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Hematological Status in Septic or Non Septic Dogs due to Parvoviral Enteritis

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Abstract

Canine parvovirus (CPV) is an important cause of morbidity and mortality for dogs younger than 1 year-old. Canine parvoviral enteritis (CPE) is a predisposing factor for the development of sepsis. The inflammatory response to the disease may have predictive value for the alterations in the presence of sepsis. Therefore, the diagnostic approach to a septic dog with CPE should include clinical examinations followed by routine laboratory examinations such as hemogram. In this study, a total of 61 dogs, aged 4-6 months, 7 healthy (Control Group) and 54 diseased dogs with clinical signs of CPE such as anorexia, vomiting and hemorrhagic enteritis (CPE Group) were used. CPE group was divided into Septic CPE (n: 25) and Non Septic CPE (n: 29) subgroups in accordance with 2001 systemic inflammatory response syndrome (SIRS) criterias. Clinical examinations and hemogram analysis from venous blood samples were performed. When compared to the Control group, the respiratory rate (RR), heart rate (HR) and body temperature of the dogs in the CPE group were higher ($p<0.000$) and the capillary refill time (CRT) was shorter ($p<0.014$). In the comparison of Septic CPE and Non Septic CPE groups, the RR was higher in the Septic CPE group ($p<0.001$). When compared to the Control group, the leukocytes (WBC), granulocyte, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and hemoglobin (Hb) values of the CPE group were lower ($p<0.031$) and the reticulocyte distribution width (RDW) value was higher ($p<0.001$). In the comparison of Septic CPE and Non Septic CPE groups, WBC, lymphocyte, monocytes and granulocyte values of the Septic CPE group were lower ($p<0.006$) and MCH values were higher ($p<0.004$). As a result, it was concluded that in accordance with the receiver operating characteristic (ROC) based diagnostic performance analysis, RR, WBC, lymphocyte, MCH, monocytes and granulocyte values can provide useful diagnostic information in differentiating dogs with septic and non septic CPE and may help identifying the disease severity earlier in triage and increase survival rate with early intervention.

Key Words: Dog, hemogram, parvoviral enteritis, sepsis.

Parvoviral Enteritise Bağlı Septik veya Septik Olmayan Köpeklerde Hematolojik Durum

Öz

1 yaşından küçük köpeklerde kanin parvovirus (CPV) önemli bir morbidite ve mortalite sebebidir. Kanin parvoviral enteritis (CPE), sepsis gelişimi için predispoze edici bir faktördür. Hastalığa verilen yangısal cevap, sepsis varlığında gözlenen değişimler için prediktif bir değere sahip olabilir. Bu sebeple, CPE'li septik bir köpeğe diagnostik yaklaşım klinik muayeneleri takiben hemogram gibi rutin laboravutar muayenelerini içermelidir. Bu çalışmada 4-6 aylık, sağlıklı 7 adet (Kontrol Grubu), anoreksi, kusma ve hemorajik enteritis gibi CPE'nin klinik bulgularına sahip 54 adet hasta (CPE Grubu), toplam 61 adet köpek kullanıldı. 2001 sistemik yangısal cevap sendromu (SIRS) kriterleri doğrultusunda CPE grubu köpekleri Septik CPE (n: 25) ve Non Septik CPE (n: 29) alt gruplarına ayrıldı. Tüm köpeklerin klinik muayeneleri ve venöz kan örneklerinden hemogram analizleri yapıldı. Kontrol grubu ile karşılaştırıldığında CPE grubu köpeklerinin solunum sayısı (RR), kalp ritmi (HR) ve vücut sıcaklığı değerleri daha yüksek ($p<0.000$), CRT değeri ise daha kısaydı ($p<0.014$). Septik CPE ve Non Septik CPE gruplarının karşılaştırılmasında ise RR değeri Septik CPE grubunda daha yüksekti ($p<0.001$). Kontrol grubu ile karşılaştırıldığında CPE grubunun lökosit (WBC), granülosit, ortalama hemoglobin miktarı (MCH), ortalama hemoglobin konsantrasyonu (MCHC) ve hemoglobin (Hb) değerleri daha düşük ($p<0.031$), retikülosit dağılım genişliği (RDW) değeri ise daha yüksekti ($p<0.001$). Septik CPE ve Non Septik CPE gruplarının karşılaştırmasında ise Septik CPE grubunun WBC, lenfosit, monosit, granülosit değerleri daha düşük ($p<0.006$), MCH değeri ise daha yüksekti ($p<0.004$). Sonuç olarak, alıcı işletim karakteristiği (ROC) temelli diagnostik performans analizi doğrultusunda RR, WBC, lenfosit, MCH, monosit ve granülosit değerlerinin ise septik ve non septik CPE'li köpeklerin ayırt edilmesinde faydalı diagnostik bilgi sağlayıp, triajda hastalık şiddetini daha erken tanımlayıp erken müdahale ile hayatta kalma oranını arttırabileceği kanısına varıldı.

Anahtar Kelimeler: Köpek, hemogram, parvoviral enteritis, sepsis.

INTRODUCTION

Canine parvoviral enteritis (CPE) is an acute, highly contagious and fatal viral disease. Although the disease affects dogs younger than 6 months-old, adult dogs with immunosuppression are also at risk. The most common form of CPE is acute hemorrhagic enteritis, characterized by severe villous damage (1). CPE is a predisposing factor for sepsis, as it

promotes intestinal bacterial translocation and severe immunosuppression (2). In addition, there are many factors contributing to the development of sepsis in canine parvovirus (CPV) infection such as cellular destruction, intestinal hypomotility, dysbiosis and tissue necrosis, and bacteremia resulting from translocation (3,4). Although the clinical manifestations of dogs with CPE are non specific, they correlate with enteritis. While symptoms such as anorexia, lethargy, and pyrexia are dominant in the initial phase, gastroenteritis findings such as vomiting and diarrhea become more evident later on. Feces may vary from mucoid to hemorrhagic (4,5). Impaired immunity with mucosal barrier damage increases susceptibility to secondary infections and significant changes are observed in hemogram parameters. Significant leukopenia (usually due to neutropenia and lymphopenia) in dogs with CPE is frequently observed as the virus targets mitotically active leukocytes, bone marrow, and lymphoid tissue. Neutropenia and bacterial overload reduce and/or prevent the elimination of luminal bacteria from the bloodstream (3,6,7), and the release of inflammatory mediators together with the progression of systemic inflammatory response syndrome (SIRS) contribute to bacterial translocation cycle and causes development of sepsis (4).

According to the most recent scientific consensus, the definition of sepsis is used to describe organ dysfunction triggered by the body's noxious inflammatory response to an infection (2,8). A conference was held in 1991 to establish a correlation between sepsis and SIRS (9). After the adaptation of the criteria determined as a result of this conference to animals, a series of modifications were proposed and it was observed that the cut-off values differed among researchers (10). Moreover, most clinicians report that the old consensus definition is not clear enough for sepsis definition and 71% of those surveyed by the European Society of Intensive Care Medicine (ESICM) did not cite a general sepsis definition despite the criteria which was set at the 1991 consensus conference (11). This gap in clinical practice and data from clinical studies had shown that SIRS and sepsis-related conditions require a revision. For this reason, the International Sepsis Definitions Conference was held in 2001 and in addition to 1991 SIRS criterias, it was emphasized that the evaluation of capillary refill time (CRT) or mucous membrane color changes can increase its specificity (2,11).

Since its transferral to veterinary practice, the definition of SIRS has been used frequently by clinicians and researchers for the diagnosis of sepsis (2). The definition of sepsis in veterinary practice is similar to the one used in human medicine and is characterized by SIRS. The clinical diagnosis of SIRS is made on the basis of abnormal findings in the heart and respiratory rate, body temperature and leukocyte counts (12). In cases of CPE, intestinal mucosal damage and villous atrophy may lead to malabsorption, diarrhea and vomiting which cause rapid shock and dehydration, and severe bacteremia may result in sepsis and death (2,13). Clinical findings vary not only depending on the damage to the originating organ, but also depending on the extent of damage to the secondary affected organs. For this reason, clinical examination and evaluation of hemogram findings are useful both in the decision of further diagnostic tests and in the prediction of the course of the disease (2).

The diagnostic approach to a septic dog with CPE should include clinical examinations followed by routine laboratory examinations such as hemogram. Hemogram analysis can reveal abnormalities in different cellular lineages. Among the hemogram parameters, hematocrit can show anemia secondary to blood loss, hemolysis, oxidative stress and decreased erythrocyte production. Polycythemia may indicate hemoconcentration and splenic contraction in hypovolemic animals. Lymphopenia and leukopenia associated with immunosuppression and lymphocyte apoptosis may also persist. In addition, disseminated intravascular coagulopathy (DIC) due to platelet consumption has also been reported as a common finding associated with thrombocytopenia (5,10,14).

For this reason, the aim of this study is to evaluate the diagnostic effectiveness of clinical and hemogram parameters comparatively and to emphasize their importance in routine examinations in dogs with CPE which were classified as septic and non-septic according to 2001 SIRS criteria.

MATERIAL AND METHODS

This study was conducted with the approval of the Harran University Animal Experiments Local Ethics Committee dated 28/03/2022, number 2022/002.

The animal material of this study consisted of a total of 61 dogs, aged 4-6 months, non-neutered (31 male, 30 female), 7 healthy (Control Group) and 54 diseased dogs with clinical signs of CPE such as anorexia, lethargy, vomiting and hemorrhagic enteritis (CPE Group). All dogs included in the study were unvaccinated and mixed breed. Breeds known to be predisposed to CPE, such as German shepherds and Dobermans, were not included in the study. Body weights were determined as 8.6 (7.9-12.4) kg in the Control Group and 8.65 (5.7-13.1) kg in the CPE Group. In addition, anamnestic data revealed that all dogs in the study were fed on a commercial dry dog food, and no treatment was given for non-specific gastroenteritis symptoms such as vomiting and diarrhea.

Inclusion and Exclusion Criteria

Inclusion criterias were the presence of acute clinical manifestations of CPE (anorexia, vomiting, lethargy, and hemorrhagic enteritis) (1,2), not receiving any treatment and positive result of canine parvovirus (CPV) rapid test (CDV/CPV/CAV-2 Antibody (Ab), Biotech Laboratories, USA) which utilizes the principle of lateral flow immunochromatographic assay technique. Dogs that were determined to have gastroenteritis or comorbid diseases of different etiologies as a result of clinical, laboratory and rapid diagnostic test kit applications were not included in the study.

Clinical Examinations

Clinical examinations included respiratory rate (RR), heart rate (HR), capillary refill time (CRT), body temperature measurements, as well as evaluation of mucous membranes, lung and heart auscultation, and examination of palpable lymph nodes. In addition, fecal samples were taken from all dogs

and microscopic (Olympus CX43, light microscope, x40 magnification, Tokyo, Japan) examinations were performed in order to investigate the presence of parasites/parasite eggs.

Application of Rapid Diagnostic Test Kits

Canine distemper virus, canine parvovirus, canine adenovirus type-2 antibody (CDV, CPV, CAV-2, Ab) rapid diagnostic test kits were applied to all the dogs in accordance with the manufacturer's instructions (CDV/CPV/CAV-2 Ab, Biotech Laboratories, USA. Compared to PCR, for CDV, specificity: 98.3% sensitivity: 96.1%; for CPV, specificity: 98.8% sensitivity: 92%; for CAV-2, specificity: 97.8% sensitivity: 100%). In addition, the rapid diagnostic test for Giardia antigen (Giardia Ag, VETSCAN, Zoetis, USA. Compared to PCR, specificity: 99.3% sensitivity: 98.1%) from fecal samples was performed according to the manufacturer's instructions. As a result of rapid diagnostic test kit application, it was determined that CPV Ab results of all the dogs with gastroenteritis were positive, and CDV Ab, CAV-2 Ab, Giardia Ag rapid test kit results and microscopic fecal examination results were negative. The same examinations and test were also applied to the dogs in the Control Group and results were found to be negative.

Forming Subgroups

Dogs included in the CPE Group as a result of clinical and laboratory examinations and rapid diagnostic test kit application results were divided into two subgroups as Septic CPE and Non Septic CPE in accordance with 2001 SIRS criteria. Confirmation of the 2001 SIRS criteria was accepted as the presence of at least two of the following criterias; body temperature <37.8 °C or >39.4 °C, heart rate >140 bpm, respiratory rate >30 breaths/minute, WBC <6000 or >16000 cells/µL (11). Considering these criterias, 25 dogs with CPE were included in the Septic CPE Group and 29 dogs in the Non Septic CPE Group.

Blood Sampling and Laboratory Examinations

Venous blood samples from vena cephalica (2-4 mL) were obtained from all the dogs with minimal restraint and patient stress. The venous blood samples were transferred into tubes containing K_3EDTA and measured without waiting using a hematology autoanalyzer (Sysmex pocH-100i, SYSMEX Corp, Japan). Within the scope of hemogram analyses, white blood cell (WBC), lymphocyte, monocyte, granulocyte, red blood cell (RBC), mean corpuscular volume (MCV), hematocrit (Hct), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), reticulocyte distribution width (RDW) and hemoglobin (Hb) measurements were performed in the central laboratory of the animal hospital.

Statistical Analysis

Statistical analysis of all data was performed using SPSS 25.00 (IBM, USA) software. Kolmogorov-Smirnov test was used to determine whether the data were parametric or non-parametric, and Mann Whitney U test was used to determine the p values. Non-parametric data were presented as median (min, max). ROC analyses were performed using the same statistical software to demonstrate the clinical significance of the parameters which were determined to have statistical significance as a result of the analysis. Within the scope of ROC analyses, area under curve (AUC, >0.600), p value (< 0.05), sensitivity and specificity (> 70%) parameters were evaluated. Statistical significance was accepted as p <0.05, CI = 95% for all the data.

RESULTS

Clinical Examination Results

As a result of clinical examinations, it was determined that character of diarrhea was hemorrhagic in all dogs in the CPE group. Vomiting was present in 50 of 54 diseased dogs. Skin turgor time was 5 (3-6) seconds in CPE group and 2 (2-4) seconds in Control group (p<0.000). The mucous membranes were hyperemic in 44 of the CPE group dogs, while 10 dogs had pallor. Lymphadenopathy was detected in 26 of 54 diseased dogs.

Compared to the Control Group, it was determined that RR, HR and body temperature values of the CPE Group were higher (p<0.000) and CRT value was shorter (p<0.014). Comparison of clinical examination findings of Control with CPE groups is presented in Table 1. In the comparison of Septic CPE and Non Septic CPE groups, RR value was higher in the Septic CPE Group (p<0.001). In the evaluation of the gingival mucous membrane, a marked hyperemic appearance was detected in dogs in the Septic CPE Group (23 out of 25 dogs). No statistical difference was observed in other clinical examination parameters (p>0.05). Comparison of clinical examination findings of Septic with Non Septic CPE groups is presented in Table 2.

Table 1. Comparison of clinical examination findings of control with CPE groups

Parameters	**Control Group** (n:7) Median (min, max)	**CPE Group** (n:54) Median (min, max)	P value
RR (breaths/min)	35 (27, 46)	88 (68, 99)	0.000
HR (beats/min)	77 (65, 88)	102 (84, 164)	0.000
CRT (seconds)	3 (2, 3)	2 (1, 3)	0.014
Temp (°C)	38.10 (37.70, 38.50)	39.25 (38.00, 40.50)	0.000

RR: Respiratory rate, HR: Heart rate, CRT: Capillary refill time, Temp: Body temperature.

Table 2. Comparison of clinical examination findings of septic with Non Septic CPE groups

Parameters	**Septic CPE Group** (n: 25) Median (min, max)	**Non Septic CPE** Group (n: 29) Median (min, max)	P value
RR (breaths/min)	92 (79, 99)	84 (68, 99)	0.001
HR (beats/min)	105 (90, 164)	101 (84, 164)	0.137
CRT (seconds)	2 (1, 3)	2 (1, 3)	0.518
Temp (°C)	39.30 (38.80, 40.50)	39.2 (38, 40.50)	0.294

RR: Respiratory rate, HR: Heart rate, CRT: Capillary refill time, Temp: Body temperature.

Hemogram Findings

Compared to the Control Group, WBC, granulocyte, MCH, MCHC and Hb values were lower ($p<0.031$) and the RDW value was higher ($p<0.001$) in the CPE group. However, no difference was detected in terms of lymphocyte, monocytes, RBC, MCV and Hct values ($p>0.05$). Comparison of hemogram results of Control with CPE groups is presented in Table 3. In the comparison of Septic CPE and Non Septic CPE groups, it was observed that WBC, lymphocyte, monocytes and granulocyte values of the Septic CPE Group were lower ($p<0.006$) and MCH values were higher ($p<0.004$). No difference was detected in terms of RBC, MCV, Hct, MCHC, RDW and Hb values ($p>0.05$). Comparison of hemogram results of Septic with Non Septic CPE groups is presented in Table 4.

Table 3. Comparison of hemogram results of Control with CPE groups

Parameters	Control Group (n: 7) Median (min, max)	CPE Group (n: 54) Median (min, max)	P value
WBC (m/mm³)	14.76 (8.80, 18.50)	9.90 (1.29, 22.47)	0.009
Lym (m/mm³)	4.17 (2.10, 5.16)	3.70 (1.01, 12.32)	0.973
Mon (m/mm³)	0.80 (0.10, 1.70)	0.54 (0.05, 5.90)	0.393
Gra (m/mm³)	9.79 (5.45, 13.40)	4.41 (0.20, 14.39)	0.004
RBC (M/mm³)	6.90 (5.79, 7.86)	7.09 (4.06, 10.57)	0.333
MCV (fl)	63.85 (56.00, 73.20)	69.20 (48.70, 91.30)	0.374
Hct (%)	44.78 (37.21, 51.56)	48.10 (26.50, 84.40)	0.122
MCH (pg)	23.80 (21.76, 25.11)	19.40 (13.00, 24.10)	0.000
MCHC (g/dl)	32.45 (28.44, 39.42)	29.30 (20.50, 35.80)	0.025
RDW (fl)	9.70 (8.26, 11.10)	10.85 (8.90, 18.00)	0.001
Hb (g/dl)	15.36 (14.47, 19.70)	14.20 (6.70, 21.40)	0.031

WBC: White blood cell, Lym: Lymphocyte, Mon: Monocyte, Gra: Granulocyte, RBC: Red blood cell, MCV: Mean corpuscular volume, Hct: Hematocrit, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Reticulocyte distribution width, Hb: Hemoglobin.

Table 4. Comparison of hemogram results of Septic with Non Septic CPE groups

Parameters	Septic CPE Group (n: 25) Median (min-max)	Non Septic CPE Group (n: 29) Median (min-max)	P value
WBC (m/mm³)	6.64 (1.29, 16.90)	13.11 (4.59, 22.47)	0.000
Lym (m/mm³)	2.77 (1.01, 6.56)	4.64 (1.24, 12.32)	0.006
Mon (m/mm³)	0.35 (0.05, 2.50)	0.95 (0.14, 5.90)	0.001
Gra (m/mm³)	1.87 (0.20, 9.33)	7.02 (1.02, 14.39)	0.000
RBC (M/mm³)	7.36 (5.13, 10.54)	6.91 (4.06, 10.57)	0.557
MCV (fl)	70.10 (62.60, 78.80)	66.20 (48.70, 91.30)	0.078
Hct (%)	53.70 (26.90, 72.50)	45.50 (26.50, 84.40)	0.356
MCH (pg)	20.70 (16.80, 24.10)	18.20 (13.00, 23.00)	0.004
MCHC (g/dl)	29.80 (24.30, 35.80)	28.70 (20.50, 32.20)	0.168
RDW (fl)	11.20 (10.00, 13.70)	10.80 (8.90, 18.00)	0.520
Hb (g/dl)	15.30 (11.00, 21.10)	12.70 (6.70, 21.40)	0.060

WBC: White blood cell, Lym: Lymphocyte, Mon: Monocyte, Gra: Granulocyte, RBC: Red blood cell, MCV: Mean corpuscular volume, Hct: Hematocrit, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Reticulocyte distribution width, Hb: Hemoglobin.

ROC Analyses Findings

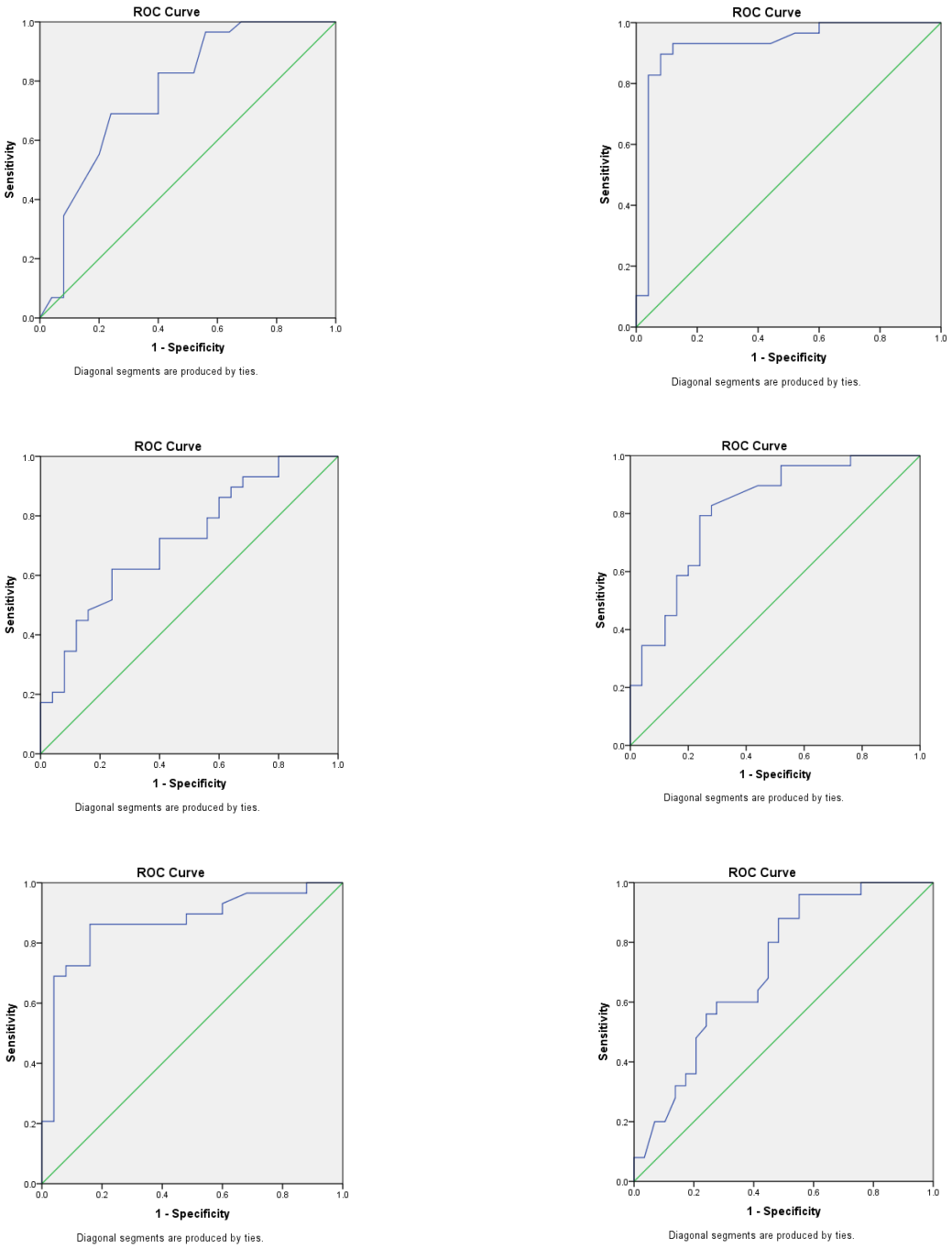
The diagnostic performances of the parameters such as respiratory rate, WBC, lymphocyte, monocyte, granulocyte and MCH values that were determined to be statistically different as a result of the comparison of the Septic CPE and Non Septic CPE groups were investigated by ROC analysis. In order to distinguish septic dogs from non-septic ones, it was determined that respiratory rate had good AUC (0.765), excellent sensitivity (100%) and low specificity (32%), WBC value had excellent AUC (0.924), sensitivity (93.1%) and specificity (88%), lymphocyte and MCH values had good AUC (0.716 and 0.717, respectively), sensitivity (72.4% and 60%, respectively) and specificity (60% and 58.6%), and monocyte and granulocyte values had good AUC (0.815 and 0.866, respectively), sensitivity (82.8% and 86.2%, respectively) and specificity (72% and 84%, respectively). ROC analysis results of Septic with Non Septic CPE groups comparison are presented in Table 5 and ROC curves of diagnostic performance analyses are presented in Graph 1.

Table 5. ROC analysis results of Septic with Non Septic CPE groups comparison

Parameters	AUC	Std. Error	AsympSig	Asymptotic 95% Confidence Interval		Cut-off value	Sensitivity	Specificity
				Lower Bound	Upper Bound			
RR (breaths/min)	0.765	0.067	0.001	0.634	0.896	77.5	100%	32%
WBC (m/mm³)	0.924	0.042	0.000	0.841	1.000	8.75	93.1%	88%
Lym (m/mm³)	0.716	0.069	0.007	0.580	0.852	2.97	72.4%	60%
Mon (m/mm³)	0.815	0.059	0.000	0.700	0.930	0.40	82.8%	72%
Gra (m/mm³)	0.866	0.052	0.000	0.764	0.968	3.84	86.2%	84%
MCH (pg)	0.717	0.069	0.006	0.580	0.853	19.20	64%	58.6%

RR: Respiration rate, WBC: White blood cell, Lym: Lymphocyte, Mon: Monocyte, Gra: Granulocyte, MCH: Mean corpuscular hemoglobin, AUC: Area under curve, Std.Error: Standard error, Asymp sig: Asymptotic significance

Graph 1. ROC curves of diagnostic performance analyses



Receiver Operating Characteristic (ROC) curve analysis of respiratory rate (A), WBC (B), lymphocyte (C), monocyte (D), granulocyte (E) and MCH (F) values. Diagonal segments are produced by ties.

DISCUSSION AND CONCLUSION

In the present study, the diagnostic performances of clinical and hemogram parameters of dogs with CPE, which were classified as septic and non septic according to 2001 SIRS criteria, were evaluated.

Dogs younger than 1 year-old are frequently diagnosed with gastrointestinal infections and among the viral agents, CPV is an important cause of morbidity and mortality (7). The virus spreads from animal to animal by the oronasal route and shows tropism to lymphoid tissue, bone marrow, and intestinal epithelium. In addition, in dogs younger than 3 week-old, the virus can also affect the myocardium (15). In addition, it has been reported that dogs less than 6 month-old, unvaccinated or given an inadequate/wrong vaccination program are susceptible to CPE (2,3,16). In the present study, the rate of sepsis development in dogs with CPE was determined as 46.29%. However it should be kept in mind that the population characteristics including an overrepresentation of animals within the susceptible age group and being unvaccinated may also have contributed for the discrepancy between the results obtained in this study and the ones previously cited.

The clinical signs of animals affected by sepsis reflect the systemic inflammatory status as well as changes in vitals such as body temperature, heart and respiratory rate. These parameters should be evaluated on admission to the hospital, and the diagnosis of sepsis should be made when the presence of infection with SIRS is detected. The inflammatory response to the disease may have predictive value for the changes observed in the presence of sepsis. It has been reported that heart and respiratory rate as well as leukocyte count considered as mortality-related parameters (2).

Non-specific findings such as pyrexia, lethargy, anorexia, increased respiratory rate are associated with viremia in 1-5 days after the onset of CPV infection. Dehydration and hypovolemia resulting from fluid loss due to vomiting and diarrhea impair tissue perfusion, and thus mucous membrane color changes, tachycardia, and prolonged CRT can be observed (7). Therefore, findings such as dryness of mucous membranes, prolonged CRT and loss of skin elasticity in CPV infections are associated with a large amount of fluid and protein loss from the gastrointestinal tract (16). In the present study, it was determined that the RR, HR and body temperature values of CPE Group were higher ($p<0.000$) and the CRT value was lower ($p<0.014$) when compared to the Control Group. These differences were thought to be related to the hemodynamic response to maintain tissue perfusion (2). In the comparison of Septic CPE and Non Septic CPE groups, only the RR value differed statistically and it was found to be higher in the Septic CPE group ($p<0.001$). RR is the sentinel and arguably most important vital sign because its normal values are breached before those of other vital signs in nearly all states of clinical decline. Changes in respiratory rate are often the earliest warning of SIRS, sepsis, respiratory insufficiency and shock among others. In these conditions, abnormalities in RR first herald the need for additional patient assessment and rapid intervention to prevent further decline. Tachypnea is often the first sign of SIRS, sepsis and respiratory insufficiency (17). Therefore, although traditional resuscitation goals such as normalization of respiratory rate may be insufficient to detect tissue hypoxia, these parameters should not be ignored (15). Optimization and normalization of mucous membrane color along with vitals increases survival rate in dogs with CPE.

Evaluation of clinical parameters such as CRT, heart and respiratory rate and hydration status along with routine laboratory tests such as hemogram provide important clinical information for diagnosis, differential diagnosis and monitoring the complications secondary to viral infection (15, 16). Depending on the tropism of CPV, clinical and hemogram findings differ according to the affected cell type. Immunosuppression may occur due to the death of myeloproliferative cells and thymic lymphocytosis (2,16). Mild to severe leukopenia has been reported in dogs with CPE (7). This is associated with viral replication in bone marrow and lymphatic tissue that destroys active mitotic myeloid precursors and lymphoid cells. It was reported that leukopenia at admission and 24 and 48 hours after admission could be used to predict outcome and increases over time in total WBC and absolute differential leukocyte counts would be associated with better outcome (1,7,10). However, the occasionally observed leukocytosis in cases of CPE may be due to primary or secondary bacterial infection, acute intravascular hemolysis, secondary to increased cell production by the bone marrow causing a shift of cells from the marginal pool to the circulation, or damage to the liver and/or other organs. In addition, it has been reported that neutrophilia and lymphopenia may be associated with a severe inflammatory reaction induced by bacterial infections in cases of CPE (18). Moreover, common hematological abnormalities such as low levels of RBC, MCH, MCHC and Hb have been reported to be associated with regenerative anemia and/or iron deficiency anemia due to viral persistence in the bone marrow. However, significant dehydration due to fluid loss from the gastrointestinal tract may mask anemia and cause relative polycythemia (19). The decrease in Hb level may be due to blood loss with feces and/or vomiting in CPE cases. Furthermore, low Hb levels may result from reduced erythropoiesis due to direct damage by CPV to the bone marrow, and accumulation of toxic waste products during the viremia and febrile phase as well as the dog's previous poor health (18,20). Besides, the changes in these parameters may be associated with hypochromic anemia caused by proinflammatory cytokines and the disruption of the development of reticulocytes by converting iron into a less usable form (16). In the present study, the WBC, granulocyte, MCH, MCHC and Hb values of the CPE Group were lower ($p<0.031$) and the RDW value was higher ($p<0.001$) when compared to the Control Group. Considering the presence of sepsis, in the Septic CPE Group, the WBC, lymphocyte, monocytes and granulocyte values were found to be lower ($p<0.006$) and MCH value was found to be higher when compared with the Non Septic CPE Group ($p<0.004$). These differences were interpreted as a result of the destruction of hematopoietic linage precursors, depletion of lymphoid organs and massive intestinal recruitment in the presence of sepsis (10). Low MCH, MCHC and Hb levels of

the CPE Group compared with the Control Group are associated with iron recovery and/or disruption of iron metabolism in erythroid precursor cells (2,16). The high MCH value observed in the Septic CPE Group was thought to be related with not having enough vitamin B12 or folic acid in the body as a result of malnutrition and/or malabsorption due to villous atrophy (10,16).

Monocytes have an essential role in CPE due to their functions such as removal of necrotic debris, viral inactivation, response to foreign bodies and phagocytosis of old or abnormal erythrocytes. In previous studies, it was reported that an increase in monocyte counts had prognostic value and were associated with higher survival rate (21,22). The low monocyte levels detected in the Septic CPE Group of the present study were consistent with previous studies, and it was thought that this finding might be related to immunosuppression due to lymphoid tissue damage (7). In addition, this finding can be explained by the fact that monocytes begin to migrate to the inflamed tissue when the inflammatory response begins as a result of infection (23).

The limitations of this study are the limited number of animals which may influence the results of the ROC-based diagnostic performance analysis results and the evaluation of hemogram analysis within the scope of routine laboratory examination.

Although interest in routine hematological parameters has increased recently (24), data on clinical and hematological parameters in dogs with parvoviral enteritis and sepsis are limited. With this study, based on the ROC-based diagnostic performance analysis, it was observed that RR, WBC, lymphocyte, monocytes, granulocyte and MCH parameters in the presence of sepsis have higher diagnostic performance and provide clinically important information in routine clinical and laboratory examinations. As a result, it was concluded that the evaluation of WBC, lymphocyte, monocytes, granulocyte and MCH values together with clinical examination findings in dogs with CPE who developed sepsis according to 2001 SIRS criteria, may improve early identification of severely ill patients at triage and allow more aggressive and timely interventions to improve the prognosis of these patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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