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Relationship between Cystatin C with some hematological and biochemical parameters in neonatal calf diarrhea

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ABSTRACT

Objectives: The purpose of this research is to determine the relationship between cystatin C (Cys-C) and some hematologic and biochemical parameters in neonatal calves diarrhea.

Materials and Methods: In this research the animal material of the study was obtained from different breeds, genders and ages (0-30 days) 10 samples have been taken from healthy neonatal calves and 22 samples from diarrhea calves which didn't received any medicine. Otherwise, the general examination has been done for all the calves. The levels of hematologic, biochemical and blood gas have been determind for both healthy calves and neonatal calves diarrhea.

Results: Depending on the control group, we have observed that the neonatal calves diarrhea hematologic parameters WBC, Neu, Hct, Hb levels ($p<0.05$) and biochemical parameter BUN ($p<0.01$) and Cr ($p<0.05$) level statistically have been increased. On the other hand, Alb ($p<0.05$) and glucose ($p<0.01$) levels have been decreased. In term of blood gas analysis and depending on the control group the level of K^+ ($p<0.05$) has been increased, the levels of pH, pO_2 and base ($p<0.05$) have been decreased. We evaluate the Cys-C level in the neonatal calves diarrhea and we have found that Cys-C level is statistically increased this was detected comparing to the control group ($p <0.01$).

Conclusion: In this research the obtained level of Cys-C can be used as normal for calves; statistically there is no relationship between Cys-C and some of the hematologic and biochemical parameters, the Cys-C level in the calves diarrhea is an important parameter it can be used to determine the diagnosis, treatment and prognosis of the disease; but still much more research about the topic should be done.

Keywords: *Neonatal calf, Diarrhea, Cystatin C*

INTRODUCTION

Diarrhea is one of the most important causes of neonatal calf deaths. Calf diarrhea is reported as one of the most important problems of cattle breeding, high morbidity and mortality associated with diarrhea occurance and causes significant economic losses (Altuğ et al., 2013; Uetake, 2013).

The early diagnosis and the effective treatment of calf diarrhea can reduce the mortality in general the expected results from early diagnosis reduce losses of existing cases and prevent the occurrence of new cases (McGuirk, 2008; Smith, 2012).

Deaths can be observed due the occurance of diarrhea that causes fluid loss in a short time which causes kidney failure as a result of hypovolemia, metabolic acidosis as a consequence of electrolyte losses HCO_3^- and/or its exchange (Na^+, K^+, H^+) and heart blockade as a result of hyperkalemia. Kidney reduces the urine production to recover the

increased fluid losses during diarrhea (Berchtold, 2009; Altuğ et al., 2013).

The main parameters used to diagnose acute and chronic kidney diseases is circulating Creatinin (Cr) and Blood Ure Nitrogen (BUN) concentrations and urine specific gravity (Almy et al., 2002; Cobrin et al., 2013; Ghys et al., 2014). In the previous years many studies examine the correlation between glomerular filtration rate (GFR) and Cys-C (Etem and Mızrak, 2015; Ustaalioğlu et al., 2015).

Serum Cr is affected by many variables such as age, gender, muscle mass. In addition, many studies observed that serum Cr values didn't change remarkably in the early period when kidney functions started to deteriorate (Etem and Mızrak, 2015). Cys-C serum concentration is independent of gender, age or muscle mass, meaning it typically reflects GFR assessment (Onopiuk et al., 2015).

Cys-C has many properties ideal for endogenous GFR marker applications; without GFR variation they are known to have constant production and plasma concentration, low individual variability, no plasma protein binding, no tubular secretion, no tubular reabsorption without catabolism and no extrarenal excretion (Briguori et al., 2010; Ghys et al., 2014; Onopiuk et al., 2015).

Cys-C is freely filtered by glomeruli and after glomerular filtration Cys-C is reabsorbed and catabolized by proximal tubular cells; that is why it does not return to its circulation and the remaining minimum part which is low in concentration is eliminated in the urine (Miyagawa et al., 2009). As a indication for GFR, serum Cys-C is more advantageous than Cr and Cys-C shows an increasing rate at it clinical usage (Toprak, 2013).

In the literature review, there are studies on Cys-C in dogs (Almy et al., 2002; Braun et al., 2002; Pagitz et al., 2007; Miyagawa et al., 2009; Monti et al., 2012; Ghys et al., 2014), but no study on Cys-C in ruminants has been found especially in calves.

In this study by revealing the relationship between kidney biochemical parameters and Cys-C levels in diarrhea calves, it was aimed to contribute to the literature how it changes and its levels according to the healthy control group.

MATERIALS and METHODS

Working approval was obtained from Van YUHADYEK with the ethical committee permission dated at 28.03.2019 and numbered 2019/03. In this study, 22 calves with diarrhea brought to clinics with the complaint of diarrhea from Van province and its districts and 10 calves with no health problems as a control group (0-30 days old, 32 in total) were included in the study.

General examinations of the calves brought to the clinic were carried out. Body temperature, heart and breathing frequencies and age were recorded. Anamnesis of calves with diarrhea was obtained, clinical examinations were performed and data were recorded. Later, fecal samples were taken to sterile fecal container with rectal stimulation. The Speed V DIAR 5 (BVT® Diagnostica Veterinaria, France) test, which enables etiological diagnosis from faeces, was performed on the faeces samples. This kit detected the antigens of the pathogen on the strip membrane by a rapid immuno-chromotographic method. According to the agents that were determined by the previous method, the rates of agents was Giardia 15.789%, E. coli 21.05%, Coronavirus 15.789%, Rotavirus 15.789%, Cryptosporidium 5.26%, Rotavirus and Coronavirus 21.05%, E. coli and Coronavirus 5.26%. Several treatment plans were followed depending on the aetiology and dehydration that were mild, moderate or severe and in most cases varying degrees of metabolic acidosis were determined. The aim of the treatment was to preserve the life of the calves, which aimed at intravenous rehydration through serum and sodium bicarbonate, and then appropriate therapeutic applications were used, whereas bacterial pathogens with antibiotics and the causes of parasites with specific anti-parasites and for the viral agents, their treatment was aimed as continuous intravenous rehydration and giving nutrients and antibiotics to prevent secondary infection.

For hematological, biochemical and blood gas examinations, blood samples were taken duly from the vena jugularis of calves to tubes- with and without anticoagulants. From the anticoagulated blood samples, hematologically red blood cells (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), white blood cells (WBC), Neutrophil (Neu), Lymphocyte (Lym), Eosinophil (Eo), Monocyte (Mo), Hematocrit (Hct) and Hemoglobin (Hb) levels were determined by veterinary blood count device (MS4-s® Veterinary Blood Count Device, Melet Schloesing Laboratoires co., France). Blood samples in tubes without anticoagulants were centrifuged and the serum obtained used to determine the biochemically; glucose, total protein (Tp), albumin (Alb), BUN, Cr and creatine kinase (CK) levels

(Mindray® BS 400 Veterinary Biochemistry, Mindray co., China) were measured.

The blood taken into the heparinized syringe evaluated by the blood gas device according to the method and the data were recorded according to the patient protocol. Blood gases pH, partial pressure of carbon dioxide (pCO_2), partial pressure of oxygen (pO_2), HCO_3^-, and serum Na^+, K^+ and Cl^- values were evaluated with the blood gases device (Radiometer® ABL80, Rdiometer co., Denmark).

The absorbance levels in the blood serum was determined by proceeding procedure of the specific ELISA test kit (YLbiont®) (Catalog No: YLA0386BO) Cys-C ELISA device (DAS®, Italy). Descriptive Statistics for the features mentioned; it is expressed as median, mean, standard deviation, minimum and maximum value. In terms of these features, Mann-Whitney test was used to compare groups.

For determining the relationship between variables, Spearman Correlation Coefficients were calculated separately in the groups. Statistical significance level was taken as 5% in calculations and SPSS (ver:13) statistical package program was used for calculations.

RESULTS

Clinically all data of calves included in the control group were at normal physiological limits. In most of the diarrhea calves presenting to the clinic, lymph nodes are swollen especially prescapular and body temperatures average 37.84±0.36 °C, heart rate average 125.28±5.12 per minute and breathing frequency average 36.28±4.17 per minute. Conjunctiva hyperemic, sunken eyes and dehaydration were detected; their stools were soft and waterly in others.

Hematological parameters in blood samples taken with anticoagulants shown at Table 1. Comparing to the control group a statistically significant increase ($p<0.05$) in WBC, Neu, Hb and Hct levels was detected in diarrhea calves.

From the serum obtained biochemically; glucose, Tp, Alb, BUN, Cr and CK levels, as well as the absorbance values obtained in Cys-C in blood serums were determined (Table 2). In diarrhea calves, there was a statistically significant increase in Cys-C, BUN ($p<0.01$) and Cr ($p<0.05$) levels, and a statistically significant decrease in glucose levels ($p<0.01$) and Alb levels ($p<0.05$) compared to the control group.

Table 1. Hematologic data of healthy and patient group

Parameters	Control Group (Mean± St. dev.) (n=10)	Patient Group (Mean± St. dev.) (n=22)
WBC (m/mm3)	8.64±1.04	14.93±8.28*
Lym (%)	56.12±8.35	40.51±20.32
Mo (%)	3.97±0.88	5.30±2.43
Neu (%)	37.87±7.81	59.01±33.87*
Eo (%)	1.63±1.10	1.86±2.20
RBC (m/mm³)	9.63±1.37	9.17±1.98
MCV (fl)	32.43±1.63	35.53±5.08
MCHC (g/dl)	38.90±3.85	39.35±4.44
Hct (%)	25.48±1.20	33.78±1.52*
Hb (g/dl)	9.38±0.82	12.73±0.59*

The difference depending on control group *: $p<0.05$, **: $p<0.01$, and ***: $p<0.001$ statisically

Table 2. Biochemical data healthy and patient group

Parameters	Control Group (Mean± St. dev.) (n=10)	Patient Group (Mean± St. dev.) (n=22)
Glycose (mg/dl)	111.86±21.86	81.63±17.18**
Tp (g/dl)	5.82±0.21	5.97±0.32
Alb (g/dl)	3.31±0.30	2.92±0.33*
BUN (mg/dl)	9.85±0.40	44.62±8.06**
Cr (mg/dl)	1.11±0.11	3.38±0.70*
CK (U/l)	242.71±39.24	607.93±123.28
Cys-C (ng/ml)	6.96±0.86	10.54±3.75**

The difference depending on control group *: $p<0.05$, **: $p<0.01$, and ***: $p<0.001$ statisically

Table 3. Blood gas data of healty and patient group

Parameters	Control Group (Mean± St. dev.) (n=10)	Patient Group (Mean± St. dev.) (n=22)
pH	7.39±0.06	7.24±0.16*
pCO2 (mm Hg)	37.45±9.84	38.38±6.29
pO2 (mm Hg)	37.13±7.51	30.92±11.53*
HCO3- (mmol/l)	22.36±6.03	17.38±7.78
Base (mmol/l)	-1.89±5.73	-9.38±9.98*
Na+ (mmol/l)	136.88±3.36	132.92±8.38
K+ (mmol/l)	4.90±0.63	6.20±1.63*
Cl- (mmol/l)	99.50±3.78	95.87±8.84

The difference depending on control group *: $p<0.05$, **: $p<0.01$, and ***: $p<0.001$ statisically

Table 4. The correlation analysis between Cys-C with pH, pCO_2, pO_2, HCO_3^-, base, Na^+, K^+, Cl^-, BUN, Cr, Hct and Hb

Parameters		Cys-C	pH	pCO2	pO2	HCO3-	Base	Na+	K+	CL-	BUN	Cr	Hct	Hb
Cys-C (ng/ml)		1.000												
	P													
pH		0.264	1.000											
	P	0.235												
pCO2 (mm Hg)		0.009	0.184	1.000										
	P	0.968	0.390											
pO2 (mm Hg)		0.145	0.016	-0.254	1.000									
	P	0.521	0.939	0.231										
HCO3- (mmol/l)		0.215	0.941**	0.458*	-0.021	1.000								
	P	0.337	0.000	0.024	0.923									
Base (mmol/l)		0.216	0.957**	0.411*	-0.055	0.990**	1.000							
	P	0.334	0.000	0.046	0.797	0.000								
Na+ (mmol/l)		0.093	-0.042	0.080	-0.084	-0.039	-0.097	1.000						
	P	0.679	0.845	0.709	0.697	0.858	0.651							
K+ (mmol/l)		-0.001	-0.354	0.081	-0.046	-0.247	-0.238	-0.598**	1.000					
	P	0.998	0.090	0.707	0.832	0.245	0.263	0.002						
CL- (mmol/l)		0.132	-0.257	-0.118	-0.117	-0.280	-0.329	0.858**	-0.485*	1.000				
	P	0.557	0.225	0.582	0.585	0.186	0.116	0.000	0.016					
BUN (mg/dl)		-0.337	-0.496	-0.245	0.166	-0.447	-0.456	-0.557*	0.688**	-0.494	1.000			
	P	0.202	0.051	0.360	0.540	0.082	0.076	0.025	0.003	0.052				
Cr (mg/dl)		-0.035	-0.218	-0.276	0.473	-0.226	-0.218	-0.628**	0.655**	-0.632**	0.784**	1.000		
	P	0.579	0.417	0.300	0.064	0.399	0.418	0.009	0.006	0.009	0.000			
Hct (%)		-0.316	-0.502*	-0.490*	0.163	-0.557**	-0.579**	0.103	0.280	0.243	0.556*	0.412	1.000	
	P	0.152	0.012	0.015	0.447	0.005	0.003	0.633	0.185	0.252	0.025	0.113		
Hb (g/dl)		-0.342	-0.545**	-0.385	0.121	-0.565**	-0.597**	0.028	0.320	0.247	0.494	0.322	0.900**	1.000
	P	0.119	0.006	0.063	0.572	0.004	0.002	0.895	0.127	0.245	0.052	0.223	0.000	

Correlation *: p <0.05, **: p <0.01, and ***: p <0.001; the value in the row is statistically significant according to the value in the column

The blood taken into the heparinized syringe in accordance with the procedure was immediately scanned in the blood gas device and the data were recorded according to the patient protocol. Blood gases (pH, pO_2, pCO_2, HCO_3^-), and serum Na^+, K^+ and Cl^- were determined by the blood gas analyzer (Table 3). In diarrhea calves a statistically significant increase in K^+ levels compared to the control group ($p<0.05$). A statistically significant decrease ($p<0.05$) was detected in pH, pO_2 and base levels. Data of the correlation analysis between Cys-C with pH, pCO_2, pO_2, HCO_3^-, base, Na^+, K^+, Cl^-, BUN and Cr were determined (Table 4).

DISCUSSION

Diarrhea can be fatal in neonatal calves as a result of dehydration and acidosis, which can result from various pathogens or factors that play a role in the development of diarrhea (Sobiech et al., 2013; Cho and Yoon, 2014; Pereira et al., 2017).

The 22 diarrhea calves that used in this study were devided into three groups depending on their daily age, and sometimes there was one or more causes of disease was observed. By evaluating these results, it was observed that Giardia, *E. coli*, Coronavirus, Rotavirus and Cryptosporidium were among the factors causing diarrhea expressed by researchers (Xiao et al., 1993; Bazeley, 2003; Gomez et al., 2013). In the clinical examination of 10 healthy calves included in the control group, all physiological parameters are in the reference range that reported by the researchers (Wilson et al., 2000; Piccione et al., 2010; Silva et al., 2016) and this is an indication that the calves that make up the control group are healthy.

In 22 diarrhea calves included in the study, clinical results support the results stated by the researchers (Millemann, 2009; Sobiech et al., 2013; Dawes et al., 2014; Bednarski and Kupczynski, 2015; Pereira et al., 2017). All clinical signs may not occur at the same time in a diarrhea calves. While some calves only have fluid and electrolyte losses, others may show severe clinical symptoms (high fever, weakening etc.) (Pereira et al., 2017). Therefore, laboratory tests in diarrhea calves can provide important information about the diagnosis, treatment and prognosis of the disease (Mohri et al., 2007). Along with hematology and biochemical analyzes, blood gas analysis is a good method to determine the severity of metabolic acidosis (Berchtold, 1999; Kasari, 1999).

The control group in this study, hematological parameters of healthy calves were found by researchers (Knowles et al., 2000; Mohri et al., 2007; Ježek et al., 2011; Bellino et al., 2012; Klinkon and Ježek, 2012; Panousis et al., 2018) found in the reference ranges expressed (Table 1). This situation supports that the calves included in the study are healthy.

By comparing the hematological parameters of the calves in the patient group and the control group, there was a significant increase ($p<0.05$) in WBC 14.93±8.28 m/m3, Neu 59.01±33.87, Hct 33.78±1.52, and Hb 12.73±0.59 g/dl values (Table 1). This situation coincides with the statements (Cambier et al., 2001; Dawes et al., 2014; Heller and Chigerwe, 2018). This situation thought to be caused by fluid and electrolyts losses and infection.

The glucose level of healthy calves included in this study was between 111.86±21.86 mg/dl (Tablo 3). This value was within the reference ranges expressed by the researchers (Knowles et al., 2000; Bellino et al., 2012). This is an indication that the control group calves included in the study are healthy.

In this study, the glucose level of diarrhea calves included in the patient group was 81.63±17.18 mg/dL (Table 2). When this situation was compared to the control group, a statistically significant decrease was observed ($p<0.01$). These data are similar to the data of the researchers (Sobiech et al., 2013; Bednarski and Kupczynski, 2015; Trefz et al., 2017) and it thought that the reason for the decrease in serum glucose levels, loss of the sucking reflex, problems with food, malnutrition, nutration and diarrhea-related losses.

In healthy calves forming the control group, the Tp level was between 5.82±0.21 g/dl, and the Alb level was between 3.31±0.30 g/dl (Table 2). These values were within the reference ranges expressed by the researchers (Knowles et al., 2000; Mohri et al., 2007; Klinkon and Ježek, 2012; Panousis et al., 2018). This is an indication that the control group calves included in the study are healthy.

In diarrhea calves included in the study, the level of Tp was 5.97±0.32 g/dl, Alb was 2.92±0.33 g/dl, and there was only a statistically decrease in Alb level compared to the control group ($p<0.05$) (Table 2). This situation is thought to occur as a result of infectious factors in the etiology of diarrhea affecting the liver, increased protein catabolism in diarrhea, protein loss through the digestive system, loss of sucking reflex, malnutrition and passive

transfer failure in neonatal calves. These findings are coincided with the statement that the decrease of serum Alb levels in calves may be a result of liver damage or protein catabolism in long term diarrhea as the researchers proved Seifi et al. (2006), Klinkon and Ježek, (2012) and Heller and Chigerwe (2018).

The control group BUN level included in this study was between 9.85±0.40 mg/dl (Table 2). These values were within the reference ranges expressed by the researchers (Mohri et al., 2007; Klinkon and Ježek, 2012; Başer and Civelek, 2013). This is an indication that the control group calves included in the study are healthy.

In diarrhea calves included in the study, a statistically significant increase ($p<0.01$) was detected in BUN levels 44.62±8.06 mg/dl compared to the control group. It was observed that this level coincided with the statements of the researchers (Klinkon and Ježek, 2012; Başer and Civelek, 2013). It is thought the reason for its appearance is due to metabolic acidosis, hypoglycaemia and increased catabolism. However, it indicates that increased dehydration and hyperkalemia affect kidney functions.

The Cr level of the healthy calves included in the study was 1.11±0.11 mg/dl (Table 2). This value appears to be within the reference ranges expressed by the researchers (Mohri et al., 2007; Gomez et al., 2013). While the Cr level in diarrhea calves included in the study was measured 3.38±0.70 mg/dL, a statistically significant increase ($p<0.05$) was found compared to the control group. In this situation, for diarrhea calves the levels appears to be coincide with the researchers expressing (Almy et al., 2002; Seifi et al., 2006; Mohri et al., 2007; Cobrin et al., 2013) as well as, kidney functions are affected due to increased Hct, fluid and electrolyte loss that associated with diarrhea.

Başer and Civelek (2013) in their study; CK level of healthy calves are 404.80±234.16 U/l, Özkan et al. (2011), in their study, reported that it is between 316.18±37.64 U/l. CK levels were found between 242.71±39.24 mg/dl in the healthy calves that constituted the control group, and these values were found to be close to the data of the researchers.

Başer ve Civelek (2013) in their study, the CK level was between 944.94±269.65 U/l for diarrhea calves, Özkan et al. (2011) reported between 884.80±196.00 U/Ll. In diarrhea calves included in the study, CK level was determined as 607.93±123.28 mg/dl (Table 2). Compared to the control group, the level of CK in diarrhea calves is not statistically significant, although it increases ($p>0.05$) (Table 2). These data are among the values expressed by the researchers (Özkan et al., 2011; Klinkon and Ježek, 2012; Başer and Civelek, 2013), this situation is due to diarrhea which causes increased metabolic acidosis, Hct, fluid and electrolyte loss, glucose and Alb losses. It is thought that these are the reasons of varying degrees of muscular dystrophy.

Blood gas analysis has been routinely used in the diagnosis and treatment of diarrhea calves (Seifi et al., 2006; Heller and Chigerwe, 2018). The pH of the healthy calves included in the study was detected as 7.39±0.06, pCO_2 37.45±9.84 mm Hg, pO_2 37.13±7.51 mm Hg (Tablo 4). These levels appear to be within the reference ranges expressed by the researchers (Bouda and Jagos, 1984; Bellino et al., 2012; Gomez et al., 2013; Sobiech et al., 2013). In the light of these data, it is an indication that the calves included in the control group are healthy.

In the blood gas analysis of diarrhea calves included in the study, a statistically significant decrease ($p<0.05$) was detected at pH 7.24±0.16 and pO_2 30.92±11.53 mm Hg compared to the control group (Table 3). However, there was no statistically change in pCO_2 level. It was observed that the values obtained coincided with the statements of the researchers (Gomez et al., 2013; Sen and Constable, 2013). The decrease in pH and pO_2 may be an indicator of malnutrition, dehydration due to diarrhea, fluid and electrolyte loss, the pCO_2 level does not change because the kidney and respiratory system are trying to respond to metabolic acidosis.

For the healthy calves included in this study HCO_3^- level was determined as 22.36±6.03 mmol/l and the base level was -1.89±5.73 mmol/l (Table 3). These levels were within the reference ranges expressed by the researchers (Bouda and Jagos, 1984; Bellino et al., 2012; Gomez et al., 2013; Sobiech et al., 2013). This indicates that the control group calves included in the study did not have any metabolic and systemic diseases.

In diarrhea calves included in this study, the HCO_3^- level was measured as 17.38±7.78 mmol/l and the base level as -9.38±9.98 mmol/l (Table 3). It was found that these levels coincide with the statements of the researchers (Gomez et al., 2013; Sen and Constable, 2013). Although there was no significant change in HCO_3^- level in diarrhea calves compared to the control group, a statistically significant decrease was observed in the base ($p>0.05$). It is thought that this condition may be due to diarrhea which causes Na^+ and HCO_3^- loss, fluid loss,

bacterial fermentation of the carbohydrates in the intestines which leads to a base excess associated with the apperance D-lactate, furthermore venous pO_2 reduction, L-lactic acid accumulation in ineffective tissue perfusion, and a decrease in H^+ excretion in ineffective renal perfusion.

Na^+ value of healthy calves included in the study was 136.88±3.36 mmol/l, K^+ 4.90±0.63 mmol/l and Cl^- 99.50±3.78 mmol/l (Table 3). It is seen that these levels are within the reference ranges given by the researchers (Maach et al., 1991; Mohri et al., 2007; Bellino et al., 2012; Klinkon and Ježek, 2012; Gomez et al., 2013).

Serum Na^+ level is significantly lower in calves with acute diarrhea (131.2±7.2 mmol/l) compared to healthy calves of the same age (140.0±9.9 mmol/l) (Klinkon and Ježek, 2012). During acute diarrhea in calves, the amount of stool may increase 40 times and electrolyte loses take place with the stool. In these calves, the Cl^- level (95.6±6.9 mmol/l) was significantly lower compared to healthy calves (103.3±6.9 mmol/l) (Klinkon and Ježek, 2012). Although this situation decreases at Na^+ 132.92±8.38 mmol/l and Cl^- 95.87±8.84 mmol/l, this decrease is not statistically significant ($p>0.05$). Gomez et al. (2013). Na^+ (78%) and Cl^- (68%) in diarrhea calves reported that they were within normal ranges.

In diarrhea calves included in the study, there is a statistically significant increase in K^+ 6.20±1.63 mmol/l level ($p<0.05$). This coincides with the statements of the researchers (Maach et al., 1992; Constable and Grünberg, 2013; Sen and Constable, 2013; Sobiech et al., 2013). Diarrhea is thought to cause dehydration, acidemia, and hyperkalemia and impaired cardiovascular and kidney functions losses.

Serum Cys-C is reported to be of clinical importance in the early diagnosis and treatment of acute kidney injury and chronic renal failure in the evaluation of renal dysfunction (Cobrin et al., 2013; Toprak, 2013; Nakhjavan-Shahraki et al., 2017). Determination of Cys-C in serum and urine can be routinely used. Their level in serum almost entirely depends on kidney function (Onopiuk et al., 2015).

In the literature searches, no research on Cys-C level in calves and even ruminants have been detected until this time. There are studies on Cys-C in dogs (Almy et al., 2002; Braun et al., 2002; Pagitz et al., 2007; Miyagawa et al., 2009; Monti et al., 2012; Ghys et al., 2014).

Normal serum Cys-C values in humans are between 0.6 and 1 mg/l (Villa et al., 2005). An overlap of plasma Cys-C concentration was observed (0.12 to 1.10 mg/lin adult dogs, 0 to 1.73 mg/l in young dogs and 0 to 1.60 mg/lin older dogs) (Ghys et al., 2014). In another study, the average Cys-C concentration in healthy dogs and dogs with kidney failure was 1.08±0.16 mg/l and 4.37±1.79 mg/l, respectively (Almy et al., 2002;). In a study on healthy dogs, they express the upper limit of Cys-C as 1.3 mg/L using an immunoturbidimetric procedure for human Cys-C (Braun et al., 2002). Onopiuk et al. (2015) they found serum Cys-C level as 0.96 µg/ml in their study on adult people.

The Cys-C level in the healthy calves that constitute the control group included in this study is 6.96±0.86 ng/ml, and in diarrhea calves; it was determined as 10.54±3.75 ng/ml. According to the control group, this increase was found to be statistically significant in diarrhea calves. This situation, thought that it may have been occurred because of the association with the buffering of metabolic acidosis resulting from anaerobic respiration due to decreased fluid volume and electrolyte loss such as pO_2 and HCO_3^- loss, excessive effort and consequently decreased glomerular filtration and destruction of glomeruli, all of these associated with diarrhea.

In the correlation test, it is seen that although there is positive and negative relation between hematological, biochemical and blood gas parameters measured in the study was detected, this relationship was not statistically significant.

CONCLUSION

As a result; due to the physiopathological changes in diarrhea, WBC, Hct, K^+, BUN and Cr levels increased, pH, base, glucose and Alb levels decreased; Cys-C level which is an indicator of kidney degeneration increased statistically significantly compared to the healthy control group, it is believed that this increase may have diagnostic significance, the Cys-C levels determined in the control group may be the normal value for calves, and there was a conviction that more researches should be conducted with more sampling.

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