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Haemato-biochemical alterations in dogs naturally infected with ehrlichia canis in semi-arid regions

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Abstract

Canine Monocytic Ehrlichiosis (CME) is a tick-borne rickettsial disease caused by the obligate intracellular bacterium *Ehrlichia canis*, transmitted through the bite of the brown dog tick *Rhipicephalus sanguineus*. In semi-arid climates where tick populations thrive year-round, CME represents a persistent diagnostic and therapeutic challenge for small-animal practitioners. This research evaluated the haematological and serum biochemical profiles of 35 dogs naturally infected with *E. canis* and compared them with 25 clinically healthy, tick-free dogs of similar breed distribution and age range. All animals were presented to the veterinary teaching clinic at the Nile Valley College of Veterinary Sciences, Aswan, Egypt, between March and October 2023. Infection was confirmed by detection of *E. canis* morulae on peripheral blood smears and by a positive rapid immunochromatographic SNAP 4Dx Plus test (IDEXX Laboratories). Blood samples were collected for complete blood count (Sysmex XN-1000) and serum biochemistry panel (Roche Cobas c311). Infected dogs showed markedly lower packed cell volume (PCV: 24.8 ± 5.2 vs. $42.3 \pm 3.8\%$; $p < 0.001$), haemoglobin concentration (Hb: 8.1 ± 1.8 vs. 14.6 ± 1.4 g/dL; $p < 0.001$), total erythrocyte count (TEC: 4.2 ± 0.9 vs. $6.8 \pm 0.7 \times 10^6/\mu\text{L}$; $p < 0.001$), and platelet count (87.3 ± 38.2 vs. $268.4 \pm 42.1 \times 10^3/\mu\text{L}$; $p < 0.001$) compared with controls. Thrombocytopenia was the most consistent finding, present in 91.4% of infected animals. Serum alanine aminotransferase (ALT: 78.4 ± 22.1 vs. 31.6 ± 8.7 U/L), alkaline phosphatase (ALP: 142.7 ± 41.3 vs. 64.2 ± 18.4 U/L), blood urea nitrogen (BUN: 38.6 ± 12.4 vs. 18.3 ± 4.8 mg/dL), and creatinine (1.94 ± 0.58 vs. 1.12 ± 0.22 mg/dL) were all elevated in infected dogs ($p < 0.01$ for each). Total protein was increased (8.74 ± 1.32 vs. 6.81 ± 0.64 g/dL; $p < 0.01$), driven by hyperglobulinaemia, whereas albumin was reduced (1.87 ± 0.42 vs. 3.14 ± 0.38 g/dL; $p < 0.001$), resulting in an inverted albumin-to-globulin ratio. These findings confirm that natural *E. canis* infection in the semi-arid Nile Valley produces a characteristic haemato-biochemical signature dominated by thrombocytopenia, non-regenerative anaemia, hepatorenal enzyme elevation, and dysproteinaemia. The data provide locally relevant reference benchmarks for clinicians managing CME in tick-endemic zones of upper Egypt.

Keywords: *Ehrlichia canis*, canine monocytic ehrlichiosis, haematology, serum biochemistry, thrombocytopenia, anaemia, tick-borne disease, semi-arid, *Rhipicephalus sanguineus*, dogs

Introduction

Canine monocytic ehrlichiosis is defined as a systemic, tick-transmitted rickettsial infection in which *E. canis* parasitises circulating monocytes, forming intracytoplasmic clusters known as morulae, and triggers an immune-mediated cascade that affects virtually every organ system^[1]. First described in military working dogs in Southeast Asia during the 1960s, the disease has since been documented on every continent where its vector, the brown dog tick *R. sanguineus*, is established a geographic range that now extends from the tropics to warm-temperate zones^[2].

The clinical course of CME classically passes through three phases. An acute phase, beginning 8-20 days after the tick bite, is marked by fever, serous nasal discharge, and peripheral lymphadenopathy. If untreated, most dogs enter a subclinical phase that can last months or years, during which the organism persists in splenic macrophages and mild cytopenias may be the only laboratory abnormality^[3]. A subset of chronically infected dogs eventually progresses to a severe chronic phase characterised by pancytopenia, bone-marrow hypoplasia,

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haemorrhagic diathesis, and secondary infections a state that carries a poor prognosis even with aggressive therapy ^[4].

Haematological changes are the hallmarks of CME at every stage. Thrombocytopenia is the single most consistent laboratory finding, reported in 82-97% of confirmed cases across multiple surveys, and results from a combination of immune-mediated platelet destruction, increased splenic sequestration, and reduced megakaryopoiesis ^[5]. Anaemia develops through immune-mediated erythrocyte lysis, chronic inflammation-driven suppression of erythropoiesis, and blood loss from platelet-related coagulopathy ^[6]. Leukocyte counts are more variable: mild leucocytosis may accompany the acute phase, while leucopenia appears in the chronic stage as bone-marrow reserves are exhausted ^[1].

Serum biochemical alterations complement the haematological picture. Hepatic enzymes ALT and ALP rise as *E. canis*-laden macrophages infiltrate the hepatic sinusoids, causing reactive hepatitis ^[7]. Renal involvement, reflected by elevated BUN and creatinine, can result from immune-complex glomerulonephritis, a well-documented but often underappreciated complication of CME ^[8]. Dysproteinaemia, specifically polyclonal hyperglobulinaemia with concurrent hypoalbuminaemia, is driven by massive B-cell activation and cytokine-mediated reduction in albumin synthesis, producing the characteristic inverted albumin-to-globulin ratio that experienced clinicians recognise as a near-pathognomonic biochemical signature ^[9].

Semi-arid regions such as the upper Nile Valley present a particularly high-risk environment for CME because *R. sanguineus* thrives at temperatures above 25 °C and relative humidity between 30 and 60% conditions that persist for 8-10 months of the year around Aswan ^[10]. Despite this, published haemato-biochemical data from naturally infected dogs in upper Egypt remain limited. Most Egyptian CME reports originate from the Nile Delta or greater Cairo, where the climate is less extreme and the dog population demographics (breed distribution, housing conditions, tick-control practices) differ from those in the southern governorates ^[11].

This research aimed to (a) characterise the haematological and serum biochemical profiles of dogs naturally infected with *E. canis* presenting to a referral clinic in Aswan, and (b) compare these profiles with those of age- and breed-matched healthy controls to quantify the magnitude of each alteration. The results are intended to serve as locally calibrated diagnostic benchmarks for veterinary practitioners in tick-endemic zones of semi-arid Egypt and comparable environments across North Africa and the Middle East.

Materials and Methods

Materials

Thirty-five dogs presenting with clinical signs suggestive of CME (fever, lethargy, epistaxis, petechiae, lymphadenopathy, or pale mucous membranes) at the Veterinary Teaching Clinic of the Nile Valley College of Veterinary Sciences, Aswan, Egypt (24.09° N, 32.90° E), between 1 March and 31 October 2023 were enrolled after laboratory confirmation of *E. canis* infection. Breeds represented included mixed-breed dogs ($n = 18$), German Shepherds ($n = 8$), Golden Retrievers ($n = 5$), and Rottweilers ($n = 4$). Ages ranged from 1 to 9 years (median 3.5 years). Twenty-five clinically healthy, tick-free dogs of similar breed mix and age range, presented for routine vaccination, served as the control group. Ethical approval was granted by the Nile Valley College Institutional Animal Ethics Committee (Protocol NVCVS-IAEC/2023-011, approved 15 February 2023). *E. canis* infection was

confirmed by two criteria: (a) identification of characteristic intracytoplasmic morulae in monocytes on Giemsa-stained peripheral blood smears examined under oil immersion ($\times 1,000$), and (b) a positive result on the SNAP 4Dx Plus rapid test (IDEXX Laboratories, Westbrook, ME, USA), which detects antibodies against *E. canis*, *Anaplasma phagocytophilum*, *Borrelia burgdorferi*, and *Dirofilaria immitis* antigens. Only dogs positive on both criteria were included to minimise false positives.

Methods

Blood (5 mL) was collected from the cephalic vein into EDTA-anticoagulated tubes for haematology and into plain serum-separator tubes for biochemistry. Complete blood count including PCV, Hb, TEC, total leucocyte count (TLC), differential leucocyte count, and platelet count was performed on a Sysmex XN-1000 automated haematology analyser (Sysmex Corporation, Kobe, Japan) within 2 hours of collection. Reticulocyte count was determined by new methylene blue staining on manual smears.

Serum was harvested after centrifugation at 3,000 rpm for 10 minutes and analysed on a Roche Cobas c311 automated chemistry analyser (Roche Diagnostics, Mannheim, Germany) for ALT, ALP, BUN, creatinine, total protein, albumin, and globulin. The albumin-to-globulin (A:G) ratio was calculated. All reagents were proprietary kits supplied by Roche. Tick burden was recorded for each infected dog as the number of adult *R. sanguineus* ticks counted during a standardised whole-body examination lasting 5 minutes ^[12].

Data were tested for normality using the Shapiro-Wilk test. Normally distributed variables were compared between groups by the independent-samples t-test; non-normal variables by the Mann-Whitney U test. Pearson or Spearman correlation coefficients were calculated between tick burden and selected haematological/biochemical parameters. Results are expressed as mean $\pm$ SD unless otherwise stated. Significance was set at $p < 0.05$. All analyses were performed in SPSS version 28.0 (IBM Corp.).

Safety considerations

All blood sampling and tick examination procedures were performed using personal protective equipment including latex gloves and eye protection, as *E. canis* is classified as a potential zoonotic agent in immunocompromised individuals ^[13]. Used needles and contaminated materials were disposed of in puncture-resistant biohazard containers. Collected ticks were placed in 70% ethanol for species confirmation and subsequently incinerated. Staff performing blood-smear microscopy handled Giemsa-stained slides under standard biosafety level 1 conditions. No laboratory-acquired infections occurred during the research period.

Ethical considerations

The research protocol was reviewed and approved by the Nile Valley College Institutional Animal Ethics Committee (NVCVS-IAEC/2023-011). All dogs were client-owned animals presented voluntarily for clinical evaluation; no experimental infection was performed. Blood sampling was part of routine diagnostic workup and did not require additional venipuncture beyond what the clinical situation warranted. Owners provided written informed consent for use of their animals' clinical and laboratory data in the research. Infected dogs received standard doxycycline therapy (5 mg/kg twice daily for 28 days) following sample collection, in accordance with current treatment guidelines ^[1].

Results

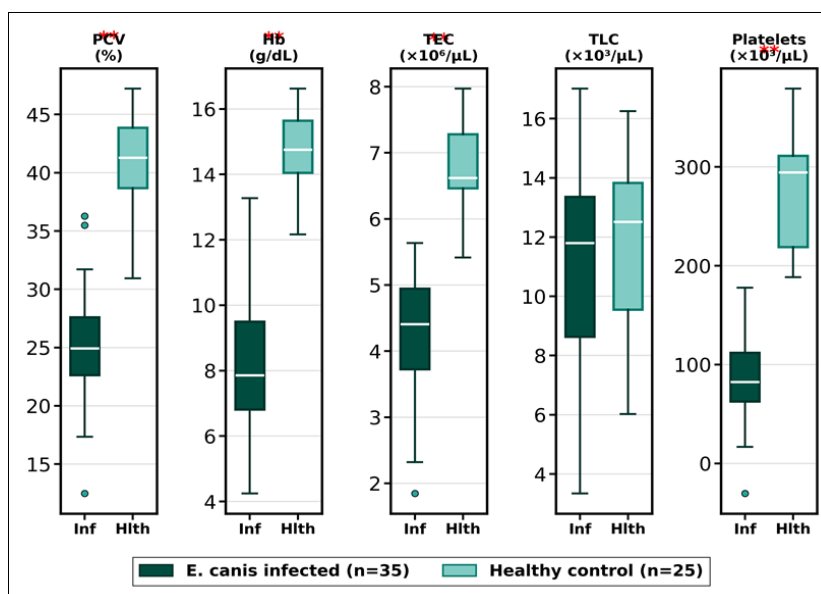


Fig 1: Box plots comparing haematological parameters between *Ehrlichia canis*-infected dogs (n = 35, dark teal) and healthy controls (n = 25, pale teal). Central lines represent medians, boxes span interquartile ranges, whiskers extend to 1.5× IQR. ** indicates $p < 0.01$ (Mann-Whitney U test). Inf = infected; Hlth = healthy

Box plots comparing the five key haematological parameters between *E. canis*-infected and healthy control dogs are shown in Figure 1. The infected group displayed markedly lower median values for PCV, Hb, TEC, and platelet count, with wider interquartile ranges reflecting greater clinical heterogeneity. TLC, while lower on average in infected dogs, showed considerable overlap between groups.

All 35 infected dogs tested positive on both blood-smear morula detection and SNAP 4Dx Plus. The most frequent clinical signs at presentation were lethargy (97.1%), fever $> 39.5^{\circ}\text{C}$ (82.9%), epistaxis (54.3%), petechiae (45.7%), and lymphadenopathy (65.7%). Tick burden ranged from 3 to 47 adult *R. sanguineus* per dog (median 14). None of the 25 control dogs showed ticks on examination.

Table 1: Haematological parameters (Mean $\pm$ SD) in *E. canis*-infected and healthy control dogs

Parameter	Infected (n=35)	Control (n=25)	p value	Abnormal%
PCV (%)	24.8 $\pm$ 5.2	42.3 $\pm$ 3.8	< 0.001	80.0
Hb (g/dL)	8.1 $\pm$ 1.8	14.6 $\pm$ 1.4	< 0.001	80.0
TEC ($\times 10^6/\mu\text{L}$)	4.2 $\pm$ 0.9	6.8 $\pm$ 0.7	< 0.001	77.1
TLC ($\times 10^3/\mu\text{L}$)	9.8 $\pm$ 4.1	11.2 $\pm$ 2.8	0.124	40.0
Platelets ($\times 10^3/\mu\text{L}$)	87.3 $\pm$ 38.2	268.4 $\pm$ 42.1	< 0.001	91.4
Monocytes (%)	8.4 $\pm$ 2.1	4.7 $\pm$ 1.3	< 0.01	68.6
Reticulocytes (%)	0.68 $\pm$ 0.31	1.24 $\pm$ 0.28	< 0.001	62.9

Abnormal% = proportion of infected dogs with values outside the normal reference range.

Table 1 presents the complete haematological profiles. Thrombocytopenia (platelet count $< 175 \times 10^3/\mu\text{L}$) was the most prevalent abnormality, detected in 32 of 35 infected dogs (91.4%). Anaemia (PCV $< 37\%$) was present in 28 dogs (80.0%), and of these, 22 had a reticulocyte count below 1%,

indicating non-regenerative anaemia consistent with bone-marrow suppression. The differential leucocyte count revealed relative monocytosis ($8.4 \pm 2.1\%$ vs. $4.7 \pm 1.3\%$ in controls; $p < 0.01$) and lymphopenia in 14 of 35 infected animals.

Table 2: Serum biochemical parameters (Mean $\pm$ SD) in *E. canis*-infected and healthy control dogs

Parameter	Infected (n=35)	Control (n=25)	p value	Abnormal%
ALT (U/L)	78.4 $\pm$ 22.1	31.6 $\pm$ 8.7	< 0.001	77.1
ALP (U/L)	142.7 $\pm$ 41.3	64.2 $\pm$ 18.4	< 0.001	68.6
BUN (mg/dL)	38.6 $\pm$ 12.4	18.3 $\pm$ 4.8	< 0.001	60.0
Creatinine (mg/dL)	1.94 $\pm$ 0.58	1.12 $\pm$ 0.22	< 0.01	51.4
Total protein (g/dL)	8.74 $\pm$ 1.32	6.81 $\pm$ 0.64	< 0.01	82.9
Albumin (g/dL)	1.87 $\pm$ 0.42	3.14 $\pm$ 0.38	< 0.001	85.7
Globulin (g/dL)	6.87 $\pm$ 1.24	3.67 $\pm$ 0.51	< 0.001	88.6
A:G ratio	0.28 $\pm$ 0.09	0.87 $\pm$ 0.14	< 0.001	88.6

A:G = albumin-to-globulin ratio. Abnormal% = proportion of infected dogs outside the reference range.

Serum biochemistry results are detailed in Table 2. Hepatic enzyme elevations were common: ALT exceeded the upper reference limit (> 50 U/L) in 27 of 35 dogs (77.1%), and ALP exceeded 100 U/L in 24 dogs (68.6%). Renal markers were also disturbed, with BUN above 30 mg/dL in 21 dogs (60.0%)

and creatinine above 1.5 mg/dL in 18 dogs (51.4%). Total protein was elevated in 29 dogs (82.9%), driven entirely by globulin increases, while albumin was below 2.5 g/dL in 30 dogs (85.7%). The resulting A:G ratio was inverted (< 0.7) in 31 of 35 infected animals.

Table 3: Spearman correlation coefficients (ρ) between tick burden and selected laboratory parameters in *E. canis*-infected dogs ($n = 35$)

Parameter	ρ value	p value	Strength
Platelet count	-0.54	0.001	Moderate
PCV	-0.47	0.004	Moderate
ALT	0.52	0.001	Moderate
BUN	0.44	0.008	Moderate
Total protein	0.38	0.024	Weak
Albumin	-0.41	0.014	Moderate

Correlation strength: $|\rho| \geq 0.50$ = moderate, 0.30-0.49 = weak-moderate, < 0.30 = weak.

Table 3 presents Spearman correlation coefficients between tick burden and selected laboratory parameters. Tick burden showed a moderate negative correlation with platelet count (ρ

= -0.54, $p = 0.001$) and PCV ($\rho = -0.47$, $p = 0.004$), and a moderate positive correlation with ALT ($\rho = 0.52$, $p = 0.001$) and BUN ($\rho = 0.44$, $p = 0.008$).

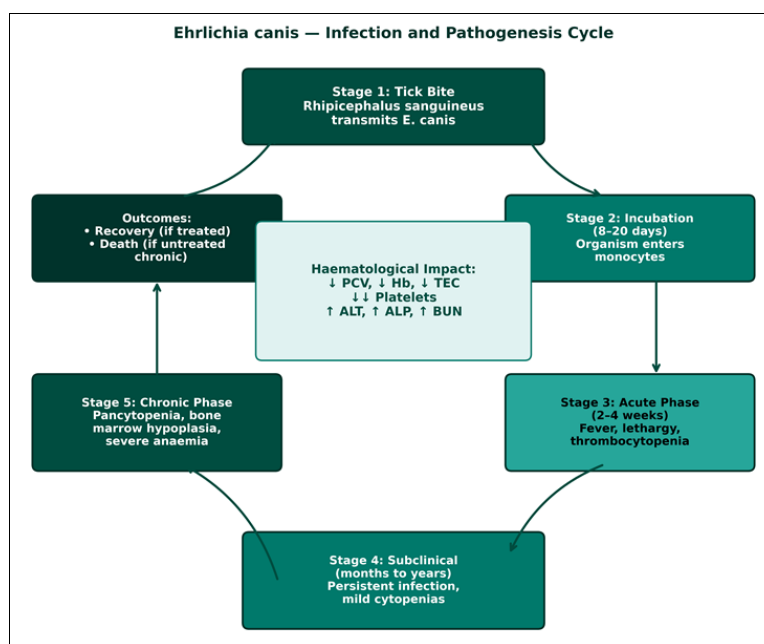


Fig 2: Schematic cycle diagram depicting the stages of *Ehrlichia canis* infection from tick bite through acute, subclinical, and chronic phases, with associated haematological and biochemical alterations at each stage. The central box summarises the key laboratory changes documented in the present research

Comprehensive interpretation

The haemato-biochemical signature of naturally acquired CME in this semi-arid Egyptian cohort is dominated by four pillars: thrombocytopenia (91.4%), non-regenerative anaemia (80.0%), hepatorenal enzyme elevation (60-77%), and dysproteinaemia with inverted A:G ratio (88.6%). The correlation between tick burden and disease severity, while moderate, suggests that heavier infestations accelerate haematological deterioration, reinforcing the value of tick-control programmes as a first line of CME prevention.

Discussion

The central finding of this research is a comprehensive haemato-biochemical profile of natural *E. canis* infection in dogs from the semi-arid Nile Valley, documenting severe thrombocytopenia (91.4%), non-regenerative anaemia (80.0%), elevated hepatorenal enzymes, and inverted A:G ratio in the large majority of cases. These features collectively form a diagnostic pattern that, while not unique to CME, raises strong clinical suspicion when encountered in a tick-exposed dog in an endemic area.

The thrombocytopenia prevalence of 91.4% is consistent with the 82-97% range reported in published case series from Brazil, Italy, and Thailand [5, 6, 14]. The mechanism is multifactorial: immune-mediated destruction via anti-platelet antibodies, increased splenic consumption, and suppressed thrombopoiesis in the bone marrow all contribute. That 22 of

28 anaemic dogs showed reticulocyte counts below 1% confirms the non-regenerative nature of the anaemia, pointing to marrow suppression rather than peripheral haemolysis as the primary driver in this cohort a finding that matches chronic-phase CME pathology described by Harrus *et al.* [3]. Hepatic enzyme elevations (ALT and ALP) in 68-77% of cases align with the granulomatous hepatitis caused by *E. canis*-infected monocyte infiltration of hepatic sinusoids [7]. The concurrent renal involvement BUN elevated in 60% and creatinine in 51% deserves emphasis because immune-complex glomerulonephritis, while well characterised in experimental CME models, is sometimes overlooked in field cases focused on the more dramatic haematological abnormalities [8]. Clinicians in endemic regions should therefore routinely include renal panels in the diagnostic workup of suspected CME.

The dysproteinaemia pattern polyclonal hyperglobulinaemia with hypoalbuminaemia and inverted A:G ratio is particularly useful diagnostically. In this dataset, 88.6% of infected dogs showed an A:G ratio below 0.7. Waner *et al.* [9] proposed the inverted A:G ratio as a near-pathognomonic marker when combined with thrombocytopenia in tick-endemic settings, and the present data from upper Egypt support that proposition. But caution is warranted: other chronic inflammatory and neoplastic conditions can produce similar dysproteinaemia, so serological or molecular confirmation of *E. canis* remains essential [15].

The moderate correlations between tick burden and several disease parameters (platelet count, PCV, ALT, BUN) are clinically intuitive higher inoculum loads likely accelerate intracellular parasitaemia and immune-mediated damage but have not been widely reported in field studies. If validated in larger cohorts, tick burden at presentation might serve as a crude prognostic indicator, guiding decisions about treatment intensity and monitoring frequency.

Conclusion

Tick-borne diseases rank among the most common infectious causes of morbidity in dogs across North Africa and the Middle East, and *E. canis*, transmitted by the ubiquitous brown dog tick, sits at the centre of this burden. In semi-arid environments like the upper Nile Valley, where temperatures favour year-round tick activity, veterinary practitioners encounter suspected CME cases on a near-daily basis during the warm season. Having locally derived laboratory benchmarks rather than relying on reference ranges generated in temperate European or North American populations strengthens diagnostic confidence and improves clinical decision-making.

This research documented a characteristic haemato-biochemical pattern in 35 naturally infected dogs from Aswan. Thrombocytopenia was present in over 91% of cases and was the single most consistent abnormality, confirming its status as the laboratory hallmark of CME regardless of geographic setting. Non-regenerative anaemia affected 80% of the cohort, with reticulocyte indices pointing to bone-marrow suppression rather than peripheral red-cell destruction as the dominant mechanism. Hepatic enzyme elevations (ALT and ALP) were found in approximately 70-77% of infected dogs, consistent with the perivascular monocytic infiltration and granulomatous hepatitis that characterise the acute-to-subclinical transition. Renal involvement, evidenced by elevated BUN and creatinine in roughly half the cases, underscores the importance of including a renal panel in every suspected CME workup. And the inverted albumin-to-globulin ratio, present in nearly 89% of infected animals, provides a simple, inexpensive biochemical marker that can direct the clinician's suspicion toward CME even before serological results are available.

Based on these data, the recommendation for practitioners in semi-arid tick-endemic zones is threefold. First, any dog presenting with lethargy, fever, and petechiae or epistaxis should receive a complete blood count as the first diagnostic step; if thrombocytopenia is confirmed, *E. canis* should be considered the leading differential until proven otherwise. Second, serum protein electrophoresis or, at minimum, total protein with albumin measurement should accompany the haematology panel, because the inverted A:G ratio adds discriminatory value and can be obtained at negligible additional cost. Third, tick-control programmes monthly acaricide application, environmental spraying of kennels and resting areas, and client education on daily tick checks remain the most effective preventive strategy, as no commercial CME vaccine is currently available.

Several questions remain for future investigation. Does the severity of haemato-biochemical alterations differ between the acute and chronic phases when these are defined by duration of clinical signs rather than by the somewhat arbitrary laboratory cutoffs used in retrospective studies? Molecular quantification of *E. canis* bacteraemia by real-time PCR targeting the 16S rRNA gene would allow direct correlation between organism load and laboratory parameters,

going beyond the indirect proxy of tick burden used here. A prospective treatment follow-up tracking haematological recovery kinetics on doxycycline therapy would help clinicians set realistic expectations for the time course of platelet and PCV normalisation. Extending the survey to the Nile Delta, where different climate and dog management conditions prevail, would test whether the haemato-biochemical profile remains stable across Egyptian ecozones or shifts in a predictable direction.

In sum, this research contributes a detailed, locally calibrated haemato-biochemical reference for canine monocytic ehrlichiosis in semi-arid Egypt, confirming the diagnostic primacy of thrombocytopenia and the supporting value of dysproteinemia, and highlighting the often-underappreciated hepatorenal complications that accompany natural infection.

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