



Research Article

Evaluation of Serum Lactate and Neutrophil-to-Lymphocyte Ratio as Early Predictors of Disease Severity in Dogs with Acute Gastroenteritis

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ABSTRACT

Introduction: Acute gastroenteritis (AGE) in dogs ranges from mild to severe, requiring supportive care. Serum lactate reflects tissue perfusion and metabolic status, while the neutrophil-to-lymphocyte ratio (NLR) marks systemic inflammation. The present study aimed to assess the value of serum lactate and NLR as early predictors of disease severity in dogs with AGE.

Materials and methods: In this prospective clinical study, 72 dogs (39 males and 33 females) with AGE and a mean age of 4.5 years were included. Clinical severity was assessed based on predefined clinical criteria, including degree of dehydration, frequency of vomiting and diarrhea, body temperature, heart rate, mental status, and need for hospitalization or intensive supportive treatment using intravenous fluid therapy and antiemetic administration. Blood samples were collected to determine serum lactate concentration and complete blood count before any treatment, including intravenous fluid therapy and antiemetic administration. The NLR was calculated from absolute neutrophil and lymphocyte counts. Correlation and regression analyses were performed to assess how these biomarkers were associated with clinical severity. Receiver operating characteristic (ROC) analysis assessed the ability of NLR to distinguish severe disease from mild-to-moderate disease.

Results: Serum lactate concentrations and NLR were higher in dogs with severe AGE compared with dogs with mild-to-moderate gastroenteritis. Serum lactate concentrations and NLR revealed significant positive correlations with clinical severity scores. Higher lactate concentrations and NLR were associated with prolonged hospitalization and the need for intensive supportive treatment. In multivariate analysis, serum lactate and NLR remained independently associated with gastroenteritis. Based on ROC analysis, combining lactate and NLR provided superior discrimination compared to using each biomarker individually; thus, the combination offered enhanced discriminative ability.

Conclusion: Serum lactate and NLR were associated with disease severity in dogs with AGE and served as markers for early clinical risk stratification.

1. Introduction

Acute gastroenteritis (AGE) is one of the most common causes of veterinary consultation in small animal medicine¹.

The clinical signs are broad, ranging from transient, self-limiting diarrhea to life-threatening conditions

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characterized by severe dehydration, systemic inflammatory response syndrome (SIRS), and sepsis^{1,2}. Many dogs with uncomplicated AGE recover with symptomatic and supportive treatment. However, some dogs progress to critical disease requiring intensive intravenous fluid therapy, antiemetic therapy, nutritional support, and, in some cases, multimodal organ function monitoring³. Acute gastroenteritis accounts for a high proportion of emergency canine diseases; rapidly and accurately identifying dogs at risk of severe disease is a clinical priority³. The ability to identify these dogs would enable timely clinical assessment and early use of therapeutic interventions, all of which may ultimately impact patient outcome³.

In routine veterinary emergency practice, initial evaluation of disease severity often relies on clinical parameters, including physical examination findings, hydration status, and owner-reported history³. However, these variables are subject to inter-observer variability and often do not reflect the underlying pathophysiology, especially early in presentation⁴. Hence, there has been increasing interest in the use of rapidly measurable biomarkers that provide complementary information on systemic perfusion, metabolic disturbance, and the magnitude of the host inflammatory response⁴. Among the candidate markers, those markers most extensively studied in both human and veterinary critical care medicine include serum lactate and neutrophil-to-lymphocyte ratio (NLR)⁵.

Serum lactate is a sensitive marker of tissue hypoperfusion, cellular hypoxia, and impending shock, a long-recognized metabolite of the dynamic balance between anaerobic glycolysis and hepatic clearance^{6,7}. The measurement of lactate is readily available, cost-effective, and easily incorporated into initial emergency assessments in dogs⁸. Meanwhile, the NLR, easily calculated from absolute neutrophil and lymphocyte counts obtained by routine complete blood count (CBC), has emerged as a robust surrogate marker of systemic inflammatory stress and immunological status⁷. Increased NLR is indicative of both enhanced innate immune activity (neutrophilia) and relative suppression of adaptive immunity (lymphopenia), a combination frequently observed in severe inflammatory or septic conditions⁹. Several veterinary studies have demonstrated the prognostic relevance of NLR in different pathological conditions, such as sepsis and parvoviral enteritis^{10,11}, but its specific role in unselected canine AGE has been less rigorously studied.

The integrated evaluation of serum lactate and NLR may offer a more precise prediction of outcomes compared to each marker individually, as these two indicators represent complementary aspects of perfusion-related metabolic dysfunction and inflammatory-immune activation, although each marker has its own utility⁹. However, prospective data assessing the simultaneous measurement of these two biomarkers at admission for early risk stratification in dogs with AGE are limited. The present study aimed to evaluate the utility of serum lactate concentration and NLR as independent early indicators of disease severity in dogs with AGE.

2. Materials and Methods

2.1. Ethical approval

The present study was conducted at Islamic University of Karaj, Faculty of Veterinary Medicine, Karaj, Iran, between March and June 2025, following approval by the Institutional Animal Care and Use Committee of the Faculty of Veterinary Medicine (IAUK.AC.1402.0215). Written informed owner consent was obtained prior to enrollment for all dogs, and all procedures were performed in accordance with the relevant guidelines and regulations for the ethical use of animals in research.

2.2. Study population and inclusion criteria

A total of 118 dogs presenting with vomiting, diarrhea, or both of acute onset (<72 hours' duration) were consecutively screened for eligibility during the study period. Of these 118 dogs, 46 dogs were excluded for different reasons, including chronic gastrointestinal disorders (n = 12), concurrent systemic diseases potentially confounding lactate or NLR interpretation (n = 9), corticosteroid or immunosuppressive therapy within the preceding 14 days (n = 8), prior fluid therapy or antiemetic administration before presentation (n = 7), history of surgery or trauma within 30 days (n = 4), and a definitive non-gastrointestinal diagnosis established during hospitalization (n = 6). Consequently, 72 dogs met the inclusion criteria and were enrolled in the study.

2.3. Assessment of clinical severity and grouping

All dogs underwent a common physical exam by a board-certified veterinary internist or senior emergency clinician at presentation. A comprehensive clinical severity scoring system was used based on six parameters, including degree of dehydration (0-3), frequency of vomiting (0-3), frequency of diarrhea (0-3), body temperature (0-3), heart rate (0-3), and mental status (0-3), which yields a total composite score ranging from 0 to 18¹². Dogs were classified as having mild-to-moderate disease with a total score of ≤ 8 , or severe disease with a total score of ≥ 9 . The severe disease category was defined as any dog that required immediate intensive care, continuous intravenous fluid therapy, or vasopressor support, regardless of numerical score. The need for hospitalization, need for intensive supportive treatment defined as administration of intravenous crystalloids, colloids, antiemetics, gastrointestinal protectants, antibiotics, or plasma transfusions, and total duration of hospitalization in days were recorded for each dog. In addition, dogs did not receive only one medication. Each dog was on a wide range of medications.

2.4. Blood sampling and laboratory analysis

The amount of 3-5 mL of peripheral blood was collected from each dog by cephalic or jugular venipuncture before initiation of any therapeutic intervention. Plasma lactate was measured in samples collected in lithium-heparin tubes and analyzed within 15 minutes of collection using a commercially available handheld lactate analyzer (Lactate Scout Vet, EKF

Diagnostics, Penarth, UK) validated for canine whole blood. All measurements were done in duplicate, and the mean value was recorded in mmol/L. Samples were collected in K2-EDTA tubes and processed within 2 hours for a CBC using an automated veterinary hematology analyzer (Sysmex XN-1000V, Sysmex Corporation, Kobe, Japan), from which absolute neutrophil and lymphocyte counts were obtained. The NLR was subsequently calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. All laboratory personnel involved in the biomarker measurements were unaware of the clinical severity status of the dogs to minimize detection bias.

2.5. Follow-up and evaluation of results

All enrolled dogs were prospectively followed from the presentation until hospital discharge, death, or euthanasia, and attending clinicians recorded clinical data daily. For dogs discharged in less than 24 hours, follow-up was performed at 48-72 hours post-discharge to confirm clinical resolution and no relapse. The primary outcome variable was disease severity classification (severe versus mild-to-moderate). Secondary outcomes were need for hospitalization, total duration of hospitalization in days, need for intensive supportive treatment, and in-hospital mortality or euthanasia directly related to complications of gastroenteritis.

2.6. Statistical analysis

Normality was assessed using the Shapiro-Wilk test. Serum lactate and NLR were compared among all dogs in the present study using a Mann-Whitney U test, and categorical variables were compared using a chi-square test with p-value set at 0.05. Spearman's rank correlation was used to assess the association between each biomarker and the

continuous severity score, avoiding information loss from dichotomization. Binary logistic regression identified independent predictors of severe disease, including lactate and NLR by design, while controlling for age, sex, and body weight. Receiver operating characteristic (ROC) curve analysis evaluated discrimination ability, with area under the curve (AUC) calculation, Youden index for cut-offs, and DeLong's test for AUC comparisons. Sample size was based on a pilot study (80% power, two-sided alpha = 0.05); a minimum of 26 dogs per group was required, but at least 70 dogs were enrolled to allow for exclusions. Analyses were performed in SPSS 27.

3. Results

3.1. Study population and baseline characteristics

The study included 72 dogs, 44 (61.1%) with mild-to-moderate gastroenteritis and 28 (38.9%) with severe gastroenteritis (Table 1). The median age of the study population was 4.5 years (range 0.5-14 years), and it consisted of 39 male (54.2%) and 33 female dogs (45.8%). The median body weight was 22.5 kg. In the mild-to-moderate group, mean body weight was 23 kg, and in the severe group, it was 21.5 kg; this difference was not significant between groups ($p > 0.05$). The most common breeds were mixed-breed dogs ($n = 18$, 25.0%), German Shepherds ($n = 9$, 12.5%), and Golden Retrievers ($n = 7$, 9.7%). The two severity groups did not differ significantly in age, sex, body weight, or breed distribution ($p > 0.05$), suggesting these variables were well balanced at baseline and unlikely to confound the primary analyses. The median total duration of signs was 18 hours (IQR = 8.0-36.0); in dogs with mild-to-moderate gastroenteritis, it was 16 hours (IQR = 6.0-32.0), and in dogs with severe gastroenteritis, it was 22 hours (IQR 10.0-48.0).

Table 1. Baseline demographic and clinical characteristics of dogs with acute gastroenteritis, stratified by disease severity, in Karaj, Iran, March-June 2025

Characteristic	Total (n = 72)	Mild-to-moderate gastroenteritis (n = 44)	Severe gastroenteritis (n = 28)	p-value
Age (median range)	4.5 years (0.5-14)	4.8 years (0.5-14)	4.0 years (0.8-12)	0.34
Body weight (median IQR)	22.5 kg (14.0-32.0)	23.0 kg (14.5-33.0)	21.5 kg (13.0-31.0)	0.41
Sex (%)				0.52
Male	n = 39 (54.2%)	n = 23 (52.3%)	n = 16 (57.1%)	
Female	n = 33 (45.8%)	n = 21 (47.7%)	n = 12 (42.9%)	
Breed (%)				0.63
Mixed-breed	n = 18 (25.0%)	n = 11 (25.0%)	n = 7 (25.0%)	
German Shepherd	n = 9 (12.5%)	n = 5 (11.4%)	n = 4 (14.3%)	
Golden Retriever	n = 7 (9.7%)	n = 5 (11.4%)	n = 2 (7.1%)	
Other breeds	n = 38 (52.8%)	n = 23 (52.3%)	n = 15 (53.6%)	
Duration of signs (median IQR)	18 hours (8.0-36.0)	16 hours (6.0-32.0)	22 hours (10.0-48.0)	0.08

n: number of dogs, IQR: Interquartile range. A p-value less than 0.05 was considered statistically significant

3.2. Biomarkers

Serum lactate concentrations were significantly higher in dogs with severe gastroenteritis (3.8 mmol/L) compared to dogs with mild-to-moderate gastroenteritis (1.6 mmol/L; Table 2; $p < 0.05$). The NLR was significantly higher in the dogs with severe gastroenteritis (median: 12.4) compared to the dogs with mild-to-moderate gastroenteritis (median:

4.2; $p < 0.05$). The percentage of dogs with hyperlactatemia (serum lactate > 2.0 mmol/L) was significantly higher in dogs with severe gastroenteritis (82.1%) compared to dogs with mild-to-moderate gastroenteritis (20.5%; $p < 0.05$). An elevated NLR (> 7.0) was observed in 78.6% of dogs with severe gastroenteritis, a proportion significantly higher than the 15.9% observed in dogs with mild-to-moderate gastroenteritis ($p < 0.05$).

Table 2. Comparison of serum lactate and neutrophil-to-lymphocyte ratio between dogs having mild-to-moderate and severe gastroenteritis in Karaj, Iran, March- June 2025

Biomarkers	Mild-to-moderate gastroenteritis (n = 44)	Severe gastroenteritis (n = 28)	p-value
Serum lactate (mmol/L; median IQR)	1.6 mmol/L (1.2-2.1) ^b	3.8 mmol/L (2.6-5.4) ^a	< 0.001
NLR (median IQR)	4.2 (2.8-6.1) ^b	12.4 (8.7-18.2) ^a	< 0.001
Hyperlactatemia (> 2.0 mmol/L)	20.5% (n = 9) ^b	82.1% (n = 23) ^a	< 0.001
Elevated NLR (> 7.0)	15.9% (n = 7) ^b	78.6% (n = 22) ^a	< 0.001

NLR: Neutrophil-to-Lymphocyte Ratio, IQR: Interquartile range, n: number of dogs. Data are presented as median (interquartile range) for continuous variables and number (percentage) for categorical variables. ^{a,b} Mean different superscript letters in a row indicate significant differences at $p < 0.05$.

3.3. Association of biomarker with clinical severity scores

Serum lactate concentrations correlated significantly and positively with composite clinical severity scores ($p < 0.05$); thus, higher lactate levels were consistently associated with increased clinical disease severity (Table 3). Similarly, NLR was significantly and positively correlated with severity scores ($\rho = 0.68$), indicating that higher inflammatory stress, as assessed by NLR, was linked to worsening clinical condition. Serum lactate concentrations ($\rho = 0.65$) and NLR ($\rho = 0.59$) were strongly correlated with

the degree of dehydration and severity score ($p < 0.05$). Mental status changes were strongly correlated with dehydration and severity score (lactate: $\rho = 0.58$, $p < 0.001$; NLR: $\rho = 0.62$, $p < 0.001$). Serum lactate was correlated with body temperature ($\rho = 0.29$, $p = 0.04$) and heart rate ($\rho = 0.22$, $p = 0.08$), while NLR correlated with body temperature ($\rho = 0.26$, $p = 0.06$) and heart rate ($\rho = 0.24$, $p = 0.07$). Significant yet weaker correlations were observed between both biomarkers and vomiting frequency (lactate: $\rho = 0.41$, $p = 0.003$; NLR: $\rho = 0.38$, $p = 0.008$), as well as diarrhea (lactate: $\rho = 0.35$, $p = 0.02$; NLR: $\rho = 0.33$, $p = 0.03$).

Table 3. Spearman's correlation coefficients between biomarkers and clinical severity score components in dogs with acute gastroenteritis during March-June 2025, Karaj, Iran

Biomarkers	Severity Score	Serum lactate severity score (ρ)	p-value	NLR severity score (ρ)	p-value
Total severity score (0-18)		0.71	< 0.001	0.68	< 0.001
Components (each scored 0-3)					
Degree of dehydration		0.65	< 0.001	0.59	< 0.001
Mental status		0.58	< 0.001	0.62	< 0.001
Frequency of vomiting		0.41	0.003	0.38	0.008
Frequency of diarrhea		0.35	0.02	0.33	0.03
Body temperature		0.29	0.04	0.26	0.06
Heart rate		0.22	0.08	0.24	0.07

NLR: Neutrophil-to-lymphocyte ratio, ρ : Spearman's rank correlation coefficient. A p-value less than 0.05 was considered statistically significant.

3.4. Clinical outcomes and biomarker associations

Dogs presenting with elevated lactate concentrations (> 2.0 mmol/L) at the time of presentation to the hospital were significantly more likely to require hospitalization compared to those with normal lactate levels (84.4% versus 35.0%; $p < 0.001$; Table 4). Among hospitalized dogs, the median duration of hospitalization was significantly higher in the hyperlactatemia group (4.0 days, IQR: 2.0-6.0 days) compared to dogs with normal lactate (1.5 days, IQR: 1.0-3.0 days; $p = 0.003$). Similarly, dogs with high NLR (> 7.0) had a significantly higher hospitalization rate (86.2% versus

37.2%; $p < 0.001$) and longer hospitalization time (median: 3.5 versus 2.0 days; $p = 0.01$) compared to dogs with normal NLR. Dogs with elevated lactate and dogs with elevated NLR were both significantly more likely to require intensive supportive care (81.3% versus 32.5%, $p < 0.001$; and 86.2% versus 32.6%, $p < 0.001$, respectively), including intravenous crystalloid fluids, antiemetics, and systemic antibiotics. Mortality was observed in 4 dogs (12.5%) in the elevated lactate group and 4 dogs (13.8%) in the elevated NLR group, with no deaths in either normal biomarker group ($p = 0.04$ and $p = 0.03$, respectively).

Table 4. Clinical outcomes in dogs with acute gastroenteritis according to serum lactate and neutrophil-to-lymphocyte ratio status

Biomarkers	Normal lactate level (n = 40)	Elevated lactate level (n = 32)	p-value	Normal NLR (n = 43)	Elevated NLR (n = 29)	p-value
Outcome						
Hospitalization (%)	n = 14 (35.0%) ^a	n = 27 (84.4%) ^b	< 0.001	n = 16 (37.2%) ^a	n = 25 (86.2%) ^b	< 0.001
Hospital stays (median IQR)	1.5 days (1.0-3.0) ^a	4 days (2.0-6.0) ^b	0.003	2 days (1.0-3.0) ^a	3.5 days (2.0-5.0) ^b	0.01
Intensive supportive treatment (%)	n = 13 (32.5%) ^a	n = 26 (81.3%) ^b	< 0.001	n = 14 (32.6%) ^a	n = 25 (86.2%) ^b	< 0.001
Mortality (%)	n = 0 (0.0%) ^a	n = 4 (12.5%) ^b	0.04	n = 0 (0.0%) ^a	n = 4 (13.8%) ^b	0.03

n: number of dogs, IQR: Interquartile range. Normal lactate: ≤ 2.0 , elevated lactate: > 2.0 , normal NLR: ≤ 7.0 , elevated NLR: > 7.0 . Normal lactate level and NLR reference: Venn et al.¹². ^{a,b} Mean different superscript letters in a row indicate significant differences at p values < 0.05 for lactate and NLR separately.

3.5. Multivariable regression analysis

A binary logistic regression analysis was performed to

determine independent predictors of severe gastroenteritis (Table 5). Serum lactate (OR: 2.84, 95% CI: 1.92-4.21, $p < 0.001$) and NLR (OR: 1.35, 95% CI: 1.18-1.54, $p < 0.001$)

were significantly associated with severe disease, whereas age (OR: 0.97, $p = 0.34$), sex (OR: 1.22, $p = 0.52$), and body weight (OR: 0.98, $p = 0.41$) were not. Both biomarkers remained independently associated after adjustment, with adjusted odds ratios of 2.96 (95% CI: 1.98-4.42, $p < 0.001$)

for serum lactate and 1.38 (95% CI: 1.20-1.59, $p < 0.001$) for NLR, while age (adjusted OR: 0.96, $p = 0.28$), sex (adjusted OR: 1.18, $p = 0.62$), and body weight (adjusted OR: 0.98, $p = 0.35$) remained non-significant.

Table 5. Univariate and multivariable logistic regression analyses of predictors for severe gastroenteritis in dogs with acute gastroenteritis

Variables	Univariate OR (95% CI)	Univariate p-value	Multivariable adjusted OR (95% CI)	Multivariable p-value
Serum lactate (per 1 mmol/L increase)	2.84 (1.92–4.21)	< 0.001	2.96 (1.98–4.42)	< 0.001
NLR (per 1 unit increase)	1.35 (1.18–1.54)	< 0.001	1.38 (1.20–1.59)	< 0.001
Age (per year increase)	0.97 (0.91–1.04)	0.34	0.96 (0.89–1.03)	0.28
Sex (Male versus Female)	1.22	0.52	1.18	0.62
Body weight (per kg increase)	0.98 (0.95–1.02)	0.41	0.98 (0.94–1.02)	0.35

OR: Odds ratio. A p-value less than 0.05 was considered statistically significant.

3.6. Receiver operating characteristic analysis

The ROC curve analysis assessed the discriminative ability of serum lactate, NLR, and their combination in differentiating severe from mild-to-moderate gastroenteritis in dogs (Table 6). The AUC for serum lactate alone was 0.84 (95% CI: 0.75-0.93), suggesting high discriminatory ability. The AUC for NLR alone was 0.82 (95% CI: 0.72-0.91), indicating comparable predictive ability. The combined model with both biomarkers had a significantly higher AUC of 0.92 (95% CI: 0.86-0.98) than lactate alone ($p = 0.03$) or NLR alone ($p = 0.02$). Using the

Youden index, the optimal cut-off for serum lactate was 2.3 mmol/L (sensitivity of 82.1%, specificity of 79.5%) for predicting severe gastroenteritis, while the optimal NLR cut-off was 7.2 (sensitivity of 78.6%, specificity of 84.1%). The combined model achieved the highest overall diagnostic accuracy, with a sensitivity of 89.3%, specificity of 88.6%, positive predictive value of 84.2%, and negative predictive value of 93.2%. These findings indicated that the combined determination of serum lactate and NLR offers higher discrimination than either biomarker alone, supporting the complementary utility of these markers in early clinical risk stratification.

Table 6. Receiver operating characteristic analysis for predicting severe gastroenteritis in dogs during March-June 2025, Karaj, Iran

Biomarker	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P-value
Serum lactate	0.84 (0.75-0.93)	2.3 mmol/L	82.1	79.5	71.9	87.5	0.03
NLR	0.82 (0.72-0.91)	7.2	78.6	84.1	75.9	86.0	0.02
Combined model	0.92 (0.86-0.98)	-	89.3	88.6	84.2	93.2	-

AUC: Area under the curve, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value, NLR: Neutrophil-to-lymphocyte ratio. Cut-off values were determined using the Youden index. Comparisons between AUCs were performed using DeLong's test. The p-values in the table (0.03 for lactate, 0.02 for NLR) refer to comparisons against the combined model, not to whether each biomarker alone is significant.

4. Discussion

This prospective clinical study demonstrated that serum lactate concentration at presentation and NLR were associated with gastroenteritis severity in dogs presenting with AGE. The combined assessment of the biomarkers provided superior discriminatory performance compared to each biomarker alone. The current results indicated that serum lactate concentration and NLR, two readily available, cost-effective biomarkers, can serve as useful early clinical risk indicators for canines with AGE, potentially influencing clinical decision-making regarding clinical assessment, hospitalization, and the intensity of supportive care.

The increased serum lactate concentration in dogs with severe gastroenteritis was consistent with lactate's known role as a sensitive marker of tissue hypoperfusion and anaerobic metabolism^{13,14}. In AGE, severe vomiting and diarrhea can cause substantial fluid losses resulting in decreased intravascular volume and decreased cardiac output with subsequent impairment of systemic oxygen delivery¹³. Inadequate oxygen delivery to meet the metabolic requirements of tissues causes cells to switch from aerobic to anaerobic glycolysis, which results in accumulation of lactate in circulation¹³. The median lactate

concentration in the current study in dogs with severe gastroenteritis (3.8 mmol/L) was similar to previous studies that described lactate concentrations of 3.0-5.0 mmol/L in dogs with severe conditions^{13,15}. The value of 2.3 mmol/L identified in the ROC analysis of the present study was similar to the upper reference limit of 2.0-2.5 mmol/L used in clinical practice for lactate¹⁶. A total of 82.1% of dogs with severe gastroenteritis had hyperlactatemia, further highlighting the clinical importance of the NLR biomarker in identifying dogs with compromised perfusion status who may require immediate resuscitation measures¹⁶. Importantly, the strong correlation between lactate and degree of dehydration, as well as mental status alterations, supported the construct validity of the present severity scoring system and reinforced the physiological link between lactate accumulation and clinical signs of impaired tissue perfusion¹⁵. Similarly, the elevated NLR in dogs with severe gastroenteritis and its strong positive correlation with clinical severity scores were consistent with previous findings of Zahorec¹⁷, who established NLR as a simple and rapid parameter of systemic inflammation and stress. Fornefett et al.¹⁸ subsequently demonstrated that NLR was elevated in dogs with SIRS. These results corroborated the

present findings in dogs with AGE, showing that NLR elevation was associated with disease severity in this population and supporting NLR as a readily available marker of systemic inflammatory stress across different clinical conditions and species. The current finding that NLR was higher in dogs with severe disease agreed with previous studies reporting NLR values of 10-15 in dogs with parvoviral enteritis or septic peritonitis^{19,20}. The association between NLR and mental status alterations in the present study was consistent with previous findings linking systemic inflammation to neurological dysfunction. Cortellini et al.²⁰ further indicated that elevated NLR was associated with worse outcomes in dogs with septic peritonitis, a condition characterized by severe systemic inflammation. In the current study, the correlation between NLR and mental status alterations suggested that systemic inflammation, as reflected by NLR, may also be associated with neurological compromise in dogs with AGE, possibly through SIRS-mediated effects on cerebral perfusion and function.

The current finding indicated that both biomarkers were independently associated with severe disease in the multivariable regression model. After adjusting for potential confounders such as age, sex, and body weight, serum lactate was a strong independent predictor (adjusted odds ratio 2.96 per 1 mmol/L increase), while NLR had an adjusted odds ratio of 1.38 per unit increase. These results indicated that each biomarker provided unique and complementary information about the pathophysiological state of the dogs. Lactate is a marker of the hemodynamic and metabolic effects of the disease, while NLR is a marker of the inflammatory and immunological properties^{21,22}. This complementary nature likely explains the combined model's superior performance in the ROC analysis compared with lactate and NLR alone. The combined model had high sensitivity (89.3%) and specificity (88.6%), indicating that measuring both biomarkers simultaneously could improve clinical decision-making by identifying most dogs at risk for severe disease while maintaining an acceptable false-positive rate. The negative predictive value of 93.2% was especially reassuring, as it indicated that dogs with normal lactate and NLR were very unlikely to develop severe disease, and this might enable safe outpatient management in a substantial proportion of cases²⁴. A recent study indicated that lactate combined with NLR provided a more accurate prognostic ability than classical scoring systems such as SIRS criteria in critically ill dogs and cats¹¹.

The observed correlations between increased biomarkers and poor clinical outcomes further supported their prognostic utility. Dogs with hyperlactatemia were almost 2.5 times more likely to be hospitalized and had notably longer hospitalization periods than dogs with normal lactate levels²². Similarly, an increased NLR was associated with a higher hospitalization rate and longer hospitalization duration²². These current findings align with earlier studies indicating that higher biomarker levels at presentation are linked to increased healthcare resource utilization in both human and veterinary medicine

populations²². The higher lactate and NLR values in dogs requiring intensive supportive treatment further support the clinical relevance of these biomarkers for identifying dogs that need early care. The mortality rate of 12.5% and 13.8% observed in the present study (all deaths occurring in the severe group) was higher than previously published mortality rates for canine gastroenteritis ranging from 3% to 10%²⁴. The notably high serum lactate and NLR levels at presentation in non-survivors indicated that these markers could help identify dogs at greatest risk of death.

Serum lactate and NLR are easily available in most veterinary clinical settings. The reliability and feasibility of lactate measurement in canine patients have been well established, with studies demonstrating predictable lactate kinetics and the clinical utility of serial lactate monitoring in dogs¹⁵. Similarly, NLR is derived from routine CBC parameters and has been validated as a practical and valuable prognostic marker in dogs with systemic inflammatory conditions, requiring no additional cost or sample processing beyond standard hematological analysis¹⁸. These characteristics make both biomarkers particularly suitable for emergency triage, where rapid, cost-effective risk stratification is essential. This accessibility makes NLR particularly suitable to be used in emergency triage, where decisions should be made on hospitalization and intensity of treatment with limited information and under time pressure²⁵. The current study proposed a pragmatic algorithm for clinical decision-making. In this algorithm, serum lactate and CBC were measured at presentation, and NLR was calculated. Dogs with both biomarkers below the specified cut-offs could be considered for outpatient management with close monitoring. Dogs with elevation in either or both biomarkers could be considered for hospitalization and more aggressive supportive care. The degree of elevation served as a surrogate for the urgency and intensity of intervention^{23,25}. Recent advances in veterinary critical care have emphasized the importance of early recognition and intervention for improved outcomes in critically ill canines, including those with acute gastrointestinal emergencies²⁵. The acute hemorrhagic diarrhea syndrome (AHDS) index was introduced to standardize clinical severity assessment in dogs with acute hemorrhagic diarrhea syndrome, underscoring the value of structured severity scoring in this population²⁶. The current findings indicated that serum lactate and NLR, two readily available biomarkers, provided complementary prognostic information for early risk stratification in dogs with AGE, further extending the conceptual framework from previous studies.

5. Conclusion

In the current study, serum lactate and NLR were independently associated with disease severity in dogs with AGE, and their combined evaluation yielded more accurate predictive performance than either biomarker alone. Both biomarkers were significantly elevated in severe cases, with median serum lactate of 3.8 mmol/L versus 1.6 mmol/L in mild-to-moderate cases, and median

NLR of 12.4 versus 4.2, respectively. Elevated lactate was associated with an 84.4% hospitalization rate compared to 35.0% in dogs with normal lactate, and elevated was associated with an 86.2% hospitalization rate compared to 37.2% in dogs with normal NLR. The high negative predictive value indicated that dogs with normal values of both biomarkers were unlikely to develop severe gastroenteritis and could be safely managed as outpatients, while elevation of either marker should prompt hospitalization. Thus, serum lactate and NLR are promising early predictors for risk stratification in dogs with AGE, and their combined use may help veterinarians to identify dogs that require closer monitoring and more intensive care. Limitations of the current study included a single-center design, a small sample size, and biomarker measurement at a single time point, which may limit generalizability. The current study also did not measure key physiological parameters, including body temperature, heart rate, and respiratory rate. Multicenter studies are needed to confirm the prognostic value of NLR and serum lactate.

Declarations

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Acknowledgments

The authors conducted the study independently and received no external contributions.

Authors' contributions

Ramtin Ghorban Pour conceptualized the study, designed the research protocol, and supervised the entire project from inception to completion. Ali Heydari served as the corresponding author, was responsible for clinical case enrollment, performed the physical examinations and severity scoring, and drafted the original manuscript. Ghazaleh Kompani contributed to clinical case enrollment and assisted in the assessment of clinical severity parameters. Sara Sadat Tavakoli was responsible for blood sample collection, laboratory analysis, and data curation. Ali Jebeli Eshrat Abadi performed the statistical analyses and contributed to the interpretation of the data. Parsa Jahani conducted the literature review and critically revised the manuscript for important intellectual content. All authors have read and approved the final version of the manuscript prior to submission. All authors have read and approved the final edition of the manuscript prior to publication in the present journal.

Competing interests

The authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the study reported in the present manuscript.

Ethical considerations

The authors confirmed that all ethical issues, including plagiarism, publication consent, research integrity, data fabrication and/or falsification, duplicate publication and/or submission, and redundancy, have been carefully considered and addressed in accordance with accepted publication ethics standards. No generative artificial intelligence tools were used to generate data, results, or conclusions. Just Grammarly used for remove grammatical errors. The authors further affirm that they are solely responsible for the accuracy, originality, and integrity of the final content both before initial submission, during the revision process, and upon final publication. The authors have checked and verified all scientific data, interpretations, and conclusions without reliance on AI for intellectual content.

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