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RESEARCH ARTICLE

Evaluation of Relationship Between C-Reactive Protein, Leukocyte Count and Platelet Indices in Dogs with Leukocytosis

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ABSTRACT

A complete blood count and acute-phase protein analyses are the laboratory tests that are used in veterinary medicine practice. Leukocytes, also known as white blood cells (WBCs), are the primary biological components of inflammatory and immunological responses. C-reactive protein (CRP) is a powerful predictor of inflammation and/or infection in veterinary medicine. Starting at that point, the investigation of the alterations and relationship between WBC count, platelet indices, and blood serum CRP levels in dogs with leukocytosis was the aim of this study. A total of 135 blood analyses records, from January 2018 to December 2022, of dogs were analyzed. The inflammatory panel of complete blood count data, including WBC, PLT, MPV, PDW, PCT, and MPV/PLT, and CRP levels in blood serum chemistry analyses were investigated. The inflammatory panel of complete blood count data was categorized according to CRP levels in blood serum chemistry analyses. There was no significant difference in platelet indices according to the blood serum levels of CRP in the dogs' blood analyses records. The WBC count in dogs with an equal or above 10 mg.dL^{-1} CRP level was significantly higher than the other levels of CRP. A moderately positive correlation was detected between CRP and WBC in the blood analyses records of all dogs, undivided according to inflammatory status, and of dogs with inflammation status regardless of etiology. Consequently, in veterinary clinical practice, C-reactive protein measures in dogs may be more applicable in cases where an important rise in WBC over the cut-off value is observed in the complete blood count, commonly used to diagnose inflammatory or infectious status.

Keywords: Complete blood count; C-reactive protein; Dog; Leukocytosis

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Lökositozlu Köpeklerde C-Reaktif Protein, Lökosit Sayısı ve Trombosit İndeksleri Arasındaki İlişkinin Değerlendirilmesi

ÖZ

Tam kan sayımı ve akut faz protein analizleri veteriner hekimlik uygulamalarında kullanılan laboratuvar testleridir. Beyaz kan hücreleri (WBC) olarak da bilinen lökositler, enflamatuar ve immünolojik yanıtların birincil biyolojik bileşenleridir. C-reaktif protein (CRP) veteriner hekimlikte enflamasyon ve/veya enfeksiyonun güçlü bir belirleyicisidir. Bu noktadan hareketle, lökositozlu köpeklerde WBC sayısı, trombosit indeksleri ve kan serumu CRP seviyeleri arasındaki değişikliklerin ve ilişkinin araştırılması bu çalışmanın amacını oluşturmuştur. Ocak 2018'den Aralık 2022'ye kadar köpeklere ait toplam 135 kan tahlili kaydı analiz edilmiştir. WBC, PLT, MPV, PDW, PCT ve MPV/PLT dahil olmak üzere tam kan sayımı verilerinin enflamatuar paneli ve kan serumu kimyası analizlerinde CRP seviyeleri araştırıldı. Tam kan sayımı verilerinin enflamatuar paneli, kan serumu kimyası analizlerindeki CRP düzeylerine göre kategorize edildi. Köpeklerin kan serumu CRP seviyelerine göre trombosit indekslerinde anlamlı bir fark bulunmadı. CRP seviyesi 10 mg/dL ve üzerinde olan köpeklerde WBC sayısı diğer CRP seviyelerine göre anlamlı derecede yüksekti. Yangı durumuna göre ayrılmamış tüm köpeklerin ve etiyoloji gözetmeksizin yangı durumu olan köpeklerin kan tahlillerinde CRP ve WBC arasında orta düzeyde pozitif bir korelasyon tespit edilmiştir. Sonuç olarak, veteriner klinik uygulamalarında, köpeklerde C-reaktif protein ölçümleri, enflamatuar ya da enfeksiyöz durumu teşhis etmek için yaygın olarak kullanılan tam kan sayımında WBC'de kesme değerinin üzerinde önemli bir artış gözlendiği durumlarda daha uygulanabilir olabilir.

Anahtar Kelimeler: C-reaktif protein; Köpek; Lökositoz; Tam kan sayımı

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INTRODUCTION

A complete blood count is a supplementary laboratory test that determines the quantity of white and red blood cells circulating in the circulation. It is commonly requested by veterinarians and serves as a regular examination of healthy and ill animals (Moruzi et al. 2023). Leukocytes, also known as white blood cells (WBCs), are the primary biological components of inflammatory and immunological responses. They defend the body against infections and neoplasia and aid in the healing of injured tissue (Moruzi et al. 2023). The leukogram, which is part of the complete blood count (CBC), is an ordered tabulation of the total nucleated cell concentration as well as the concentrations of particular WBC types found in the blood sample, also known as the WBC differential (Kritsepi-Konstantinou and Oikonomidis 2016; Wood 2022b). Leukogram abnormalities include quantitative or numerical concentration abnormalities as well as morphologic abnormalities in WBCs (Wood 2022a). WBC concentrations are evaluated by comparing them to species-specific reference values (Wood 2022a). The reference values of WBC concentrations for dogs range approximately within 5.0-14.5×10^3.μL^{-1} (Kritsepi-Konstantinou and Oikonomidis 2016; Fielder 2022; McCourt and Rizzi 2022). Only absolute numbers should be considered when making interpretations (Wood, 2022a). Abnormalities in total WBC concentration only serve to alert the physician to search for and evaluate abnormalities in cell distributions in the differential (Wood, 2022a). Even if the overall WBC counts are normal, the differential may have one or more distributional abnormalities (Wood, 2022a). Leukocytosis is a rise in total WBC concentration, whereas leukopenia is a reduction in total WBC concentration (Wood, 2022a). Inflammatory, infectious, and immunologic responses can be interpreted by using a leukogram (McCourt and Rizzi 2022; Wood 2022b).

Acute-phase proteins (APP), being a response to release proinflammatory cytokines, are produced in situations ranging from infectious diseases to trauma (Murata et al. 2004; Kocaturk et al. 2010; Anziliero et al. 2013; Ok et al. 2015). In veterinary medicine, clinic-laboratory examinations have included the use of APPs to assess healthy and sick animals (Murata et al. 2004; Ok et al. 2015). C-Reactive Protein (CRP) is recognized as a powerful predictor of inflammation and/or infection in veterinary medicine (Anziliero et al. 2013). CRP activities rely on its ability to attach to bacteria and stimulate complement binding, allowing phagocytes to pick up bacteria (Alves et al. 2020). CRP also stimulates monocytes and macrophages to produce cytokines, inhibits chemotaxis, and modulates neutrophil activity (Alves et al. 2020; Malin and Witkowska-Pilaszewicz 2022). CRP is recognized to be a significant APP in dogs, and increased CRP values have been found in dogs with systemic inflammation (Anziliero et al. 2013; Christensen et al. 2014; Ok et al. 2015). Infectious or inflammatory conditions can cause CRP serum concentrations to rapidly rise from <1 mg.L^{-1} to >100 mg.L^{-1} in dogs (Eckersall and Bell 2010). Various studies have produced various upper-point values for the reference interval (RI) for CRP (Otabe et al. 1998; Martínez-Subiela et al. 2004; Kjelgaard-Hansen 2010; Casella et al. 2013; Malin and Witkowska-Pilaszewicz 2022). The technique, procedure, reagents and anticoagulants, and equipment may all be contributing factors to this difference between studies or laboratories (Malin and Witkowska-Pilaszewicz 2022).

Many automated hematology analyzers frequently used in veterinary clinics measure platelet number, size, and total platelet mass, which might offer clinically important information in some situations (Smith et al. 2014; Llewellyn et al. 2017). The platelet indices (PIs) include the following parameters: the number of platelets (PLT) that circulate in blood flow; the mean platelet volume (MPV), quantifying platelet size; the plateletcrit (PCT), which estimates platelet mass; and the platelet distribution width (PDW), revealing platelet size variability (Smith et al. 2014; Llewellyn et al. 2017). In many instances, elevated MPV and PDW indicate the presence of bigger, immature platelets released into the circulation in response to increased platelet synthesis (Llewellyn et al. 2017). The increase in plasma thrombopoietin concentration is caused by a decrease in platelet mass, which contributes to an increase in megakaryocytopoiesis. This condition may be further exacerbated when inflammatory cytokines are present (Yuri Gasparyan et al. 2011; Llewellyn et al. 2017). So, it is expressed that MPV serves as a marker of inflammation, disease activity, and the efficiency of anti-inflammatory therapy in various chronic inflammatory illnesses (Yuri Gasparyan et al. 2011). In addition, it is also stated that the size of circulating platelets may vary depending on the intensity of inflammation (Yuri Gasparyan et al. 2011). It is informed that the alterations for MPV, PCT, and PDW in PI were detected in dogs with inflammatory or infectious conditions (Smith et al. 2014).

The purpose of this study was to investigate the alterations and relationships between WBC count, platelet indices, and blood serum CRP levels in dogs with leukocytosis.

MATERIALS AND METHODS

Materials

The blood analyses data, including both complete blood counts and blood chemistry analyses of dogs, comprised the materials of the study. A total of 135 blood analyses records, from January 2018 to December 2022, of dogs admitted to the department of internal medicine clinic of Hatay Mustafa Kemal University, Veterinary Health, Practice, and Research center were obtained.

Methods

The blood analyses were performed via automated blood count device (MS4e, Melet Schloesing Laboratoires, France) and automated biochemistry analysis device (Chem 200vet, Gesan, Italy). The existence of both complete blood counts and blood serum chemistry analyses of each dog was used as inclusion criteria for blood analyses records. Another inclusion criteria was the existence of C-reactive protein (CRP) analysis in the blood serum chemistry analysis and the existence of white blood cells (WBC), platelet indices (PI) including platelets (PLT), platelet distrubution width (PDW), main platelet volume (MPV), and plateletcrit (PCT) counts in the complete blood count. The main platelet volume-to-platelet ratio (MPV/PLT) was also calculated. Data collection was conducted by using patient registries and patient monitoring software (EVET, Hasvet, Türkiye). The inflammatory panel of complete blood count data, including WBC, PLT, MPV, PDW, PCT, and MPV/PLT, were categorized according to CRP levels in blood serum chemistry analyses. The presence of infection or inflammation was considered when the WBC level in the complete blood count was above the upper value of the reference limit (Fielder 2022). The reference interval of CRP was accepted at 0.0–1 $mg.dL^{-1}$, as defined by the manufacturer of the reagents (Gesan, Italy) for the automated biochemistry analysis device.

Statistical Analysis

For categorical variables, descriptive statistics were presented as frequencies and percentages, and for continuous variables, as arithmetic means and standard errors. The normality assumption was checked with Shapiro Wilk Test. The blood analyses records were classified as normal or having an infection according to the WBC count, and the Mann-Whitney U test was used to detect the difference between platelet indices parameters in the complete blood count and blood serum CRP levels since the normality assumption was not fulfilled. The difference between inflammatory panel parameters of the complete blood count, categorized according to CRP levels, was determined with the Kruskal-Wallis test because the normality assumption was not held. One-way ANOVA test with Dunnett T3 post hoc test was used for the determination of difference within the categorized parameters. The accuracy of blood serum CRP level in predicting the presence of infection and the accuracy of WBC count in predicting CRP level were estimated by receiver operating characteristic (ROC) analysis by calculating Area Under the Curve (AUC) and 95% confidence intervals. The optimal cut-off point maximizing the Youden's J statistic of each parameter to predict the existence of infection and the inflammatory level of CRP was also determined [J=max (sensitivity+specificity-1)]. The relationships between complete blood count parameters and CRP in dogs without inflammatory status and those with inflammatory status according to CRP levels were specified with Spearman's rank correlation coefficient due to the normality assumption not holding. A p value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS Statistics for Windows, Version 26.0 (IBM Corp, Armonk, NY, USA).

RESULTS

The blood analyses records of dogs grouping having infection or not according to WBC count in CBC were given in Table 1. According to blood serum levels of CRP, alterations in CRP and blood parameters, including the inflammatory panel, were given in Table 2. There was no significant difference in PI according to blood serum levels of CRP of dogs' bloodwork records (Table 2). The WBC count in dogs having an equal or above 10 $mg.dL^{-1}$ CRP level was significantly higher than the other levels of CRP (Table 2). AUC results for CRP and WBC in blood analyses of dogs were given in Table 3, and were showed in Figure 1. The relationships between complete blood count parameters and CRP in dogs without inflammatory status and those have an inflammatory status according to CRP levels were given in Table 4, 5, and 6. A moderate positive correlation was detected between CRP and WBC in the bloodwork of all dogs, undivided according to inflammatory status (Table 4), and of dogs with an inflammatory status (Table 6).

Table 1. Descriptives of blood records of dogs grouping having leukocytosis or not according to WBC.

Parameters	Normal (N:83)	Having leukocytosis (N:52)	p[1]
White Blood Cells$\times 10^3.\mu L^{-1}$	13.148±0.781	21.809±1.927	0.000
CRP $mg.dL^{-1}$	5.028±0.544	14.270±1.821	0.000
Platelet$\times 10^3.\mu L^{-1}$	360.289±15.871	386.192±35.018	0.605
Main Platelet Volume fL	8.571±0.112	8.508±0.113	0.906
Platelet Distribution Width %	11.562±0.488	11.469±0.734	0.285
Plateletcrit	0.361±0.044	0.290±0.025	0.340
MPV to PLT ratio	0.033±0.004	0.032±0.003	0.603

[1] Mann-Whitney U test

Table 2. Changes in CRP and inflammatory blood parameters when blood data were grouped according to CRP levels (mean±SEM).

Parameters	Grouping in CRP levels (mg.dL^{-1})				p[1]
	0 – ≤1 (N:23)	1< – <5 (N:44)	5 – <10 (N:30)	≥10 (N:38)	
CRP mg.dL^{-1}	0.274±0.079^{d}	3.298± 0.149^{c}	6.747±0.232^{b}	21.198±1.784^{a}	0.000
White Blood Cells×10^{3}.µL^{-1}	13.743±2.120^{b}	12.827±0.966^{b}	14.483±1.631^{b}	23.958±2.238^{a}	0.000
Platelet×10^{3}.µL^{-1}	346.528±27.184	345.909±21.873	356.600±42.096	423.632±37.849	0.459
Main Platelet Volume fL	8.539±0.158	8.541±0.177	8.610±0.156	8.508±0.135	0.907
Platelet Distribution Width %	10.165±0.854	11.259±0.716	12.085±1.041	12.218±0.702	0.144
Plateletcrit	0.368±0.077	0.361±0.072	0.294±0.033	0.312±0.028	0.845
MPV to PLT ratio	0.029±0.003	0.032±0.004	0.038±0.006	0.030±0.007	0.456

[1] Kruskal Wallis,

[a,b,c,d] Superscripts in the same row define the difference at the 0.05 level between the columns

Table 3. AUC results for CRP and WBC in blood analyses of dogs.

	AUC (95%)	Cut-off	p	Sensitivity (%)	Specificity (%)
CRP levels[a]	0.736 (0.644-0.827)	5.45 mg.dL^{-1} 7.15 mg.dL^{-1}*	0.000	67.3 59.6*	65.1 80.7*
CRP levels ≤1 mg.dL^{-1}[b]	0.511 (0.211-0.811)		0.941		
CRP levels 1-5 mg.dL^{-1}[b]	0.547 (0.353-0.741)		0.645		
CRP levels 5-10 mg.dL^{-1}[b]	0.479 (0.228-0.729)		0.856		
CRP levels ≥10 mg.dL^{-1}[b]	0.805 (0.656-0.953)	16.75 mg.dL^{-1} 18.25 mg.dL^{-1}*	0.004	77.8 70.4*	81.8 90.9*
WBC counts[c]	0.665 (0.536-0.793)	11.55×10^{3}.µL^{-1} 10.65×10^{3}.µL^{-1}*	0.013	66.1 77.7*	65.2 65.2*
WBC counts[d]	0.731 (0.555-0.906)	15.90×10^{3}.µL^{-1} 14.40×10^{3}.µL^{-1}*	0.010	79.2 87.5*	64.3 57.1*

*The optimal cut-off point maximizing the Youden's J statistic

[a] AUC results for CRP in dogs with leukocytosis.

[b] AUC results for CRP in dogs with leukocytosis and divided to CRP levels (mg.dL^{-1}) in blood serum.

[c] AUC results for WBC in dogs having inflammation according to CRP levels greater than 1 mg.dL^{-1} in blood serum.

[d] AUC results for WBC in dogs having inflammation according to CRP levels ≥10 mg.dL^{-1} in blood serum.

Table 4. Correlations between CRP, WBC, and PIs parameters in blood records of dogs.

	CRP mg.dL^{-1}	White Blood Cells	Platelet	Main Platelet Volume	Platelet Distribution Width	Plateletcrit	MPV to PLT ratio
CRP mg.dL^{-1}	1	-0.305	0.029	0.254	0.320	-0.031	0.002
White Blood Cells		1	-0.448*	-0.047	0.138	-0.278	0.437*
Platelet			1	-0.027	-0.335	0.807**	-0.972**
Main Platelet Volume				1	0.154	0.187	0.190
Platelet Distribution Width					1	-0.292	0.391
Plateletcrit						1	-0.795**
MPV to PLT ratio							1

** Correlation is significant at the 0.01 level

* Correlation is significant at the 0.05 level

Table 5. Correlations between inflammatory parameters of the blood-works of dogs without leukocytosis.

	CRP mg.dL^{-1}	White Blood Cells	Platelet	Main Platelet Volume	Platelet Distribution Width	Plateletcrit	MPV to PLT ratio
CRP mg.dL^{-1}	1	0.450**	0.065	0.021	0.196*	0.026	-0.072
White Blood Cells		1	0.002	0.019	0.035	-0.047	0.005
Platelet			1	-0.190*	-0.140	0.903**	-0.981**
Main Platelet Volume				1	0.033	-0.023	0.343**
Platelet Distribution Width					1	-0.082	0.120
Plateletcrit						1	-0.853**
MPV to PLT ratio							1

** Correlation is significant at the 0.01 level
* Correlation is significant at the 0.05 level

Table 6. Correlations between inflammatory parameters of the blood-work records of dogs with leukocytosis.

	CRP mg.dL^{-1}	White Blood Cells	Platelet	Main Platelet Volume	Platelet Distribution Width	Plateletcrit	MPV to PLT ratio
CRP mg.dL^{-1}	1	0.477**	0.074	0.051	0.129	0.046	-0.070
White Blood Cells		1	0.093	0.053	-0.076	0.015	-0.077
Platelet			1	-0.225*	-0.113	0.915**	-0.982**
Main Platelet Volume				1	0.035	-0.072	0.372**
Platelet Distribution Width					1	-0.046	0.090
Plateletcrit						1	-0.869**
MPV to PLT ratio							1

** Correlation is significant at the 0.01 level
* Correlation is significant at the 0.05 level

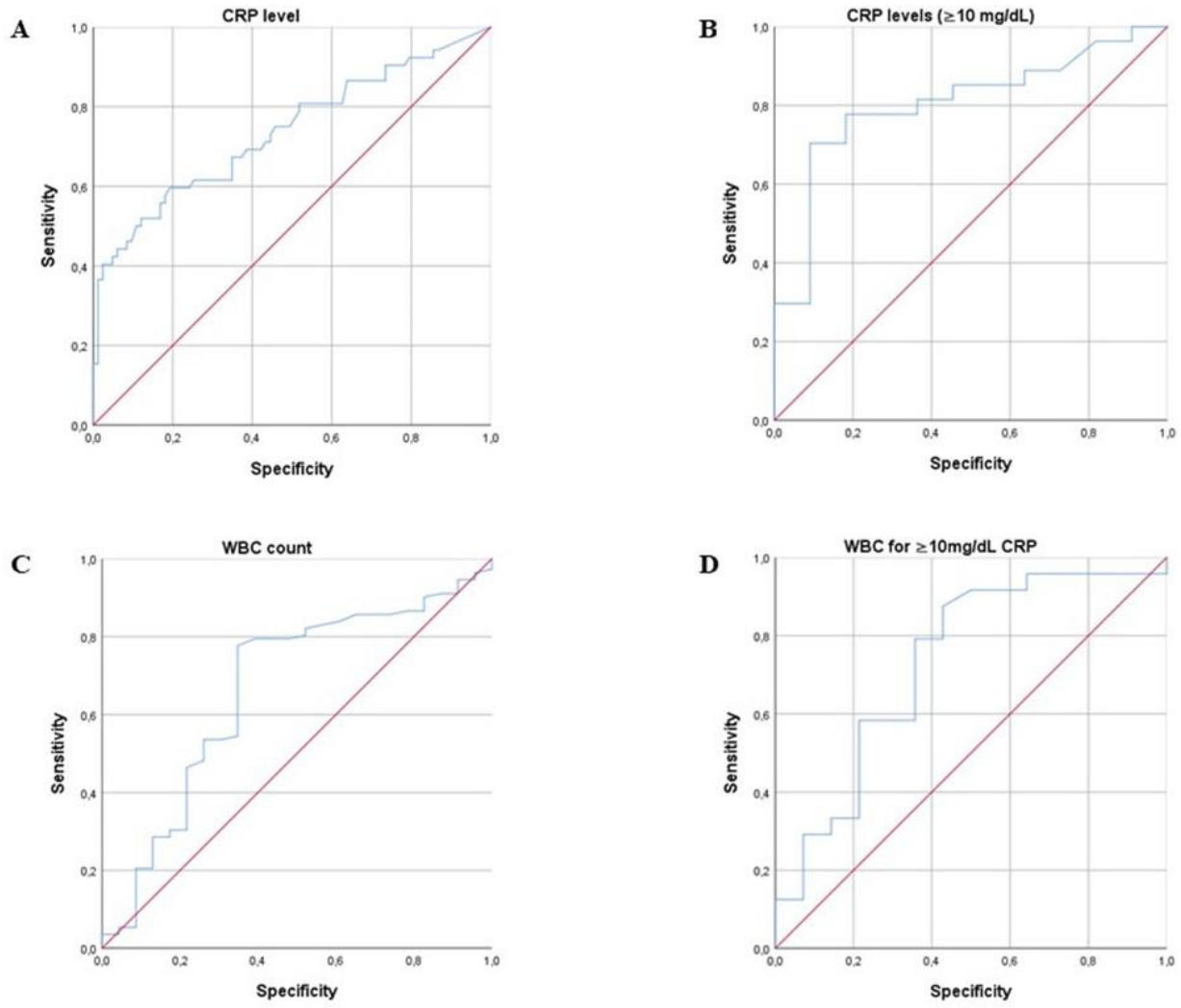

Figure 1: A: ROC curve of CRP in dogs with infection according to blood leucocyte count; **B**: ROC curve of CRP in dogs with infection according to blood leucocyte count and having CRP levels greater than 10 mg.dL^{-1} in blood serum; **C**: ROC curve of WBC in dogs having inflammation according to CRP levels greater than 1 mg.dL^{-1} in blood serum; **D**: ROC curve of WBC in dogs having inflammation according to CRP levels equal or greater than 10 mg.dL^{-1} in blood serum.

DISCUSSION

Diagnostic workups for veterinary patients include decision-making (Friedrichs et al. 2022). A detailed history and physical examination are used to make preliminary differential diagnosis (Friedrichs et al. 2022). Decisions to rule in or rule out differential diagnoses are then made based on the interpretation of laboratory tests such as hematology and other clinical pathological data (Friedrichs et al. 2022). For many regular hematological and biochemical tests, time-series data analysis provides a more accurate indication of the organ or cell's pathological status than data collected at a single time point (Honda et al. 2016). Furthermore, several standard tests must be utilized in conjunction to assess the patient's clinical condition. As a result, doing a single test at a particular time point is inadequate to provide a diagnosis (Honda et al. 2016).

A complete blood count is a laboratory analysis test that is highly demanded in the veterinary clinical routine due to its low budget and ease of application, as well as providing information about the instantaneous physiological or pathological state of the patient to which it is applied. The CBC analyzes blood components in the form of an erythrogram, a leukogram, and a platelet count, as well as the quantitative and qualitative outcomes of these parameters. (Rejec et al. 2017; Oliveira et al. 2020). Leukocytosis is defined as an elevated total leukocyte count in the circulatory blood flow (Weltan et al. 2008). Leukocytosis was reported in various clinical conditions such as diskospondylitis (Trub et al. 2021), canine demodicosis (Jaheen et al. 2022), sepsis (Ok et al. 2015), lower respiratory disease (Köse et al. 2021; Köse et al. 2023b). In this study, an increase in WBC level was identified in the blood analysis results of dogs, as in previous studies (Ok et al. 2015; Köse et al. 2021; Trub et al. 2021; Jaheen et al. 2022; Köse et al. 2023b), and was connected with inflammatory status (Table 2). In addition, according to the upper value of the WBC reference interval (5.0-14.5×103.µL-1), an increase of approximately 60% in the WBC count was observed in the blood analyses results of dogs with CRP levels greater than 10 mg.dL-1 (Table 2). On the other hands, it was found that WBC counts were within the reference range in the blood analyses results with CRP levels in the reference range and below 10 mg.dL-1 (Table 2). It is reported that serum CRP concentrations rise significantly 4 hours after the beginning of inflammation, while WBC counts do not rise at the same time (Cerón et al. 2005; Galezowski et al. 2010). Cut-off value of WBC in dogs with CRP levels greater than 10 mg.dL-1 was found as 14.40×103.µL-1 (Table 3). According to the results of the study, in the light of the literature, when a marked increase in WBC value (14.40×103.µL-1<) is determined in the blood analyses results, it is thought that the inflammatory process is older than four hours and the blood serum CRP value may be 10 mg.dL-1 or higher.

In many inflammatory and infectious situations, the liver produces acute phase proteins in response to the release of proinflammatory cytokines (De Laforcade et al. 2008; Ok et al. 2015). C-reactive protein is a valuable measure for identifying inflammation in humans and animals (Eckersall and Bell 2010; Christensen et al. 2014; Ok et al. 2015). The canine CRP reference values (<10–20 mg.L-1) (Klenner et al. 2010; Hillström et al. 2014; Hindenberg et al. 2018; Hindenberg et al. 2020) assayed by several methods, including ours (<1 mg.dL-1), seem to be approximately the same. In dogs with an inflammatory leukogram, it was firstly reported that CRP levels were increased (Burton et al. 1994). It is informed that serum CRP levels increased in the dogs with acute inflammatory disease (Tecles et al. 2005). The increase in CRP levels was reported in various clinical conditions such as demodicosis (Jaheen et al. 2022), parvoviral enteritis (Kubesy et al. 2019; Başbuğ et al. 2020), sepsis (Ok et al. 2015), systemic inflammatory response syndrome (SIRS)(Gebhardt et al. 2009). Similar to previous studies (Ok et al. 2015; Başbuğ et al. 2020; Jaheen et al. 2022), in this study, an increased CRP level was observed in the blood analyses results of dogs with leukocytosis. C-reactive protein cut-off value in dogs with parvoviral enteritis was reported as 120.5 mg.L-1 (Başbuğ et al. 2020), as well as 7.15 mg.dL-1 in the blood analyses with leukocytosis in this study (Table 3). In another study, it is reported that CRP levels were increased in dogs with SIRS (Gebhardt et al. 2009). On the other hand, in this study, the cut-off value for CRP was also detected as 16.75 mg.dL-1 in the blood analyses results with leukocytosis and including CRP levels ≥10 mg.dL-1 (Table 3). In a study conducted in dogs with acute abdominal syndrome, it was reported that there was no correlation between CRP level and WBC count at the time of admission to the clinic, but there was a positive correlation in these blood values 48–72 hours later, and both values showed a decrease (Galezowski et al. 2010). C-reactive protein, in this study, was positively correlated with WBC ($r=0.477$, $p<0.01$) (Table 6). The correlation coefficient was observed to be higher in this study than the firstly defined ($r=0.34$) by (Burton et al. 1994). The correlation coefficient ($r=0.44$) determined in another study (Nakamura et al. 2008) was quite similar to that in this study. It is thought that this increase in CRP level may be related to the inflammatory response in response to the condition causing leukocytosis. The correlation between CRP and WBC determined in this study also seems to support this idea.

In addition to their involvement in homeostasis, platelets play a crucial role in the inflammatory process by actively regulating host defenses and partnering in the occurrence of inflammation and tissue healing (Rejec et al. 2017). Platelet indices including mean platelet volume (MPV), platelet size distribution width (PDW), and plateletcrit (PCT) may now be measured

using automated blood cell analyzers (Moritz et al. 2005; Yilmaz et al. 2008). According to reports, the MPV/PLT ratio can be employed as a marker of the systemic inflammatory response, especially related to malignancy (Rejec et al. 2017; Köse et al. 2023a). It is informed that no differences could be determined in terms of platelet count and MPV/PLT ratio in dogs with periodontitis and oral malignancies (Rejec et al. 2017). Consistent with a previous study (Ok et al. 2015), there was no alteration in platelet count in this study. In the blood analyses of dogs with leukocytosis, platelet count was negatively correlated with main platelet volume ($r=-0.225$, $p<0.05$) and MPV/PLT ($r=0.982$, $p<0.01$), but it was positively correlated with plateletcrit ($r=0.915$, $p<0.01$) (Table 6).

CONCLUSION

It is obvious that the analysis of C-reactive protein in veterinary practice is a valuable supportive laboratory measure for identifying inflammation in dogs, as well as WBCs count. Considering the study results, it is concluded that in veterinary clinical practice, C-reactive protein measurements in dogs may be more useful in cases where a marked increase in WBC above the cut-off value is detected in the complete blood count routinely used to assess inflammatory or infectious status. The lack of etiology causing leukocytosis in the blood analyses of dogs may be the main limitation of this study. Therefore, it may be appropriate to conduct more comprehensive studies in this area, including etiology.

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Ethical approval: According to the legislation titled "Working Procedures and Ethics Committees of Animal Experiments" numbered 28914 published on February 15, 2014, in Turkey, the 8th article clearly suggested that clinical applications for diagnostic and therapeutic purposes are not subject to ethical committee approval. The data, information and documents presented in this article were obtained within the framework of academic and ethical rules.

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REFERENCES

Alves, A. E., Mota, F. C. D., Fujimoto, T. A. S., Sousa, W. M. R., & Di Filippo, P. A. (2020). Acute Phase Proteins response and their clinical application in veterinary medicine. Veterinária Notícias, 26(1), 82–111. https://doi.org/10.14393/VTN-v26n1-2020-53216

Anziliero, D., Bassi, E., Pain, K. M., Valle, S. D. F., & Kreutz, L. C. (2013). Serum C-reactive protein (CRP) measurement in dogs with altered hematological parameters. Ciência Animal Brasileira, 14(2), 265–272. https://doi.org/10.5216/cab.v14i2.9054

Başbuğ, O., Aydoğdu, U., & Ağaoğlu, Z. T. (2020). Evaluation of C-reactive protein, albumin, neopterin, urokinase type plasminogen activator receptor and leukocyte count as prognostic parameters in dogs with parvoviral enteritis. Kocatepe Veterinary Journal, 13(4), 375–382. https://doi.org/10.30607/kvj.736869

Burton, S. A., Honor, D. J., Mackenzie, A. L., Eckersall, P. D., Markham, R. J. F., & Horney, B. S. (1994). C-Reactive protein concentration in dogs with inflammatory leukograms. American Journal of Veterinary Research, 55(5), 613–618. https://doi.org/10.2460/ajvr.1994.55.05.613

Casella, S., Fazio, F., Russo, C., Giudice, E., & Piccione, G. (2013). Acute phase proteins response in hunting dogs. Journal of Veterinary Diagnostic Investigation, 25(5), 577–580. https://doi.org/10.1177/1040638713495851

Cerón, J. J., Eckersall, P. D., & Martínez-Subiela, S. (2005). Acute phase proteins in dogs and cats: current knowledge and future perspectives. Veterinary Clinical Pathology, 34(2), 85–99. https://doi.org/10.1111/j.1939-165X.2005.tb00019.x

Christensen, M. B., Langhorn, R., Goddard, A., Andreasen, E. B., Moldal, E., Tvarijonaviciute, A., Kirpensteijn, J., Jakobsen, S., Persson, F., & Kjelgaard-Hansen, M. (2014). Comparison of serum amyloid A and C-reactive protein as diagnostic markers of systemic inflammation in dogs. Canadian Veterinary Journal, 55(2), 161–168.

De Laforcade, A. M., Rozanski, E. A., Freeman, L. M., & Li, W. (2008). Serial Evaluation of Protein C and Antithrombin in Dogs with Sepsis. Journal of Veterinary Internal Medicine, 22(1), 26–30. https://doi.org/10.1111/j.1939-1676.2007.0021.x

Eckersall, P. D., & Bell, R. (2010). Acute phase proteins: Biomarkers of infection and inflammation in veterinary medicine. Veterinary Journal, 185(1), 23–27. https://doi.org/10.1016/j.tvjl.2010.04.009

Fielder, S. E. (2022, November). Hematology Reference Ranges. Merck Veterinary Manual Online. https://www.merckvetmanual.com/special-subjects/reference-guides/hematology-reference-ranges

Friedrichs, K. R., Jensen, A. L., & Kjelgaard-Hansen, M. (2022). Reference Intervals and Decision Limits. In M. B. Brooks, K. E. Harr, D. M. Seelig, K. J. Wardrop, & D. J. Weiss (Eds.), Schalm's Veterinary Hematology (7th ed., pp. 1273–1284). Wiley. https://doi.org/10.1002/9781119500537.ch140

Galezowski, A. M., Snead, E. C. R., Kidney, B. A., & Jackson, M. L. (2010). C-Reactive Protein as a Prognostic Indicator in Dogs with Acute Abdomen Syndrome. Journal of Veterinary Diagnostic Investigation, 22(3), 395–401. https://doi.org/10.1177/104063871002200308

Gebhardt, C., Hirschberger, J., Rau, S., Arndt, G., Krainer, K., Schweigert, F. J., Brunnberg, L., Kaspers, B., & Kohn, B. (2009). Use of C-reactive protein to predict outcome in dogs with systemic inflammatory response syndrome or sepsis. Journal of Veterinary Emergency and Critical Care, 19(5), 450–458. https://doi.org/10.1111/j.1476-4431.2009.00462.x

Hillström, A., Hagman, R., Tvedten, H., & Kjelgaard-Hansen, M. (2014). Validation of a commercially available automated canine-specific immunoturbidimetric method for measuring canine <scp>C</scp> -reactive protein. Veterinary Clinical Pathology, 43(2), 235–243. https://doi.org/10.1111/vcp.12150

Hindenberg, S., Bauer, N., & Moritz, A. (2020). Extremely high canine C-reactive protein concentrations > 100 mg/l – prevalence, etiology and prognostic significance. BMC Veterinary Research, 16(1), 147. https://doi.org/10.1186/s12917-020-02367-7

Hindenberg, S., Keßler, M., Zielinsky, S., Langenstein, J., Moritz, A., & Bauer, N. (2018). Evaluation of a novel quantitative canine species-specific point-of-care assay for C-reactive protein. BMC Veterinary Research, 14(1), 99. https://doi.org/10.1186/s12917-018-1415-2

Honda, T., Uehara, T., Matsumoto, G., Arai, S., & Sugano, M. (2016). Neutrophil left shift and white blood cell count as markers of bacterial infection. In Clinica Chimica Acta (Vol. 457). https://doi.org/10.1016/j.cca.2016.03.017

Jaheen, A. H., Kubesy, A. A., Rakha, G. M., Salem, S. I., & El-Sherif, M. A. (2022). Diagnostic value of procalcitonin, C-reactive protein, and leukocyte count in canine ehrlichiosis and canine demodicosis. Comparative Clinical Pathology, 31(3), 529–536. https://doi.org/10.1007/s00580-022-03350-4

Kjelgaard-Hansen, M. (2010). Comments on measurement of C-reactive protein in dogs. Veterinary Clinical Pathology, 39(4), 402–403. https://doi.org/10.1111/j.1939-165X.2010.00276.x

Klenner, S., Bauer, N., & Moritz, A. (2010). Evaluation of Three Automated Human Immunoturbidimetric Assays for the Detection of C-Reactive Protein in Dogs. Journal of Veterinary Diagnostic Investigation, 22(4), 544–552. https://doi.org/10.1177/104063871002200408

Kocaturk, M., Martinez, S., Eralp, O., Tvarijonaviciute, A., Ceron, J., & Yilmaz, Z. (2010). Prognostic value of serum acute-phase proteins in dogs with parvoviral enteritis. Journal of Small Animal Practice, 51(9), 478–483. https://doi.org/10.1111/j.1748-5827.2010.00965.x

Köse, S. İ., Köse, A. M., Ürer, E. K., Bahan, O., Gözer, A., & Ambarcıoğlu, P. (2023a). Diagnosis of Transmissible Venereal Tumors in Bitches - Platelet Indices Are a Remarkable Marker? Acta Scientiae Veterinariae, 51(1921). https://doi.org/10.22456/1679-9216.132008

Köse, S. İ., Özer, B., Gönenci, R., & Cantekin, Z. (2023b). The Effect of Cefovecin Sodium in Shelter Dogs with Bacterial Lower Respiratory Disease. Brazilian Archives of Biology and Technology, 66, e23230096. https://doi.org/10.1590/1678-4324-2023230096

Köse, S., Maden, M., & Sayın, Z. (2021). Clinical and bacteriological analysis of respiratory tract infections in sheltered dogs and determination of antibacterial treatment options. Journal of the Hellenic Veterinary Medical Society, 72(4), 3491–3502. https://doi.org/10.12681/jhvms.29441

Kritsepi-Konstantinou, M., & Oikonomidis, I. L. (2016). The interpretation of leukogram in dog and cat. Hellenic Journal of Companion Animal Medicine, 5(2), 62–68.

Kubesy, A. A., Rakha, G. M., Salem, S. I., & Jaheen, A. H. (2019). Altered blood procalcitonin, C-reactive protein, and leucocytes count in association with canine parvovirus (CPV) enteritis. Comparative Clinical Pathology, 28(4), 1095–1099. https://doi.org/10.1007/s00580-019-02941-y

Llewellyn, E. A., Todd, J. M., Sharkey, L. C., & Rendahl, A. (2017). A pilot study evaluating the prognostic utility of platelet indices in dogs with septic peritonitis. Journal of Veterinary Emergency and Critical Care, 27(5), 569–578. https://doi.org/10.1111/vec.12628

Malin, K., & Witkowska-Piłaszewicz, O. (2022). C-Reactive Protein as a Diagnostic Marker in Dogs: A Review. In Animals (Vol. 12, Issue 20, p. 2888). https://doi.org/10.3390/ani12202888

Martínez-Subiela, S., Cerón, J. J., & Ginel, P. J. (2004). Effects of different glucocorticoid treatments on serum acute phase proteins in dogs. Veterinary Record, 154(26), 814–817. https://doi.org/10.1136/vr.154.26.814

McCourt, M. R., & Rizzi, T. E. (2022). Hematology of Dogs. In M. B. Brooks, K. E. Harr, D. M. Seelig, K. J. Wardrop, & D. J. Weiss (Eds.), Schalm's Veterinary Hematology (7th ed., pp. 969–982). Wiley. https://doi.org/10.1002/9781119500537.ch108

Moritz, A., Walcheck, B. K., & Weiss, D. J. (2005). Evaluation of flow cytometric and automated methods for detection of activated platelets in dogs with inflammatory disease. American Journal of Veterinary Research, 66(2), 325–329. https://doi.org/10.2460/ajvr.2005.66.325

Moruzi, R. F., Morar, D., Văduva, C., Boboc, M. G., Dumitrescu, E., Muselin, F., Puvača, N., & Cristina, R. T. (2023). Leukogram patterns significance and prevalence for an accurate diagnosis in dogs. Journal of the Hellenic Veterinary Medical Society, 74(1), 5193–5202. https://doi.org/10.12681/jhvms.28696

Murata, H., Shimada, N., & Yoshioka, M. (2004). Current research on acute phase proteins in veterinary diagnosis: an overview. The Veterinary Journal, 168(1), 28–40. https://doi.org/10.1016/S1090-0233(03)00119-9

Nakamura, M., Takahashi, M., Ohno, K., Koshino, A., Nakashima, K., Setoguchi, A., Fujino, Y., & Tsujimoto, H. (2008). C-Reactive Protein Concentration in Dogs with Various Diseases. Journal of Veterinary Medical Science, 70(2), 127–131. https://doi.org/10.1292/jvms.70.127

Ok, M., Er, C., Yıldız, R., Çöl, R., Aydoğdu, U., Şen, İ., & Güzelbekteş, H. (2015). Sepsisli Köpeklerde Akut Faz Proteinler, Bazı Sitokinler ve Hemostatik Parametrelerin Değerlendirilmesi. Kafkas Universitesi Veteriner Fakultesi Dergisi, 21(5), 761–766. https://doi.org/10.9775/kvfd.2015.13418

Oliveira, P. L. de, Souza, S. L., Bonatto, N. C. M., Silva, N. L. T. da, Mancebo, A. M., Bosculo, M. R. M., Barros, L. D. de, Floriano, B. P., & Almeida, B. F. M. de. (2020). Effect of food intake on complete blood count of healthy dogs. Revista Agraria Academica, 3(6), 105–116. https://doi.org/10.32406/v3n62020/105-116/agrariacad

Otabe, K., Sugimoto, T., Jinbo, T., Honda, M., Kitao, S., Hayashi, S., Shimizu, M., & Yamamoto, S. (1998). Physiological levels of C-reactive protein in normal canine sera. Veterinary Research Communications, 22(2), 77–85. https://doi.org/10.1023/A:1006071211779

Rejec, A., Butinar, J., Gawor, J., & Petelin, M. (2017). Evaluation of Complete Blood Count Indices (NLR, PLR, MPV/PLT, and PLCRi) in Healthy Dogs, Dogs With Periodontitis, and Dogs With Oropharyngeal Tumors as Potential Biomarkers of Systemic Inflammatory Response. Journal of Veterinary Dentistry, 34(4), 231–240. https://doi.org/10.1177/0898756417731775

Smith, J. R., Smith, K. F., & Brainard, B. M. (2014). Platelet parameters from an automated hematology analyzer in dogs with inflammatory clinical diseases. The Veterinary Journal, 201(3), 406–411. https://doi.org/10.1016/j.tvjl.2014.07.009

Tecles, F., Spiranelli, E., Bonfanti, U., Cerón, J. J., & Paltrinieri, S. (2005). Preliminary Studies of Serum Acute-Phase Protein Concentrations in Hematologic and Neoplastic Diseases of the Dog. Journal of Veterinary Internal Medicine, 19(6), 865–870. https://doi.org/10.1111/j.1939-1676.2005.tb02779.x

Trub, S. A., Bush, W. W., Paek, M., & Cuff, D. E. (2021). Use of C-reactive protein concentration in evaluation of diskospondylitis in dogs. Journal of Veterinary Internal Medicine, 35(1), 209–216. https://doi.org/10.1111/jvim.15981

Weltan, S. M., Leisewitz, A. L., & Goddard, A. (2008). A case-controlled retrospective study of the causes and implications of moderate to severe leukocytosis in dogs in South Africa. Veterinary Clinical Pathology, 37(2), 164–172. https://doi.org/10.1111/j.1939-165X.2008.00037.x

Wood, R. D. (2022a, October). Leukogram Abnormalities in Animals. Merck Veterinary Manual Online. https://www.msdvetmanual.com/circulatory-system/leukocyte-disorders/leukogram-abnormalities-in-animals?query=white%20blood%20cell%20counts

Wood, R. D. (2022b, October). Overview of Leukocyte Disorders in Animals. Merck Veterinary Manual Online. https://www.msdvetmanual.com/circulatory-system/leukocyte-disorders/overview-of-leukocyte-disorders-in-animals

Yilmaz, Z., Eralp, O., & Ilcol, Y. O. (2008). Evaluation of platelet count and its association with plateletcrit, mean platelet volume, and platelet size distribution width in a canine model of endotoxemia. Veterinary Clinical Pathology, 37(2), 159–163. https://doi.org/10.1111/j.1939-165X.2008.00023.x

Yuri Gasparyan, A., Ayvazyan, L., P. Mikhailidis, D., & D. Kitas, G. (2011). Mean Platelet Volume: A Link Between Thrombosis and Inflammation? Current Pharmaceutical Design, 17(1), 47–58. https://doi.org/10.2174/138161211795049804