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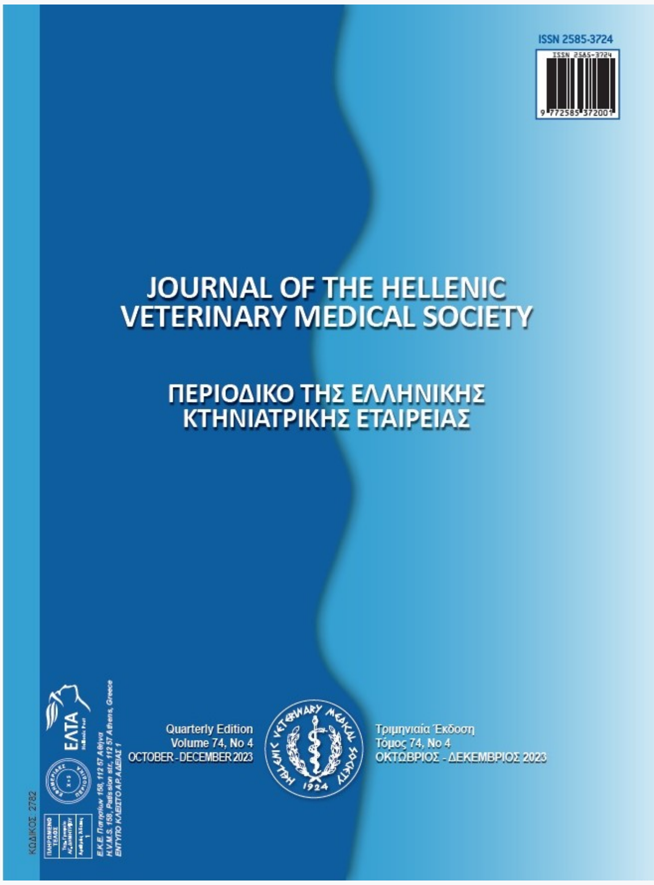

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CardiacBiomarkers in Calves with Diarrhea-Induced Neonatal Sepsis

C. Ayvazoğlu[1*], E. Akyüz[2], A. Harmankaya[3], M. Sezer[4], Y.U. Batı[5], T. Gezer[6], M. Kuru[7]

[1]*Nihat Delibalta Göle Vocational High School, Ardahan University, Ardahan, 75100, Türkiye*

[2,4,5,6]*Department of Internal Diseases, Faculty of Veterinary Medicine, Kafkas University, Kars, 36100, Türkiye*

[3]*Department of Biohemistry, Faculty of Science and Letter, Kafkas University, Kars, 36100, Türkiye*

[7]*Obstetrics and Gynecology of Department, Faculty of Veterinary Medicine, Kafkas University, Kars, 36100, Türkiye*

ABSTRACT: In this study; it was aimed to determine the levels of cardiac biomarkers [cardiac troponin I (cTnI), atrialnatriureticpeptide (ANP), N-terminal pro-brainnatriureticpeptide (NT-proBNP), homocysteine (HCY), creatinekinase-myocardialband (CK-MB)] and C-reactive protein (CRP), and the correlations between the semarkers in calves with diarrhea-induced neonatal sepsis, which causes great economic losses, especially genetic material. In the study, 40 neonatal calves with diarrhea-induced neonatal sepsis and 10 clinically healthy neonatal calves aged 0-14 days were used. The study revealed that the serum cTnI, ANP, NT-proBNP, HCY, CK-MB and CRP levels of the calves with neonatal sepsis were statistically significantly higher than those in the control group($P<0.001$). The correlation study also showed that there was a high correlation between the cardiac markers here of and the highest correlation was found between ANP and CK-MB ($R=0.836$**). In conclusion, cTnI, ANP, NT-proBNP, HCY and CK-MB can be suggested as useful prognostic and diagnostic biomarkers of cardiac dysfunctions in calves with suspected sepsis. Furthermore, according to the results of the study; although the suggest that an approximately 10-fold increase in ANP level would be the best marker for early diagnosis of sepsis, ANP may not be an ideal marker due to its short half-life and instability. Therefore, we believe that NT-proBNP, which correlates very significantly with all other markers and increases approximately 7-fold in calves with sepsis, is an important marker in the detection and early diagnosis of sepsis.

***Keywords*:** homocysteine; natriuretic peptide; neonatal calves; sepsis; troponin

Corresponding Author:
C. Ayvazoğlu, Nihat Delibalta Göle Vocational High School, Ardahan University, Ardahan, Türkiye.
E-mail address: cemayvazoglu@hotmail.com

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INTRODUCTION

Digestive system diseases and neonatal diarrhea have an important impact on calves in postpartum period between 0-28 days (Pardon and Depres, 2018; Akyüz and Kükürt, 2021) and bacteremia or viremia develops as a result of infection and causes sepsis (Gökçe et al., 2021). Systemic inflammatory response syndrome (SIRS), triggered by infection and affecting the whole body, is a result of severe sepsis (Beydilli and Gökçe, 2020; Gökçe et al., 2021; Naseri et al., 2021; Akyüz and Gökce, 2021). Therefore, SIRS findings (where SIRS criteria ≥2) can be used to define sepsis(Gökçe et al., 2021). Sepsis and its complications progress rapidly in the body, causing serious damage and almost making treatment impossible, often leading to the death of the patient (Kakihana et al., 2016; Akyüz et al., 2022). Therefore, early diagnosis and treatment of sepsis is very important to reduce the mortality rate in patients. Because, it has been reported that each one-hour delay in treatment increases the mortality rate by 6% (Levy et al., 2003).

The most important cause of death in sepsis, which has a mortality rate of approximately 30% in humans and animals, is organ failure, with the heart being the leading cause (Başoğlu et al., 2018; Naseri et al., 2019; Beydilli and Gökçe, 2020). In human studies, cardiac dysfunction was reported in 66% of sepsis cases and approximately 70% of these patients died(Landesberg et al., 2015; Kakihana et al., 2016). Studies in calves have also reported that sepsis causes cardiac dysfunction (Beydilli and Gökçe, 2020; Kırbaş et al., 2021; Naseri et al., 2021)

Different studies have reported that various biomarkers [cardiac troponin I (cTnI), atrial natriuretic peptide (ANP), N-terminal pro-brain natriuretic peptide (NT-proBNP), homocysteine (HCY), creatine kinase-myocardial band (CK-MB), C-reactive protein (CRP), etc.] can be used to detect myocarditis and cardiac dysfunction (Aydoğdu et al., 2016; Labonté et al., 2018; Aygün and Yıldız, 2018; Beydilli and Gökçe, 2020; Ogawa et al., 2021; Kozat et al., 2021).

The aim of this study was to determine the levels of cardiac biomarkers (cTnI, ANP, NT-proBNP, HCY, CK-MB) and CRP, and the correlations between these markers in sepsis, which causes great economic losses, especially in terms of genetic material. In this way, it was aimed to increase the use of biomarkers for the prognosis, early diagnosis and treatment of the disease and to reduce the mortality rate by performing a comprehensive examination of sepsis.

MATERIAL AND METHODS

This study was carried out after the approval (KAÜ-HADYEK 2022-069) received from Kafkas University Animal Experiments Local Ethics Committee.

Animals

The animal material of this study consisted of 0-14 days old Simmental and Simmental crossbred calves with sepsis brought to Kafkas University Faculty of Veterinary Medicine, Department of Internal Medicine clinics with diarrhea complaints. In the study, 40 sick animals (sepsis group) and 10 healthy calves of the same age group constituted the control group. Healthy animals consisted calves born at Kafkas University Faculty of Veterinary Medicine Prof. Dr. Ali Rıza Aksoy Research and Application Farm.

Procedures and evaluation of sepsis criteria

Calves with clinical signs of depression, diarrhea, low or absent sucking reflex, dehydration, and constant desire to lie down were examined and SIRS/sepsis criteria were evaluated. According to this evaluation, SIRS criteria for neonatal calves include body temperature >39.5°C or <37°C, pulse rate <100 or >160 per minute, respiratory rate >45 per minute, leukocyte count $>12\times10^3/\mu L$ or $<4\times10^3/\mu L$ (Akyüz and Gökce, 2021; Akyüz et al., 2022).The presence of at least 2 of the specified criteria was considered as sepsis and included in the study. In addition, a rapid test kit (BoviD-5 Ag Test Kit®, Bionote Inc., Korea) was used for the detection of etiologic agent in feces of calves with suspected neonatal sepsis meeting SIRS criteria.

Blood collection

From the calves in the sepsis and control groups, 8 mL blood samples were taken once from *V. jugularis* using a retainer and compatible sterile needle tip (Vacuette®, Greiner Bio-One GmbH, Austria).Vacuum gel serum tubes were used for serum samples and vacuum EDTA blood tubes were used for hematological measurements (BD Vakutainer®, BD, UK).Blood samples taken into vacuum gel serum tubes were kept at room temperature for about 1 hour and then centrifuged at 3500 rpm for 10 minutes (Hettich Rotina 380R®, Hettich, Germany).Serum samples were stored at -20ºC until cTnI, ANP, NT-proBNP, HCY, CK-MB and CRP levels were measured.Although troponin concentrations can remain stable for a long time at -70/-80ºC, it has been reported that they remain stable for a maximum of 3 months at -20ºC (Langhorn and Willesen, 2016). Therefore, serum samples used in this study were stored for a maximum of 60 days.

Measurement of cardiac markers and CRP

Serum cTnI, ANP, NT-proBNP, HCY CK-MB and CRP levels were determined with an ELISA device (ELISA Reader®-DAS Italy and ELISA Reader-Elecsys® 2010-Roche) and calculated with a commercial test kit (ELK Biotechnology, P.R.C.) as indicated by the manufacturer (ng/mL, pg/mL, pg/mL, µmol/L, U/L, µg/mL, respectively).

Hematological analysis

White blood cell (x10^3/µL) count was determined from the whole blood samples obtained by using a complete blood count device (VGMS4e®, Melet Schloesing, France)

Statistical analysis

The statistical comparison of the data was performed using the SPSS® software program (SPSS 26.0, Chicago, IL, USA). The distribution of the data was tested for conformity to a normal distribution by the Shapiro-Wilk test. Calves were grouped as sepsis and control. Then, the healthy versus ill were compared using an independent sample T test. Pearson correlation coefficients were calculated to define the correlation between variables. Data are expressed as Mean±SE (standard error) and the statistical significance was set at P<0.05.

RESULTS

In our study, 40 calves with sepsis (20 females, 20 males) and 10 healthy calves (5 females, 5 males) between 0-14 days postpartum were used.

As a result of the causative agent detection in feces with a rapid test kit, Rotavirus was detected in 10% (4/40), Coronavirus in 15% (6/40), *E. coli* K99 in 35% (14/40), *E. coli*K99+Coronavirus in 20% (8/40), *E. coli* K99+Rotavirus in 10% (4/40), Rotavirus+Coronavirus in 7.5% (3/40) and *E. coli* K99+Coronavirus in 10% (4/40) of calves with sepsis (Table 1).

Physical examination findings and evaluation of the levels of cardiac biomarkers in calves with sepsis and control group calves in the study are presented in Table 2. Among the physical examination findings, respiratory rate (RR; P<0.001), heart rate (HR; P=0.006) and capillary refill time (CRT; P=0.002) were statistically significantly higher in calves with sepsis compared to the control (Table 2). White blood cells (WBC) level was statistically significantly higher in calves with sepsis compared to the control (P<0.001, Table 2). In addition, biomarkers cTnI, NT-proBNP, ANP, HCY, CK-MB and CRP were significantly higher in calves with sepsis compared to the control (P<0,001, Table 2).

Table 3 shows the Pearson correlation of the data in the study.The study revealed a high correlation between cardiac markers and the most significant correlation was found between ANP and CK-MB (R=0.836**, Table 3).

DISCUSSION

Sepsis encountered during the neonatal period leads to serious economic losses in cattle breeding. The most important economic losses in this regard include the death of the calf, loss of genetic material, treatment costs or performance and yield failures despite recovery (Tokgöz et al., 2013; Demir et al., 2019). Cardiac markers (cTnI, ANP, NT-proBNP, NT-proBNP, HCY and CK-MB) and CRP, are important biomarkers that assist in the detection of cardiac diseases by increasing in serum concentrations even before the symptoms thereof (Mellanby et al., 2009; El-Ashker et al., 2013; Neamat-allah, 2015; Attia, 2016; Kılıçalp and Kozat, 2017; Ogawa et al., 2021). Our study aimed to determine the importance and ef-

Table 1. Enteropathogens evaluated in calfdiarrhea with sepsis and their prevalence

Disease Agent	N	Rate (%)
Rotavirus	4	10
Coronavirus	6	15
E. coli K99	14	35
E. coli K99+Coronavirus	8	20
E. coli K99+Rotavirus	4	10
Rotavirus+Coronavirus	3	7.5
E. coli K99+Rotavirus+Coronavirus	1	2.5
TOTAL	**40**	**100**

Table 2. Physical Examination Findings and Levels of Cardiac Biomarkers in Calves with Sepsis and Healthy Calves

Parameters	Groups	N	Mean±SE	P Value
RT (°C)	Sepsis	40	38.54±0.29	0.299
	Control	10	38.21±0.12	
RR (breaths/min)	Sepsis	40	43.13±3.10	<0.001
	Control	10	23.80±1.67	
HR (beats/min)	Sepsis	40	104.40±6.42	0,006
	Control	10	82.80±3.73	
CRT(sec)	Sepsis	40	2.93±0.24	0.002
	Control	10	1.50±0.17	
WBC(x10^3/μL)	Sepsis	40	16.66±1.77	<0.001
	Control	10	9.23±0.66	
cTnI (ng/mL)	Sepsis	40	0.19±0.01	<0.001
	Control	10	0.04±0.00	
NT-proBNP (pg/mL)	Sepsis	40	405.94±16.19	<0.001
	Control	10	60.02±3.06	
ANP (pg/mL)	Sepsis	40	228.35±10.75	<0.001
	Control	10	21.21±0.87	
Homocysteine (µmol/L)	Sepsis	40	26.38±1.04	<0.001
	Control	10	14.17±0.34	
CRP (µg/mL)	Sepsis	40	52.07±1.65	<0.001
	Control	10	24.05±1.83	
CK-MB (U/L)	Sepsis	40	139.18±3.36	<0.001
	Control	10	65.31±1.98	

RT: Rectaltemperature; RR: Respiration rate; HR: Heart rate; CRT: Capillaryrefll time WBC: White bloodcells; cTnI: cardiactroponin I; ANP: atrialnatriureticpeptide; NT-proBNP: N-terminal pro-brainnatriureticpeptide; HCY: Homocysteine; CRP: C-reactive protein; CK-MB: creatinekinase-myocardialband; P<0.05 indicates statistical significance between groups.

Table 3. Pearson Correlation of all data in the study

Parameters	RT (°C)	RR	HR	CRT	WBC	cTnI	NT-proBNP	ANP	HCY	CRP
RR (breaths/min)	0.023									
HR (beats/min)	-0.077	0.039								
CRT (sec)	0.124	0.281	0.100							
WBC (x10^3/µL)	-0.216	0.196	0.163	0.405**						
cTnI (ng/mL)	0.048	0.467**	0.333*	0.409**	0.203					
NT-proBNP (pg/mL)	0.069	0.434**	0.295	0.427**	0.373*	0.685**				
ANP (pg/mL)	0.155	0.333*	0.264	0.507**	0.230	0.751**	0.743**			
Homocysteine (µmol/L)	0.155	0.364*	-0.009	0.332*	0.186	0.535**	0.623**	0.596**		
CK-MB (U/L)	0.025	0.522**	0.240	0.415**	0.254	0.786**	0.797**	0.836**	0.654**	0.722**

RT: Rectaltemperature; RR: Respiration rate; HR: Heart rate; CRT: Capillaryrefll time WBC: White bloodcells; cTnI: cardiactroponin I; ANP: atrialnatriureticpeptide; NT-proBNP: N-terminal pro-brainnatriureticpeptide; HCY: Homocysteine; CRP: C-reactive protein; CK-MB: creatinekinase-myocardialband; **:Correlation is significant at the 0.01 level (2-tailed); *: Correlation is significant at the 0.05 level (2-tailed).

fectiveness of biomarkers in early diagnosis of sepsis by identifying the changes in cTnI, ANP, NT-proBNP, HCY, CK-MB, CRP levels and Pearson correlations between these cardiac markers in calves with diarrhea-induced neonatal sepsis.In this way, early diagnosis of sepsis will become possible and economic losses due to unconscious treatment practices and drug/veterinary costs will be avoided.

Recently, immunochromatographic test kits have been used in the diagnosis of pathogenic agents causing diarrhea (Çitil et al., 2004). The sensitivity of these test kits has been reported to be between 60-94.9% for coronavirus, 93% for *E. coli* K99, 70-100% for rotavirus and 75-100% for *C. parvum* (Klein et al., 2009; Altuğ et al., 2013). In different studies conducted with immunochromatographic test kits, it has been reported that the highest diarrhea agent is *E. coli* at rates ranging from 24% to 40% (Sezer, 2021; Akyüz et al., 2022).In addition, it has been reported that *E. coli* causes 40% of the disease in the first week of the postpartum period(Al and Balıkçı, 2012).In our study, in parallel with the literature, the rate of *E. coli* in calves with sepsis was determined as 35%.

It is very difficult to establish sepsis criteria in calves due to the variability of clinical findings in sepsis (Pardon and Depres, 2018; Beydilli and Gökçe, 2020). However; depression, weak sucking reflex, changes in CRT, tachycardia, tachypnea, hypovolemia, hypotension and dehydration are clinically evident in sepsis (Çitil and Gökçe, 2013; Bonelli et al., 2018). Nevertheless, it has also been reported that rectal temperature (RT) is variable (Kırbaş et al., 2021). Different studies have reported that HR, RR, CRT and hematocrit levels are high in calves with sepsis (Aydoğdu et al., 2018; Yıldız et al., 2018; Akyüz and Gökçe, 2021). Our study also found that HR, RR, CRT and WBC were significantly elevated which was in line with the literature. However, in our study, although RT was found to increase numerically in our study, it was not statistically significant. Increased RR in calves with sepsis indicates a decrease in the vital capacity of the lungs (Poulsen et al., 2010). The possible reason for the increase in WBC values is thought to be due to the increase in the defense mechanism against infectious agents and hemoconcentration due to dehydration (Asati et al., 2008; Brar et al., 2015). Prolonged CRT in sepsis is a result of multiple organ dysfunction and the resulting negative effects on the cardiovascular system (Fecteau et al., 2009).

The most important cause of death in sepsis is organ failure, and cardiac dysfunctions are the leading cause (Fecteau et al., 2009; King et al., 2014; Beydilli and Gökçe, 2020). Studies on humans have reported that cardiovascular abnormalities are common in sepsis cases, resulting in myocardial damage due to non-coronary artery disease (Fenton and Parker, 2016). In different studies, it has been reported that serum activities of cTnI and CK-MB increase during myocardial damage (Kemp et al., 2004; Aydoğdu et al., 2016), but CK-MB expression is not limited to the heart but can also be expressed in other tissues such as skeletal muscle and gastrointestinal system (Babuin and Jaffe, 2005; Hanedan et al., 2015). This explains why cTnI is more sensitive and specific than CK-MB for myocardial damage (Tunca et al., 2008; Akasha et al., 2015; Hanedan et al., 2015). When cardiac injury occurs, cTnI peaks in the blood within 6-12 hours and remains constant at this point for 14-21 days (Undhand et al., 2012; Chow et al., 2017). In addition, cTnI remains in circulation longer than CK-MB (Leonardi et al., 2008) and gives accurate results although CK-MB value returns to normal in the advanced stages of the disease (Başbuğan et al., 2010). In different studies, it was reported that cTnI and CK-MB levels were significantly increased in calves with sepsis (Beydilli and Gökçe, 2020; Kırbaş et al., 2021; Naseri et al., 2021). In our study, similar to the literature, cTnI and CK-MB levels were found to be significantly increased. In addition, cTnI has been reported to be the gold standard for cardiac damage (Langhorn and Willesen, 2016), and the elevation of cTnI and CK-MB in animals with sepsis indicates that myocardial damage occurs in these animals. On the other hand, the pathophysiology of troponin elevation in sepsis is thought to be due to myocardial dysfunction (Kırbaş et al., 2021).

The ANP concentration, which reflects the clinical stages of mitral valve disease (Ruskoaho, 2003), has a half-life of approximately 4 minutes and has no stability (Ogawa et al., 2021). Whereas NT-proBNP is released into the bloodstream mainly in response to ventricular myocyte stretch and has a long half-life (Kellihan et al., 2011). In addition, plasma ANP levels were found to be quite high in calves with congenital heart failure and it was suggested that it could be used for diagnostic purposes (Hori et al., 2009). In healthy calves; ANP level was reported as 36±8.16 pg/mL (Hori et al., 2009) and NT-proBNP level was reported as 131.32±13.1 pg/mL (Beydilli and Gökçe 2020). In our study, ANP and NT-proBNP levels in healthy calves were 21.21±0.87 pg/mL and 60.02±3.06 pg/

mL, respectively. In a study conducted on mice with sepsis, it was reported that ANP levels increased significantly (Li et al., 2014). However, no data on ANP levels in calves with sepsis were found in the literature review. Therefore, our study is the first in this field. Our study reported that the ANP level in calves with sepsis was 228.35±10.75 pg/mL and the 10-fold increase in ANP level compared to healthy calves was statistically very significant (P<0.001). A study conducted on calves with sepsis reported that NT-proBNP level increased significantly (Beydilli and Gökçe, 2020). Moreover, a study on the use of NT-proBNP in the determination of heart failure stated that values up to 300 pg/mL could not be a marker for the disease (Mueller et al., 2007). Our study, on the other hand, showed that NT-proBNP level in calves with sepsis was approximately 7 times higher (405.94 ± 16.19 pg/mL) compared to healthy calves and this result was statistically significant. This indicates that sepsis causes myocardial damage.

In human medicine, HCY is used to assess complications of renal, cardiovascular and other diseases (Amin et al., 2016; Long and Nie, 2016). HCY is an independent risk factor for cardiovascular disease in renal patients (Kavaklı et al., 2010) and a study on calves with diarrhea reported that HCY levels were significantly increased compared to healthy calves (Kozat et al., 2021). Furthermore, in a study conducted by Kılıçalp and Kozat (2017), it was reported that serum HCY values obtained from healthy cows can be used for the diagnosis of cardiovascular diseases. In our study, HCY level was found to be significantly increased in calves with diarrhea-induced sepsis compared to healthy calves. This increase may be caused by increased production rate of HCY (transmethylation), decreased HCY excretion, decreased HCY remethylation or transsulfuration rate (Kozat et al., 2021).

C-reactive protein is a positive acute phase protein that is often used as a biomarker of general inflammation and infection (Magliulo et al., 2016). Acute phase proteins are plasma proteins whose production and serum concentrations are up-regulated in response to inflammation, infection, cardiovascular disease, cancer and tissue damage (Bradford, 2019). A study conducted in calves with suspected sepsis reported that CRP levels increased (Akgül et al., 2019). Our study also showed results parallel to the study by Akgül et al. and significant increases were observed in CRP levels. In addition, in a study conducted on middle-aged people, it was reported that CRP levels >10 µg/mL were associated with cardiovascular diseases (Dhingra et al., 2007). However, it is not possible to determine whether the elevation of CRP levels in calves with sepsis is due to infection or cardiac damage. Therefore, it is thought that more detailed studies on the subject are needed.

CONCLUSIONS

In conclusion, cTnI, ANP, NT-proBNP, HCY and CK-MB can be suggested as useful prognostic and diagnostic biomarkers of cardiac dysfunctions in calves with suspected sepsis. Furthermore, according to the results of the study; although the suggest that an approximately 10-fold increase in ANP level would be the best marker for early diagnosis of sepsis, ANP may not be an ideal marker due to its short half-life and instability. Therefore, we believe that NT-proBNP, which correlates very significantly with all other markers and increases approximately 7-fold in calves with sepsis, is an important marker in the detection and early diagnosis of sepsis.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

REFERENCES

Akasha R, Mohammed A, Syed PA, Sirageldin E, Mohammed E, AllahMG (2015)Assessment of acutemyocardialinfarctionbytheuse of specialbiochemicalmarkers. UMJ 1:68-73.https://doi.org/10.5455/umj.20150416122936

Akgül Y, Akgül Ö, Kozat S, Özkan C, Yılmaz N (2019) Evaluation of intercellularadhesion molecule-1 (ICAM-1), Tumornecrosisfactor α (TNF-α), Interleukins (IL-6, IL-8) and C-reactive protein (CRP) levels in neonatal calveswithpresumedsepticemia. Van Vet J 30:167-173. https://doi.org/10.36483/vanvetj.577392

Akyüz E, Gökce G (2021)Neopterin, procalcitonin, clinicalbiochemistry, andhematology in calveswith neonatal sepsis. Trop Anim HealthProd 53:354.https://doi.org/10.1007/s11250-021-02779-z

Akyüz E, Kükürt A (2021) Evaluation of oxidativestressındexandsomebiochemicalparameters in neonatal calveswithdiarrhea. ActaSciVet 3:58-63.

Akyüz E, Sezer M, KuruM,Naseri A (2022)Changes in hematology, someclinicalbiochemicalparametersand mineral levels in neonatal calveswithsepsis duetodiarrhea. Van Vet J 33:26-30.https://doi.org/10.36483/vanvetj.1066050

Al M, Balıkçı E (2012) Neonatal ishalli buzağılarda rotavirus, coronavirus, E. coli K99 ve Cryptosporidiumparvum'un hızlı test kitleri ile teşhisi ve enteropatojen ile maternal immünite ilişkisi. FÜ Sağ Bil VetDerg 26:73-78.

Altuğ N, Yüksek N, Özkan C, Keleş İ, Başbuğan Y, Ağaoğlu ZT, Kaya

A, Akgül Y (2013) Neonatal buzağıishalerininimmunokromotografik test kitleri ile hızlı etiyolojik teşhisi. Van Vet J 24:123-128.

Amin HK, El-SayedMIK,Leheta OF (2016)Homocysteine as a predictivebiomarker in earlydiagnosis of renal failuresusceptibilityandprognosticdiagnosisforendstages renal disease. Ren Fail 38:1267-1275. https://doi.org/10.1080/0886022X.2016.1209382

Asati CK, Roy S, Roy M (2008)Hemato-biochemicalstudyanddiagnosis of colibacilosis in calves. IntasPolivet 9:245-248.

Attia NE (2016)Cardiacbiomarkersandultrasonography as tools in predictionanddiagnosis of traumaticpericarditis in Egyptianbuffaloes. Vet World 9:976.https://doi.org/10.14202/vetworld.2016.976-982

Aydogdu U, Coskun A, Yildiz R,Guzelbektes H, Sen I (2018)Clinicalimportance of lipid profile in neonatal calveswith sepsis. J HellenicVetMedSoc 69:1189-1194.https://doi.org/10.12681/jhvms.15926

Aydogdu U, Yildiz R, Guzelbektes H, Coskun A, Sen I (2016)Cardiacbiomarkers in prematurecalveswithrespiratorydistresssyndrome. ActaVetHung 64:38-46.https://doi.org/10.1556/004.2016.004

Aygün O, Yıldız R (2018) Evaluation of thrombomodulinand pentraxin-3 as diagnosticbiomarkersin calveswith sepsis. VetMed 63:313-320. https://doi.org/10.17221/159/2017-VETMED

Babuin L, Jaffe AS (2005)Troponin: thebiomarker of choiceforthedetection of cardiacinjury. CMAJ 173:1191-1202.

Başbuğan Y, Ağaoğlu Z, Yüksek N (2010) An investigation on serum troponinconcentration in healthyruminants. Kafkas UnivVet Fak Derg 16:641-645.https://doi.org/10.9775/kvfd.2009.1358

Basoglu A, Sen I, Meoni G, Tenori L, Naseri A (2018) NMR-basedplasmametabolomics at set intervals in newborndairycalveswith severe sepsis. MediatorsInflamm 2018.https://doi.org/10.1155/2018/8016510

Beydilli Y, Gökçe Hİ (2020) Investigations of cardiacfunctionsand organ damages in neonatal calveswithsuscepted sepsis. MAE Vet Fak Derg 5:140-145. https://doi.org/10.24880/maeuvfd.815632

Bonelli F,Meucci V, Divers TJ, Boccardo A, Pravettoni D, Meylan M, Sgorbini M (2018)Plasmaprocalcitoninconcentration in healthycalvesandthosewithsepticsystemicinflammatoryresponsesyndrome. Vet J 234:61-65.https://doi.org/10.1016/j.tvjl.2018.02.003

Bradford DJ (2019)Thedevelopment of a medicalbiomarker test toaid in rapidscreeningforthe presence of infectiousdiseases. PhDThesis. StellenboschUniversity, Institute of HealthScience, 2019.

Brar TK, Singh KD, Kumar A (2015)Effect of differentphases of menstrualcycle on heartrate variability (HRV). J ClinDiagnosticRes 9:CC01. https://doi.org/10.7860/JCDR/2015/13795.6592

Chow SL, Maisel AS, Anand I, Bozkurt B, De Boer RA, Felker GM, Zile MR (2017) Role of biomarkersfortheprevention, assessment, andmanagement of heartfailure: a scientificstatementfromtheAmericanHeartAssociation. Circ J 135:e1054-e1091. https://doi.org/10.1161/CIR.0000000000000490

Çitil M, Arslan MÖ, Güneş V, Erdoğan HM (2004) Neonatal buzağı ishallerinde Cryptosporidium ve Eimeria enfeksiyonlarının rolü. Kafkas ÜnivVet Fak Derg 10:59-64.

Çitil M, Gokce E (2013) Neonatal septicemia. Türk Klin J VetSci 4:62-70.

Demir PA, Aydin E, Ayvazoğlu C (2019)Estimation of theEconomicLossesRelatedtoCalfMortalities Kars Province, in Turkey. Kafkas UnivVet Fak Derg 25:283-290.https://doi.org/10.9775/kvfd.2018.20471

Dhingra R, Gona, P, Nam BH, D'AgostinoSr RB, Wilson PW, Benjamin EJ,O'Donnell, CJ (2007) C-reactive protein, inflammatoryconditions, andcardiovasculardisease risk. Am J Med 120:1054-1062.https://doi.org/10.1016/j.amjmed.2007.08.037

El-Ashker M, Salama M, El-Boshy M (2013)Traumaticreticuloperitonitis in waterbuffalo (Bubalusbubalis): Clinicalfindingsandtheassociatedinflammatoryresponse. J VetMed 808656:1-6.http://dx.doi.org/10.1155/2013/808656

Fecteau G, Smith BP, George LW (2009)Septicemiaandmeningitis in thenewborncalf. VetClin North AmFood Anim 25:195-208.https://doi.org/10.1016/j.cvfa.2008.10.004

Fenton KE, Parker MM (2016)Cardiacfunctionanddysfunction in sepsis. ClinChestMed 37:289-298.https://doi.org/10.1016/j.ccm.2016.01.014

Gökçe E, Sözmen M, Gülmez C, Bozukluhan K, Gökce G, Atakişi E, Erdoğan HM (2021)Carnitineconcentrations in healthyandsepticaemiasuspected neonatal calvesanditsrelationtopassiveimmunty. Turkish J Vet Anim Sci 45:229-237.https://doi.org/10.3906/vet-2011-49

Hanedan B, Kirbas A, Dorman E, Mehmet OT, Kandemir MF, Alkan O (2015)Cardiactroponin-I concentration in weanedcalveswithbovinerespiratorydisease. ActaVet 65:454-462. https://doi.org/10.1515/acve-2015-0038

Hori Y,Kikuchi M, Nakagawa A, Yonezawa T, MiuraH,Ohnami Y (2009) Plasmaatrialnatriureticpeptide in healthycalvesandcalveswithcongenitalheartdisease. J VetInternMed 23:653-656. https://doi.org/10.1111/j.1939-1676.2009.0293.x

Kakihana Y, Ito T, Nakahara M, Yamaguchi M, Yasuda T (2016) Sepsis-inducedmyocardialdysfunction: pathophysiologyandmanagement. J IntensiveCare 4:1-10. https://doi.org/10.1186/s40560-016-0148-1

Kavaklı HS, Altıntaş ND, Tanrıverdi F (2010)HomocysteineLevels in AcuteIschemicStrokePatients. Eurasian J EmergMed 9:169-171. https://doi.org/10.5152/jaem.2010.007

Kellihan HB, MacKie BA, Stepien, RL (2011) NT-proBNP, NT-proANPandcTnIconcentrations in dogswithpre-capillarypulmonaryhypertension. J VetCardiol 13:171-182.https://doi.org/10.1016/j.jvc.2011.04.003

Kemp M, Donovan J, Higham H, Hooper J (2004)Biochemicalmarkers of myocardialinjury. Br J Anaesth 93:63-73.https://doi.org/10.1093/bja/aeh148

Kılıçkap A, Kozat S (2017)Research of serum homocysteinelevels in healthycows. J VetSci Anim Husb 5:103.

Kırbaş A, Değirmençay Ş, Kilinc A, Eroğlu M (2021) Evaluation of serum cardiactroponin-I concentrationandcardiacenzymeactivities in neonatal calveswith sepsis. Israel J VetMed 76:4-11.

King EG, Bauzá GJ, Mella JR, Remick DG (2014). Pathophysiologicmechanisms in septicshock. LabInvest 94:4-12. https://doi.org/10.1038/labinvest.2013.110

Klein D, Kern A, Lapan G, Benetka V, Möstl K, Hassl A, Baumgartner W (2009) Evaluation of rapidassaysforthedetection of bovine coronavirus, rotavirus A andCryptosporidiumparvum in faecalsamples of calves. Vet J 182:484-486.https://doi.org/10.1016/j.tvjl.2008.07.016

Kozat S, Özkan C, Okman EN (2021) Evaluation of homocysteinelevels in neonatal calveswithdiarrhea. Kafkas UnivVet Fak Derg 27:271-277.https://doi.org/10.9775/kvfd.2020.24894

Labonté J, Dubuc J, Roy JP, Buczinski S (2018)Prognosticvalue of cardiactroponin I and l-lactate in blood of dairycowsaffectedbydownercowsyndrome. J VetInternMed 32:484-490. https://doi.org/10.1111/jvim.14874

Landesberg G, Levin PD, Gilon D, Goodman S, Georgieva M, Weissman C (2015)Myocardialdysfunction in severe sepsis andsepticshock: nocorrelationwithınflammatorycytokines in real-lifeclinicalsetting. Chest 148:93-102. https://doi.org/10.1378/chest.14-2259

Langhorn R, Willesen JL (2016)Cardiactroponins in dogsandcats. J VetInternMed 30:36-50.https://doi.org/10.1111/jvim.13801

Leonardi F, Passeri B, Fusari A, De Razza P, Beghi C, Lorusso R, Botti P (2008)Cardiactroponin I (cTnI) concentration in an ovine model of myocardialischemia. ResVetSci 85:141-144.https://doi.org/10.1016/j.rvsc.2007.09.010

Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Ramsay G (2003) 2001 sccm/esicm/accp/ats/sis international sepsis definitionsconference. IntensiveCareMed 29:530-538.https://doi.org/10.1007/s00134-003-1662-x

Li X, Jiang L, Lin S, He Y, ShenG, Cai Z, Zhang M (2014)Inhibition of mTORC1 renderscardiacprotectionagainstlipopolysaccharide. Int J ClinExpPathol 7:8432.

Long Y, Nie J (2016)Homocysteine in renal injury. KidneyDis 2:80-87. https://doi.org/10.1159/000444900

Magliulo M, De Tullio D, Vikholm-Lundin I, Albers WM, Munter T, Manoli K, Torsi L (2016)Label-free C-reactive protein electronicdetectionwith an electrolyte-gatedorganicfield-effect transistor-basedimmunosensor. Anal BioanalChemRes 408:3943-3952.https://doi.org/10.1007/s00216-016-9502-3

Mellanby RJ, Henry JP, Cash R, Ricketts SW, Bexiga R, Truyers I, Mellor DJ (2009) Serum cardiactroponin I concentrations in cattlewithcardiacandnoncardiacdisorders. J VetInternMed 23:926-930.https://doi.org/10.1111/j.1939-1676.2009.0330.x

Mueller C, Breidthardt T, Laule-Kilian K, Christ M, Perruchoud AP (2007)Theintegration of BNP and NT-proBNPintoclinicalmedicine.

SwissMedWkly 137:4-12.

Naseri A, Sen I, Turgut K, Guzelbektes H, Constable PD (2019)Echocardiographicassessment of leftventricularsystolicfunction in neonatal calveswithnaturallyoccurring sepsis orsepticshockduetodiarrhea. ResVetSci 126:103-112.https://doi.org/10.1016/j.rvsc.2019.08.009

Naseri A, Şen I, Turgut K, Guzelbektes H (2021) Evaluation of coagulationabnormalitiesandcardiacbiomarkers in calveswithnaturallyoccurring severe sepsis orsepticshock. Van Vet J 32:28-32.https://doi.org/10.36483/vanvetj.855449

Neamat-Allah ANF (2015)Alterations in somehematologicalandbiochemicalparameters in Egyptianbuffaloessufferingfromtraumaticreticuloperitonitisanditssequelae. Bull UASVM VetMed 72:117-122.https://doi.org/10.15835/buasvmcn-vm: 11021

Ogawa M, Hori Y, Kanno N, Iwasa N, Toyohuku T, Isayama N, Takemura N (2021)Comparison of N-terminal pro-atrialnatriureticpeptideandthreecardiacbiomarkersfordiscriminatoryability of clinicalstage in dogswithmyxomatous mitral valvedisease. J VetMedSci 83:705-715. https://doi.org/10.1292/jvms.20-0629

Pardon B, Deprez P (2018)Rationalantimicrobialtherapyfor sepsis in cattle in face of thenewlegislation on criticallyimportantantimicrobials. VlaamsDiergeneeskd. Tijdschr 87:37-46.

Poulsen KP, Foley AL, Collins MT,McGuirk SM (2010)Comparison of passive transfer of immunity in neonatal dairycalves fed colostrumorbovine serum-basedcolostrumreplacementandcolostrumsupplementproducts. J AmVetMed 237:949-954.https://doi.org/10.2460/javma.237.8.949

Ruskoaho H (2003)Cardiachormones as diagnostictools in heartfailure. EndocrRev 24:341-356.https://doi.org/10.1210/er.2003-0006

Tokgöz BS, Özdemir R, Turut N, Mirioğlu M, İnce H, Mahanoğlu B, Tuzcu N (2013) Adana Bölgesinde görülen neonatal buzağı enfeksiyonlarının morbidite ve mortaliteleri ve risk faktörlerinin belirlenmesi. AVKAE Derg 3:7-14.

Tunca R, Sozmen M,Erdogan H, Citil M, Uzlu E, Ozen H, Gokçe E (2008) Determination of cardiactroponin I in thebloodandheart of calveswithfoot-and-mouthdisease. J VetDiagnInvest 20:598-605.https://doi.org/10.1177/104063870802000510

Undhad VV, Fefar DT, Jivani BM, Gupta H, Ghodasara DJ, Joshi BP, Prajapati KS (2012)Cardiactroponin: an emergingcardiacbiomarker in animalhealth. Vet. World 5:508-511.https://doi.org/10.5455/vetworld.2012.508-511

Yıldız R, Beslek M, Beydilli Y, Ozcelik M, Bicici O (2018) Evaluation of platelet activatingfactor in neonatal calveswith sepsis. J TurkishVetMedSoc 89:66-73.