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Original Article

Hormonal, biochemical and hematological changes in neonatal calves with sepsis induced by enteritis

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Abstract

Background: Diarrhea is one of the most important problems seen in calves during the neonatal period. Sepsis caused by diarrhea is the main cause of death. In the case of sepsis, many hormonal, hematological and biochemical changes occur in calves. It is extremely important to evaluate these parameters together. **Aims:** The present study aimed to investigate hormonal, biochemical, and hematological changes in neonatal calves affected by septic enteritis to obtain more information about the pathogenesis of sepsis. **Methods:** The study included a sepsis group consisting of 40 calves aged 0-15 days with enteritis, and a control group composed of 20 clinically and hematologically healthy calves of similar age. Calves presenting with enteritis, anorexia, severe dehydration, and general condition deterioration were examined, and those meeting the sepsis criteria were included in the study. Hematological, hormonal, and biochemical measurements were performed on blood samples obtained from the calves. Additionally, pathogenic agents causing enteritis were identified using immunochromatographic methods on fecal samples. **Results:** In the sepsis group, creatinine, total protein, and urea levels, as well as the enzymatic activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma-glutamyl transferase (GGT), and creatine kinase (CK) were significantly higher compared with the healthy group ($P<0.05$), while cholesterol levels were significantly lower ($P<0.001$). The total leukocyte count (WBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and granulocyte count were also found to be higher in the sepsis group compared with the control group ($P<0.05$). Furthermore, calves in the sepsis group were determined to be hypothermic, tachycardic and tachypneic compared with the control group ($P<0.05$). In the sepsis group, notable reductions in free T3, free T4 and erythropoietin (EPO) levels were observed ($P<0.05$). However, cortisol, insulin, and adrenocorticotropic hormone (ACTH) levels were significantly higher than those in the healthy group ($P<0.05$). **Conclusion:** Sepsis causes significant hematological, biochemical and hormonal changes in neonatal calves.

Key words: Calf, Hematology, Hormone, Neonatal period, Sepsis

Introduction

Cattle breeding is of great importance in meeting the world population's need for animal products, such as meat and milk. In enterprises where breeding is carried out, the calf obtained from a cow annually is the most important factor determining the profit of that enterprise. Since calves will be evaluated as breeding, they are important for the future of the enterprise. Since calves are consumers until a certain age, their care and feeding are not taken into consideration. Accordingly, calf losses are frequently encountered (Yüceer, 2008).

The first 28 days after birth are referred to as the neonatal period. This phase is a highly critical and risky time for calves as they are particularly vulnerable to diseases during this period (Tokgöz *et al*., 2013). Diarrhea is one of the most important causes of death in calves during the neonatal period (Şahal *et al*., 2018). Economic losses are seen due to reasons such as deaths caused by diarrhea, genetic loss, developmental delay, treatment costs, increased labor force, loss of productivity, and laboratory expenses for diagnosis (Tokgöz *et al*., 2013).

Clinically, diarrhea is defined as an increase in the consistency and volume of feces, along with an increased frequency of defecation caused by inflammation of the gastrointestinal system (Sezer, 2021). Diarrhea causes dehydration and metabolic disorders in a short time (Bal, 2019).

The etiology of diarrhea involves infectious agents, environmental factors, and the immune system of the calf. Research frequently identifies *E. coli* and its strains,

rotavirus, coronavirus, and *Cryptosporidium parvum* as significant bacterial, viral, and parasitic pathogens (Akyüz *et al*., 2017). These infectious agents are held responsible for approximately 80% of diarrheal cases (Bal, 2019).

Noninfectious causes of diarrhea include environmental factors (Bal, 2019), immunological factors (Sezer, 2021), maintenance and feeding conditions, vitamin-mineral substance, trace element deficiencies (Al and Balıkçı, 2012), genetic factors and toxic factors (Bal, 2019), and the type of farm management (Sezer, 2021). In farms where hygiene conditions are inadequate, umbilical cord care is neglected, improper husbandry and feeding practices are implemented, and colostrum administration is insufficient, neonatal diarrhea cases are frequently observed (Akyüz *et al*., 2017). Contaminated umbilical cords, equipment, colostrum, milk, and similar feeds constitute the primary sources of infection (Constable, 2007).

Sepsis is defined as the acute dissemination of pathogenic agents and their toxic substances to tissues, organs, and systems via the circulatory system (Silverstein and Otto, 2012). Despite therapeutic interventions, the occurrence of hypotension, inadequate perfusion, and functional impairments in systems is referred to as septic shock (Eroğlu and Kırbaş, 2020). In cases of diarrhea that lead to septic shock with high mortality rates, rapid detection of the causative agent and timely initiation of treatment are of critical importance in terms of saving lives (Al and Balıkçı, 2012).

In a calf, 75% of the fluid in the body is intracellular and 25% is extracellular. The passage of this fluid through cell membranes is provided by osmotic pressure. Osmotic pressure is balanced by electrolytes (Bal, 2019). In diarrhea, fluid and electrolyte loss occurs through feces (Başer and Civelek, 2013). As a result of these losses, electrolyte imbalance, dehydration (Zeybek, 2013) and hypovolemic shock occur. The body's metabolic balance is disrupted (Akyüz *et al*., 2017). Extracellular fluid loss causes a decrease in plasma volume and a decrease in blood pressure (Traş *et al*., 2012). As a result, internal organ functions are impaired and the life of the creature is in danger (Gülşen and Umucalılar, 2009). In response to the stress caused by sepsis, the organism develops an adaptive mechanism through autonomic nervous system innervation, the immune system, and the hypothalamic-pituitary axis. This mechanism ensures metabolic homeostasis via the cardiovascular system. Significant changes occur in the levels of various hormones, particularly thyroid and adrenal hormones.

Hematological, hormonal and biochemical analyses performed on blood and serum are frequently used in animals to diagnose diseases, evaluate the efficacy of treatments, monitor patients, and gain insights into prognosis (Akyüz *et al*., 2020). To better understand the pathogenesis of sepsis, it is essential to evaluate the hormonal, hematological and biochemical profile. This study aimed to identify changes in hematological, biochemical, and hormonal parameters in neonatal calves with diarrhea and sepsis.

Materials and Methods

Ethical approval

This study was conducted after obtaining approval from the Kafkas University Animal Experiments Local Ethics Committee (KAU-HADYEK/2022-094).

Animal grouping

The sepsis group for this study consisted of 40 calves aged 0-15 days that met the criteria for enteritis and sepsis (Table 1). The sepsis group consisted of 20 male and 20 female calves. Samples were collected from calves brought to the Animal Hospital of the Veterinary Faculty of Kafkas University for examination. Samples were collected during the winter season in December, January and February. When creating the sepsis group, the literature information given in Table 1 was taken into consideration. As a result of the examinations, those who showed at least two of the following findings/signs: hypothermia/hyperthermia, tachycardia/bradycardia, tachypnea, leukocytosis/leukopenia were included in the sepsis group. The control group consisted of 20 calves of the same age who were clinically and hematologically healthy. The control group consisted of 10 male and 10 female calves. Calves presenting within the first 15 days after birth with diarrhea, anorexia, lateral recumbency, severe dehydration, tachypnea, tachycardia, or bradycardia indicating circulatory disturbance were examined, and those meeting the sepsis criteria were included in the study.

Table 1: Sepsis criteria in neonatal calves (Akyüz and Gökce, 2021)

Parameters	Criteria
Total leukocyte count ($\times 10^3/\mu L$)	$<5 \times 10^3/\mu L$ or $>12 \times 10^3/\mu L$
Respiratory rate (/min)	>45/min
Pulse rate (/min)	<90/min or >120/min
Band neutrophil percentage (%)	>10%
Body temperature (°C)	>39°C or <36.6°C

Vital signs, such as rectal body temperature, respiratory rate, and heart rate per minute, were recorded for animals in both groups. Additionally, fresh fecal samples obtained from the rectum were tested using 5-in-1 rapid immunochromatographic test kits (targeting rotavirus, coronavirus, cryptosporidium, *E. coli K99*, and giardia), (BoviD-5 Ag Test Kiti®, Bionote Inc., Kore), applied according to the manufacturer's instructions. These tests were used to identify the pathogen(s) responsible for sepsis.

Biochemical, hematological, and hormonal analyses

Blood samples were taken from septic calves and healthy calves into vacuum tubes with gel+clot activator and tubes with K3 EDTA. The blood samples in gel+clot

activator vacuum tubes were centrifuged at 100.62 × r (cm) for 10 min, and the resulting serum was separated for biochemical and hormonal analyses. Biochemically, enzyme activities including alanine aminotransferase (ALT, IU/L), aspartate aminotransferase (AST, IU/L), alkaline phosphatase (ALP, IU/L), gamma-glutamyl transferase (GGT, IU/L), creatine kinase (CK, IU/L), and lactate dehydrogenase (LDH, IU/L) were measured. Levels of glucose (mg/dL), total cholesterol (mg/dL), creatinine (Crea, mg/dL), urea (mg/dL), total protein (TP, g/dL), albumin (ALB, g/dL), triglycerides (mg/dL), and iron (Fe, mg/dL) measured using commercial kit (Mindray BS120®, China, Hasvet Medikal) were also determined. These measurements were performed on an automatic analyzer (Mindray BS120®, China, Hasvet Medikal) using a spectrophotometric method.

Hormonal parameters including free triiodothyronine (fT3) (pg/ml), thyroxine (fT4) (ng/dL), cortisol (µg/dL), insulin (mIU/L), adrenocorticotropic hormone (ACTH, pg/ml), and erythropoietin (EPO, mU/ml) levels were analyzed and assessed. These analyses were performed using the chemiluminescence method (Snibe Diagnostics®, China).

Blood samples collected in K3 EDTA tubes were analyzed using an automated complete blood count analyzer (MS4E®, Vega Group, Melet Schloesing). Parameters measured included total leukocyte count (WBC, $\times 10^3/\mu L$), lymphocyte count (LYM, $\times 10^3/\mu L$), granulocyte count (Gra, $\times 10^3/\mu L$), erythrocyte count (RBC, $\times 10^6/\mu L$), mean corpuscular volume (MCV, fL), hematocrit percentage (HCT, %), mean corpuscular hemoglobin (MCH, pg), mean corpuscular hemoglobin concentration (MCHC, g/dL), hemoglobin concentration (Hb, g/dL), and platelet count ($\times 10^3/\mu L$).

Statistical analysis

All statistical analyses were performed using SPSS® software (Version 26.0, IBM Corp., Chicago, IL, USA). The normality of data distribution in each group was evaluated using the Shapiro-Wilk test, and the homogeneity of variances was examined using Levene's test.

For pairwise comparisons, data showing normal distribution and homogeneity of variances were analyzed using the Independent Samples t-test. When the assumption of homogeneity of variances was not met, the results of the Welch's t-test (equal variances not assumed) were considered. For data that did not follow a normal distribution, the Mann-Whitney U-test was used as a nonparametric alternative.

In the comparison of multiple groups classified according to the causative pathogen, the Kruskal-Wallis H test was applied since some subgroups (e.g., *Cryptosporidium parvum*, n=3) had very small sample sizes and the data did not meet the assumptions of normality and variance homogeneity. When statistically significant differences were found, post-hoc pairwise comparisons were performed using the Mann-Whitney U test with Bonferroni correction to control for type I error.

Correlations between continuous variables were assessed using Pearson's correlation coefficient when the assumptions of normality were met. When these assumptions were not satisfied, Spearman's rank correlation was applied to confirm the robustness of associations.

All data were expressed as mean ± standard deviation (SD), and differences were considered statistically significant at a level of $P<0.05$. Due to the small sample size in some subgroups, statistical power was limited, and results from these comparisons should therefore be interpreted with caution.

Results

Clinical findings

Clinical examination of septic calves revealed severe enteritis, dehydration ranging from 10-12%, weakness, mental depression, lateral recumbency, loss of suckling reflex, and hypothermia. Clinical examinations conducted in septic calves revealed that their rectal body temperature was significantly lower ($P<0.001$), while their respiratory rate ($P=0.01$) and heart rate were significantly higher ($P<0.001$) compared with the control group (Table 2).

Findings on the identification of pathogenic agents

In the sepsis group of calves, *E. coli* was detected in 9 cases, *Cryptosporidium parvum* in 3 cases, *rotavirus+coronavirus* in 11 cases, and mixed infections in 17 cases.

Biochemical findings

In the sepsis group, creatinine ($P<0.001$), total protein ($P<0.001$), and urea levels ($P<0.001$), along with AST ($P<0.001$), ALT ($P<0.001$), ALP ($P=0.008$), LDH ($P=0.002$), GGT ($P<0.001$), and CK ($P<0.001$) enzyme activities were found to be significantly higher compared with the healthy group. Cholesterol levels, however, were significantly lower in the sepsis group than in the control group ($P<0.001$) (Table 2). The remaining biochemical data did not show significant difference.

Hematological findings

In the sepsis group, WBC ($P=0.05$), MCV ($P=0.002$), and MCH ($P=0.028$) values as well as the granulocyte count ($P=0.007$) were found to be significantly higher compared with the control group (Table 2). Other hematological data did not show any significant difference.

Hormonal findings

In the sepsis group, free T3 ($P<0.001$), free T4 ($P=0.001$) and EPO ($P<0.001$) concentrations were found to be significantly lower compared with the control group. In contrast, cortisol, insulin, and ACTH concentrations were significantly higher than those in the healthy group ($P<0.001$) (Fig. 1).

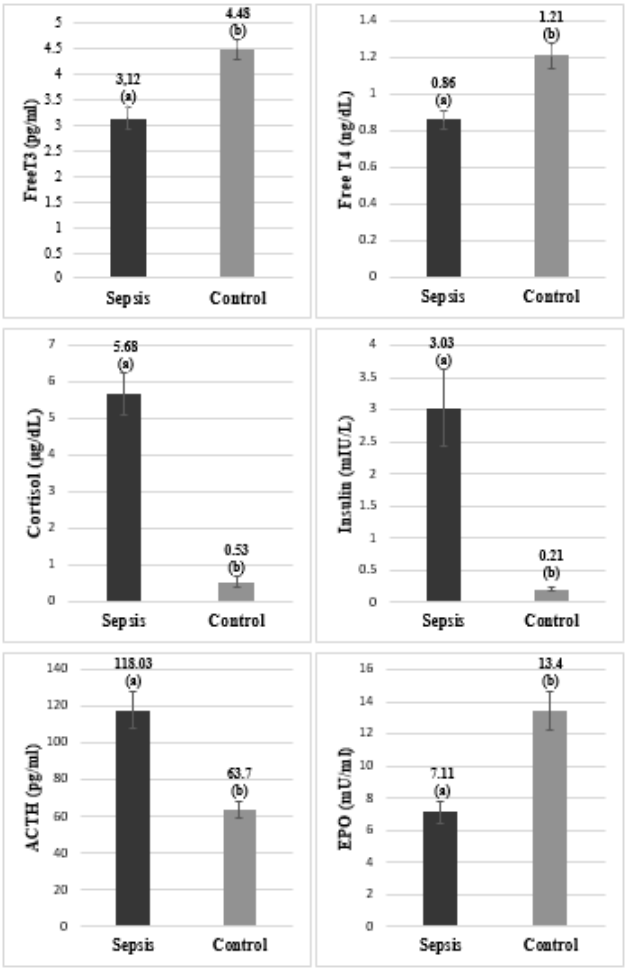

Fig. 1: Charts depicting comparative hormone levels across groups are presented with error bars representing standard deviations (SD). (a) and (b) show the statistical difference between groups

Comparison results of vital signs, biochemical, hematological, and hormonal parameters by pathogen

In the pathogen-based comparison, body temperature was found to be significantly lower in the *Cryptosporidium parvum* (P=0.034) and mixed infection (P=0.002) groups compared with the control group. The number of pulsations per minute was significantly higher in the *E. coli* (P=0.003), viral (P=0.001), and mixed infection (P<0.001) groups than in the control group. Creatinine (P=0.026) and AST (P=0.002) levels were found to be significantly higher in the mixed infection group compared with the control group. ALT levels were also significantly higher in the *E. coli* (P=0.016) and mixed infection (P<0.001) groups than in the control group. Cholesterol levels were significantly lower across all affected groups compared with the control group, regardless of the pathogen (P<0.05). ALP enzyme activity was significantly higher in the *E. coli K99*-positive group (P=0.02) compared with the control group. Similarly, LDH enzyme activity was significantly elevated in the mixed infection (P=0.014) compared with the control group. In the *E. coli K99*-positive group, both GGT (P<0.001) and CK (P=0.009) enzyme activities were found to be significantly higher than in the control group. Serum urea levels were significantly elevated in the *E. coli* (P=0.003), *Cryptosporidium parvum* (P=0.008), viral infection (P=0.005), and mixed groups (P<0.001) compared with the control group. In contrast, other biochemical parameters showed no statistically significant differences among the groups when compared by pathogen (Table 3).

Granulocyte count was found to be significantly higher in the viral infection group (P=0.04), while mean corpuscular volume (MCV) was significantly elevated in the group with mixed infections (P=0.011) compared with the control group. Platelet count was found to be significantly higher in the *Cryptosporidium parvum*-positive group than in the group with mixed infections (P=0.039). No statistically significant differences were observed in other hematological parameters among the groups (Table 3). Free T3 and T4 levels were found to be significantly lower in the mixed infection group compared with the control group (P=0.003 and P=0.02, respectively). Cortisol levels were significantly higher in the septic groups compared with the control group, regardless of pathogen type (P<0.05). ACTH levels were significantly elevated in the *E. coli K99*-positive (P=0.002) and viral infection (P<0.001) groups compared with the control group. Erythropoietin levels were significantly lower in the *E. coli K99*-positive (P=0.002) and mixed infection (P=0.016) groups compared with the control group (Table 3).

Comparison of results between male and female animals

In order to determine whether there were sex-based differences in the hormonal profile, both the healthy and septic groups were further divided into male and female subgroups. The evaluations revealed no statistically significant differences in hormonal parameters between female and male calves within the healthy and septic groups (Table 4).

In the comparison of hormonal parameters between female animals in the sepsis group and healthy female animals, free T4 (P=0.016) and EPO levels (P=0.001) were found to be significantly lower in the sepsis group. In contrast, cortisol (P<0.001), insulin (P=0.003), and ACTH (P=0.001) levels were significantly higher in female animals in the sepsis group compared with healthy female animals (Table 4).

In the comparison of hormonal parameters between male animals in the sepsis group and healthy male animals, free T3 (P<0.001), free T4 (P=0.048), and EPO levels (P=0.005) were found to be significantly lower in the sepsis group. On the other hand, cortisol (P<0.001), insulin (P=0.01), and ACTH (P<0.001) levels were significantly higher in male animals in the sepsis group compared with healthy male animals (Table 4). Correlation coefficients describing the relationships among hormonal, biochemical, and hematological parameters, as well as vital signs, are presented in Table 5.

Table 2: Comparison of vital signs, biochemical parameters, hematological parameters between septic and control groups

Parameters	Sepsis (n=40)	Control (n=20)	P-value
Body temperature (°C)	36.73±0.31	38.71±0.11	<0.001
Heart rate (min)	134.05±3.30	104.70±2.10	<0.001
Respiratory rate (min)	40.30±1.66	33.10±1.49	0.01
Glucose (mg/dL)	68.40±7.65	62.30±3.10	0.941
Crea (mg/dL)	2.86±0.38	0.83±0.03	<0.001
TP (g/L)	58.15±2.80	44.84±1.96	0.001
ALB (g/L)	21.92 ±0.81	19.99±0.74	0.134
AST (IU/L)	69.3±6.92	36.55±2.56	<0.001
ALT (IU/L)	18.55±2.05	7.60±0.56	<0.001
Cholesterol (mg/dL)	31.78±2.59	78.25±4.56	<0.001
Triglycerid (mg/dL)	20.58±2.22	25.40±4.21	0.206
ALP (IU/L)	307.53±33.02	164.25±17.21	0.008
LDH (IU/L)	829.08±63.99	432.45±68.66	0.002
GGT (IU/L)	355.35±75.18	19.55±2.23	<0.001
CK (IU/L)	631.73±103.82	158.25±18.50	0.001
Fe (mg/dL)	89.00±9.61	103.30±6.95	0.042
Urea (mg/dL)	95.43±14.53	22.35±2.18	<0.001
WBC (m/mm^3)	20.61±2.58	10.84±0.49	0.05
Lym (m/mm^3)	7.90±1.82	5.06±0.35	0.336
Gra (m/mm^3)	12.04±1.58	5.50±0.45	0.007
RBC (m/mm^3)	9.16±0.41	9.41±0.35	0.863
MCV (fl)	44.23±0.71	40.25±0.91	0.002
HCT (%)	40.69±2.11	38.00±1.76	0.355
MCH (pg)	13.28±0.28	12.13±0.45	0.028
MCHC (g/dL)	30.28±0.62	30.39±1.11	0.930
Hb (g/dL)	12.15±0.57	11.27±0.34	0.145
Platelet count (m/mm^3)	492.08±47.08	557.15±47.91	0.388

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase, CK: Creatine kinase, LDH: Lactate dehydrogenase, Crea: Creatinine, TP: Total protein, ALB: Albumin, Fe: Iron, WBC: Total leukocyte count, LYM: Lymphocyte count, Gra: Granulocyte count, RBC: Erythrocyte count, MCV: Mean corpuscular volume, HCT: Hematocrit percentage, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, and Hb: Hemoglobin concentration. The data are presented as mean±SD. P<0.05 is considered to be significant. The data are presented as mean±SD. P<0.05 is considered to be significant

Table 3: Comparison of vital signs, biochemical parameters, hematological parameters, hormonal parameters by pathogen

Parameters	*E. coli* (n=9)	Crypto (n=3)	Rota-Corona (n=11)	Mix (n=17)	Control (n=20)	P-value
Body temperature (°C)	36.91±0.73^{ab}	35.16±1.09^{a}	37.77±0.72^{ab}	36.25±0.33^{a}	38.71±0.11^{b}	0.001
Heart rate (beats/min)	134.44±9.21^{a}	112.67±6.36^{ab}	135.64±4.38^{a}	136.59±5.07^{a}	104.70±2.10^{b}	<0.001
Respiratory rate (beats/min)	41.78±3.40	44.00±4.00	39.82±4.70	39.18±1.76	33.10±1.49	0.081
Glucose (mg/dL)	75.78±12.43	43.33±8.57	57.27±11.76	76.12±14.84	62.30±3.10	0.491
Crea (mg/dL)	2.93±0.66^{b}	3.55±1.39^{ab}	2.70±0.78^{ab}	2.81±0.66^{b}	0.83±0.03^{a}	0.002
TP (g/L)	62.07±6.56	58.56±8.61	59.16±3.69	55.35±4.99	44.84±1.96	0.051
ALB (g/L)	23.14±1.66	25.73±4.54	22.54±0.83	20.20±1.38	19.99±0.74	0.148
AST (IU/L)	65.33±13.96^{ab}	49.67±3.48^{ab}	71.31±16.52^{ab}	72.88±10.33^{b}	36.55±2.56^{a}	0.005
ALT (IU/L)	18.44±4.93^{b}	27.33±15.3^{ab}	17.00±3.92^{ab}	18.06±2.33^{b}	7.60±0.56^{a}	<0.001
Cholesterol (mg/dL)	30.78±3.59^{a}	25.67±9.82^{a}	42.36±5.27^{a}	26.53±3.89^{a}	78.25±4.56^{b}	<0.001
Triglyceride (mg/dL)	28.33±6.16	17.00±8.50	24.36±4.73	14.65±1.66	25.40±4.21	0.255
ALP (IU/L)	383.22±51.87^{b}	165.33±8.74^{ab}	247.30±59.13^{ab}	331.52±59.42^{ab}	164.25±17.21^{a}	0.028
LDH (IU/L)	749.78±84.67^{ab}	720.33±139.24^{ab}	956±160.95^{ab}	808.12±98.32^{b}	432.45±68.66^{a}	0.03
GGT (IU/L)	529±219.88^{b}	45.67±24.09^{ab}	297.45±104.25^{b}	355.53±114.10^{b}	19.55±2.23^{a}	<0.001
CK (IU/L)	747.44±272.26^{a}	413.33±247.44^{ab}	679.36±238.4^{ab}	578.18±129^{ab}	158.25±18.50^{b}	0.01
Fe (mg/dL)	65 ±10.32	157.33±55.88	85.36±19.91	92.00±14.16	103.30±6.95	0.098
Urea (mg/dL)	82.89±23.67^{b}	211.33±85.30^{b}	99.82±29.67^{b}	78.76±19.37^{b}	22.35±2.18^{a}	<0.001
WBC (m/mm^3)	23.77±7.22^{ab}	16.22±7.32^{ab}	22.77±2.68^{b}	18.31±4.41^{ab}	10.84±0.49^{a}	0.039
Lym (m/mm^3)	7.61±5.03	3.71±0.16	8.75±2.65	8.28±3.08	5.06±0.35	0.249
Gra (m/mm^3)	15.67±4.80^{b}	12.08±7.04^{ab}	12.95±2.16^{b}	9.53±2.11^{ab}	5.50±0.45^{a}	0.025
RBC (m/mm^3)	8.92±0.61	8.28±0.55	9.46±0.45	9.24±0.88	9.41±0.35	0.637
MCV (fl)	44.96±0.54^{ab}	40.03±2.08^{ab}	43.71±1.18^{ab}	44.92±1.38^{b}	40.25±0.91^{a}	0.004
HCT (%)	40.01±2.68	33.33±4.04	41.35±2.40	41.92±4.49	38.00±1.76	0.553
MCH (pg)	13.61±0.33	11.86±0.76	13.76±0.55	13.05±0.49	12.13±0.45	0.172
MCHC (g/dL)	30.42±0.80	29.76±0.37	31.60±0.87	29.44±1.27	30.39±1.11	0.465
Hb (g/dL)	12.20±0.92	9.96±1.31	13.09±0.87	11.90±1.12	11.27±0.34	0.260
Platelet count (m/mm^3)	556.11±101.0^{ab}	923±208.65^{a}	487.45±64.94^{ab}	385.12±66.68^{b}	557.15±47.9^{ab}	0.039
Free T3 (pg/ml)	3.26±0.43^{ab}	2.79±0.08^{ab}	3.51±0.41^{ab}	2.84±0.36^{b}	4.48±0.19^{a}	0.005
Free T4 (ng/dL)	0.81±0.11^{ab}	0.98±0.29^{ab}	0.96±0.09^{ab}	0.81±0.09^{b}	1.21±0.07^{a}	0.023

Cortisol (µg/dL)	5.60±1.35[b]	7.06±2.22[b]	5.60±1.22[b]	5.54±0.87[b]	0.53±0.15[a]	<0.001
Insulin (mIU/L)	2.04±1.02[b]	6.20±3.97[b]	3.38±1.34[b]	2.77±0.81[b]	0.21±0.04[a]	0.005
ACTH (pg/ml)	157.17±35.02[a]	79.16±0.33[ab]	132.80±12.94[a]	94.60±8.93[ab]	63.71±4.40[b]	<0.001
EPO (mu/ml)	5.49±1.02[b]	6.61±4.69[ab]	8.84±0.98[ab]	6.95±1.24[b]	13.40±1.19[a]	0.001

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase, CK: Creatine kinase, LDH: Lactate dehydrogenase, Crea: Creatinine, TP: Total protein, ALB: Albumin, Fe: Iron, WBC: Total leukocyte count, LYM: Lymphocyte count, Gra: Granulocyte count, RBC: Erythrocyte count, MCV: Mean corpuscular volume, HCT: Hematocrit percentage, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, Hb: Hemoglobin concentration, EPO: Erythropoietin, and ACTH: Adrenocorticotropic hormone. [a, b]: Values marked with different letters within the same row show statistically significant differences. The data are presented as mean ± SD. P<0.05 is considered to be significant

Table 4: Comparison of hormonal parameters between male and female calves in the control group/sepsis group

Parameters	Control female (n=10)	Control male (n=10)	P-value
Free T3 (pg/ml)	4.32±0.30	4.65±0.24	0.404
Free T4 (ng/dL)	1.11±0.10	1.30±0.10	0.143
Cortisol (µg/dL)	0.60±0.22	0.46±0.23	0.280
Insulin (mIU/L)	0.24±0.006	0.9±0.07	0.436
ACTH (pg/ml)	65.63±7.20	61.80±5.41	0.676
EPO (mu/ml)	12.92±1.76	13.89±1.68	0.696
Parameters	Sepsis female (n=20)	Sepsis male (n=20)	P-value
Free T3 (pg/ml)	3.36±0.31	2.87±0.28	0.231
Free T4 (ng/dL)	0.78±0.06	0.95±0.09	0.148
Cortisol (µg/dL)	5.36±0.76	6.00±0.90	0.591
Insulin (mIU/L)	3.28±0.92	2.78±0.83	0.748
ACTH (pg/ml)	111.36±9.75	124±17.81	0.904
EPO (mu/ml)	6.37±0.90	7.86±1.10	0.306
Parameters	Sepsis female (n=20)	Control female (n=10)	P-value
Free T3 (pg/ml)	3.36±0.31	4.32±0.30	0.06
Free T4 (ng/dL)	0.78±0.06	1.11±0.10	0.016
Cortisol (µg/dL)	5.36±0.76	0.60±0.22	<0.001
Insulin (mIU/L)	3.28±0.92	0.24±0.06	0.003
ACTH (pg/ml)	111.36±9.75	65.63±7.20	0.001
EPO (mu/ml)	6.37±0.90	12.92±1.76	0.001
Parameters	Sepsis male (n=20)	Control male (n=10)	P-value
Free T3 (pg/ml)	2.87±0.28	4.65±0.24	0.001
Free T4 (ng/dL)	0.95±0.09	1.30±0.10	0.048
Cortisol (µg/dL)	6.00±0.90	0.46±0.23	<0.001
Insulin (mIU/L)	2.78±0.83	0.19±0.07	0.015
ACTH (pg/ml)	124.70±17.81	61.80±5.41	<0.001
EPO (mu/ml)	7.86±1.10	13.89±1.68	0.005

EPO: Erythropoietin, and ACTH: Adrenocorticotropic hormone. The data are presented as mean±SD. P<0.05 is considered to be significant

Table 5: Correlation coefficients between hormonal, biochemical, hematological parameters and vital signs

Parameters	Free T3	Free T4	Cortisol	Insulin	ACTH	EPO
Body temperature	0.427**	0.119	-0.489**	-0.193	-0.119	0.225
Heart rate	-0.283*	-0.371**	0.375**	0.078	0.358**	-0.479**
Respiratory rate	-0.291*	0.075	0.418**	0.232	0.238	-0.139
Glucose	0.114	-0.212	-0.129	0.309*	-0.121	-0.159
Crea	-0.134	0.025	0.654**	0.220	0.369**	-0.247
TP	-0.195	0.033	0.489**	0.200	0.253	-0.362**
ALB	-0.047	0.099	0.286*	0.232	0.033	-0.192
AST	-0.274*	-0.116	0.479**	0.080	0.190	-0.262*
ALT	-0.223	-0.146	0.481**	0.153	0.262*	-0.219
Cholesterol	0.423**	0.432**	-0.431**	-0.342**	-0.331**	0.342**
Triglyceride	0.237	0.550**	0.019	-0.016	0.106	0.097
ALP	-0.258*	0.034	0.447**	0.128	0.184	-0.341**
LDH	-0.202	-0.001	0.480**	0.123	0.244	-0.103
GGT	-0.334**	-0.235	0.528**	0.318*	0.468**	-0.402**
CK	-0.162	-0.023	0.554**	0.013	0.247	-0.198
Fe	-0.036	0.093	-0.225	-0.235	-0.284*	0.030
Urea	-0.241	-0.250	0.492**	0.308*	0.268*	-0.286*
WBC	-0.044	-0.141	0.107	0.340**	0.089	-0.101
LYM	0.064	0.250	0.002	-0.100	-0.034	0.238

GRA	-0.101	-0.366**	0.119	0.484**	0.118	-0.279*
RBC	0.014	0.157	0.181	-0.050	0.026	0.031
MCV	-0.300*	0.171	0.430**	0.094	0.378**	-0.052
HCT	-0.082	0.139	0.323*	-0.046	0.170	0.012
MCH	-0.347**	0.167	0.309*	-0.013	0.357**	0.069
MCHC	-0.176	0.089	0.008	-0.009	0.084	0.084
HGB	-0.171	0.221	0.398**	-0.067	0.205	0.073
Platelet count	0.172	0.236	-0.146	0.056	-0.275*	-0.086
Free T3	-	0.325*	-0.392**	-0.252	-0.271*	0.338**
Free T4	0.325*	-	-0.014	-0.372**	-0.063	0.374**
Insulin	-0.252	-0.372**	0.240	-	0.227	-0.222
ACTH	-0.271*	-0.063	0.393**	0.227	-	-0.220
EPO	0.338**	0.374**	-0.326*	-0.222	-0.220	-

* Correlation is significant at the 0.05 level (2-tailed), and ** Correlation is significant at the 0.01 level (2-tailed). ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase, CK: Creatine kinase, LDH: Lactate dehydrogenase, Crea: Creatinine, TP: Total protein, ALB: Albumin, Fe: Iron, WBC: Total leukocyte count, LYM: Lymphocyte count, Gra: Granulocyte count, RBC: Erythrocyte count, MCV: Mean corpuscular volume, HCT: Hematocrit percentage, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, Hb: Hemoglobin concentration, EPO: Erythropoietin, and ACTH: Adrenocorticotropic hormone

Discussion

In neonatal calves with diarrhea, clinical signs such as lethargy, inability to stand, anorexia, tachycardia, anuria or oliguria, hypothermia, tachypnea and muscle weakness (Constable, 2007), enophthalmos, and loss of skin elasticity can be observed (Akyüz *et al*., 2017; Sezer and Gökce, 2024). Similarly, in the present study, septic calves exhibited clinical symptoms including hypothermia, lateral/sternal recumbency, loss of suckling reflex, reduced skin elasticity, enophthalmos, tachycardia, and tachypnea.

In the diagnosis of sepsis, complete blood count, particularly the evaluation of total leukocyte count, is of great importance (De Clue, 2017). Leukopenia or leukocytosis has been reported in the literature as a possible finding in cases of sepsis (Akyüz and Gökce, 2021; Sezer and Gökce, 2024). In this study, leukocytosis and granulocytosis were identified in the 40 calves within the sepsis group. Relevant literature suggests that the primary cause of leukocytosis and granulocytosis is an increase in neutrophils. This neutrophilia is considered a response by the body to an infection occurring in the gastrointestinal system (Kozat and Tuncay, 2018).

In cases of diarrhea-induced fluid loss, blood volume can decrease by up to 40%, leading to increased plasma protein concentration. This reduction in the liquid portion of blood results in elevated Hct, Hb, and RBC values a condition known as polycythemia (Eroğlu and Kırbaş, 2020). Conversely, a decrease in Hct levels, Hb concentration, and RBC count defines anemia. Anemia is commonly observed in calves with diarrhea due to both malnutrition and bleeding caused by damage to the gastrointestinal tract (Eroğlu and Kırbaş, 2020; Sezer and Gökce, 2024). In the present study, some calves in the septic group were found to have anemia, while others exhibited polycythemia.

MCV and MCH values increase as hemoglobin concentration rises (Kozat and Tuncay, 2018). Consistent with this observation, the present study found that the mean corpuscular volume and mean corpuscular hemoglobin levels in the sepsis group were significantly higher than those in the control group.

Toxemia in septic calves frequently leads to liver damage. This damage has been reported to cause increased AST and ALT enzyme activities (Başer and Civelek, 2013). Furthermore, endotoxemia contributes to passive congestion, ruminal distension, and muscle breakdown, which also affect these elevations (Merhan *et al*., 2016; Sezer and Gökce, 2024). In the present study, ALT and AST enzyme activities in the sepsis group were found to be higher than those in the control group due to these factors.

GGT and ALP enzyme activities have been reported to increase in septic animals due to conditions such as cholestasis, acute hepatic necrosis, and renal failure (Merhan *et al*., 2016; Sezer and Gökce, 2024). In this study, serum GGT and ALP enzyme activities were also found to be significantly higher in the sepsis group compared with the control group, consistent with the aforementioned factors.

Serum urea and creatinine levels increase due to protein catabolism in conditions such as infection, starvation, and high fever (Merhan *et al*., 2016). In calves, diarrhea-induced dehydration results in lowered blood pressure and reduced glomerular filtration rate. As kidney function deteriorates, serum urea and creatinine levels rise (Uzlu *et al*., 2010; Eroğlu and Kırbaş, 2020; Sezer and Gökce, 2024). A positive correlation has been reported between these increases and the severity of diarrhea (Sezer, 2021). In the present study, serum urea and creatinine levels in the septic group were also elevated, consistent with these underlying factors.

Myopathy, one of the most significant complications of sepsis, is known to cause increases in serum CK and LDH enzyme activities (Akyüz and Gökce, 2021). In this study, a significant increase in serum CK and LDH enzyme activities was also observed, associated with myopathy in the septic group.

Total protein levels are reported to increase in cases of diarrhea. One main reason for this rise is hemoconcentration resulting from reduced plasma volume due to dehydration (Eroğlu and Kırbaş, 2020).

Another contributing factor is an elevation in serum sialic acid levels. Inflammation-induced tissue damage leads to increases in fibrinogen and globulin levels. Accelerated synthesis of sialoproteins in the liver further raises TP levels in the blood serum (Uzlu *et al*., 2010; Merhan *et al*., 2016; Sezer and Gökce, 2024). In this study, TP levels in the septic group were also found to have increased as a result of dehydration and inflammation.

In calf diarrhea cases, infection and inflammation have been reported to adversely affect lipid profiles (Tothova *et al*., 2016). In many inflammatory diseases, cytokine release and enteropathy result in a decrease in total cholesterol levels (Lekkou *et al*., 2014). Similarly, in this study, serum cholesterol levels in the sepsis group were found to be significantly reduced.

Thyroid hormones are synthesized in thyroid gland follicles and play many critical roles in life. The two primary forms of thyroid hormones, thyroxine (T4) and triiodothyronine (T3), are the main actors in regulating these functions (Squires, 2003). To assess thyroid hormone levels, the concentrations of free T3 and free T4 in blood serum are commonly measured. It has been suggested that factors illnesses can alter thyroid hormone levels. Examining these changes raises the possibility of using thyroid hormones as prognostic markers (Perello *et al*., 2006; Mebis and Van den Berghe, 2011; Hajimohammadi *et al*., 2015). Disease-related declines in thyroid hormone levels particularly reductions in free T3 and, in severe cases, free T4 are referred to as "euthyroid sick syndrome" or "nonthyroidal illness syndrome" (Cho and Yoon, 2014). The primary causes of this condition include reduced thyroid-stimulating hormone (TSH) secretion and starvation due to anorexia. Additionally, impaired thyroid functions may lead to insufficient binding of serum T4 and T3, further contributing to this condition (Melmed *et al*., 2011). In veterinary medicine, studies have reported decreased levels of free T4 and free T3 in calves experiencing severe diarrhea-induced dehydration (Hajimohammadi *et al*., 2015; Çorapsız and Birdane, 2023). This decrease is attributed to thyroid dysfunction caused by cytokine release and endotoxemia, both of which are associated with the severity of the disease. During the acute phase of illnesses particularly sepsis thyroxine-binding globulin (TBG) levels are reported to drop, resulting in reduced serum T4 levels (den Brinker *et al*., 2005). Moreover, cytokines released during severe illness suppress TSH release from the pituitary gland and decrease the activity of thyroxine 5´-deiodinase (5´D) enzymes in the thyroid gland and liver (Kahl *et al*., 2000). In the present study, lower levels of free T3 and free T4 were detected in the sepsis group.

Glucocorticoids play a vital role in adaptation to infectious and non-infectious stress, as well as severe inflammatory diseases (De Castro *et al*., 2019). During stress and severe illness, the endocrine system is stimulated, activating the hypothalamic-pituitary-adrenal (HPA) axis. The hypothalamus stimulates the pituitary gland which, in turn, triggers ACTH. ACTH reaches the adrenal cortex through the bloodstream, leading to cortisol secretion (Andanson *et al*., 2020). Cortisol by controlling inflammation, it induces vasoconstriction and fluid retention, thereby supporting the cardiovascular system (Van den Berghe *et al*., 2022). Additionally, cortisol regulates intestinal permeability and helps maintain tissue and organ development (Brückmann *et al*., 2000). It has been reported that ACTH and cortisol levels increase in conditions such as sepsis, endotoxemia, and septic shock, particularly those involving *E. coli* infections. This increase is primarily attributed to inflammation-related stress and cytokine storms (Gold *et al*., 2007). Consequently, cortisol levels in the blood are frequently evaluated in studies of stress, inflammation, and the immune system (Whittaker and Gallagher, 2019; Brückmann *et al*., 2000). In patients with sepsis, adrenal hormone levels are monitored as indicators of prognosis. High cortisol levels are associated with a guarded prognosis and increased mortality (De Castro *et al*., 2019). In the present study, cortisol and ACTH levels were found to be higher in the sepsis group compared with the control group. This observation is thought to result from factors such as severe inflammation, circulation failure due to dehydration, endotoxemia, cytokine release, and stress in the sepsis group.

Insulin is secreted by the β-cells of the pancreas's langerhans islets and plays a critical role in regulating blood glucose homeostasis by facilitating the uptake of glucose into cells (Greenspan and Gardner, 2004). During sepsis, an increase in serum cortisol levels occurs, impairing the function of insulin receptors. As a result, patients develop insulin resistance along with hyperinsulinemia. Another contributing factor to insulin resistance is mitochondrial dysfunction in cells caused by sepsis (Melis *et al*., 2023). The severe cytokine release and subsequent oxidative stress during sepsis further exacerbate insulin resistance, leading to hyperinsulinemia (Savaş and Gültekin, 2017). In cases of enteritis caused by pathogens such as *E. coli*, *rotavirus*, and *coronavirus*, increased serum insulin levels have been reported (Brückmann *et al*., 2000). In this study, serum insulin levels were also found to be elevated in the sepsis group, consistent with the reasons outlined above.

Erythropoietin, also known as a hematopoietic growth factor, is a hormone produced by the kidneys. This glycoprotein stimulates red blood cell production (Tamion *et al*., 2005; Walden *et al*., 2010). It is synthesized by peritubular interstitial fibroblasts in the renal cortex and functions via a specific cell surface receptor called EpoR. EpoR is activated through Janus tyrosine kinase-2 (Jak-2), regulating red blood cell production. Additionally, EpoR is found in the brain, retina, heart, kidney, smooth muscle cells, myoblasts, and vascular endothelium. EpoR activation promotes red blood cell production, reduces apoptosis, and extends cell lifespan (Walden *et al*., 2010). Anemia frequently occurs in cases of renal, prerenal, and postrenal kidney failure. The primary cause of this anemia is decreased erythropoietin production due to impaired kidney function and increased blood urea levels, which inhibit circulating erythropoietin (Eschbach *et al*., 1984). In this

study, the decline in EPO levels in the sepsis group was found to be due to kidney dysfunction associated with prerenal azotemia. Although the present study provides valuable insights into the hormonal, biochemical, and hematological changes associated with neonatal calf sepsis, some limitations should be considered. The number of animals within certain pathogen subgroups, particularly the *Cryptosporidium parvum* group (n=3), was relatively small, which may have reduced the statistical power to detect subtle intergroup differences. Therefore, the results related to these subgroups should be interpreted with caution. Nevertheless, the trends observed—especially in biochemical and hormonal parameters of the Cryptosporidium subgroup—were consistent with the pathophysiological alterations reported in previous studies (El-Deeb *et al*., 2022; Dengler *et al*., 2023) on protozoal infections in neonatal ruminants.

In calves, diarrhea-induced dehydration results in lowered blood pressure and reduced glomerular filtration rate. As kidney function deteriorates, serum urea levels and creatinine enzyme activity rise (Uzlu *et al*., 2010; Eroğlu and Kırbaş, 2020; Sezer and Gökce, 2024). Erythropoietin is an erythropoietic glycoprotein hormone produced in the renal interstitium. Its production site is the proximal renal tubular cells, renal cortex and peritubular capillary endothelial cells of the renal medulla. Erythropoietin levels decrease in functional disorders occurring in the kidneys. Therefore, erythropoietin hormone levels reflect renal function (Rahman *et al*., 2016). Therefore, we believe that the reason for the decrease in erythropoietin levels in the sepsis group is both the decrease in the glomerular filtration rate as a result of fluid loss and the damage to the kidneys due to the inflammation that occurs.

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Conflict of interest

The authors declare no conflict of interest associated with the results of this study.

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Use of generative AI and AI-assisted technologies statements

Generative artificial intelligence and artificial intelligence-assisted technology was not used in the preparation of this article.

References

Akyüz, E and Gökce, G (2021). Neopterin, procalcitonin, clinical biochemistry, and hematology in calves with neonatal sepsis. Trop. Anim. Health Prod., 53: 354-362.

Akyüz, E; Naseri, A; Erkılıç, EE; Makav, M; Uzlu, E; Kırmızıgül, AH and Gökce, G (2017). Neonatal calf diarrhea and sepsis. KAUFBED. 10: 181-191.

Akyüz, E; Ölmez, M; Kuru, M; Merhan, O; Makav, M; Öğün, M; Bozukluhan, K; Naseri, A; Uzlu, E and Gökce, G (2020). Evaluation of some biochemical parameters in female Gurcu goats before, during and after pasture. Dicle Univ. J. Fac. Vet. Med., 13: 33-38.

Al, M and Balıkçı, E (2012). Diagnosis of rotavirus, coronavirus, *E. coli K99* and *Cryptosporidium parvum* in calves with neonatal diarrhea using rapid test kits and the relationship between enteropathogen and maternal immunity. Fırat Univ. Vet. J. Health Sci., 26: 73-78.

Andanson, S; Boissy, A and Veissier, I (2020). Conditions for assessing cortisol in sheep: the total form in blood v. the free form in saliva. Animal. 14: 1916-1922.

Bal, D (2019). Etiological studies on neonatal calf diarrhea in Manisa region. MSc Thesis, Afyon Kocatepe University, Afyonkarahisar. PP: 7-65.

Başer, DF and Civelek, T (2013). Correlation between venous acid-base status and renal function in neonatal calves with acute diarrhea. Kocatepe Vet. J., 6: 25-31.

Brückmann, A; Höck, C; Linke, K; Hennies, M and Schallenberger, E (2000). Alterations of growth hormone, cortisol, luteinizing hormone, and insulin concentrations in early-postnatal calves affected with diarrhea. Domest. Anim. Endocrinol., 18: 187-197.

Cho, YI and Yoon, KJ (2014). An overview of calf diarrhea-infectious etiology, diagnosis, and intervention. J. Vet. Sci., 15: 1-17.

Constable, PD (2007). General medicine. In: Radostits, OM (Ed.), *Veterinary medicine*. (10th Edn.), Philadelphia, USA, Saunders Elsevier. PP: 51-58.

Çorapsız, MF and Birdane, FM (2023). Evaluation of thyroid and some blood-serum parameters in neonatal calf diarrhea. MSc Thesis, Afyon Kocatepe University, Afyonkarahisar. PP: 1-20.

De Castro, R; Ruiz, D; Lavín, BA; Lamsfus, JA; Vazquez, L; Montalban, C; Marcano, G; Sarabia, R; Paz-Zulueta, M; Blanco, C and Santibanez, M (2019). Cortisol and adrenal androgens as independent predictors of mortality in septic patients. PLoS One. 14: e0214312-e0214325.

De Clue, A (2017). Sepsis and the systemic inflammatory response syndrome. In: Ettinger, SJ; Feldman, EC and Cote, E (Eds.), *Textbook of veterinary ınternal medicine*. (8th Edn.), St. Louis, Missouri, Saunders. PP: 523-527.

den Brinker, M; Joosten, KF; Visser, TJ; Hop, WC; de Rijke, YB; Hazelzet, JA; Boonstra, VH and Hokken-Koelega, AC (2005). Euthyroid sick syndrome in meningococcal sepsis: the impact of peripheral thyroid hormone metabolism and binding proteins. J. Clin. Endocrinol. Metab., 90: 5613-5620.

Dengler, F; Hammon, HM; Liermann, W; Görs, S; Bachmann, L; Helm, C and Ulrich, R and Delling, C (2023). *Cryptosporidium parvum* competes with the intestinal epithelial cells for glucose and impairs systemic glucose supply in neonatal calves. Vet. Res., 54: 40-56.

El-Deeb, W; Iacob, O; Fayez, M; Elsohaby, I; Alhaider, A; Mkrtchyan, HV; Ibrahim, A and Alhumam, N (2022). Assessment of the immune response of clinically infected

calves to *Cryptosporidium parvum* infection. Agriculture. 12: 1151-1164.

Eroğlu, MS and Kırbaş, A (2020). Systemic inflammatory response syndrome and sepsis. Fırat Univ. Vet. J. Health Sci., 34: 61-67.

Eschbach, JW; Mladenovic, J; Garcia, JF; Wahl, PW and Adamson, JW (1984). The anemia of chronic renal failure in sheep. Response to erythropoietin-rich plasma *in vivo*. J. Clin. Invest., 74: 434-41.

Gold, JR; Divers, TJ; Barton, MH; Lamb, SV; Place, NJ; Mohammed, HO and Bain, FT (2007). Plasma adrenocorticotropin, cortisol, and adrenocorticotropin/ cortisol ratios in septic and normal-term foals. J. Vet. Intern. Med., 21: 791-796.

Greenspan, FS and Gardner, DG (2004). *Basic and clinical endocrinology*. 7th Edn., New York, Mc Graw Hill. PP: 1-976.

Gülşen, N and Umucalılar, HD (2009). *Calf nutrition and nutritional diseases.* 1st Edn., Konya, Turkey, Konya SU Printing Office. PP: 91-100.

Hajimohammadi, A; Roshan-Ghasrodashti, A; Forouzesh, SM and Saeb, M (2015). A survey on relationships between thyroid hormone levels and clinical findings in dairy calf diarrhea. Vet. Sci. Dev., 5: 5835-5838.

Kahl, S; Elsasser, T and Blum, J (2000). Effect of endotoxin challenge on hepatic 5′-deiodinase activity in cattle. Domest. Anim. Endocrinol., 18: 133-143.

Kozat, S and Tuncay, İ (2018). Prevalence of rotavirus, coronavirus, *cryptosporidium spp*, *Escherichia coli K99* and *Giardia lamblia* agents in calves with neonatal diarrhea in Siirt region. Van Vet. J., 29: 17-22.

Lekkou, A; Mouzaki, A; Siagris, D; Ravani, I and Gogos, CA (2014). Serum lipid profile cytokine production and clinical outcome in patients with severe sepsis. J. Crit. Care. 29: 723-727.

Mebis, L and Van den Berghe, G (2011). Thyroid axisfunction and dysfunction in critical illness. Best Pract. Res. Clin. Endocrinol. Metab., 25: 745-757.

Melis, MJ; Miller, M; Peters, VBM and Singer, M (2023). The role of hormones in sepsis: an integrated overview with a focus on mitochondrial and immune cell dysfunction. Clin. Sci., 137: 707-725.

Melmed, S; Polonsky, KS; Larsen, PR and Kronenberg, HM (2011). *Williams textbook of endocrinology* E-Book. 12th Edn., Philadelphia, USA, Elsevier Health Sciences. PP: 545-577.

Merhan, O; Bozukluhan, K; Gökçe, G and Yılmaz, O (2016). Investigation of haptoglobin, ceruloplasmin and some biochemical parameter levels in diarrheic calves. Fırat Univ. Vet. J. Health Sci., 30: 195-198.

Perello, M; Friedman, T; Paez-Espinosa, V; Shen, X; Stuart, RC and Nillni, EA (2006). Thyroid hormones selectively regulate the posttranslational processing of prothyrotropin-releasing hormone in the paraventricular nucleus of the hypothalamus. Endocrinology. 147: 2705-2716.

Rahman, M; Haque, M; Towhidul, A; Amin, N; Parveen, H; Al Mahmuda, N and Abbas G (2016). Serum erythropoietin level in chronic kidney disease patients with anemia: A baseline study at Chittagong Medical College, Chittagong, Bangladesh. J. Clin. Exp. Med., 4: 20-25.

Şahal, M; Terzi, OS; Ceylan, E and Kara, E (2018). Calf diarrhea and prevention methods. Lalahan Hay. Araşt. Enst. Derg., 58: 41-49.

Savaş, HB and Gültekin, F (2017). Insulin resistance and its clinical significance. Med. J. SDU, 24: 116-125.

Sezer, M (2021). Studies on sTREM-1, Mr-Pro-Adrenomedullin (Mr-Pro-ADM), clinical biochemistry and hematology in calves suspected of sepsis. Ph.D. Thesis, Kafkas University, Kars. PP: 1-40.

Sezer, M and Gökce, G (2024). sTREM-1, MR-Pro-Adrenomedullin, clinical biochemistry and hematology in calves with neonatal sepsis. J. Hell. Vet. Med. Soc., 74: 6481-6490.

Silverstein, D and Otto, CM (2012). Sepsis. In: Greene, CE (Ed.), *Infectious diseases of the dog and cat*. (4th Edn.), St. Louis, Missouri, USA, Saunders Elsevier. PP: 359-369.

Squires, EJ (2003). *Applied animal endocrinology*. 1st Edn., Trowbridge, UK, CABI Publishing. PP: 1-234.

Tamion, F; Le Cam-Duchez, V; Menard, JF; Girault, C; Coquerel, A and Bonmarchand, G (2005). Serum erythropoietin levels in septic shock. Anaesth. Intens. Care. 33: 578-584.

Tokgöz, BS; Özdemir, R; Turut, N; Mirioğlu, M; İnce, H; Mahanoğlu, B; Yoldas, A and Tuzcu, N (2013). Determination of morbidity and mortality rates and risk factors of neonatal calf infections observed in the Adana region. AVKAE. J., 3: 7-14.

Tothova, C; Nagy, O; Kovac, G and Nagyova, V (2016). Changes in the concentrations of serum proteins in calves during the first month of life. J. Appl. Anim. Res., 44: 338-346.

Traş, B; Yazar, E and Elmas, M (2012). *Veterinary medicine*. 1st Edn., Olgun-Çelik Printing, Konya. PP: 125-140.

Uzlu, E; Karapehlivan, M; Çitil, M; Gökçe, E and Erdoğan, HM (2010). Investigation of serum sialic acid and certain biochemical parameters in calves exhibiting diarrhea symptoms. Van Vet. J., 21: 83-86.

Van den Berghe, G; Teblick, A; Langouche, L and Gunst, J (2022). The hypothalamus-pituitary-adrenal axis in sepsis- and hyperinflammation-induced critical illness: Gaps in current knowledge and future translational research directions. E-Bio Med., 84: 104284-104294.

Walden, AP; Young, JD and Sharples, E (2010). Bench to bedside: A role for erythropoietin in sepsis. Crit. Care. 14: 227-235.

Whittaker, AC and Gallagher, S (2019). Caregiving alters immunity and stress hormones: a review of recent research. Curr. Opin. Behav. Sci., 28: 93-97.

Yüceer, B (2008). The effect of colostrum on immunity, growth, disease incidence, and survival rate in calves that received colostrum. MSc Thesis, Ankara University, Ankara, Turkey. PP: 1-84.

Zeybek, S (2013). Time-dependent effects of intravenous isotonic sodium bicarbonate administration on venous acid-base status and renal function in neonatal calves with acute diarrhea. MSc Thesis, Afyon Kocatepe Univ, Afyonkarahisar. PP: 39-46.