## Evaluation of the Efficacy of Blood Gases and Hemogram Parameters in the Diagnosis of non Neurogenic Distemper and Parvoviral Enteritis in Dogs with Acute Gastroenteritis

### Evaluación de la Eficacia de los Gases en Sangre y los Parámetros del Hemograma en el Diagnóstico del Distemper no Neurogénico y Enteritis Parvoviral en Perros con Gastroenteritis Aguda

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### ABSTRACT

Canine parvovirus (CPV) and canine distemper virus (CDV), which are seen mostly in dogs younger than 6 months (mos) old with high mortality despite early diagnosis and treatment, cause various hematological abnormalities and clinical symptoms accompanied by gastroenteritis findings. Since the methods developed for definitive ante-mortem diagnosis are time-consuming and require expertise and equipment, routine laboratory tests such as blood gases and hemogram analyzes still maintain their importance in the diagnosis and monitoring the complications associated with the viruses. The animal material of the study was consisted of a total of 50 dogs: 40 dogs (Experimental Group; 24 male, 16 female) aged between 2-6 mos, from medium to large breeds such as Anatolian shepherd, Boxer and mixed breed with gastroenteritis symptoms; 10 healthy dogs (Control Group; 8 male, 2 female) aged between 2-6 mos. from similar breeds. All were brought to the hospital either for diagnosis/treatment or for routine check-up. Based on the results of rapid antigen tests performed following the clinical and laboratory analyzes, the Experimental Group was divided into two subgroups: Canine Parvovirus Group (CPV Group, n=22) and Canine Distemper Virus Group (CDV Group, n=18). As a result of laboratory analyzes, differences in respiratory rate, capillary refill time and body temperature (P=0.000) in the clinical examinations; leukocyte (WBC) (P=0.003), granulocyte (P=0.000) and mean corpuscular volume (MCV) (P=0.001) levels in the hemogram; pH (P=0.001), lactate (P=0.004) and HCO<sub>2</sub> (P=0.001) levels in the blood gases analysis were detected in the CPV and CDV groups. Based on the Receiver operating characteristic (ROC) evaluation of the parameters, which were determined to vary in the Experimental Group, it was concluded that low pH and HCO, with high lactate levels in blood gases along with low WBC, granulocyte and high MCV levels in the hemogram may be useful parameters in establishing a routine laboratory test panel for diferentiation between CPV and CDV.

Key words: Canine parvovirus; canine distemper virus; hemogram; blood gases; dog

### RESUMEN

El parvovirus canino (CPV) y el virus del moquillo canino (CDV), que se observan principalmente en perros menores de 6 meses (mes) con una alta mortalidad a pesar del diagnóstico y tratamiento precoces, causan diversas anomalías hematológicas y síntomas clínicos acompañados de hallazgos de gastroenteritis. Dado que los métodos desarrollados para el diagnóstico ante-mortem definitivo requieren mucho tiempo y experiencia y equipo, las pruebas de laboratorio de rutina, como los análisis de gases en sangre y hemogramas, aún mantienen su importancia en el diagnóstico y seguimiento de las complicaciones asociadas con los virus. El material animal del estudio estuvo constituido por un total de 50 perros: 40 perros (Grupo Experimental; 24 machos, 16 hembras) con edades comprendidas entre 2-6 mes, de razas medianas a grandes como Pastor de Anatolia, Boxer y mestizos con síntomas de gastroenteritis; 10 perros sanos (Grupo de Control: 8 machos, 2 hembras) de 2 a 6 mes de edad, de razas similares. Todos fueron llevados al hospital para diagnóstico/ tratamiento o para chequeos de rutina. Con base en los resultados de las pruebas rápidas de antígenos realizadas tras los análisis clínicos y de laboratorio, el Grupo Experimental se dividió en dos subgrupos: Grupo de Parvovirus Canino (Grupo CPV, n = 22) y Grupo de Virus del Moquillo Canino (Grupo CDV, n = 18). Como resultado de análisis de laboratorio, diferencias en frecuencia respiratoria, tiempo de llenado capilar y temperatura corporal (P = 0,000) en los exámenes clínicos; niveles de leucocitos (WBC) (P = 0,003), granulocitos (P = 0,000) y volumen corpuscular medio (MCV) (P = 0,001) en el hemograma; niveles de pH (P = 0,001), lactato (P = 0,004) y HCO<sub>3</sub> (P = 0,001) en el análisis de gases en sangre se detectaron en los grupos CPV y CDV. Con base en la evaluación de la característica operativa del receptor (ROC) de los parámetros, que se determinó que variaban en el Grupo Experimental, se concluyó que pH bajo y HCO, con niveles altos de lactato en los gases sanguíneos junto con niveles bajos de leucocitos, granulocitos y altos niveles de MCV en el hemograma puede ser un parámetro útil para establecer un panel de pruebas de laboratorio de rutina para la diferenciación entre CPV y CDV.

Palabras clave: Parvovirus canino; virus del moquillo canino; hemograma; gases en sangre; perro



### INTRODUCTION

Acute gastroenteritis (AG) describes a syndrome characterized by a sudden onset of vomiting and/or diarrhea due to gastrointestinal mucosal inflammation. Clinical examinations, elimination of other potential causes are important in its diagnosis and histopathological evaluation is rarely used [45]. There are no pathognomonic specific physical examination findings for the diagnosis of AG and some affected dogs (*Canis familiaris*) may not have significant abnormalities [32]. Findings consistent with AG are lethargy, ptyalism and abdominal distension. Besides, evaluation of mucous membranes, capillary refill time, skin elasticity and hydration status is important in deciding further diagnostic tests [24]. Laboratory analyzes are important for the elimination of non-gastrointestinal causes such as acute kidney injury, acute hepatitis, pancreatitis and metabolic complications of gastroenteritis that may cause gastroenteritis findings [32, 45].

There are several causative factors that can cause gastroenteritis in dogs. These are viruses such as Parvovirus, Coronavirus [27] and Distemper virus [47]; bacteria such as Salmonella spp. and Escherichia coli [10]; endoparasites such as Dipyllidium caninum [15] and Ancylostoma caninum [30]. Two important viral infections that usually cause hemorrhagic gastroenteritis in dogs are Canine Parvovirus (CPV) [20] and Canine Distemper virus (CDV) [6]. CPV infection is an acute, contagious and fatal viral disease that can cause both hemorrhagic gastroenteritis and myocarditis, which is more common in puppies less than 8 weeks (w) old [16, 22, 31]. Although severe clinical findings are mostly seen in dogs younger than 6 months (mos), adult dogs with immunosuppression are also potentially at risk [35]. CDV infection, which is the most important cause of mortality in domestic dogs after rabies [43], causes fever, respiratory symptoms such as cough, nasal and/or ocular discharge as well as gastroenteritis characterized by vomiting and diarrhea [3, 14, 21].

Due to its pantropic nature, CDV infection causes immunosuppression and induces a wide variety of clinical findings [3, 17, 34]. Similarly, the initial findings of CPV infection are non-specific such as anorexia, depression, fever and diarrhea that can vary from mucoid to hemorrhagic [20]. It has been reported that definitive ante-mortem diagnosis is difficult due to non-specific clinical and laboratory findings such as anemia, lymphopenia, neutropenia/neutrophilia [6, 14, 20, 31]. For this reason, various techniques such as enzyme linked immunosorbent assay (ELISA), electron microscopy, viral isolation, fecal hemagglutination, latex agglutination, counter immunoelectrophoresis, immunochromatography and polymerase chain reaction (PCR) to detect CPV antigen in stool; immunofluorescence, immunocytochemistry, antigen immunecapture ELISA, ferret inoculation test and in situ hybridization to detect CDV antigen [5, 6, 18, 19, 41] have been developed. However, most of these techniques require expertise and equipment, and are reported to be tiring and time-consuming [1, 18, 42]. Therefore, as reported, some routine laboratory tests may be useful in the diagnosis and differentiation between CDV and CPV infections and also monitoring the complications associated with the viruses [17, 40, 46].

Although blood gases and hematological parameters are not sufficiently specific to identify the etiology of gastroenteritis cases, they provide clinically important information in terms of establishing a differential diagnosis list. That is why, this study aims to reveal prominent blood gases and hemogram parameters that are important in the determination of CDV and CPV infections prior to rapid antigen test applications and to establish a routine laboratory test panel for the diagnosis of the diseases.

### MATERIALS AND METHODS

### Animal design

The animal material of the study was consisted of a total of 50 dogs: 40 dogs (Experimental Group; 24 male, 16 female), which were brought for diagnosis/ treatment, aged between 2-6 mos from medium to large breeds such as Anatolian shepherd, Boxer and mixed breed with gastroenteritis symptoms such as anorexia, vomiting and diarrhea: 10 healthy dogs (Control Group: 8 male, 2 female), which were brought for vaccination and/or routine check-up, aged between 2-6 mos from similar breeds. In order not to affect the results, the dogs included in the study were not selected among dog breeds such as Rottweiler, Doberman, German shepherd known to be susceptible to viral diseases [9]. All were admitted to Harran University Veterinary Faculty Animal Hospital. Anamnestic data revealed that none of the dogs in the present study were neither vaccinated nor dewormed and all were fed on commercial dry food. Also, it was learned that the dogs in the Experimental Group had had symptoms for the last 1-2 days (d) before admission, and that no treatment had been received.

This study protocol was approved by the ethics committee of the Faculty of Veterinary Medicine, Harran University (session and permit number: 2021-005/01-14).

### **Clinical examinations**

Clinical examinations of all dogs included in the study were performed in the same exam room specific to canine patients by the same personnel with minimal restrain in order not to influence the examination results. Within the scope of clinical examinations, body temperature, respiratory and heart rate measurements, lung and heart auscultation, mandibular, prescapular, superficial inguinal and popliteal lymph node palpations were performed. Stool samples were taken from all the dogs with rectal swab to investigate the presence of parasites and microscopic examination of the samples was performed (light microscope, 40x magnification, Olympus®). Dogs with comorbid diseases such as neurological (dogs that were possibly affected with CDV but without gastroenteritis findings), respiratory or dermatosis-related conditions and with any parasites were excluded from the study. That is, only dogs with AG were enrolled in the Experimental Group.

### **Collection of blood samples**

Venous blood samples from all dogs were taken from the vena cephalica (5-10 milliliters (mL)) venepuncture with minimal restrain. 3-5 mL of blood was added into tubes containing ethylenediaminetetraacetic acid ( $K_3$ EDTA) to be used for hemogram and the rest was collected with injectors containing heparin to be used for blood gases analysis.

### Blood gases and hemogram analysis

Blood gases (hydrogen ion concentration (pH), partial pressure of carbondioxide (pCO<sub>2</sub>), partial pressure of oxygen (pO<sub>2</sub>), base excess (BE), bicarbonate (HCO<sub>3</sub>), lactate, potassium,

sodium, chlorine concentrations and glucose levels) analysis was performed from heparinized blood samples with the GEM Premier Plus 3000 (74351, Blood Gas/Electrolyte Analyzer, Model 5700, Instrumentation Laboratories, USA) autoanalyzer. Hemogram analysis (leukocyte, lymphocyte, monocyte, granulocyte, erythrocyte (RBC), MCV, hemoglobin (Hb), hematocrit (Hct) mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and red cell distribution width (RDW)) was performed from venous blood samples with K<sub>3</sub>EDTA using MS4 (CFE 279, Hematology Analyzer, France) autoanalyzer as well. Blood gases and hemogram analyzes were performed within 5-10 minutes after sampling.

# Rapid antigen test applications and dividing experimental group into subgroups

In order to differentiate diseases causing gastrointestinal symptoms similar to CPV and CDV; Canine Adenovirus 2, Canine Influenza virus, Canine Coronavirus (Asan Easy Test CAV2/CIV/ CCV Ag, ASAN Pharm. Co., Ltd. Gyeonggi-do Korea, relative sensitivity: 93.10 %, relative specificity: 97.50 %) tests were performed according to the manufacturer's instructions. All test results were determined to be negative. Following blood gases and hemogram analyzes of all dogs in the Experimental Group, Canine Parvovirus (Asan Easy Test CPV Ag, ASAN Pharm. Co., Ltd. Gyeonggi-do Korea, relative sensitivity: 97.96 %, relative specificity: 97.50 %) and Canine Distemper Virus (Asan Easy Test CDV Ag, ASAN Pharm. Co., Ltd. Gyeonggi-do Korea, relative sensitivity: 97.96 %, relative specificity: 97.50 %) antigen tests were performed in accordance with the manufacturer's instructions. Based on the test results, the Experimental Group was divided into two subgroups: Canine Parvovirus (CPV Group) and Canine Distemper virus (CDV Group). The same tests (CAV2/CIV/CCV Ag, CPV and CDV Ag) were also applied to the dogs in the Control Group and the results were determined to be negative. Based on the results of rapid antigen tests, 18 dogs were enrolled in the CDV Group and 22 dogs in the CPV Group.

### Statistical analysis

The data were evaluated using SPSS 21.00 (SPSS for Windows®) statistical software. One sample Kolmogorov-Smirnov test [48] was applied to determine whether all data were parametric or non-parametric. Non-parametric data were evaluated as median (min, max) and parametric data as mean ( $\pm$ SD) with Mann Whitney U, Kruskal-Wallis test [47]. Receiver operating characteristic curve (ROC) analysis was used to determine the diagnostic cut-off values of the measured values, which were found to be useful in the differential diagnosis of the disease as a result of the comparison of blood gases and hemogram parameters. Statistical significance was considered as P<0.05 for all data.

### **RESULTS AND DISCUSSION**

### **Clinical examinations**

Clinical examinations including heart and respiratory rate, capillary refill time and body temperature measurements of the Control (n:10), CDV (n:18) and CPV groups (n:22) were determined to be different from each other (P=0.000). Besides, comparing the CPV and CDV groups, respiratory rate, capillary refill time and

body temperature were determined to be different from each other (P=0.000). Clinical examination findings are shown in TABLE I.

| TABLE I<br>Clinical examination findings |                              |                          |                          |                     |  |  |  |  |
|--|------------------------------|--------------------------|--------------------------|---------------------|--|--|--|--|
| Parameters                               | Control Group<br>(mean ± SD) | CDV Group<br>(mean ± SD) | CPV Group<br>(mean ± SD) | P value<br>(P<0.05) |  |  |  |  |
| RR (min)                                 | 35.9 ± 6.82c                 | 89.5 ± 5.37a             | 65.18 ± 15.05b           | 0.000               |  |  |  |  |
| HR (min)                                 | 79.50 ± 8.68b                | 100.22 ± 8.12a           | 108.09±21.14a            | 0.000               |  |  |  |  |
| CRT (sec)                                | 2.6 ± 0.51a                  | 1.83 ± 0.78b             | 2.86 ± 0.77a             | 0.000               |  |  |  |  |
| Temp (°C)                                | 38.1 ± 0.3c                  | 39.29 ± 0.28a            | 38.72 ± 0.88b            | 0.000               |  |  |  |  |

RR: Respiration rate, HR: Heart rate, CRT: Capillary fill time, Temp: Body temperature

### Hemogram findings

In all the groups, statistical differences were determined in the hemogram parameters such as WBC, granulocyte, MCV, MCH and MCHC values (P<0.05). Among these parameters, WBC (P=0.003), granulocyte (P=0.000) and MCV (P=0.001) values of the CPV Group were determined to be different from those of the CDV Group. Hemogram findings are shown in TABLE II.

| TABLE II<br>Hemogram findings |                              |                          |                          |                     |  |  |  |  |
|-------------------------------|------------------------------|--------------------------|--------------------------|---------------------|--|--|--|--|
| Parameters                    | Control Group<br>(mean ± SD) | CDV Group<br>(mean ± SD) | CPV Group<br>(mean ± SD) | P value<br>(P<0.05) |  |  |  |  |
| WBC                           | 14.73 ± 2.86a                | 17.61 ± 9.75a            | 8.50 ± 8.15b             | 0.003               |  |  |  |  |
| Lymphocyte                    | 4.08 ± 1.41                  | 3.86 ± 2.57              | 4.11 ± 2.96              | 0.950               |  |  |  |  |
| Monocyte                      | 0.97 ± 0.55                  | 1.32 ± 0.92              | 0.66 ± 1                 | 0.088               |  |  |  |  |
| Granulocyte                   | 9.68 ± 2.39a                 | 12.42 ± 8.54a            | 3.71 ± 5.36b             | 0.000               |  |  |  |  |
| RBC                           | 6.86 ± 0.78                  | 7.58 ± 1.51              | 6.81 ± 1.46              | 0.194               |  |  |  |  |
| MCV                           | 64.56 ± 6.52b                | 64.44 ± 8.21b            | 72.30 ± 5.31a            | 0.001               |  |  |  |  |
| НСТ                           | 45.71 ± 6.07                 | 48.42 ± 9.62             | 48.22 ± 14.89            | 0.823               |  |  |  |  |
| MCH                           | 23.07 ± 1.75a                | 19.60 ± 2.65b            | 20.55 ± 1.43b            | 0.000               |  |  |  |  |
| MCHC                          | 33.67 ± 4.22a                | 30.53 ± 2.03b            | 28.5 ± 1.79b             | 0.000               |  |  |  |  |
| RDW                           | 10.21 ± 1.23b                | 11.81 ± 2.52a            | 11.14 ± 0.95ab           | 0.075               |  |  |  |  |
| Hb                            | 15.51 ± 1.78                 | 14.73 ± 2.68             | 14.02 ± 3.05             | 0.352               |  |  |  |  |

WBC: White blood cell, RBC: Red blood cell, MCV: Mean corpuscular volume, HCT: Hematocrit, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, Hb: Hemoglobin

### **Blood gases analysis**

Parameters such as pH, Na, Cl, lactate and HCO<sub>3</sub> were determined to have statistical differences (P<0.05) as a result of blood gases analysis. Comparing the CPV and CDV groups, pH (P=0.001), lactate (P=0.004) and HCO<sub>3</sub> (P=0.001) levels were determined to be different from each other as well. Blood gases findings are shown in TABLE III.

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| Blood gases findings |                              |                          |                          |                     |  |  |  |  |  |
|----------------------|------------------------------|--------------------------|--------------------------|---------------------|--|--|--|--|--|
| Parameter            | Control Group<br>(mean ± SD) | CDV Group<br>(mean ± SD) | CPV Group<br>(mean ± SD) | P value<br>(P<0.05) |  |  |  |  |  |
| рН                   | 7.40 ± 0.34a                 | 7.37 ± 0.08a             | 7.29 ± 0.07b             | 0.001               |  |  |  |  |  |
| pCO <sub>2</sub>     | 36.71 ± 2.38                 | 35.82 ± 4.86             | 35.45 ± 6.48             | 0.824               |  |  |  |  |  |
| pO <sub>2</sub>      | 29.27 ± 2.05b                | 37.16 ± 10.50a           | 33.34 ± 8.63ab           | 0.072               |  |  |  |  |  |
| К                    | 4.10 ± 0.37                  | 3.97 ± 0.46              | 4.03 ± 0.69              | 0.846               |  |  |  |  |  |
| Na                   | 146.30 ± 4.62b               | 153.22 ± 7.87a           | 148.18 ± 6.78ab          | 0.022               |  |  |  |  |  |
| Ca                   | 1.05 ± 0.13                  | 1.06 ± 0.18              | 0.92 ± 0.23              | 0.085               |  |  |  |  |  |
| Cl                   | 113 ± 3.01b                  | 115.05 ± 7.41ab          | 109.54 ± 7.41a           | 0.044               |  |  |  |  |  |
| Glucose              | 113.20 ± 10.22               | 97.55 ± 21.79            | 92.31 ± 30.92            | 0.098               |  |  |  |  |  |
| Lactate              | 1.80 ± 0.25b                 | 1.76 ± 0.85b             | 3.13 ± 1.87a             | 0.004               |  |  |  |  |  |
| Base excess          | -2.57 ± 3.58                 | -3.78 ± 4.30             | -6.84 ± 7.72             | 0.119               |  |  |  |  |  |
| HCO <sub>3</sub>     | 21.80 ± 1.21a                | 20.71 ± 3.37a            | 17.66 ± 3.57b            | 0.001               |  |  |  |  |  |

pH: Power of hydrogen, pCO<sub>2</sub>: Partial pressure of carbon dioxide, pO<sub>2</sub>: Partial pressure of oxygen, K: Potassium, Na: Sodium, Ca: Calcium, Cl: Chlorine, HCO<sub>2</sub>: Bicarbonate

### Receiver operating characteristic curve analysis

Receiver operating characteristic curve (ROC) analysis of the parameters, which were determined to differ in the CPV from CDV Group as a result of hemogram analysis, was performed. Within the scope of ROC analysis, the calculated results for WBC were: Area under curve (AUC): 0.871, 95 % confidence interval (CI), Cut-off: 7.45, sensitivity: 72 %, specificity: 100 %; for granulocyte: AUC: 0.907, 95 % CI, Cut-off: 2.865, sensitivity: 77 %, specificity: 100 %; For MCV, AUC: 0.777, 95 % CI, Cut-off: 69.35, sensitivity: 81 %, specificity: 77 %, respectively. The ROC analysis findings and figures of hemogram parameters are shown in TABLE IV and FIG. 1, respectively.

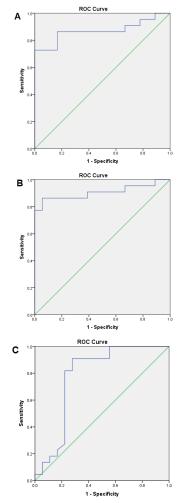


FIGURE 1. ROC analysis of WBC (A), granulocyte (B) and MCV (C) values. Diagonal segments are produced by ties

ROC analysis of statistically significant parameters of blood gases was performed. In the ROC analysis of blood gases parameters, which were determined to differ between the CPV and CDV groups, the calculated results for pH were: AUC: 0.821, 95 % Cl, Cut-off: 7.381, sensitivity: 90 %, specificity: 60.7 %; for lactate: AUC: 0.778, 95 % Cl, Cut-off: 2.15, sensitivity: 72 %, specificity: 75 %; For HCO<sub>3</sub>, AUC: 0.797, 95 % Cl, Cut-off: 21, sensitivity: 90 %, specificity: 64.3 %, respectively. ROC analysis findings and figures of blood gases parameters are shown in TABLE V and FIG. 2, respectively.

| <i>TABLE IV</i><br>ROC analysis findings of hemogram parameters                                      |       |       |       |       |       |       |      |                |        |
|--|-------|-------|-------|-------|-------|-------|------|----------------|--------|
| Asymp. 95 % CI   Parameter AUC Std. Error P value Asymp. 95 % CI Cut-off Sensitivity Specifity Obset |       |       |       |       |       |       |      | Observed Power |        |
| WBC  | 0.871 | 0.060 | 0.000 | 0.753 | 0.990 | 7.450 | 72 % | 100 %          | 88.0 % |
| Gra  | 0.907 | 0.052 | 0.000 | 0.804 | 1.000 | 2.865 | 77 % | 100 %          | 96.9 % |
| MCV  | 0.777 | 0.085 | 0.003 | 0.610 | 0.943 | 69.35 | 81 % | 77 %           | 94.5 % |

Gra: Granulocyte, AUC: Area under curve, Std. Error: Standard error, Asymp. CI: Asymptotic confidence interval, WBC: White blood cell, MCV: Mean corpuscular volume

*TABLE V* DC analysis findings of blood gases parameters

| Parameter        | AUC   | Std. Error | P value | Asymp. 95 % CI<br>Lower Bound Upper Bound |       | Cut-off | Sensitivity | Specifity | Observed Power |
|------------------|-------|------------|---------|---|-------|---------|-------------|-----------|----------------|
| рН               | 0.790 | 0.075      | 0.002   | 0.643                                     | 0.938 | 7.306   | 88 %        | 54 %      | 78.6 %         |
| Lactate          | 0.777 | 0.074      | 0.003   | 0.632                                     | 0.921 | 2.600   | 83 %        | 60 %      | 80.0 %         |
| HCO <sub>3</sub> | 0.759 | 0.080      | 0.005   | 0.602                                     | 0.916 | 17.20   | 88 %        | 50 %      | 76.3 %         |

AUC: Area under curve, Std. Error: Standart error, Asymp. CI: Asymptotic confidence interval, pH: Power of hydrogen, HCO<sub>2</sub>: bicarbonate

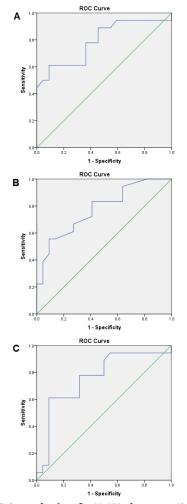


FIGURE 2. ROC analysis of pH (A), lactate (B) and HCO<sub>3</sub> (C) values. Diagonal segments are produced by ties

CPV and CDV infections cause various clinical findings with gastroenteritis, mostly in dogs younger than 6 mos and despite early diagnosis and therapeutic approaches, mortality rates have been reported to be 4-7 % [38] and 95 % [33], respectively. Considering that the techniques developed for definitive *ante-mortem* diagnosis are tiring, timeconsuming and require expertise and equipment [1, 18, 41], the importance of routine laboratory tests such as blood gases and hemogram measurements become evident in terms of diagnosis, differentiation and monitoring the complications associated with the viruses [17, 40, 46].

Clinical manifestations of CDV infection depend on viral virulence, environmental conditions and host immunity [14]. The main organ systems affected by CDV infection are respiratory, gastrointestinal and central nervous systems [4]. Fever, anorexia and lethargy are usually associated with viremia (1-3 d after the onset of infection). Since the typical neurological form is mostly observed in 1-3 w after the acute infection, respiratory findings such as conjunctivitis, pneumonia and gastrointestinal findings such as vomiting and diarrhea, which are usually hemorrhagic, are prominent in the acute period [2, 6, 13, 46]. Considering these findings, dogs with only gastroenteritis symptoms were included in this study within the scope of clinical manifestation of acute CDV infection in accordance with previous reports [6, 46].

Similarly, non-specific clinical findings such as fever, lethargy, anorexia and stagnation observed in CPV infection are associated with viremia (1-5 d after the onset of infection). In both CPV and CDV infections, findings related to dehydration and hypovolemia such as oral mucous membrane dryness, prolonged capillary refill time and loss of skin elasticity are associated with high-volume fluid and protein losses in the gastrointestinal tract [14, 36]. Capillary refill time (CRT) (2.86  $\pm$  0.77, P=0.000), which was determined to be higher in the CPV Group compared to the CDV Group, indicate that the fluid loss from the gastrointestinal tract in CPV infection is higher and tissue perfusion is more severely affected.

In previous reports, increased respiratory rate has been reported in CDV infection as a result of respiratory disorders such as interstitial pneumonia [25]. Compared to the CPV group, the higher respiratory rate ( $89.5 \pm 5.37$ , P=0.000) in the CDV group was consistent with this finding. It has been reported that high fever in CDV and CPV infections is associated with the viremia period [6, 20, 21, 31]. The characteristic of fever seen in the CDV and CPV groups ( $39.29 \pm 0.2$  and  $38.72 \pm 0.88$  °C, P=0.000) of the present study was interpreted as biphasic fever for CDV and CPV infections, which is often associated with viremia [7, 14].

Evaluation of blood gases in critical cases (such as CDV, CPV infections) in veterinary medicine makes it possible to detect physiological disorders early, warn the clinician against possible decompensations and guide treatment options [26]. Any change in bicarbonate or carbon dioxide pressure keeps the pH in balance by stimulating the compensation mechanism [11]. The medical treatment of diseases that cause severe gastroenteritis includes fluid therapy, nutritional care, antiemetic and antimicrobial drug applications [37, 40]. Decreased bicarbonate levels and base excess have been reported in dogs with CPV [36, 39] and dogs with CDV [17]. In addition, it has been reported that the increased pH value despite the low bicarbonate level is associated with the compensation mechanism and low bicarbonate and high

lactate levels are required for classification of metabolic acidosis [36]. Electrolyte disturbances due to vomiting and diarrhea are inevitable in dogs affected either by CPV or CDV infection, which causes gastroenteritis due to its pantropic nature [29]. As a result of blood gases analysis, significant differences were determined in pH (P=0.001), lactate (P=0.004) and HCO<sub>3</sub> (P=0.001) levels between the CPV and CDV groups in the present study. The lower pH and base excess along with higher lactate levels of the CPV group may indicate that dehydration and protein loss from the intestines are more severe and energy metabolism is more severely affected [8, 11]. Also, the chlorine level was detected to be lower in the Experimental Group than that of the Control Group (P=0.044). These findings were interpreted depending on the presence of relative free water deficit [12] in the dogs of the Experimental Group.

Many differences have been reported as a result of hematological analyzes performed in dogs with CDV or CPV [9, 16, 17, 20, 32, 34]. In addition to hematological analyzes, blood gases measurements are reported to be useful diagnostic and prognostic methods that are frequently used both for tentative diagnosis and confirmation of the diagnosis [8, 14, 22]. CDV persists in the bone marrow of infected dogs. This persistence causes erythroid hypoplasia and explains the anemia detected in CDV-infected dogs [17]. In addition, the fact that iron becomes less useful for the body as a result of the release of interleukin-6 also contributes to the formation of anemia [16, 31].

Similarly, it has been reported that low hemoglobin, hematocrit, MCV, MCH and MCHC levels determined in CPV infection are related to the disruption of iron recovery and/or iron metabolism in erythroid precursor cells [28]. Viral replication in lymph nodes observed in viral infections causes lymphopenia in the acute phase and subsequently leukopenia. After the initially observed leukopenia, lymphocytosis and thus leukocytosis have also been reported [17, 23]. In the hemogram analysis of the present study, WBC (P=0.003), granulocyte (P=0.000) and MCV (P=0.001) levels in the CPV Group were found to be different than those of the CDV Group. Also, differences were observed in terms of MCH (P=0.000) and MCHC (P=0.000) levels between the Experimental and Control groups. The more severe findings in the CPV Group compared to the CDV Group can be explained by the fact that the agent tends to replicate very rapidly in the gastrointestinal tract, lymphoid tissue and bone marrow cells, resulting in more severe immunosuppression [44].

In the comparative ROC analysis of the CPV and CDV groups of the present study, it was determined that pH (sensitivity: 90 %, specificity: 60.7 %, observed power: 78.6 %), lactate (sensitivity: 72 %, specificity: 75 %, observed power: 80 %) and HCO<sub>3</sub> (sensitivity: 90 %, specificity: 64.3 %, observed power: 76.3 %) in the blood gases analysis; WBC (sensitivity: 72 %, specificity: 100 %, observed power: 88 %), granulocytes (sensitivity: 77 %, specificity: 100 %, specificity: 90.9 %) and MCV (sensitivity: 81 %, specificity: % 77, observed power: 94.5 %) levels in the hemogram analysis were useful in establishing a routine laboratory test panel to make an etiological differentiation list.

### CONCLUSIONS

Although blood gases and hematological parameters do not have sufficient specificity in determining the etiology of diseases with gastroenteritis findings, they are highly important in terms of forming a differential diagnosis list and providing useful clinical information. As a result, it was concluded that the evaluation of WBC, granulocyte and MCV levels in hemogram and pH, lactate and HCO3 levels in blood gases as a routine laboratory test panel may be useful in differentiating between CPV infection and CDV infection in dogs only with AG as clinical manifestation.

### **CONFLICT OF INTEREST**

The authors declare that they have no conflicts of interest in the research.

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