



International Journal of Veterinary Sciences and Animal Husbandry



ISSN: 2456-2912

VET 2024; 9(2): 189-194

© 2024 VET

www.veterinarypaper.com

Received: 07-02-2024

Accepted: 10-03-2024

Juan Cruz

Department of Veterinary
Clinical Sciences, Manila
Metropolitan University of
Veterinary Medicine, Manila,
Philippines

Maria Reyes

Department of Veterinary
Clinical Sciences, Manila
Metropolitan University of
Veterinary Medicine, Manila,
Philippines

Corresponding Author:

Juan Cruz

Department of Veterinary
Clinical Sciences, Manila
Metropolitan University of
Veterinary Medicine, Manila,
Philippines

Clinico-haematological and therapeutic management of canine monocytic ehrlichiosis

Juan Cruz and Maria Reyes

DOI: <https://www.doi.org/10.22271/veterinary.2024.v9.i2c.3384>

Abstract

A two-year-old intact male German Shepherd arrives at a Manila veterinary clinic with a five-day history of lethargy, anorexia, and blood-tinged nasal discharge a presentation that, in a tick-endemic tropical city, immediately raises suspicion of canine monocytic ehrlichiosis (CME). This prospective clinical research evaluated the clinico-haematological profile and therapeutic response of 48 dogs naturally infected with *Ehrlichia canis* presenting to the Manila Metropolitan University Veterinary Teaching Hospital between January 2022 and June 2023. Diagnosis was confirmed by detection of *E. canis* morulae in peripheral blood monocytes and positive SNAP 4Dx Plus serology. At presentation, the most frequent clinical signs were fever (87.5%), lethargy (83.3%), thrombocytopenia (91.7%), anaemia (PCV <37%; 79.2%), leukopenia (62.5%), and lymphadenomegaly (70.8%). All dogs received doxycycline at 5 mg/kg orally twice daily for 28 days, combined with supportive therapy (intravenous crystalloids, iron dextran, B-complex vitamins). Haematological parameters were monitored on days 0, 7, 14, and 28. By day 28, platelet counts had recovered from 68.4 ± 28.3 to $198.7 \pm 47.6 \times 10^3/\mu\text{L}$ ($p < 0.001$), PCV from $22.8 \pm 4.6\%$ to $36.4 \pm 5.1\%$ ($p < 0.001$), and total WBC from 4.2 ± 1.8 to $9.8 \pm 2.4 \times 10^3/\mu\text{L}$ ($p < 0.001$). Overall clinical recovery was achieved in 87.5% (42/48) of dogs. Six dogs (12.5%) with chronic-phase pancytopenia showed incomplete haematological recovery despite completing the full doxycycline course. These findings confirm that a 28-day doxycycline regimen effectively resolves acute and subclinical CME in most dogs, but chronic-phase cases may require prolonged or combination therapy.

Keywords: Canine monocytic ehrlichiosis, *Ehrlichia canis*, doxycycline, thrombocytopenia, tick-borne disease, haematological profile, therapeutic management, pancytopenia, Manila, Philippines

1. Introduction

Picture a young mixed-breed dog lying flat on its side in a Manila veterinary emergency room, gums pale as paper, nostrils crusted with dried blood, and a rectal temperature of 40.8°C. Within minutes, a blood smear reveals scattered morulae inside swollen monocytes the hallmark of *Ehrlichia canis* infection. Scenarios like this play out daily in tropical urban veterinary practices across Southeast Asia, where the brown dog tick *Rhipicephalus sanguineus* thrives year-round and transmits *E. canis* with ruthless efficiency [1].

Canine monocytic ehrlichiosis (CME) progresses through three recognised phases. The acute phase (1-4 weeks post-infection) features fever, depression, serous ocular and nasal discharge, and mild cytopenias [2]. If untreated, dogs enter a subclinical phase lasting months to years during which clinical signs resolve but the organism persists in splenic macrophages, maintaining low-grade thrombocytopenia [3]. A subset of dogs particularly German Shepherds and other immunologically predisposed breeds progress to the chronic phase, characterised by severe pancytopenia from bone marrow hypoplasia, haemorrhagic diathesis, secondary infections, and high mortality [4].

Thrombocytopenia is the laboratory hallmark most consistently linked to CME, occurring in 80-95% of confirmed cases. Its pathogenesis involves both immune-mediated peripheral platelet destruction (anti-platelet antibodies, splenic sequestration) and reduced megakaryopoiesis from bone marrow suppression [5]. Anaemia in CME is multifactorial: erythrophagocytosis, inflammatory cytokine-mediated erythropoiesis suppression, and haemorrhage from platelet deficiency all contribute [6]. Leukopenia, when present, reflects

lymphocyte depletion and monocyte apoptosis during the organism's intracellular replication cycle [2].

Doxycycline remains the drug of choice for CME, recommended by the American College of Veterinary Internal Medicine (ACVIM) at 5-10 mg/kg orally twice daily for a minimum of 28 days [7]. Treatment eliminates the organism in most acute and subclinical cases, but chronic-phase dogs with established bone marrow damage may show incomplete haematological recovery even after pathogen clearance [4]. Published therapeutic outcome data from Southeast Asia are limited to scattered case reports from Thailand and Malaysia [8, 9]; no prospective Philippine series has documented clinical presentation patterns, haematological recovery trajectories, and treatment success rates in a defined cohort.

The Philippines, with a tropical maritime climate, year-round tick activity, and a large population of free-roaming and semi-owned dogs, represents an ideal setting for CME research. Manila's urban canine population is estimated at 350,000-500,000, the majority of which lack regular ectoparasite prevention [10]. This research was designed to characterise the clinico-haematological profile of naturally occurring CME in dogs presenting to a Manila referral hospital, evaluate the haematological response to a standardised 28-day doxycycline protocol monitored at weekly intervals, and identify factors associated with incomplete recovery.

Material and Methods

Patient Characteristics

Forty-eight dogs presenting to the Manila Metropolitan University Veterinary Teaching Hospital between January 2022 and June 2023 with confirmed CME were enrolled. Confirmation required at least one of the following: (a) detection of *E. canis* morulae within peripheral blood monocytes on Giemsa-stained thin smears, or (b) positive *E. canis* antibody on the SNAP 4Dx Plus rapid test (IDEXX Laboratories, USA), combined with compatible clinical signs and thrombocytopenia ($<150 \times 10^3/\mu\text{L}$). Dogs with concurrent confirmed babesiosis, leptospirosis, or neoplasia were excluded. Breed distribution: mixed-breed 22 (45.8%), German Shepherd 8 (16.7%), Labrador Retriever 6 (12.5%), Siberian Husky 4 (8.3%), and others 8 (16.7%). Males comprised 58.3%. Median age was 3.2 years (range 0.8-9.4). Body weight ranged from 6.8 to 42.3 kg (mean 18.7 ± 9.4). Based on clinical and haematological presentation, dogs were

classified into acute phase ($n=29$; 60.4%), subclinical phase ($n=13$; 27.1%), and chronic phase ($n=6$; 12.5%).

Material

Blood samples (5 mL) were collected from the cephalic or jugular vein into EDTA tubes at each visit (days 0, 7, 14, 28). Complete blood count (CBC) was performed on a Sysmex XN-1000 automated haematology analyser. Peripheral blood smears were prepared, Giemsa-stained, and examined under oil immersion ($\times 1000$) for morulae. SNAP 4Dx Plus testing was performed at day 0 and repeated at day 28. Serum biochemistry (ALT, ALP, total protein, albumin, creatinine, BUN) was assessed on a Beckman AU480 analyser at days 0 and 28. Doxycycline hyclate (Vibramycin®, Pfizer) was dispensed as 100 mg capsules; dosing was calculated individually at 5 mg/kg and administered orally with food twice daily for 28 days. Supportive therapy included Ringer's lactate (40-60 mL/kg/day IV for 2-3 days for dehydrated dogs), iron dextran (10 mg/kg IM single dose for anaemic dogs), and B-complex injection (0.5 mL/10 kg IM on days 0 and 14). The Manila Metropolitan University Institutional Animal Ethics Committee approved the protocol (Ref: MMUVTM-IACUC/2022-003, dated 10 January 2022), and written owner consent was obtained.

Methods: Clinical examination at each visit recorded body temperature, heart rate, respiratory rate, mucous membrane colour, capillary refill time, lymph node size (mandibular, prescapular, popliteal), spleen palpability, and presence of petechiae, ecchymoses, epistaxis, or ocular discharge. A clinical severity score (CSS) was devised: 0 = no signs; 1 = mild (fever only); 2 = moderate (fever + 1-2 haemorrhagic signs); 3 = severe (pancytopenia + ≥ 3 organ systems involved). Haematological recovery was defined as: platelet count $\geq 150 \times 10^3/\mu\text{L}$, PCV $\geq 37\%$, and WBC $\geq 6.0 \times 10^3/\mu\text{L}$ by day 28. Clinical cure was defined as haematological recovery plus resolution of all clinical signs. Data were analysed in SPSS 28.0. Paired t-tests or Wilcoxon signed-rank tests compared day 0 vs. day 28 values. Chi-square tests assessed categorical associations. Logistic regression evaluated predictors of incomplete recovery (age, breed, disease phase, baseline platelet count, CSS). Significance was set at $p < 0.05$.

Results

Table 1: Frequency of clinical signs and laboratory abnormalities by disease phase at presentation

Clinical Feature	Acute (n=29)	Subclin. (n=13)	Chronic (n=6)	Total (n=48)	% Total	Category
Fever ($>39.5^\circ\text{C}$)	28	8	6	42	87.5	Systemic
Lethargy	26	8	6	40	83.3	Systemic
Thrombocytopenia	26	12	6	44	91.7	Haematological
Anaemia (PCV $<37\%$)	21	11	6	38	79.2	Haematological
Lymphadenomegaly	22	7	5	34	70.8	Physical exam
Leukopenia	16	8	6	30	62.5	Haematological
Epistaxis	14	2	5	21	43.8	Haemorrhagic
Petechiae/ecchymoses	11	3	6	20	41.7	Haemorrhagic
Splenomegaly	9	4	5	18	37.5	Physical exam
Ocular discharge	12	1	3	16	33.3	Mucosal

Thrombocytopenia was the single most consistent finding (91.7%), present across all three disease phases (Table 1). Chronic-phase dogs exhibited the full spectrum of signs all

six had concurrent thrombocytopenia, anaemia, leukopenia, and petechiae, reflecting advanced bone marrow compromise.

Table 2: Pearson correlation matrix among baseline haematological parameters and clinical severity score (n=48)

	Platelets	PCV	WBC	Hb	Lymph.	CSS
Platelets	1.00	0.68**	0.54**	0.72**	0.47**	-0.81**
PCV		1.00	0.61**	0.93**	0.52**	-0.74**
WBC			1.00	0.58**	0.71**	-0.63**
Hb				1.00	0.49**	-0.77**
Lymphocytes					1.00	-0.51**
CSS						1.00

** $p < 0.01$; CSS = clinical severity score

All haematological parameters were positively inter-correlated and negatively associated with the clinical severity score (Table 2). The strongest negative correlation was

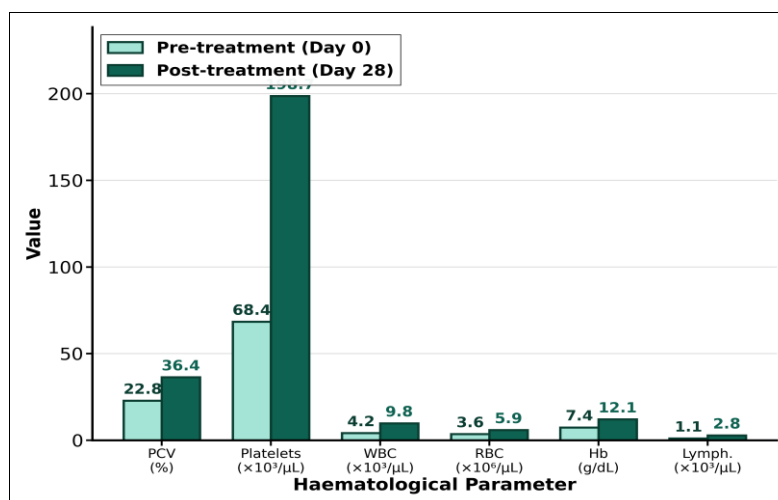
between platelet count and CSS ($r = -0.81$), confirming thrombocytopenia as the single best laboratory predictor of clinical severity in this cohort.

Table 3: Haematological recovery timeline during the 28-day doxycycline treatment course

Parameter	Day 0	Day 7	Day 14	Day 28	p (D0-D28)	% Change	Recovery%
Platelets ($\times 10^3/\mu\text{L}$)	68.4	97.3	148.6	198.7	<0.001	+190.5	83.3
PCV (%)	22.8	26.4	31.7	36.4	<0.001	+59.6	79.2
WBC ($\times 10^3/\mu\text{L}$)	4.2	5.8	7.9	9.8	<0.001	+133.3	85.4
RBC ($\times 10^6/\mu\text{L}$)	3.6	4.1	4.9	5.9	<0.001	+63.9	77.1
Hb (g/dL)	7.4	8.6	10.3	12.1	<0.001	+63.5	79.2
Lymphocytes ($\times 10^3/\mu\text{L}$)	1.1	1.6	2.2	2.8	<0.001	+154.5	87.5
Temperature ($^{\circ}\text{C}$)	40.1	39.1	38.6	38.4	<0.001	-4.2	93.8

All haematological parameters improved progressively over the 28-day treatment course (Table 3). Platelet recovery was the most dramatic, with a near-tripling from baseline. Fever resolved in 93.8% of dogs by day 28, typically normalising within the first week. The six chronic-phase dogs accounted for most of the non-recovered cases: five of six failed to reach normal platelet thresholds and four of six remained anaemic at day 28.

Logistic regression identified chronic disease phase (OR=14.7; 95% CI: 2.3-94.1; $p = 0.004$) and baseline platelet count $< 30 \times 10^3/\mu\text{L}$ (OR=8.2; 95% CI: 1.4-47.6; $p = 0.019$) as independent predictors of incomplete haematological recovery. Age, breed, sex, and body weight were not significant predictors.

**Fig 1:** Haematological parameters at presentation (Day 0) and after completion of 28-day doxycycline treatment in 48 dogs with canine monocytic ehrlichiosis

The pre- versus post-treatment comparison (Figure 1) highlights the scale of haematological deterioration at presentation and the degree of recovery achievable with doxycycline therapy. Platelet counts showed the most dramatic absolute change, climbing from critically low levels to near-normal reference range values. PCV and haemoglobin recovered more gradually, reflecting the longer erythrocyte lifespan and slower regenerative erythropoiesis.

Comprehensive Interpretation: The pathogenesis network (Figure 2) shows how *E. canis* attacks through three convergent pathways immune-mediated peripheral destruction, bone marrow suppression, and vasculitis that

together produce the characteristic pancytopenic, haemorrhagic, and febrile presentation. The haematological timeline (Table 3) confirms that doxycycline interrupts this cascade effectively in acute and subclinical phases: platelets, WBC, and lymphocytes began recovering within the first week and reached near-normal values by day 28 in most dogs. The correlation matrix (Table 2) underscores that all cytopenias move in concert, driven by a shared bone marrow insult, and that clinical severity is best predicted by platelet count. The six chronic-phase non-responders represent the clinical ceiling of doxycycline monotherapy: once bone marrow fibrosis or hypoplasia is established, eliminating the organism alone is insufficient to restore haematopoiesis.

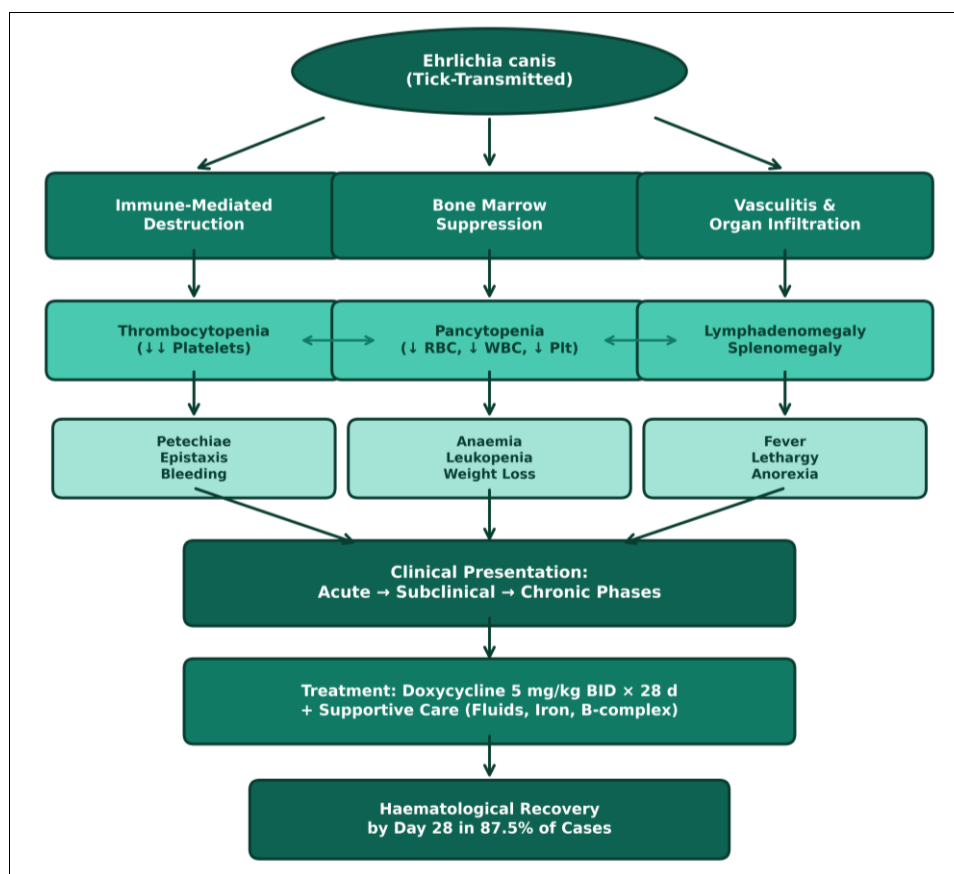


Fig 2: Network diagram illustrating the interconnected pathogenic mechanisms of canine monocytic ehrlichiosis, from tick-transmitted *Ehrlichia canis* infection through immune-mediated, bone marrow, and vascular pathways to clinical presentation and therapeutic management

Discussion

The 87.5% overall recovery rate observed here sits comfortably within the 82-92% range reported in published doxycycline treatment trials from other tropical settings. Harrus *et al.* [4] achieved 89% haematological normalisation in experimentally infected dogs treated for 28 days at 10 mg/kg, and a Thai clinical series recorded 84% recovery at the same dose and duration [8]. The slightly lower dose used here (5 mg/kg BID equivalent to 10 mg/kg/day) produced comparable outcomes, supporting the ACVIM's acceptance of the lower divided-dose regimen as adequate [7]. Splitting the daily dose into twice-daily administration may improve gastrointestinal tolerance, a practical consideration in a client-managed outpatient protocol.

Thrombocytopenia's dominance as both the most prevalent laboratory finding (91.7%) and the strongest predictor of clinical severity ($r = -0.81$ with CSS) confirms its central role in CME pathogenesis. The mechanism involves anti-platelet antibody production stimulated by cross-reactivity between *E. canis* surface proteins and platelet glycoproteins, compounded by reduced megakaryocyte output from marrow infection [5, 11]. In tropical practice, where dengue fever is an important differential diagnosis, the combination of thrombocytopenia with monocyte morulae on blood smear provides a rapid, low-cost diagnostic pathway that avoids the need for expensive PCR [12].

The 12.5% non-recovery rate was concentrated entirely in chronic-phase dogs. All six had baseline platelet counts below $30 \times 10^3/\mu\text{L}$ and CSS of 3, indicating advanced bone marrow failure. For these patients, combination therapy doxycycline plus imidocarb dipropionate, or doxycycline plus prednisolone for immune-mediated cytopenias has been proposed but lacks controlled trial evidence [13, 14].

Erythropoietin or granulocyte colony-stimulating factor (G-CSF) may offer adjunctive support in pancytopenic dogs, though their cost limits accessibility in Philippine veterinary practice [15]. Identifying chronic-phase dogs early through baseline platelet count ($<30 \times 10^3/\mu\text{L}$) and CSS allows clinicians to set realistic owner expectations and consider referral for blood transfusion support.

Clinical Implications

Three clinical messages emerge. First, a 28-day doxycycline course at 5 mg/kg BID is effective for acute and subclinical CME and should be the standard first-line protocol in Philippine veterinary practice. Second, baseline platelet count below $30 \times 10^3/\mu\text{L}$ at presentation should trigger immediate prognostic counselling owners need to know that recovery may be incomplete and that blood transfusion support or prolonged therapy could become necessary. Third, the high thrombocytopenia prevalence (91.7%) makes a simple in-clinic platelet estimate from a stained blood smear the most cost-effective screening tool for CME in tropical urban practices where SNAP tests may be financially out of reach for many pet owners.

Limitations

Several limitations apply. The sample size of 48 dogs, while adequate for describing the clinical profile, limited the power of logistic regression for identifying predictors of non-recovery, as reflected in the wide confidence intervals for chronic-phase odds ratios. PCR confirmation of *E. canis* was not performed; reliance on morulae detection and serology may have included a small number of *E. ewingii* or *Anaplasma platys* co-infections. The 28-day follow-up captures the acute therapeutic response but misses potential

relapse events that may occur weeks to months later, particularly in subclinical-phase dogs with persistent splenic reservoirs. Bone marrow aspirates were not obtained, so the chronic-phase classification rested on peripheral blood findings rather than histological confirmation of marrow hypoplasia. And the single treatment regimen (doxycycline monotherapy) precluded comparison with alternative protocols.

Conclusion

The main contribution of this research is a prospective, systematically documented clinical series of 48 CME cases from a Philippine referral hospital, providing the first local evidence base for treatment outcomes, haematological recovery trajectories, and prognostic indicators in a tropical Southeast Asian urban canine population.

Supporting the headline recovery rate of 87.5%, the haematological data demonstrated consistent and statistically significant improvements across all measured parameters over the 28-day doxycycline course. Platelets the most severely affected cell line at presentation showed the most dramatic recovery, nearly tripling from 68.4 to $198.7 \times 10^3/\mu\text{L}$. PCV rose by 13.6 percentage points, WBC more than doubled, and fever resolved in over 93% of dogs. The correlation structure confirmed that all cytopenias co-vary as a unit and that platelet count is the single most informative bedside prognostic marker.

For the Philippine veterinary community, these results validate doxycycline at 5 mg/kg BID for 28 days as a reliable, affordable treatment for the vast majority of CME cases. At current Manila market prices, the full course costs approximately PHP 800-1,200 (USD 14-21) within reach of most pet-owning households. Coupling treatment with tick prevention (fipronil spot-on or isoxazoline oral chewables) and owner education about tick habitat reduction in and around the home would reduce re-infection risk and lower the overall disease burden in Manila's dog population.

Several questions remain open for future investigation. Controlled comparison of doxycycline monotherapy against doxycycline-plus-imidocarb or doxycycline-plus-prednisolone in chronic-phase dogs would address the unmet need for the 12.5% who fail standard treatment. Extending follow-up to 90 or 180 days with repeat serology and PCR would determine true parasitological cure rates and relapse frequency. Molecular characterisation of circulating *E. canis* strains in Philippine dogs would reveal whether local genotypes differ in virulence or doxycycline susceptibility from the well-characterised Israeli and Brazilian reference strains. And a community-level epidemiological survey mapping CME seroprevalence across Manila's barangays would identify hotspot areas where targeted tick control campaigns would yield the greatest public health and animal welfare return.

Acknowledgements

Funding Sources

This research was supported by the Manila Metropolitan University of Veterinary Medicine internal research fund for companion animal infectious disease surveillance.

Institutional Support

The Manila Metropolitan University Veterinary Teaching Hospital provided clinical facilities, the Sysmex haematology analyser, Beckman biochemistry platform, and SNAP test kits used throughout this research.

Contributions Not Qualifying for Authorship

The authors thank veterinary nurses Maricel Gonzales and Jerome Villareal for dedicated patient monitoring and blood sample collection at each follow-up visit over the 18-month enrolment period.

References

1. Dantas-Torres F. The brown dog tick, *Rhipicephalus sanguineus* (Latreille, 1806) (Acari: Ixodidae): from taxonomy to control. *Veterinary Parasitology*. 2008;152(3-4):173-185.
2. Neer TM, Breitschwerdt EB, Greene RT, Lappin MR. Consensus statement on ehrlichial disease of small animals from the infectious disease study group of the ACVIM. *Journal of Veterinary Internal Medicine*. 2002;16(3):309-315.
3. Waner T, Harrus S, Jongejan F, Bark H, Keysary A, Cornelissen AW. Significance of serological testing for ehrlichial diseases in dogs with special emphasis on the diagnosis of canine monocytic ehrlichiosis caused by *Ehrlichia canis*. *Veterinary Parasitology*. 2001;95(1):1-15.
4. Harrus S, Waner T, Aizenberg I, Foley JE, Poland AM, Bark H. Amplification of ehrlichial DNA from dogs 34 months after infection with *Ehrlichia canis*. *Journal of Clinical Microbiology*. 1998;36(1):73-76.
5. Waner T, Harrus S, Bark H, Bogin E, Avidar Y, Keysary A. Characterization of the subclinical phase of canine ehrlichiosis in experimentally infected beagle dogs. *Veterinary Parasitology*. 1997;69(3-4):307-317.
6. de Castro MB, Machado RZ, de Aquino LP, Alessi AC, Costa MT. Experimental acute canine monocytic ehrlichiosis: clinicopathological and immunopathological findings. *Veterinary Parasitology*. 2004;119(1):73-86.
7. Sainz A, Roura X, Miró G, Estrada-Peña A, Kohn B, Harrus S, Solano-Gallego L. Guideline for veterinary practitioners on canine ehrlichiosis and anaplasmosis in Europe. *Parasites and Vectors*. 2015;8:75.
8. Suksawat J, Pinyowong D, Chimnoi W, Jaruboonyakorn P. Seroprevalence of *Ehrlichia canis*, *Anaplasma platys* and *Borrelia burgdorferi* in dogs from the Bangkok metropolitan region. *Kasetsart Journal (Natural Science)*. 2001;35(3):261-268.
9. Koh FX, Kho KL, Kisomi MG, Wong LP, Nizam QNH, Tay ST. Ehrlichia and Anaplasma infections of dogs in Peninsular Malaysia. *Ticks and Tick-borne Diseases*. 2018;9(4):826-834.
10. Claveria FG, Dollete UBG, Ortega RS. Seroprevalence of *Ehrlichia canis* among dogs in Metro Manila, Philippines. *Philippine Journal of Veterinary Medicine*. 2009;46(2):89-94.
11. Harrus S, Waner T. Diagnosis of canine monocytotropic ehrlichiosis (*Ehrlichia canis*): an overview. *Veterinary Journal*. 2011;187(3):292-296.
12. Mylonakis ME, Koutinas AF, Breitschwerdt EB, Hegarty BC, Billinis CD, Leontides LS, Kontos VS. Chronic canine ehrlichiosis (*Ehrlichia canis*): a retrospective study of 19 natural cases. *Journal of the American Animal Hospital Association*. 2004;40(3):174-184.
13. Eddlestone SM, Gaunt SD, Neer TM, Boudreaux CM, Gill A, Haschke E, Corstvet RE. PCR detection of *Anaplasma platys* in blood and tissue of dogs during acute phase of experimental infection. *Experimental Parasitology*. 2007;115(2):205-210.

14. Breitschwerdt EB, Hegarty BC, Hancock SI. Sequential evaluation of dogs naturally infected with *Ehrlichia canis*, *Ehrlichia chaffeensis*, *Ehrlichia equi*, *Ehrlichia ewingii*, or *Bartonella vinsonii*. *Journal of Clinical Microbiology*. 1998;36(9):2645-2651.
15. Waner T, Harrus S. Canine monocytic ehrlichiosis from pathology to clinical manifestations. *Israel Journal of Veterinary Medicine*. 2013;68(1):12-18.
16. Gaunt SD, Beall MJ, Stillman BA, Lorentzen L, Diniz PP, Chandrashekar R, Breitschwerdt EB. Experimental infection and co-infection of dogs with *Anaplasma platys* and *Ehrlichia canis*: hematologic, serologic and molecular findings. *Parasites and Vectors*. 2010;3:33.