



Prognostic markers of multiple organ dysfunction syndrome in critically ill dogs: albumin, creatinine, platelets, RNL, RPL, and shock index

[Marcadores prognósticos da síndrome da disfunção orgânica múltipla em cães críticos: albumina, creatinina, plaquetas, RNL, RPL e índice de choque]

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Abstract: Systemic Inflammatory Response Syndrome (SIRS) is a severe condition in hospitalized dogs, particularly when associated with multiple organ dysfunction syndrome (MODS), which is linked to increased mortality. This study included 39 dogs meeting SIRS criteria, aiming to evaluate clinical and laboratory parameters as prognostic tools at admission. The following variables were analyzed: hematocrit ($\leq 25\%$), platelet count ($\leq 200,000/\mu\text{L}$), albumin ($\leq 2.5\text{ g/dL}$), creatinine ($\geq 1.6\text{ mg/dL}$), serum lactate, shock index (SI), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR). Dogs were stratified into three groups according to disease severity: Group A (three abnormal laboratory parameters), Group B (two abnormal parameters), and Group C (one abnormal parameter). Mortality was highest in Group A (60 %), followed by Group B (53.8 %) and Group C (36.4 %). Statistically significant differences were observed among groups for hematocrit ($p = 0.002$), platelet count ($p = 0.002$), and albumin ($p = 0.014$). ROC curve analysis demonstrated high sensitivity of the shock index (88.9 %) for predicting mortality. The integrated assessment of simple laboratory parameters and the shock index was useful for risk stratification, whereas the predictive performance of admission lactate and NLR/PLR when evaluated in isolation was limited, possibly influenced by the static nature of measurement and sample size.

Keywords: Prognosis; systemic inflammatory response syndrome; clinical triage.

Resumo: A Síndrome da Resposta Inflamatória Sistêmica (SIRS) é uma condição grave em cães hospitalizados, especialmente quando associada à disfunção orgânica múltipla (MODS), condição que eleva as taxas de mortalidade. Este estudo avaliou 39 cães com triagem de SIRS positivo, com o objetivo de analisar diferentes parâmetros clínicos e laboratoriais como ferramentas prognósticas na triagem inicial. Foram avaliados: hematócrito ($\leq 25\%$), contagem de plaquetas ($\leq 200\text{ mil}/\mu\text{L}$), albumina ($\leq 2,5\text{ g/dL}$), creatinina ($\geq 1,6\text{ mg/dL}$), lactato sérico, índice de choque (IC) e as relações neutrófilo-linfócito (RNL) e plaqueta-linfócito (RPL). Os cães foram divididos em três grupos de gravidade: Grupo A (três parâmetros laboratoriais alterados), Grupo B (dois parâmetros alterados) e Grupo C (um parâmetro alterado). A mortalidade foi superior no Grupo A (60 %), seguido do Grupo B (53,8 %) e Grupo C (36,4 %). Diferenças estatisticamente significativas entre os grupos foram identificadas para hematócrito ($p=0,002$), plaquetas ($p=0,002$) e albumina ($p=0,014$). A análise da curva ROC demonstrou elevada sensibilidade do IC (88,9 %) para predição de óbito. Conclui-se

que a avaliação integrada de parâmetros laboratoriais simples e do IC é eficaz na determinação do prognóstico, enquanto a acurácia do lactato admissional isolado e dos índices RNL/RPL pode sofrer influência da natureza estática da coleta e do tamanho amostral.

Palavras-chave: Prognóstico; Síndrome da resposta inflamatória sistêmica; triagem clínica.

1. Introduction

Systemic inflammatory response syndrome (SIRS) and sepsis are severe clinical conditions encountered in veterinary inpatient settings and are associated with high mortality, particularly when they progress to Multiple Organ Dysfunction Syndrome (MODS), involving one or more organ systems ^(1, 2).

Veterinary studies have reported variable mortality rates for SIRS, ranging from 20% to 68 % ⁽³⁾, and rates may exceed 70 % when MODS is present ^(4, 5). This elevated mortality is largely attributed to delayed diagnosis and exacerbated progression of the inflammatory cascade, and worsening endothelial dysfunction ^(5, 6).

Since publication of the Sepsis-3 consensus in 2016, the SOFA (Sequential Organ Failure Assessment) and qSOFA (Quick Sequential Organ Failure Assessment) scores have been adopted in human medicine as screening tools for early identification of organ dysfunction ⁽⁷⁾. These scoring systems are based on integrated assessment of six organ systems: respiratory, hematologic, hepatic, cardiovascular, central nervous system, and renal. Higher scores are associated with poorer prognosis ^(6, 8).

However, application of these tools in veterinary medicine remains limited. Scarcity of studies validating SOFA and qSOFA in small animals reduces confidence in their clinical utility for veterinary patients. Moreover, common structural limitations in veterinary practice, such as difficulty obtaining PaO₂/FiO₂ ratios for respiratory assessment, restrict routine hospital use of these instruments ⁽⁹⁻¹¹⁾.

Given these practical limitations associated with complex scoring systems in veterinary medicine, this study aimed to evaluate systemic dysfunction in critically ill dogs through integration of accessible clinical and laboratory variables. Rather than relying on isolated measurements, the study focused on combined assessment of multiple organ systems as prognostic screening tools ^(4, 12).

2. Material and methods

The study was approved by the Ethics Committee on Animal Use under protocol 027/2023, ensuring ethical compliance and welfare of all animals involved.

Thirty-nine dogs (18 males and 21 females) of various breeds and ages, ranging from three months to 18 years, admitted for veterinary hospitalization were included. Dogs were enrolled based on the presence of clinical and hematologic criteria for Systemic Inflammatory Response Syndrome (SIRS), presented in Table 1. Animals were classified as having SIRS when two or more parameters were abnormal, according to Sepsis-3 consensus guidelines and recommendations described by Harvey ⁽¹³⁾, Rabelo ⁽⁹⁾, and Cortellini et al. ⁽¹⁰⁾.

Table 1. Criteria for identification of SIRS in hospitalized dogs.

Parameter	Criterion (dogs)
Temperature (°C)	< 38.1 or > 39.2
Heart rate (bpm)	> 120
Respiratory rate (rpm)	> 20
Leukocytes ($\times 10^3/\mu\text{L}$)	< 6 or > 16
Band cells (%)	> 3

Note: Presence of ≥ 2 criteria characterizes SIRS. Source: Adapted from Rabelo ⁽⁹⁾.

Clinical data were obtained from medical records provided by the attending veterinarian. Underlying diseases were classified as infectious, reproductive, traumatic, immune-mediated, or neoplastic. Lactate concentration (>1 mmol/L) was measured, and the Glasgow Coma Scale (score ≤ 17) was applied.

For severity stratification, dogs were allocated to three groups (A, B, and C) according to the number of abnormalities in the following variables: creatinine (≥ 1.6 mg/dL), albumin (≤ 2.5 g/dL), platelet count ($\leq 200,000/\mu\text{L}$), and hematocrit ($\leq 25\%$) ^(9, 14).

Group A (high severity): 15 dogs with three abnormal laboratory variables.

Group B (moderate severity): 13 dogs with two abnormal laboratory variables.

Group C (low severity): 11 dogs with one abnormal laboratory variable.

2.1 Laboratory Analysis

Peripheral venous whole blood samples were collected from the jugular or cephalic vein into tubes containing K_1EDTA (0.5 mL) and tubes without anticoagulant for biochemical analysis (1 mL), following antisepsis with 70 % alcohol. All samples were refrigerated and analyzed within two hours of collection. Blood smears were prepared on glass slides and stained using the May-Grünwald/Giemsa method (New Prov®).

Erythrocyte count, hemoglobin concentration, total leukocyte count, and platelet count were determined using an automated hematology analyzer (BC-2200 Vet, Mindray®). Hematimetric indices (MCV, MCH, and MCHC) were calculated as described by Weiss and Wardrop ⁽¹⁴⁾.

Hematocrit was confirmed by the microhematocrit method after centrifugation at 11,000 rpm for 5 min (Fanem®, Excelsa Flex 3400), followed by reading on a specific scale card. Total plasma protein was measured using a manual refractometer (Kasvi®).

On stained smears, differential leukocyte count, neutrophil morphological evaluation, qualitative erythrocyte assessment, and estimated platelet count were performed according to Stockham and Scott ⁽¹⁵⁾, using a 100 $\times$ oil immersion objective on a light microscope (Olympus BX41®).

Whole blood samples collected in tubes without anticoagulant were centrifuged at 4,000 rpm for 5 min in a benchtop centrifuge (Hoffmann®, HCL-4) to obtain serum. Biochemical analyses were performed using an automated analyzer (Mindray®, BS200) with commercial

reagents (Bioclin®). Serum lactate and creatinine were determined by kinetic methods, whereas albumin was measured by the bromocresol green monoreagent method. All procedures followed manufacturer instructions.

In addition to derived indices, absolute counts of total leukocytes, segmented neutrophils, and lymphocytes were included for intergroup comparisons and association with clinical outcomes.

The segmented neutrophil-to-lymphocyte ratio (SNR) was calculated according to Jager et al.⁽¹²⁾, by dividing absolute segmented neutrophil count by absolute lymphocyte count. The platelet-to-lymphocyte ratio (PLR) was calculated by dividing absolute platelet count by absolute lymphocyte count in peripheral blood ^(16, 17).

2.2 Clinical Analysis

Shock index was calculated on day 0, before venous blood collection, as the ratio between heart rate (bpm) and systolic blood pressure (mmHg) ($SI = HR/SBP$), according to Balhara et al. ⁽¹⁷⁾. Heart rate was determined by cardiac auscultation with a stethoscope, whereas systolic blood pressure was measured using Doppler equipment and a veterinary sphygmomanometer appropriate for species and body size.

2.3 Statistical Analysis

Means, medians, standard deviations, minimum values, and maximum values were calculated. Comparisons among Groups A, B, and C, as well as between G1 and G2, were performed using one-way ANOVA for parametric variables and the Kruskal–Wallis test for nonparametric variables. Statistical significance was set at $p < 0.05$. Mortality rate was calculated as relative frequency of deaths during the observation period.

To evaluate diagnostic accuracy and prognostic performance of hemodynamic markers (serum lactate and shock index) in relation to outcome (death or survival), receiver operating characteristic (ROC) curve analysis was performed. Overall test performance was determined by area under the curve (AUC). Optimized cutoff values for the study sample were identified using the Youden index, with corresponding sensitivity and specificity values. Analyses were conducted using Jamovi software (version 2.3).

3. Results and discussion

When the three study groups were compared, mortality rates were 60% in Group A (dogs with three abnormal laboratory variables), 53.8% in Group B (dogs with two abnormal variables), and 36.4 % in Group C (dogs with one abnormal variable), demonstrating a progressive increase in mortality with greater clinical severity. This pattern is consistent with previous reports showing higher mortality in patients with SIRS and organ dysfunction as multiple systems become compromised ^(2,3).

A higher frequency of infectious and reproductive causes (pyometra) was observed across all groups, representing 66.66 % of the total sample. This distribution reinforces the role of infectious foci as major triggers of SIRS in small animal clinical practice.

Group A, which showed the highest mortality rate (60 %) and the highest mean age (6.73 years), included more cases of severe hemoparasitic disease, pyometra, and extensive trauma (lacerations with myiasis), suggesting that Multiple Organ Dysfunction Syndrome (MODS) may already have been established at initial evaluation. Although mean age was similar among groups (5.0 to 6.7 years), the sample showed wide age variation, reflecting the heterogeneous nature of

SIRS in small animal practice, where it may arise as a common consequence of multiple disorders with distinct pathophysiologic mechanisms and prognoses^(11,18). In this context, prognosis depends not only on inflammatory response but also on individual patient characteristics.

For example, acute infectious diseases such as parvoviral infection, observed mainly in younger dogs, are associated with rapid progression and high mortality due to severe dehydration, secondary sepsis, and bacterial translocation ^(7, 19, 20). In contrast, in neoplasia and metastatic disease, SIRS is associated with chronic inflammation combined with disease progression, often with an irreversible course ^(20, 21).

Differences in etiology and age represent important limitations of this study, since prognosis may vary substantially according to underlying disease and intrinsic characteristics of each dog. Geriatric patients with trauma-associated SIRS may have reduced capacity to respond to systemic stress, whereas young dogs with acute infectious diseases may deteriorate rapidly because of pathogen virulence despite greater functional reserve ^(11, 20).

Within this scenario, prognostic markers evaluated in this study, such as lactate, albumin, and shock index, should be interpreted as indicators of systemic severity at the time of assessment, reflecting perfusion status and intensity of inflammatory response. However, their prognostic value should be considered in the context of the underlying disease and individual patient condition. In potentially reversible disorders, such as trauma and acute infections, these variables may help guide fluid resuscitation and clinical monitoring ⁽¹¹⁾. In chronic or irreversible conditions, such as advanced neoplasia, they may primarily reflect disease progression regardless of therapeutic intervention ⁽²⁰⁾. Table 2 presents the distribution of etiologies and age profile according to severity groups.

Table 2. Distribution of etiologies and age profile according to severity groups (n=39).

Group	N	Mean age (years)	Median age (years)	Examples from the sample
Group A	15	6.73	6	Infectious (4), Reproductive (4), Traumatic (6), Inflammatory/Orthopedic (1)
Group B	13	5.07	4	Infectious (5), Reproductive (2), Traumatic (2), Neoplastic (2), Imune-mediated (1), Metabolic (1)
Group C	11	5.65	4	Infectious (6), Reproductive (3), Traumatic (1), Metabolic (1)

In the present study, most dogs had serum lactate concentrations above 3 mmol/L, highlighting hyperlactatemia as a marker of inadequate tissue perfusion and supporting its role as a biomarker in SIRS screening ^(6, 22, 23). Group A showed the highest mean lactate concentration (4.25 mmol/L) and the highest mortality rate, suggesting an association between persistent hyperlactatemia and poorer clinical outcome, as previously reported in critically ill dogs ^(22, 23).

Regarding shock index (SI), although differences among groups were small, all groups showed mean values greater than 1, consistent with hemodynamic compromise. Studies in critically ill dogs have shown that elevated SI values are associated with increased mortality, reflecting circulatory dysfunction and inadequate perfusion ^(17, 24). In

addition, the present findings agree with Berger et al.⁽²⁴⁾, who reported that the combination of increased SI and hyperlactatemia amplifies risk of death. When clinical outcome (death vs. discharge) was analyzed in the present study, SI differed significantly between groups ($p = 0.038$), supporting its use as an early marker of circulatory dysfunction and adverse prognosis, particularly when values approach or exceed 2 in critically ill patients, consistent with previous reports^(17, 24).

However, when evaluated individually, both variables showed limited ability to predict mortality. ROC curve analysis demonstrated an area under the curve (AUC) of 0.646 for shock index and 0.467 for serum lactate. At a cutoff value of 1.12, SI showed high sensitivity (88.9 %) but low specificity (44.4 %). For lactate, a cutoff value of 2.2 mmol/L yielded sensitivity of 77.8 % and specificity of 33.3 %. It is important to note that lactate concentrations in this study represented a single static measurement obtained at admission (day 0). Serial monitoring may provide better assessment of therapeutic response and restoration of tissue perfusion. The ROC curve is presented in Figure 1.

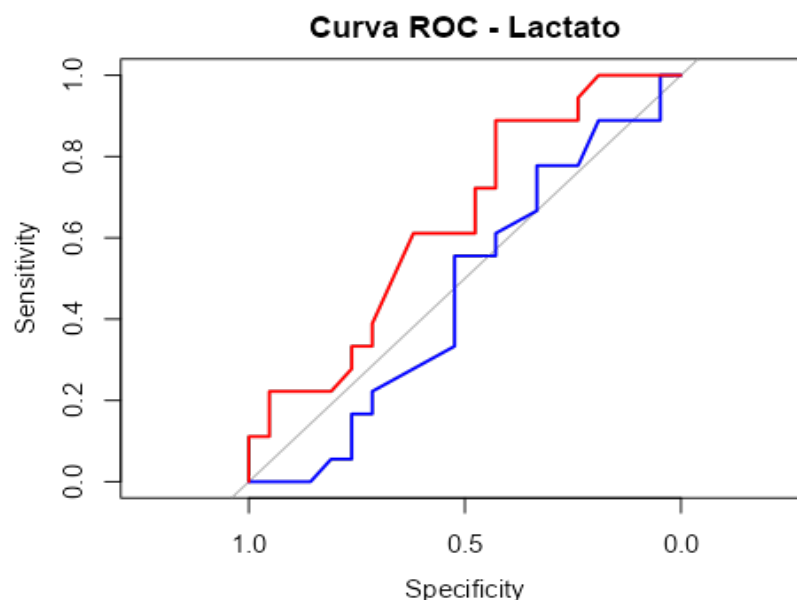


Figure 1. Receiver operating characteristic (ROC) curves of shock index (SI) and serum lactate for prediction of mortality in dogs with SIRS.

When groups were analyzed according to the number of abnormal laboratory variables, significant differences among Groups A, B, and C were observed for hematocrit ($p = 0.002$), platelet count ($p = 0.002$), and serum albumin ($p = 0.014$), indicating greater hematologic and inflammatory involvement in dogs classified with higher severity. These findings reinforce the multisystemic nature of SIRS and MODS in critically ill dogs^(10, 18).

Post hoc analysis was performed for hematocrit and demonstrated significant differences between Groups A and C for both hematocrit and albumin. Between Groups B and C, only hematocrit differed significantly, whereas no significant differences were observed between Groups A and B. From a clinical perspective, hematocrit showed greater discriminatory ability between patients with low severity and those with established systemic dysfunction, but lower sensitivity for distinguishing more advanced stages of clinical involvement. Hematocrit, platelet count, and albumin values are presented in Figures 2, 3, and 4, respectively.

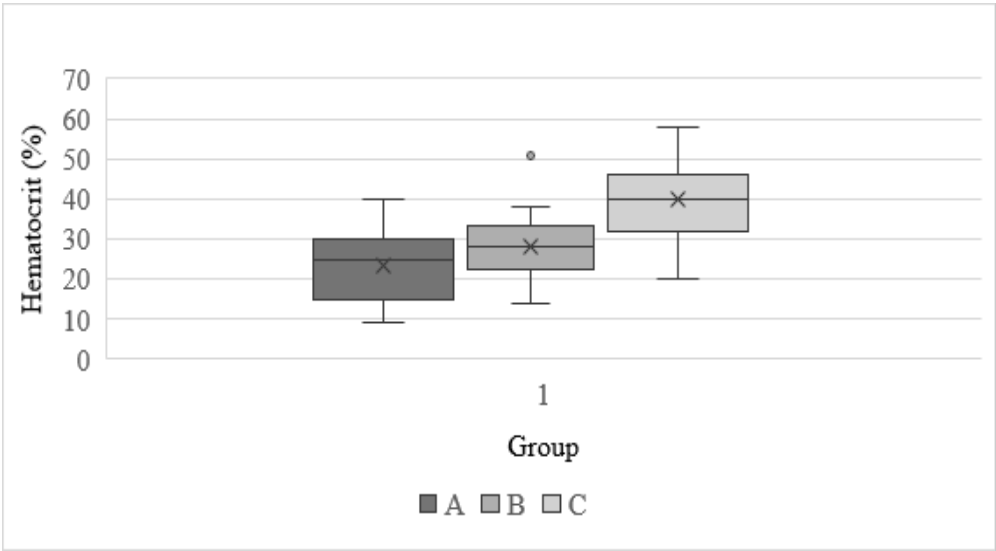


Figure 2. Distribution of hematocrit values (%) among groups A, B, and C.

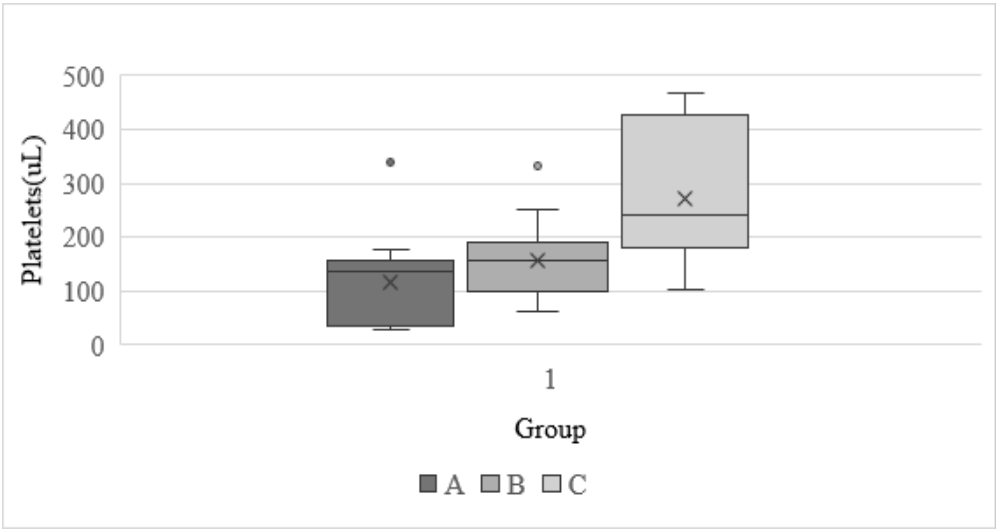


Figure 3. Distribution of platelet counts (thousands) among groups A, B, and C.

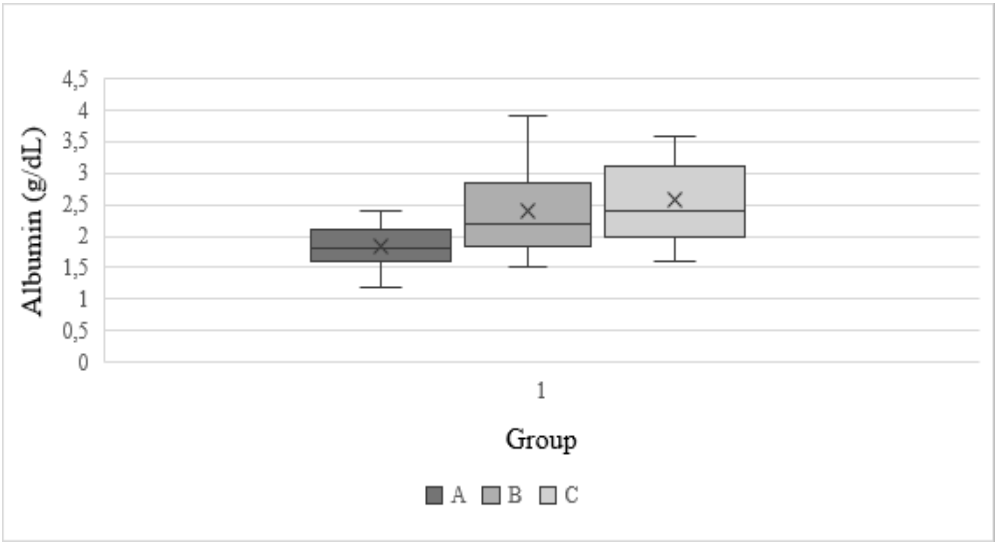


Figure 4. Distribution of albumin values (g/dL) among groups A, B, and C.

The reduction in hematocrit values observed in the more severe groups may be associated with mechanisms such as hemodilution, anemia of inflammation, peripheral consumption, and impaired erythropoiesis, all of which have been described in critically ill and septic patients ^(14, 15, 25, 26).

Likewise, thrombocytopenia observed in the most severely affected dogs may reflect platelet consumption and endothelial dysfunction. Dogs in Group C (lower severity), which showed platelet counts within the reference interval, had more favorable clinical outcomes, supporting the relevance of this variable during screening, since thrombocytopenia has been associated with poorer prognosis in dogs with sepsis ^(1, 13, 27, 28).

Hypoalbuminemia has also been described as an important marker of severity and mortality in hospitalized patients, acting as a negative acute-phase protein ^(9, 29). Its reduction in the setting of SIRS reflects not only intensity of systemic inflammation and increased vascular permeability, but also redistribution of hepatic protein synthesis in response to proinflammatory cytokines such as IL-1 and IL-6, contributing to poorer prognosis ^(9, 29, 30, 31). Serum albumin analysis showed that dogs with concentrations above 2.5 g/dL (Group C) had lower mortality, whereas Groups A and B, characterized by hypoalbuminemia, had higher mortality rates. These results reinforce the value of integrated assessment of simple and widely available laboratory variables as adjunctive tools for risk stratification and prognosis in dogs with SIRS and MODS ^(8, 10).

Although no statistically significant difference in serum creatinine concentration was observed among groups, descriptive analysis indicated a progressive increase according to clinical severity, with higher mean values in Group A. Lack of statistical significance may be related to limited sample size, preserved renal compensatory capacity during early stages of disease, and limitations of creatinine as a renal biomarker, since increases generally occur only after substantial reduction in glomerular filtration rate. Therefore, creatinine may remain within the reference interval during early dysfunction. In addition, compensatory renal mechanisms may mask early changes, particularly in critically ill patients ^(6, 29).

In this context, recent studies suggest that urinary biomarkers may provide greater sensitivity for early detection of acute kidney injury in dogs and may identify renal impairment before increases in serum creatinine occur ⁽²⁹⁾. These findings indicate that, although widely used, creatinine has limitations as an isolated marker for early recognition of renal dysfunction in patients with SIRS.

Overall, findings of this study indicate that albumin, platelet count, and hematocrit may serve as useful prognostic markers in dogs with SIRS by reflecting extent of organ dysfunction (MODS). Table 3 presents a descriptive analysis of hematocrit, platelet count, albumin, and creatinine values.

Table 3. Analysis of hematocrit (%), platelet (mL/ μ L), albumin (g/dL), and creatinine (mg/dL) values in dogs from groups A (three abnormal variables), B (two abnormal variables), and C (one abnormal variables). Different letters within the same row indicate a statistically significant difference among Groups ($p < 0.05$).

	Group	N	Mean	Median	Standard-deviation	Minimum	Maximum
Hematocrit (%)	A	15	23.60 ^a	25	9.18	9	40
	B	13	28.30 ^a	28	9.63	14	51
	C	11	39.90 ^b	40	10.85	20	58
Platelets (mil/ μ L)	A	15	117.66 ^a	136	82.05	28	340
	B	13	157.38 ^a	156	74.92	62	332
	C	11	270.27 ^b	240	123.93	103	468
Albumin g/dL	A	15	1.84 ^a	1.80	0.37	1.20	2.40
	B	13	2.40 ^{ab}	2.20	0.69	1.50	3.90
	C	11	2.57 ^b	2.40	0.69	1.60	3.60
Creatinine mg/dL	A	15	1.85 ^a	0.80	1.96	0.50	7.00
	B	13	0.83 ^a	0.80	0.24	0.30	1.20
	C	11	0.79 ^a	0.70	0.35	0.40	1.50

Analysis of mean leukocyte, neutrophil, and total lymphocyte counts, as well as PLR (platelet-to-lymphocyte ratio) and NLR (neutrophil-to-lymphocyte ratio), among severity groups and clinical outcomes (discharge or death) did not reveal statistically significant differences. The absence of significance likely reflects limited statistical power due to sample size (type II error). In addition, many critically ill patients are referred after previous treatment, including corticosteroid administration and fluid therapy, which may mask initial leukocyte and platelet responses and directly affect calculation of these indices at admission ^(16, 33).

Despite these limitations, assessment of NLR and PLR remains a promising approach in veterinary intensive care, where available studies are still limited ^(16, 34). We agree with Macfarlane et al.⁽³⁴⁾, who suggested that measurement of NLR may be more informative than isolated cell counts because it integrates systemic inflammatory response. However, its prognostic applicability in heterogeneous SIRS populations still requires validation in studies with larger sample sizes. Table 4 presents a descriptive analysis of evaluated variables (lactate, SI, PLR, and NLR) in the three groups.

Table 4. Descriptive analysis of lactate (mmol/L), shock index (SI), PLR, and NLR values in dogs from groups A (three abnormal variables), B (two abnormal variables), and C (one abnormal variable).

	Group	N	Mean	Median	Standard-deviation	Minimum	Maximum
Lactate	A	15	4.25 ^a	4.20	2.17	1.00	8.60
	B	13	3.34 ^a	3.00	1.51	1.40	6.00
	C	11	3.09 ^a	2.40	1.10	2.00	4.70
SI	A	15	1.32 ^a	1.00	0.50	0.71	2.50
	B	13	1.48 ^a	1.11	0.71	0.78	2.86
	C	11	1.09 ^a	1.00	0.35	0.50	1.76
PLR	A	15	190.74 ^a	105.19	366.61	5.12	1500.00
	B	12	293.58 ^a	85.93	475.95	41.40	1706.66
	C	11	441.46 ^a	284.40	472.30	19.33	1550.00
NRL	A	15	26.81 ^a	21.25	24.93	3.33	89.00
	B	13	34.27 ^a	12.00	38.82	4.42	122.00
	C	11	24.60 ^a	15.20	25.96	1.45	92.00

Literature highlights the complexity of organ dysfunction in small animals and the need for integrative diagnostic screening approaches, as reviewed by Cortellini et al. ⁽¹⁰⁾. Accordingly, combined assessment of multiple clinical and laboratory variables, together with indicators such as lactate >3 mmol/L and shock index >1.0, proved more effective in estimating risk of death than isolated analysis of individual variables.

4. Conclusion

Integrated assessment of simple laboratory variables (hematocrit, platelet count, and serum albumin), combined with monitoring of serum lactate and shock index (SI), proved useful for screening and predicting clinical outcome in dogs with SIRS. Identification of a greater number of abnormal variables, particularly when associated with increased lactate concentrations and elevated SI values, was associated with higher mortality risk. In contrast, within this case series, NLR and PLR did not perform as independent predictors of death. Combined use of these hemodynamic and laboratory markers represents an accessible tool for early risk stratification in critically ill patients.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Data availability statement

The complete dataset supporting the findings of this study is available from the corresponding author upon reasonable request.

Author contributions

Conceptualization: Rueda, T. L., Ditrich, R. L.; Formal analysis: Rueda, T. L.; Supervision: Ditrich, R. L.; Writing: Rueda, T. L., Ditrich, R. L.

Generative AI use statement

The authors did not use generative artificial intelligence tools or technologies in creating or editing any part of this manuscript.

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