported that fasting GH levels varied with age in both sexes ($P < 0.001$) and declined in older human males and females. Data showed that the highest level of GH was recorded at weaning (Table 2) and then it decreased gradually in the same group (Figure 2). Compatible results with those displayed by Mohamed *et al*. (2019) who observed the Baladi calves at 3 months old had higher

levels of GH from 6 -18 months old. In the opposite trend with GH, it was observed that the leptin level rose linearly during the experimental period (Figure 2). Similar linear increases in leptin concentrations in the peripubertal period have been noted in some studies (Díaz-Torga *et al.*, 2001; Garcia *et al.*, 2002), but not in others (Block *et al.*, 2003; Chelikani *et al.*, 2009).

The relationship between leptin and GH is intricate, since Carro *et al.* (2000) reported that different leptin concentrations in the body cause a rise or diminish in GH secretion concentrations. Also, the leptin presence is fundamental to the exertion of the GH's physiological influences, yet GH itself does not directly impact leptin levels (Cady *et al.*, 2017). Furthermore, Neuropeptide Y (NPY) is suggested to be the main mediator of leptin's effects in the hypothalamus, regulating luteinizing hormone (LH) and growth hormone (GH) secretion (Barb and Kraeling, 2004). A living body's adipose tissue plays a crucial role in regulating GH secretion. GH and IGF-1 are involved in obesity, and their levels are frequently lower in obese individuals (Casabiell *et al.*, 2001). Clement *et al.* (1998) reported a change in the GH level in blood plasma followed by genetic changes in the leptin/ob gene or its receptors.

Male calves consistently exhibited higher levels of GH and lower leptin levels compared to females in the same group (Table 2, and Figure 2). Similar differences in GH levels were observed by, Mohamed *et al.* (2019) and Suwitil *et al.* (2017) between male and female calves. However, for leptin levels, females have greater circulating leptin than males, even after correcting for differences in body fat mass (Wabitsch *et al.*, 1997) in humans. It has been observed that in typically developing children, leptin levels rise prior to puberty and peak at the onset of puberty (Garcio-Mayor *et al.*, 1997). Following that, boys' plasma leptin levels start to decrease while girls' levels continue to rise, depending on their body fat percentage (Taleb *et al.*, 2014).

Current results showed a significant superiority for group C in ADG by 10.1, 23.6%; 15.6, and 20.9%, compared with the B and A groups in Friesian male and female calves (Figure 2). These findings align with Wauters *et al.* (2000), who reported that GH affects the body's composition and fat circulation and plays a major part in growth and development. Also, Klindt *et al.* (1998) indicated that GH enhances lean tissue deposition and increases farm animals' feed efficiency. Furthermore, according to (Brown *et al.*, 2008), GH enhances growth performance, milk yield, and production efficiency in practice and metabolism in animal species like cattle or pigs.

On the other hand, our findings support the concept that leptin is pivotal for the long-term control of BW in cattle (Chelikani *et al.*, 2009). Also, Ferraz *et al.* (2023) claimed that higher serum leptin levels were more related to higher BW. Leptin concentrations were generally positively associated with ADG (Foote *et al.*, 2016). Moreover, Strauch *et al.* (2003) found a significant positive correlation between leptin and Brahman cows BW.

Skeletal Growth

Linear body measurements are often utilized alongside weight to indicate growth (Rodríguez-Sánchez et al., 2018). Current results showed that skeletal measurements at 18 months of age (Figure 3); BL, HW, and HG ranged from 140.00 to 120.80 cm, 132.80 to 128.00 cm, and 170.60 to 162.20 cm for male calves, and 124.00 to 118.40 cm, 129.6 to 125 cm, and 155.2 to 162.60 cm for female calves, respectively. This roughly matched the values for male calves (at ~17 months of age) reported by Ibrahim *et al.* (2005), which are 123.6 to 127.8 cm BL, 126.4 to 130.2 cm HW, and 170.8 to 175.8 cm HG; and for female calves (at ~16 months of age) reported by El-Samahy *et al.* (2010) in Friesian cattle, which are 121.01 to 123.85 cm HW, and 162.14 to 164.69 cm HG. Our data showed the superiority of the C group followed by the B group and then the A group. These data are consistent with Mohamed *et al.* (2019). They indicated a positive association between body dimensions, ADG, and GH levels in male and female Baladi calves. Current data supports this association and completes it by leptin levels. Leptin is one of a complex network of endocrine signals that contributes to longitudinal bone growth through actions on chondrocytes and osteoblasts (Nilsson *et al.*, 2005). In juvenile animals, leptin is thought to stimulate bone growth, whereas it may decrease bone remodeling in the mature skeleton and, hence, influence bone mass (Thomas, 2004). It is important to monitor the development of skeletal measurements to determine the timing of puberty that allows females to achieve full growth and increased skeletal mineralization, before the demands of pregnancy, lactation, and raising offspring (Duittoz *et al.*, 2016).

Reproductive Performance of Bulls

Current results indicated that bulls in the C group reached maturity significantly younger (29.4, 49.6 d) and heavier (2.5, 7.8 %) than bulls in the B and A groups, respectively (Table 3). This superiority could be linked to the corresponding peak in GH levels (Table 1, 2, and Figure 2). A similar observation also reported by Abd El-Hafeez *et al.* (2020) in Baladi bulls substantiates the present study's finding. Also, the data displayed a positive relationship between GH and leptin levels with testosterone concentrations. Numerous investigations have indicated that testicular growth during the peripubertal and early pubertal periods was positively related to circulating levels of metabolic hormones, including leptin and GH (Brito *et al.*, 2007); these hormones influence the proliferation and differentiation of testicular cells.

Leptin increases releasing of gonadotrophin-releasing hormone (GnRH) from the hypothalamus, and consequently FSH and LH release from the anterior pituitary. These then increase the release of testosterone from the testes in the male and estrogen from the ovaries in the female. Leptin exerts its effect on the hypothalamic GnRH neurons indirectly, as the GnRH neurons are devoid of leptin receptors, presumably involving the kisspeptin neurons, premammillary nucleus, agouti-related protein (AgRP) and NPY neurons in the hypothalamus, which are well endowed with leptin receptors (Malik *et al*., 2019). Stimulation of the GnRH neurons by kisspeptin, NPY, and AgRP neurons seems to involve the upregulation of sirtuins, particularly sirtuin 1 (sirt1). Sirtuins are believed to act as sensors of cellular stress, helping regulate mitochondrial and nuclear activity (Yamamoto and Takahashi, 2018; Khawar *et al*., 2022).

The effects of leptin on the differentiation of Leydig cells and testosterone secretion are dependent: positive at low doses and negative at higher doses (Seetharam *et al*., 2022). Feeding restriction may elevate testosterone levels, as observed by Sangsritavong *et al*. (2002) and Vasconcelos *et al*. (2003), who noted that a minor, whether acute or chronic, reduction in energy consumption led to a notable decrease in liver blood flow, thereby raising the levels of circulating steroid hormones.

The results of the present study suggested that increased body fat accumulation as reflected by leptin concentrations elevation in favorable testicular growth, as the testes' circumference increases with increased leptin levels. The enhancement in the latency period for Friesian bulls in the C group could be due to the elevation in testosterone concentrations. This assumption is emphasized by the negative association between testosterone level and the latency period (Table 3). The current result elaborates on that of Benia *et al*. (2013), showing that testosterone hormone plays a crucial role in controlling sexual behavior. Specifically, testosterone regulates the expression of nitric oxide synthase in the penis. Similar findings were reported by Karaca *et al*. (2015) and Swelum *et al*. (2017), who discovered that rams had higher testosterone concentrations and shorter reaction times. Other researchers, however, have not discovered any relationship between rams' sexual libido and their blood levels of testosterone (Moghaddam *et al*., 2012).

According to O'Donnell *et al*. (2000), larger testes are assumed to indicate a higher abundance of Sertoli cells and, thus, the ability to support more sperm throughout the bull's lifetime. This would indicate better spermatogenic capability. This may explain the improvement of all physical characteristics of semen, except semen pH, at maturity in association with GH and leptin levels in Friesian bulls among experimental groups (Table 3). Oocyte penetration depends on sperm motility characteristics, and effective penetration heavily depends on progressive motility (Zarazaga *et al*., 2009). Mohamed *et al*. (2016) indicated that rams with greater testosterone concentrations had significantly higher physical semen characteristics during sexual maturity.

Reproductive Performance of Heifers

Enhancement of the age at puberty onset, fertility, and reproductive performance of Friesian female calves perhaps due to increasing ADG, GH, and leptin levels of the C group followed by the B group, and delaying A group (Table 4). The present findings are compatible with those shown by Mohamed *et al*. (2019) who stated that higher levels of ADG, and GH may be indicators for improving reproductive performance in Baladi heifers.

The results showed that the Friesian heifers in group C were heavier and reached puberty 14.5 d and 29 d earlier at significant rates of 3.8% and 9.40% and than their counterparts in the B and A groups, respectively (Table 4). Observations indicated a raising in leptin levels throughout pubertal development as shown in (Figure 2), reflecting that heifers with higher circulating levels would attain puberty at a younger age. Body mass notably influences altering in GH throughout aging, particularly from early life until puberty, since the effects of fat accretion in the body (Figures 1 and 2). Through increased leptin production and release in the body, fat accumulation plays a crucial role in puberty and the onset of estrus (Matty and Hassan, 2020). This makes sense and is consistent with and emphasizes present results, which reveal a rise in leptin concentration as age advances and elevations in body weight (Daniel *et al*., 2013, Alali and Rahawy, 2022). Our results are consistent with those of Rosales Nieto *et al*. (2013), who found that the concentration of leptin hormone in ewe lambs was positively correlated with an earlier onset of puberty and correlated with age at first estrus, contingent on the timing of ovarian activity and body weight at first estrus.

Likewise, a positive effect of leptin level on the attainment of puberty was also indicated by Prajapati and Anand Laxmi (2015), in Murrah buffalo heifers, and a negative impact of leptin level with age at puberty (Garcia *et al*., 2002) in dairy cattle heifers, substantiates the findings of the present study. Sarkar *et al*. (2010) and Kumar *et al*. (2012) discovered that leptin receptors in the corpus luteum can regulate P_4 releasing, potentially allowing Friesian heifers to reach puberty earlier, as observed in the C group. In ewes-lambs with high BW compared to those with low BW, the progesterone concentration was more notable with high BW (Alali and Rahawy, 2022).

Puberty is a hormonally controlled process that occurs only when the body's energy reserves are sufficient (Mukherjee *et al*., 2023). It has been suggested that NPY serves as the main interface of leptin action in the hypothalamus, con-

trolling the release of LH and GH (Barb and Kraeling, 2004). In addition, leptin directly activates the ventral pre-mammillary nucleus (PMV), which then triggers its GnRH neurons downstream (Leshan *et al*., 2009). It is presumed that leptin functions as a permissive signal for puberty (Maciel *et al*., 2004; Barb and Kraeling, 2004) rather than being the cause of puberty triggers, although leptin can inhibit NPY expression (Gamba and Pralong, 2006), modulate the expression of kisspeptin receptors (Stephens *et al*., 2015), and subsequently hasten puberty.

From the present study, it has been observed that Friesian heifers in the C, B, and A groups received the first service when their BWs were 67.3, 63.9, and 61.2% of adult BW, respectively (Table 4), displaying a little elevation compared with available reports on Friesian heifers stated that they received the 1st service when their body weight was 50 – 60% of adult body weight (Wathes *et al*., 2014). However, reaching 65% of mature BW at breeding was advised by Kasimanickam *et al*. (2021), who concluded that 55% of mature BW at breeding harmed heifers' and their progeny heifers' reproductive performance.

After displaying their first estrous, the first AI investigated after 65, 68, and 74.5 d in the C, B, and A groups, respectively. Puberty at 30 to 45 days is one of the main goals of heifer replacement programs prior to mating (Gasser, 2013), due to the conception rate rising beyond the pubertal estrous (Byerley *et al*., 1987), which is achieved in the current experiment.

Decreasing the number of AI services per conception simultaneously shortens the service period for the heifers in the C group compared with counterparts in the A group (Table 4). The positive relation between the concentration of leptin with fertility, and the reproductive rate (Rosales Nieto *et al*., 2013) in Marino ewe-lambs, which may be due to increasing BW at the start of insemination substantiates the findings in the present study. In addition, Strauch *et al*. (2003) found a negative association between the postpartum interval and serum leptin hormone in multiparous Brahman cows, which was associated with higher rates of first-service conception. About 40% of dairy cows had anomalies in their postpartum reproductive cycles, according to Mann *et al*. (2005), who also found a correlation between lower plasma leptin concentrations and aberrant reproductive function. Also, lower serum leptin concentrations were observed in repeat breeder cows by Guzel and Tanriverdi (2014), compared to fertile cows.

The improvement of the growth, weight, and body size (Table 2, Figures 1, 2, and 3) of the heifers in the C and B groups were able to deliver without any difficulties (Table 4), as there was just one case in the A group of dystocia cases registered, while recorded zero in the C, and B groups.

Table 5: Blood serum constituents of Friesian male and female calves post-weaning till maturity.

Items	Groups			±MSE	P value
	L	M	H		
Males					
Growth hormone (ng/dl)	8.21^{c}	9.38^{b}	10.62^{a}	0.88	<0.0001
Leptin (ng/dl)	4.27^{b}	5.05^{a}	5.55^{a}	0.22	0.0007
Total protein (g/dl)	6.59^{c}	6.99^{b}	7.50^{a}	0.09	<0.0001
Albumin (g/dl)	3.41^{c}	3.75^{b}	4.09^{a}	0.12	0.0005
Globulin (g/dl)	3.18^{a}	3.24^{a}	3.41^{a}	0.16	0.5926
Albumin / Globulin ratio	1.07^{a}	1.16^{a}	1.20^{a}	0.10	0.8027
Glucose (mg/dl)	78.47^{b}	78.77^{b}	85.58^{a}	2.15	0.0377
Cholesterol (mg/dl)	154.11^{b}	161.55^{b}	181.73^{a}	4.79	0.0005
Triglycerides (mg/dl)	47.33^{b}	52.33^{a}	51.99^{a}	1.5	0.0049
High Density Lipoprotein (mg/dl)	46.89^{b}	50.89^{a}	52.63^{a}	1.40	0.0175
Low density lipoproteins (mg/dl)	97.75^{b}	100.19^{b}	118.70^{a}	4.83	0.0063
Very low density lipoprotein (mg/dl)	9.47^{b}	10.47^{a}	10.40^{a}	0.23	0.0049
Females					
Growth hormone (ng/dl)	8.57^{c}	8.69^{b}	9.05^{a}	0.76	<0.0001
Leptin (ng/dl)	5.58^{b}	6.38^{b}	7.73^{a}	0.29	<0.0001
Total protein (g/dl)	7.04^{c}	7.42^{b}	7.86^{a}	0.11	<0.0001
Albumin (g/dl)	3.50^{c}	3.71^{b}	3.86^{a}	0.09	0.0420
Globulin (g/dl)	3.54^{a}	3.71^{a}	4.00^{a}	0.15	0.1115
Albumin / Globulin ratio	0.99^{a}	1.00^{a}	0.97^{a}	0.07	0.9679
Glucose (mg/dl)	71.16^{b}	74.17^{b}	81.84^{a}	1.97	0.0011
Cholesterol (mg/dl)	145.14^{b}	159.62^{b}	183.19^{a}	3.84	<0.0001
Triglycerides (mg/dl)	54.73^{b}	59.40^{a}	59.73^{a}	1.17	0.0057
High Density Lipoprotein (mg/dl)	44.13^{b}	49.87^{a}	48.13^{a}	1.39	0.0162
Low density lipoproteins (mg/dl)	90.06^{b}	97.87^{b}	123.11^{a}	4.46	<0.0001
Very low density lipoprotein (mg/dl)	10.95^{b}	11.88^{a}	11.95^{a}	0.23	0.0057

$^{a, b \text{ and } c}$: Means within each row with different superscripts are significantly differ ($P < 0.05$).

Endocrine and Metabolic Parameters

Mean values of serum total protein, albumin, glucose, cholesterol, triglycerides, HDL, LDL, and VLDL were significantly (P<0.01) elevated in the C groups along with the rise in ADG, GH, and leptin levels, in male and female calves (Table 5). The higher GH level contributed in superiority in favor of the C group, to its impact on serum total protein than the B and A groups. Growth hormone increases feed conversion rate, promotes protein synthesis, and is essential for many physiological functions (Gao *et al*., 2006). Moreover, GH controls well-lipolytic function and the body's overall energy consumption (Lee *et al*., 2006). Additionally, Brian *et al*. (2004) demonstrated that GH possessed the ability to influence feed intake, whole-body

fat deposition, and increase rate. Renaville *et al.* (2002) observed that GH is produced in the pituitary gland and binds to the growth hormone receptor (GHR) in the liver and adipose tissue to directly regulate gluconeogenesis, proteosynthesis, lipogenesis, and insulin secretion.

Interestingly, the structure of leptin is similar to that of GH, and leptin is likely to bind to growth hormone-binding proteins (Saleem *et al.*, 2015). The site of expression for leptin receptors in the hypophysis cerebri, where the growth hormone secretion is mediated by leptin (Shimon *et al.*, 1998). Intra-cerebro-ventricular (ICV) administration of leptin demonstrated that leptin was involved in growth hormone release (Saleem *et al.*, 2015).

Systemic leptin levels rise in proportion to increases in body fat (Landry *et al.*, 2013), and this hormone is crucial for maintaining energy balance (Ahima and Hileman, 2000). Ahmadi *et al.* (2016) reported that physiological leptin concentration in plasma varies between 1 and 10 ng/ml, which is in consistent with the current results (Table 5). Females typically have higher amounts of fatty tissue mass and subcutaneous fat than lean body mass, however, males have more lean body mass than fatty tissue mass, on the other hand (Kasper *et al.*, 2005). The metabolism of proteins, lipids, and glucose depends on leptin (Haluzik *et al.*, 1999; Henry *et al.*, 1999).

Taleb *et al.* (2014) found a notable relationship between LDL, HDL, and total cholesterol with leptin, however, no correlation was observed between triglycerides and leptin in adolescents. Leptin showed a positive association with glucose in both dairy (German Holstein) and beef (Charolaise) bulls (r=0.32 and 0.47), however, there was a negative correlation (r=-0.66) between leptin and HDL-cholesterol in Charolaise bulls (Bellmann *et al.*, 2004). Likewise, Hussein *et al.* (2011) observed, in Friesian cows, a positive relationship (r=0.31) between leptin and total cholesterol. In contrast, Chan *et al.* (2011) reported that leptin reduces triglycerides and total fat mass while raising HDL, which in turn regulates body fat.

Finally, the blood metabolites were within the normal physiological range, it did not indicate a negative energy balance in both male and female calves in groups.

CONCLUSIONS AND RECOMMENDATIONS

This investigation demonstrates the hypothesis that both GH and leptin levels in serum play a key function in growth performance, fertility, and reproductive performance in Friesian male or female calves. Thus, data on ADG related to GH and leptin levels may be a viable selection tool early in life for selecting high-performing individuals for better productivity. However, the relationship between GH and other metabolic hormones such as IGF-1, insulin, and thyroxine and their association with growth rate and fertility will be applied in future studies.

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NOVELTY STATEMENT

Possibility of selecting calves with high growth and reproductive potential at an early age (at weaning; 105 days) based on the relationship between the average daily gain from birth to weaning with the concentration of growth hormone and leptin.

AUTHOR'S CONTRIBUTIONS

Al-Moataz Bellah Mahfouz Shaarawy conceived the presented idea and carried out the experiments, collected and cured the data. Mahmoud Yassin Mohamed developed the theory, has revised the experimental design, and wrote the manuscript with input and support from all authors. Mahmoud Sayed Sayah supervised the experimental procedures, revised the manuscript, and paraphrased some paragraphs. Ashraf Ali Mehany worked out almost all of the technical details, and performed the numerical calculations for the suggested experiment. Ezzat Arafa Ahmed El-Beltagi has performed the experimental procedures. Shimaa M. Ali cured the data, performed the data analysis, prepared and revised the manuscript. All authors discussed the results, provided critical feedback, helped shape the research, and contributed to the final manuscript.

Ethics Statement

All research procedures were carried out in compliance with the standards set forth guidelines for the care and use of experimental animals by the Animal Ethics Committee of APRI, ARC, Egypt. The experimental work of the present study achieved the Institutional Animal Care and Use Committee (IACUC) protocol Number (ARC/APRI/79/24) for the protection of animals used for scientific purposes and feed legislation.

Conflict of Interest

All authors declare that there is no conflict of interest in this study.

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