*Short Research Article*

Tracking Systemic Inflammatory Progression in Dogs: Blood indices as Predictive Tools

ABSTRACT

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| **Aims:** To evaluate the alterations in haematological indices such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII) in dogs diagnosed with systemic inflammatory response syndrome (SIRS), and to further assess the changes in these parameters in cases that progress to multiple organ dysfunction syndrome (MODS).  **Study design:**  **Place and Duration of Study:** The study was conducted in the Department of Veterinary Clinical Medicine. Ethics and Jurisprudence, College of Veterinary and Animal Sciences, Pookode, Wayanad- 673576 between July 2024 and June 2025.  **Methodology:** Dogs meeting the inclusion criteria for SIRS were enrolled in the study. Based on organ dysfunction parameters, they were categorized into two groups: Group I, comprising dogs that did not develop MODS, and Group II, comprising those that progressed to MODS. Comprehensive haematological analyses were performed and their relevance in disease progression was interpreted.  **Results:** NLR values were significantly elevated in both groups compared to the control group (6.3 ± 0.93 in Group I, 8.09 ± 0.86 in Group II, and 3.28 ± 0.14 in controls). Although PLR values did not show a statistically significant difference between Group I and the control group, Group II exhibited a significantly lower PLR (90.21 ± 16.65) compared to controls (169.15 ± 16.14; **P = 0.003**). SII values were markedly increased in both groups relative to the control animals.  **Conclusion:** The study highlights the prognostic significance of NLR, PLR, and SII as inflammatory biomarkers in dogs with SIRS, with notable differences observed between those that developed MODS and those that did not. |

*Keywords: SIRS, MODS, NLR, PLR, SII*

1. INTRODUCTION

Systemic inflammatory response syndrome (SIRS) occurs as a widespread reaction to infectious or non-infectious diseases, driven by a significant release of inflammatory mediators. Assessing the severity and progression of SIRS in dogs remains challenging, as conventional diagnostic methods may not always provide early insights into immune dysregulation. Various biomarkers for the diagnosis and prognostication of sepsis have been assessed in veterinary medicine with mixed results (Hodgson *et al.,* 2018). The neutrophils being a key component of the innate immune system, will have a dramatic increase when there are any inflammatory reactions are taking place in the body. However, with continued septic states, neutrophil function is decreased and apoptosis is delayed (Hotchkiss *et al*., 2013). The neutrophil-to-lymphocyte ratio (NLR) is an easily accessible and cost-effective biomarker derived from a complete blood count, used to evaluate the balance of the body's inflammatory response (Salciccioli *et al.,*2015). Zahorec (2001) first proposed the use of the NLR as a marker of infection in a clinical setting in human medicine. The NLR and platelet-to-lymphocyte ratio (PLR) are recognized as prognostic indicators in existing literature, valued for their simplicity, accessibility, and cost-effectiveness. Additionally, the systemic immune-inflammation index (SII) and systemic inflammatory response index are emerging as crucial markers for assessing the severity of SIRS in animals. Numerous studies in human medicine have identified the NLR as a reliable independent predictor of morbidity and mortality across various clinical conditions, including sepsis, cardiovascular disease, neoplasia, and infectious diseases.

In dogs, various etiological agents can trigger SIRS, which, if left unmanaged, may progress to multiple organ dysfunction syndrome (MODS), depending on the severity of infection and the timeliness of medical intervention. Early assessment of inflammation levels is essential to prevent disease progression. Given the critical nature of SIRS, prompt and appropriate care is required to mitigate complications in affected dogs.

This study primarily aims to assess variations in the NLR, PLR, and SII in dogs diagnosed with SIRS, contributing to the refinement of early detection methodologies and optimized therapeutic interventions. Additionally, the study seeks to evaluate changes in these indices as SIRS progresses to MODS. By leveraging simple and cost-effective biomarkers, this research aims to enhance accessible diagnostic tools, ultimately improving the standard of care for critically ill canine patients.

2. material and methods

Dogs having clinical signs like lethargy, weakness, respiratory distress, cough, hyporexia/anorexia, vomiting, diarrhoea, fever and altered mentation irrespective of age, sex and breed presented to veterinary hospitals under Kerala Veterinary and Animal Sciences University, Pookode were screened and those dogs meeting the inclusion criteria of SIRS (2/4) (Thomas and Boller, 2018) were selected. SIRS criteria included heart rate more than 120beats /minute, respiratory rate more than 40 breaths per minute, hypothermia (temperature < 100.60F) or hyperthermia (temperature > 102.60F) and leucopaenia (< 6000/µL) or leucocytosis (> 16000/µL). The dogs satisfying any two of the above criteria were taken as having SIRS and detailed study was carried out. Those dogs diagnosed with chronic kidney disease were excluded, leaving a final cohort of dogs.

Each dog underwent a complete blood count using a veterinary haematology analyzer (Mindray, BC 30 Vet). Non-invasive blood pressure measurements were conducted using an automatic, portable oscillometric blood pressure device (PetTrust Blood Pressure Monitor, BioCare Corporation, Taiwan). Functional oxygen saturation of arterial haemoglobin (SpO₂) was monitored non-invasively in all dogs using a handheld veterinary pulse oximeter H 100 (Hygeia, Plutus Enterprise Limited, Jordan, Hong Kong). For coagulation assessment, a 2 mL sample of whole blood was collected in a citrated vial to evaluate prothrombin time and activated partial thromboplastin time. The analysis was performed using an automated coagulation analyser (Mispa Clog, Agape Diagnostic Ltd., Ernakulam, Kerala) based on the turbo-densitometric measuring principle. Serum creatinine and total bilirubin levels were estimated with a semi-automatic biochemical analyser (MISPAVIVA 2578-10/17, Agappe, Kochi, Kerala) using appropriate kits. These dogs were further evaluated for MODS based on established organ dysfunction criteria (Ripanti *et al*., 2012; Troia *et al.,* 2018) as mentioned below.

1. Cardiovascular dysfunction– systolic blood pressure < 90mmHg despite adequate fluid (oscillometric method) resuscitation

2. Haemostatic dysfunction – prothrombin time > 7.5seconds or activated partial thromboplastin time > 16.5seconds or platelet count < 160 x 103/µL

3. Hepatic dysfunction– serum bilirubin > 0.35mg/dL (in the absence of haemolysis or biliary obstruction)

4. Renal dysfunction – serum creatinine > 1.35mg/dL

5. Respiratory dysfunction – saturation of peripheral oxygen < 95 per cent

6. Central nervous system dysfunction – Modified Glasgow Coma Scale Score ≤ 14 (Platt *et al*., 2001)

The dogs were categorised under MODS if two or more organ systems dysfunction was there.

They were classified into two groups: group 1-those without the development of MODS and group 2, those diagnosed with MODS.

Control group - Apparently healthy dogs formed the control group to obtain the normal parameters under study.

The laboratory tests included absolute neutrophil count, absolute lymphocyte count , platelet count, NLR, PLR and SII

**Definition of NLR, PLR and SII**

NLR – Neutrophil ÷ Lymphocyte

PLR – Platelet ÷ Lymphocyte

SII - Platelet x neutrophil ÷ Lymphocyte counts.

**Statistical analysis**

Independent t-test was done for comparing different variables between two groups.

3. results and discussion

A total of 41 dogs met the inclusion criteria for SIRS. After excluding seven dogs diagnosed with chronic kidney disease, 34 cases were selected for detailed evaluation. Of these, 22 (64.7 per cent) were male, and 12 (35.2 per cent) were female. The most represented breeds included Labrador Retriever (8/34, 23.5 per cent), Rottweiler (5/34, 14.7 per cent), Spitz (5/34, 14.7 per cent), Dobermann (3/34, 8.8 per cent), Dachshund (3/34, 8.8 per cent), German Shepherd (2/34, 6.8 per cent), Pug (2/34, 6.8 per cent), Beagle (1/34, 2.9 per cent), and Great Dane (1/34, 2.9 per cent). Additionally, two dogs (11.8 per cent) were of mixed breed. Hodgson *et al.* (2018) observed an over presentation of mixed breed dogs in their study on SIRS affected dogs. The age of the affected animals ranged from 10 months to 13 years.

Among the 34 cases selected, 15 (44.1 per cent) dogs did not develop MODS and were categorized under Group I. The remaining 19 (55.9 per cent) dogs met the criteria for MODS and were classified under Group II. The various haematological parameters were estimated and compared with the control group.

Although neutrophil and lymphocyte play a crucial role in the body’s defence against pathogens, a patient’s white blood cell count may present false negatives or may be delayed in reflecting the progression of inflammatory disease. Recent studies have demonstrated that white blood cell count ratios such as NLR and PLR may act as potential inflammation biomarkers in a variety of diseases.

The parameters NLR, PLR and SII were compared with the control animals. The NLR values were significantly higher for both the group I and group II animals than the control animals (table.1). Li *et al*. (2024) reported a higher incidence of mortality among septic patients that are having higher values for NLR and PLR. Shen *et al.* (2019) also reported that a high level of PLR on admission was associated with mortality in septic patients. Macfarlane *et al*. (2016) observed in the dogs with soft tissue sarcoma, the neutrophil-to-lymphocyte ratio was significantly increased compared to those with benign soft tissue tumors. In our study we could get an increase in the NLR values in dogs that developed MODS than the dogs that was not having MODS but it was not statistically significant. Azab *et al*. (2011) in their study in patients with acute pancreatitis observed that NLR is superior to total WBC in predicting adverse outcomes of acute pancreatitis. And they suggested a NLR cut off value of >4.7 as a simple indicator of severity in patients presenting with acute pancreatitis. In our study, we got a higher NLR value in both group I and group II, 6.3 ± 0.93 and 8.09 ± 0.86 respectively, that was significantly higher than the values for the control group (3.28 ± 0.14) (table I, II). In agreement with our findings Hodgson *et al.* (2018) observed that an NLR ≥ 6 had an 84.39% sensitivity and 86.95% specificity to identify dogs with systemic inflammatory states. They also noted that none of the ratios could distinguish septic and non-septic causes. In our study also, even though there was an increase of NLR in dogs with MODS compared to that of dogs without MODS, no statically significant change was observed in the values between the groups (table 3). In agreement with these findings, Salciccioli *et al.* (2015) reported that NLR was not associated with 28-day mortality in patients with sepsis. Pierini *et al.* (2019) found out that the median NLR was 11.69 and NLR was lower in septic dogs compared to non-septic ones. The systemic inflammatory response present in both populations was known to result in the development of neutrophilia and lymphopaenia. An increased release from the bone marrow and delayed apoptosis of circulating neutrophils typically results in increased numbers of circulating neutrophils of various degrees of maturation (Lewis *et al*., 2012). Cortisol mediated apoptosis and margination and redistribution of lymphocytes contribute to the development of lymphopaenia (Hotchkiss *et al*., 2013). Increased NLR signifies an increased inflammatory response in the body and has been significantly associated with an increased risk of multiorgan failure, also sepsis development in critically ill human patients (Akilli *et al*., 2014). [Mutz](https://onlinelibrary.wiley.com/authored-by/Mutz/M.) *et al*. (2015) also reported a poor outcome in lymphoma affected dogs with increased NLR.

Recent studies indicate that platelets play a crucial role in both immunomodulation and inflammation. They facilitate the release of inflammatory cytokines and interact with various bacteria and immune cells such as neutrophils, T-lymphocytes, natural killer (NK) cells, and macrophages thereby contributing to the onset or intensification of the inflammatory response (Cho *et al.,* 2014). In our study, PLR values did not exhibit significant variation between Group I and the control animals. However, a statistically significant reduction (***P = .003***) in PLR was observed in Group II animals compared to the control group (Table 2). In our study population majority of the cases with SIRS were having reduced platelet count that might be the reason for the reduction in the PLR values. Conversely, Neumann (2021) reported elevated PLR values in dogs and cats diagnosed with pancreatitis relative to control subjects, while also noting the absence of correlation between PLR and disease severity. Reactive thrombocytosis occurring in these conditions might be the reason for increased PLR (Voudoukis *et al*.,2014). Rejec *et al*. (2017) found no statistically significant difference in PLR between healthy animals and dogs affected by periodontitis.

The SII reflected the local immune response and systemic inflammation (Yazlık *et al*., 2022). As a biomarker of the inflammatory process in human medicine, it has found its place as a prognostic factor in different malignancies (Sun *et al.,* 2019). In our study, the SII values exhibited significant variation between group I (dogs without MODS) and the control animals, with Group I showing higher SII values compared to the healthy control group (table.1). Notably, dogs affected by MODS (group II) demonstrated even higher SII values, which were significantly elevated relative to the control animals (table 2). In our study we could not observe any significant changes in the SII value among the dogs with MODS and the dogs without MODS (table 3). Cristobal *et al*. (2022) reported increased NLR, PLR, and SII in dogs suffering from chronic inflammatory enteropathy. These values normalized following clinical improvement, highlighting their potential as biomarkers for disease progression and recovery. Similarly, Duran-Galea *et al.* (2024) observed elevated NLR and SII levels in dogs diagnosed with leishmaniosis compared to the control group. However, in contrast to chronic inflammatory enteropathy, no significant changes in PLR were noted in these animals. Tuna and Ulutas (2024) demonstrated a positive correlation between SII and C reactive protein in their study in obese dogs.

**Table 1. Comparison of different parameters between group I (dogs without**

**MODS) and control group**

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | Group I | Control | t-value (P-value) |
| TLC | 27.99 ± 5.36 | 7.82 ± 0.98 | 3.699\*\* ***(.002)*** |
| Neutrophil count | 20.47 ± 3.92 | 5.47 ± 0.58 | 3.779\*\* ***(.002)*** |
| Lymphocyte count | 3.94 ± 0.91 | 1.83 ± 0.35 | 2.173\* ***(.043)*** |
| NLR | 6.3 ± 0.93 | 3.28 ± 0.14 | 3.223\*\* ***(.006)*** |
| Platelet count | 250.27 ± 53.37 | 267.85 ± 22.63 | 0.287ns ***(.776)*** |
| PLR | 110.6 ± 23.89 | 169.15 ± 16.14 | 1.967ns ***(.060)*** |
| Systemic immune inflammatory index | 1519.53± 265.36 | 853.02 ± 53.9 | 2.461\* ***(.026)*** |

*\*\* Significant at 0.01 level; \* Significant at 0.05 level; ns non-significant*

**Table II. Comparison of different parameters between group II (dogs with MODS) and control group**

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| **Variable** | **Group II** | **Control** | **t-value(P-value)** |
| TLC | 28.25 ± 5.22 | 7.82 ± 0.98 | 3.843\*\*(***.001)*** |
| Neutrophil count | 23.46 ± 4.51 | 5.47 ± 0.58 | 3.953\*\****(.001)*** |
| Lymphocyte count | 3.29 ± 0.59 | 1.83 ± 0.35 | 2.125\* ***(.043)*** |
| NLR | 8.09 ± 0.86 | 3.28 ± 0.14 | 5.548\*\****(<.001)*** |
| Platelet count | 205.11 ± 35.3 | 267.85 ± 22.63 | 1.342ns ***(.190)*** |
| PLR | 90.21 ± 16.65 | 169.15 ± 16.14 | 3.263\*\* ***(.003)*** |
| Systemic immune inflammatory Index (SII) | 1617.17±361.93 | 853.02 ± 53.9 | 2.088\* ***(.050)*** |

*\*\* Significant at 0.01 level; \* Significant at 0.05 level; ns non-significant*

**Table 3. Comparison of different parameters between group I and group II**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Group I** | **Group II** | **t-value (P-value)** |
| TLC | 27.99 ± 5.36 | 28.25 ± 5.22 | 0.034ns ***(.973)*** |
| Neutrophil count | 20.47± 3.92 | 23.46 ± 4.51 | 0.485ns ***(.631)*** |
| Lymphocyte count | 3.94 ± 0.91 | 3.29 ± 0.59 | 0.617ns ***(.541)*** |
| NLR | 6.3 ± 0.93 | 8.09 ± 0.86 | 1.411ns ***(.168)*** |
| Platelet count | 250.27 ± 53.37 | 205.11 ± 35.3 | 0.731ns ***(.470)*** |
| PLR | 110.6 ± 23.89 | 90.21 ± 16.65 | 0.721ns ***(.476)*** |
| Systemic immune inflammatory index | 1519.53 ± 265.36 | 1617.17 ± 361.93 | 0.207ns ***(.837)*** |

*ns non-significant*

4. Conclusion

Based on the findings of this study, dogs with SIRS/MODS showed significant haematological changes, with NLR, PLR and SII serving as potential biomarkers for inflammation severity. The elevated NLR in dogs diagnosed with MODS aligns with previous studies highlighting its association with systemic inflammation, although the observed increase was not statistically significant between affected groups. PLR exhibited a significant decrease in MODS-affected dogs, contrasting with some prior reports, emphasizing the variability of inflammatory markers in different disease conditions. This may be the first documented report of significant reduction in PLR in dogs with MODS. SII values demonstrated a notable increase in both groups, reinforcing its relevance in assessing immune responses. While these haematological ratios may aid in understanding inflammatory progression, their clinical utility in distinguishing disease severity requires further validation. Future research could focus on refining threshold values and exploring their predictive capability for therapeutic interventions in critically ill canine patients.

Ethical approval

All manuscripts which deal with animal subjects must be approved by an Institutional Review Board (IRB), Ethical Committee, or an Animal Utilization Study Committee. , and this statement, and approval number, must accompany the submission. If required, author should be ready to submit a scanned copy of the IRB or Ethical Committee Approval at any stage of publication (Pre of post publication stage). The manuscript should contain information about any post-operative care and pain management for the animals.

All authors hereby declare that the study was conducted after the approval of the Director of Academic and Research, Kerala Veterinary and Animal Sciences University (No KVASU/DAR/A2/1924/2024(2) Pookode, dated 06/07/2024.

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