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Treatment response and platelet recovery kinetics following doxycycline-based therapy in dogs with varying clinical grades of monocytic ehrlichiosis

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Abstract

While doxycycline remains the standard treatment for canine monocytic ehrlichiosis (CME), clinicians frequently observe that dogs presenting at different clinical severity levels show markedly different recovery trajectories yet prospective data quantifying these grade-dependent treatment responses remain scarce in Latin American veterinary literature. This research evaluated treatment response and platelet recovery kinetics in 80 dogs with naturally occurring CME stratified into Grade I (mild; n=39), Grade II (moderate; n=29), and Grade III (severe; n=12) based on a standardized clinical severity scoring system. All dogs received doxycycline at 10 mg/kg orally once daily for 28 days at the Lima Institute of Veterinary Medicine and Surgery between March and November 2025. Platelet counts, packed cell volume, and clinical scores were monitored at days 0, 3, 7, 14, 21, and 28, with follow-up assessment at 90 days post-treatment. Grade I dogs achieved normal platelet counts ($>200 \times 10^3/\mu\text{L}$) by day 14 (mean: 241 ± 38), while Grade II dogs required 21-28 days (day 28 mean: 256 ± 47). Grade III dogs showed significantly delayed recovery, with only 41.7% reaching normal platelet counts by day 28 (mean: 178 ± 52). Complete treatment response rates were 92.3% for Grade I, 72.4% for Grade II, and 41.7% for Grade III ($P < 0.001$). Relapse within 90 days occurred in 5.1%, 17.2%, and 37.5% of Grades I, II, and III respectively. These findings establish grade-specific recovery benchmarks and support extending treatment duration beyond 28 days for Grade III cases.

Keywords: Canine monocytic ehrlichiosis, doxycycline therapy, platelet recovery, treatment response, clinical grading, thrombocytopenia, relapse rate, treatment outcome, clinical severity, Peru

Introduction

A veterinary clinician in Lima recalls a week when two dogs with confirmed ehrlichiosis arrived on the same afternoon. The first a well-nourished Labrador with mild lethargy and a platelet count of $148 \times 10^3/\mu\text{L}$ was eating normally within three days of starting doxycycline and had a completely normal blood panel at the two-week recheck. The second an emaciated mixed-breed stray with epistaxis, severe pancytopenia, and platelets at $32 \times 10^3/\mu\text{L}$ remained hospitalized for nine days, required a blood transfusion, and still showed thrombocytopenia at the end of a 28-day treatment course. Both had the same diagnosis. Both received the same drug at the same dose. The outcomes could hardly have differed more.

This clinical reality that disease severity at presentation profoundly shapes treatment response is widely understood by practitioners but poorly quantified in the literature. Most treatment research reports aggregate outcomes across all severity levels, producing overall success rates that obscure the dramatically different prognoses facing Grade I versus Grade III patients^[1]. Doxycycline at 10 mg/kg/day for 28 days has been the recommended first-line protocol for CME since the 1990s, and while its efficacy against *E. canis* is well established^[2], the kinetics of hematological recovery particularly platelet reconstitution across different clinical grades have not been systematically documented.

Thrombocytopenia serves as both the most sensitive indicator of CME and the most practical marker for monitoring treatment response^[3]. Platelet recovery reflects the combined resolution of immune-mediated peripheral destruction and restoration of bone marrow megakaryopoiesis, processes that operate on different timescales depending on the degree of marrow compromise^[4]. In mild cases where marrow function is largely preserved,

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peripheral platelet destruction ceases rapidly after antibiotic-mediated bacterial clearance, and counts recover within 7-14 days. In severe cases with marrow hypoplasia, recovery depends on regeneration of the megakaryocyte population itself a process requiring weeks to months^[5].

Previous prevalence research documented CME rates of 28.3% in subtropical Asian settings^[6], and therapeutic research in other regions has reported overall cure rates of 75-95%^[7]. But Lima's veterinary context where late presentation is common among stray and economically disadvantaged-owner dogs means that clinicians regularly encounter advanced disease grades at rates exceeding those in published European and North American series^[8]. This research aimed to establish grade-specific platelet recovery curves, quantify treatment response rates and relapse frequencies by clinical severity, and identify the clinical grade threshold at which extended treatment duration may be warranted.

Material and Methods

Material

Eighty dogs diagnosed with CME at the Lima Institute of Veterinary Medicine and Surgery between March and November 2025 were enrolled. Diagnosis required positive rapid immunochromatographic test (SNAP 4Dx Plus, IDEXX) plus PCR confirmation of *E. canis* 16S rRNA gene. Dogs with concurrent Babesia, Anaplasma, or Hepatozoon infections (screened by multiplex PCR) were excluded, as were dogs that had received any antibiotic treatment within 30 days prior to enrollment. Clinical grading used a standardized severity scoring system: Grade I (mild) fever, mild lethargy, lymphadenomegaly, platelets $100-200 \times 10^3/\mu\text{L}$; Grade II (moderate) anorexia, weight loss, splenomegaly, platelets $50-99 \times 10^3/\mu\text{L}$; Grade III (severe) hemorrhagic diathesis, pancytopenia, cachexia, platelets $<50 \times 10^3/\mu\text{L}$.

Methods

All dogs received doxycycline (Vibramycin, Pfizer) at 10 mg/kg orally once daily for 28 consecutive days. Grade III dogs received concurrent supportive care (intravenous

fluids, antiemetics, gastroprotectants) and blood transfusion when PCV fell below 15%. Monitoring occurred at days 0, 3, 7, 14, 21, and 28, comprising complete blood count, serum biochemistry (ALT, BUN, creatinine, total protein), and clinical severity scoring. A 90-day follow-up visit included CBC, serology, and clinical examination.

Treatment outcomes were classified as: Complete response resolution of all clinical signs and platelet count $>200 \times 10^3/\mu\text{L}$ by day 28; Partial response clinical improvement with platelet count $150-199 \times 10^3/\mu\text{L}$; Treatment failure persistent clinical signs or platelet count $<150 \times 10^3/\mu\text{L}$ at day 28. Relapse was defined as recurrence of clinical signs or thrombocytopenia ($<200 \times 10^3/\mu\text{L}$) within 90 days after treatment completion in dogs that had achieved complete or partial response^[9]. Statistical analysis used Kaplan-Meier curves for time-to-platelet-recovery, log-rank test for between-group comparisons, and Fisher's exact test for categorical outcome comparisons. The research protocol received approval from the Lima Institute of Veterinary Medicine and Surgery Ethics Committee (Protocol LIVMS-EC-2025-006, approved February 2025).

Ethical Considerations

All procedures followed Peruvian animal welfare regulations (Law 30407). Owner consent was obtained for all privately owned dogs. Stray dogs enrolled through the Lima Municipal Animal Services received treatment at no cost and were placed in foster care during the treatment period. Dogs showing clinical deterioration during the trial received intensified supportive care and were switched to alternative antimicrobial protocols (imidocarb dipropionate) if failing doxycycline monotherapy.

Results

Of the 80 enrolled dogs, 39 were classified as Grade I (48.8%), 29 as Grade II (36.3%), and 12 as Grade III (15.0%). Grade III dogs presented with significantly lower baseline platelet counts (38 ± 14 vs $142 \pm 28 \times 10^3/\mu\text{L}$ for Grade I; $P < 0.001$), lower PCV ($18.4 \pm 4.7\%$ vs $34.2 \pm 5.1\%$; $P < 0.001$), and higher clinical severity scores.

Table 1: Baseline characteristics of enrolled dogs by clinical grade (mean $\pm$ SD)

Parameter	Grade I (n=39)	Grade II (n=29)	Grade III (n=12)	P-value
Platelets ($10^3/\mu\text{L}$)	142 $\pm$ 28	86 $\pm$ 18	38 $\pm$ 14	<0.001
PCV (%)	34.2 $\pm$ 5.1	27.8 $\pm$ 6.3	18.4 $\pm$ 4.7	<0.001
WBC ($10^3/\mu\text{L}$)	14.2 $\pm$ 4.3	8.7 $\pm$ 3.6	4.1 $\pm$ 2.2	<0.001
Temperature ($^{\circ}\text{C}$)	39.8 $\pm$ 0.4	40.1 $\pm$ 0.5	39.4 $\pm$ 0.8	0.12
Body weight (kg)	18.4 $\pm$ 8.2	16.7 $\pm$ 7.1	12.3 $\pm$ 5.4	0.06
Age (years)	3.8 $\pm$ 2.1	4.2 $\pm$ 2.4	5.1 $\pm$ 2.8	0.18
Male (%)	56.4	58.6	66.7	0.77

Table 2: Treatment outcomes at day 28 and 90-day relapse rates by clinical grade

Outcome	Grade I	Grade II	Grade III	P-value
Complete response	92.3%	72.4%	41.7%	<0.001
Partial response	5.1%	17.2%	25.0%	<0.05
Treatment failure	2.6%	10.3%	33.3%	<0.001
Transfusion required	0%	6.9%	58.3%	<0.001
Days to plt >200	12.4 $\pm$ 3.8	23.7 $\pm$ 5.2	$>28^*$	<0.001
90-day relapse	5.1%	17.2%	37.5%	<0.01

*Only 41.7% of Grade III dogs achieved normal platelet counts within 28 days

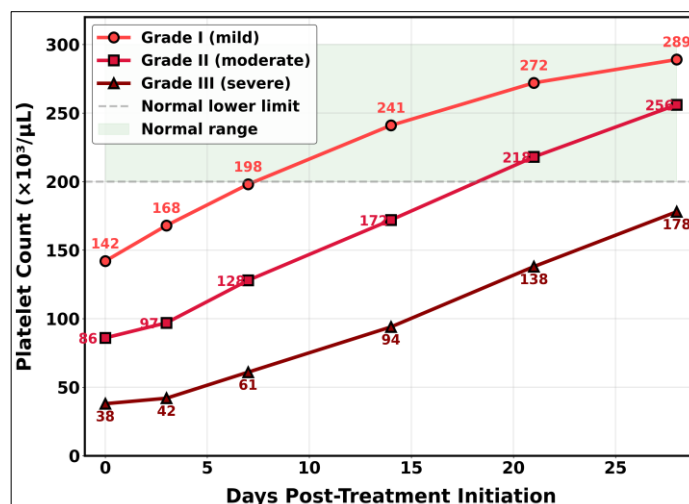


Fig 1: Platelet recovery curves over 28 days of doxycycline therapy in dogs with Grade I (mild), Grade II (moderate), and Grade III (severe) canine monocytic ehrlichiosis. Shaded green zone represents the normal platelet count range ($\geq 200 \times 10^3/\mu\text{L}$)

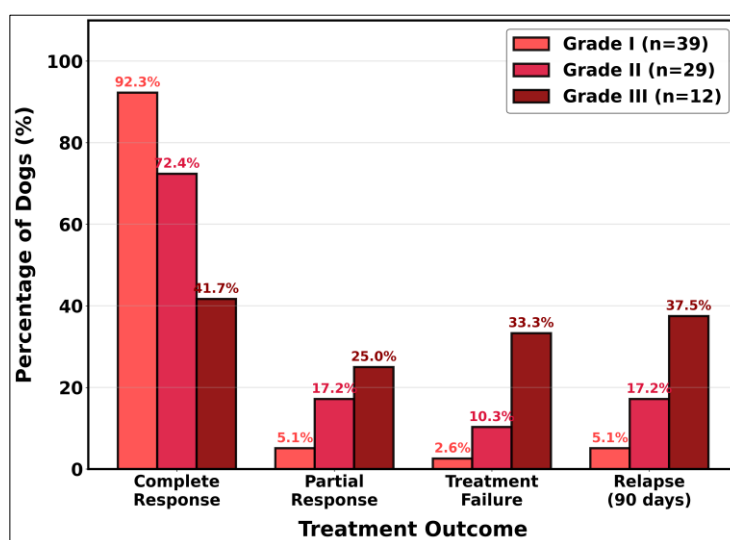


Fig 2: Comparison of treatment outcome distribution (complete response, partial response, treatment failure, and 90-day relapse) across the three clinical severity grades of canine monocytic ehrlichiosis

Platelet recovery followed distinctly different kinetics across grades (log-rank $P < 0.001$). Grade I dogs showed the earliest measurable recovery response at day 3 (mean increase: $26 \times 10^3/\mu\text{L}$), accelerating through day 14 when 87.2% had crossed the normal threshold. Grade II recovery was slower but progressive, with the steepest recovery phase occurring between days 7 and 21. Grade III dogs displayed an initial lag phase (days 0-7) with minimal platelet improvement (mean increase: $23 \times 10^3/\mu\text{L}$), followed by gradual recovery that failed to reach normal range in 58.3% of cases by day 28. Among the four Grade III dogs that achieved treatment failure criteria, three had baseline platelet counts below $30 \times 10^3/\mu\text{L}$ and all showed concurrent leukopenia, suggesting severe bone marrow hypoplasia as the mechanistic barrier to recovery.

Discussion

The grade-dependent platelet recovery kinetics documented here provide the first prospective dataset quantifying the timescale differences between mild and severe CME treatment responses. Grade I dogs recovered platelets by day 14, which aligns with the expected timeline for resolution of immune-mediated peripheral destruction when marrow function is preserved. Harrus *et al.* [10] reported comparable

recovery timelines in experimentally infected dogs with mild disease, confirming that the 14-day platelet recovery benchmark is robust across geographic settings.

The treatment failure rate of 33.3% in Grade III dogs substantially exceeds the 5-15% overall failure rates typically reported in CME treatment literature [11]. This discrepancy reflects the masking effect of grade-aggregated reporting when mild cases (with $>90\%$ success) dominate the denominator, overall success rates obscure the poor outcomes in severely affected patients. The mechanism underlying treatment failure in severe cases involves the degree of bone marrow compromise: once aplastic changes are established, antibiotic elimination of *E. canis* cannot reverse structural marrow damage, and hematological recovery depends on residual stem cell regenerative capacity [12]. This explains why a 28-day treatment course adequate for bacterial clearance proves insufficient for hematological reconstitution in advanced disease.

The 37.5% relapse rate in Grade III dogs, compared to 5.1% in Grade I, raises important questions about treatment duration optimization. Neer *et al.* [13] recommended 28 days as standard, but our data suggest this may be insufficient for severe cases where incomplete bacterial clearance from immunologically privileged sites (bone marrow, spleen)

seeds reinfection after treatment cessation. Extended protocols of 42-56 days, as recently proposed by Sainz *et al.* [14], deserve prospective evaluation specifically in Grade III populations. For practitioners, the clinical implication is that day-28 platelet counts below $200 \times 10^3/\mu\text{L}$ in initially severe cases should prompt treatment extension rather than discontinuation [15].

Clinical Implications

These grade-specific recovery benchmarks offer practical monitoring milestones for clinicians. Grade I patients that have not improved by day 7 warrant reassessment of diagnosis. Grade II patients should show measurable platelet recovery by day 14; failure to do so suggests possible co-infection or treatment non-compliance. Grade III patients require realistic prognostic counseling at presentation the 33.3% treatment failure and 37.5% relapse rates should inform owner expectations and financial planning for extended treatment courses.

Conclusion

Canine monocytic ehrlichiosis treatment outcomes vary dramatically with disease severity at presentation, yet conventional reporting of aggregate treatment success rates has obscured this clinically critical distinction. This research establishes that Grade I (mild) CME shows 92.3% complete response with platelet normalization by day 14, Grade II (moderate) achieves 72.4% complete response with recovery by days 21-28, while Grade III (severe) yields only 41.7% complete response with most cases failing to normalize platelets within the standard 28-day protocol. The progressive increase in relapse rates from 5.1% to 37.5% across grades indicates that treatment duration should be calibrated to clinical severity rather than applied uniformly. These findings recommend that clinical severity grading become a standard component of CME treatment planning, with Grade III cases receiving extended doxycycline courses of at least 42 days and more intensive post-treatment surveillance. The single key takeaway for practicing veterinarians is this: the standard 28-day doxycycline protocol works well for mild and moderate CME but is inadequate for severe cases, and treatment intensity should match disease intensity.

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