RESEARCH ARTICLE

Haemato-Biochemical Changes and Therapeutic Outcomes in Cerebral Babesiosis in Dogs

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Abstract

Canine cerebral babesiosis is a rare, but life threatening neurological manifestation of *Babesia gibsoni* infection with scant documentation in India. The aim of the present study was to evaluate the clinical, haemato-biochemical changes with response to treatment in dogs with cerebral babesiosis (n=11). Cerebral babesiosis was initially suspected based on the presence of characteristic neurological signs and subsequently confirmed by microscopic examination of stained peripheral blood smears, and molecular confirmation by species-specific PCR targeting the *18S rRNA* gene of *Babesia gibsoni*, which yielded the expected 670-bp amplicon. Eleven dogs diagnosed with cerebral babesiosis were treated with diminazene aceturate, doxycycline, enrofloxacin, metronidazole, and supportive medications. Clinical, haematological and serum biochemical parameters were assessed on days 0, 3, 7, 14 and 28 post-treatment. Neurological signs included ataxia, hind limb stiffness, paddling, opisthotonus, seizures, head pressing, stupor, circling, nystagmus, blindness and paraplegia, which mostly improved slowly after treatment. Haematological evaluation showed anaemia, leukocytosis and marked changes in the lymphocyte, eosinophil and monocyte profiles in the early phase. Haemoglobin and erythrocyte parameters improved progressively after therapy and leukocyte abnormalities progressively approached the values recorded in apparently healthy dogs. Serum biochemical analysis showed significant changes in albumin, ALT, ALP, total bilirubin, direct bilirubin and BUN. High concentrations of ALT, ALP, bilirubin and BUN were observed at the beginning of the study and gradually decreased with treatment, while albumin concentration increased in the direction of the normal range. There were no significant differences in globulin, A/G ratio, creatinine, indirect bilirubin, glucose and magnesium. Results suggest cerebral babesiosis is associated with a poor prognosis despite intensive therapy, and combination chemotherapy with appropriate supportive care improved clinico-pathological and haemato-biochemical parameters and recovery of surviving dogs. Early diagnosis and treatment are thus still important to improve clinical outcomes.

Key words: *Babesia gibsoni*, Cerebral babesiosis, Dogs, Haematology, Neurological signs, Serum biochemistry.

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Introduction

The widespread occurrence of *Babesia gibsoni,* its impact on canine well-being, and the challenges associated with its diagnosis and treatment render it important in India (Reddy *et al.,* 2022). Indicators of *Babesia gibsoni* infection encompass fever, fatigue, anaemia, jaundice, and in severe cases, organ failure. The parasite may induce a recurring illness and is often associated with more enduring, subclinical infections, complicating diagnosis and therapy (Malinovska, 2024). Canine cerebral babesiosis affects dogs with central nervous systems, representing a rare yet severe Babesia infection that typically leads to neurological manifestations such as seizures, ataxia, and changes in mental state. *Babesia canis* or *Babesia gibsoni* are more prone to induce it, and when it manifests in the brain, it is often associated with a severe systemic infection (Liu *et al.,* 2012). Limited case studies have documented cerebral involvement in babesiosis, however it is not the predominant presentation (Sivajothi and Reddy, 2017). Cerebral babesiosis is presumed when canines display neurological symptoms, and a Babesia infection is diagnosed; concurrent infections must be excluded, and in the event of canine fatalities, the detection of protozoa in the brain should be validated through histopathological or molecular analyses (Adaszek *et al.,* 2012). The present study reports on clinical signs, haemato-biochemical changes and therapy outcomes in cerebral babesiosis in dogs.

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Materials and Methods

The research encompassed cerebral babesiosis affected dogs (n=11) presented to the Department of Veterinary Medicine at the College of Veterinary Science in Proddatur in the YSR districts of Andhra Pradesh, India, from October 2023 to September 2024. The research omitted canines with a background of trauma, uraemic encephalopathy, congestive heart failure, idiopathic epilepsy, canine distemper, rabies, or intermittent seizures. The choice of dogs was determined by their medical background, clinical manifestations, and diagnoses validated with blood smear analysis and PCR. Clinical and haemato-biochemical findings in dogs afflicted with cerebral babesiosis were recorded, and the post-treatment response was evaluated on days 0, 3, 7, 14 and 28 following therapy. Cerebral babesiosis was initially suspected based on the presence of characteristic neurological signs and subsequently confirmed by microscopic examination of stained peripheral blood smears, which revealed intraerythrocytic *Babesia* organisms (Reddy *et al.,* 2014; Sivajothi *et al.,* 2023) and further confirmed by PCR.

For PCR, blood samples (200 µL) collected from 11 dogs with neurological signs suggestive of babesiosis were collected into EDTA-coated tubes and stored at −20°C. Genomic DNA was extracted using the QIAamp DNA Blood Mini Kit (Qiagen®, Germany; Cat. No. 51104) according to the manufacturer's instructions with minor modifications. DNA concentration and purity were assessed using a NanoDrop 1000 spectrophotometer (Thermo Scientific, USA), and samples with an A260/A280 ratio of 1.7-1.9 were considered suitable for PCR. DNA was standardized to 100 ng/µL, and integrity was confirmed by electrophoresis on a 0.7% agarose gel prepared in 1× TAE buffer. Species-specific PCR was performed for *Babesia gibsoni* using a thermal cycler. The PCR conditions consisted of initial denaturation at 95°C for 5 min, followed by 40 cycles of denaturation at 95°C for 30 s, annealing at 60°C for 30 s and extension at 72°C for 100 s, with a final extension at 72°C for 5 min. Amplified products were subsequently analysed by agarose gel electrophoresis, which yielded a specific 670-bp amplicon corresponding to the *Babesia gibsoni 18S rRNA* gene.

Dogs in the current study received a variety of medications according to predetermined dosages and schedules. Deep intramuscular injection that contained diminazene aceturate (70 mg/mL) was administered in two doses at 48-h intervals @ 3.5 mg/kg body weight. For 21 days, doxycycline with lactic acid bacillus tablet, was given orally @ 5 mg/kg body weight every 12-h. Tab. enrofloxacin was administered orally for 21 days @ 10 mg/kg body weight every 24-h (Birkenheuer *et al.,* 2004). Metronidazole was given orally every 12-h for 21 days @ 15 mg/kg body weight. Inj. Iron Dextran was administered intramuscularly once weekly for 4 doses @ 10 mg/kg body weight. Syrup Hatplat (herbal platelet enhancer) which contains extracts of *Carica papaya*, goat milk powder, almond, wheatgrass, kiwi, pomegranate was another supportive therapy administered @ 5 mL for animals weighing up to 10 kg, 10 mL for 10-20 kg, and 20 mL for animals weighing > 20 kg, and Syrup Ferrimin (with folic acid, ferric ammonium chloride (12.2 mg/5 mL), and vitamins B_1, B_2, B_6, and B_{12}) was also given according to body weight, for 4 days. Tab. 40 mg of pantoprazole was given orally @ 1 mg/kg body weight every 24-h. Animals weighing less than 5 kg received 5 mL of Syrup Silytek, which contained silymarin buclizine hydrochloride (35 mg/5 mL) (Gonde *et al.,* 2016; Thakur *et al..* 2024; Malinovska, 2024).

On the 0^{th}, 3^{rd}, 7^{th}, 14^{th}, and 28^{th} days following treatment, the resolution of clinical symptoms and the improvement in haematological and biochemical parameters were used to gauge the clinical recovery of dogs with cerebral babesiosis. Using sterile disposable syringes, 3 mL of blood were drawn from the dogs' cephalic veins and placed in vacutainers that contained the anticoagulant EDTA. Following the standard procedures haematological parameters were assessed by automatic blood analyzer. 5 mL of blood were drawn in clot activator vacutainers in order to separate the serum. Following clotting, the serum was separated using centrifugation and stored at -20°C until analysis. Using standard procedures and kits, the serum biochemical parameters were analysed on a semi-automatic analyser.

The student's t-test was employed to evaluate the haemato-biochemical information employing SPSS version 20.00. The outcomes were subjected to statistical analysis through the established procedures.

Results and Discussion

In this study, a standard therapeutic approach was initiated on all 11 dogs with cerebral babesiosis along with post-treatment evaluations conducted on the 0^{th}, 3^{rd}, 7^{th}, 14^{th}, and 28^{th} day. Neurological examinations were performed on all 11 dogs at the time of presentation; 9 dogs on the 3^{rd} day; 8 dogs on 7^{th} day, 4 dogs on 14^{th} day and 2 dogs on 28^{th} day of examination, as few dogs gradually died during the study period of 28 days. The recorded clinical parameters and haematological changes and serum biochemical parameters are presented in the Tables 1-3; Fig.1A and 1B.

Although several clinical signs showed an apparent reduction by day 14 and day 28, particularly stiffness, paddling, opisthotonus, twitching, stupor, and paraplegia, the differences were not statistically significant ($p>0.05$). Chi-square analysis utility was limited (n=2) also limits statistical power.

Table 1: Post-therapeutic clinical assessment of dogs with cerebral babesiosis

Neurological findings	Post therapy days of observation (% dogs with cerebral babesiosis)					P value
	0th day (11)	3rd day (9)	7th day (8)	14th day (4)	28th day (2)	
Ataxia	72.72% (8/11)	77.77% (7/9)	62.50% (5/8)	50.00% (2/4)	50% (1/2)	0.826
Stiffness of hind limbs	63.63% (7/11)	77.77% (7/9)	62.50% (5/8)	25.00% (1/4)	0% (0/2)	0.183
Paddling	63.63% (7/11)	77.77% (7/9)	75.00% (6/8)	25.00% (1/4)	0% (0/2)	0.130
Opisthotonus	54.54% (6/11)	55.55% (5/9)	62.50% (5/8)	25.00% (1/4)	0% (0/2)	0.448
Twitching of hind limbs	54.54% (6/11)	66.66% (6/9)	62.50% (5/8)	25.00% (1/4)	0% (0/2)	0.344
Seizures	54.54% (6/11)	55.55% (5/9)	37.50% (3/8)	50.00% (2/4)	50% (1/2)	0.951
Head pressing	36.36% (4/11)	22.22% (2/9)	25.00% (2/8)	25.00% (1/4)	0% (0/2)	0.849
Stupor	36.36% (4/11)	33.33% (3/9)	25.00% (2/8)	0.00% (0/4)	0% (0/2)	0.568
Decerebrate rigidity	36.36% (4/11)	33.33% (3/9)	37.50% (3/8)	50.00% (2/4)	0% (0/2)	0.825
Decerebellate rigidity	36.36% (4/11)	44.44% (4/9)	25.00% (2/8)	25.00% (1/4)	0% (0/2)	0.748
Circling	27.27% (3/11)	22.22% (2/9)	25.00% (2/8)	50.00% (2/4)	0% (0/2)	0.744
Nystagmus	18.18% (2/11)	22.22% (2/9)	12.50% (1/8)	25.00% (1/4)	0% (0/2)	0.931
Blindness	18.18% (2/11)	22.22% (2/9)	25.00% (2/8)	25.00% (1/4)	0% (0/2)	0.949
Paraplegia	18.18% (2/11)	22.22% (2/9)	12.50% (1/8)	0% (0/4)	0% (0/2)	0.813



Fig. 1: (A) Dog with cerebral form of babesiosis exhibiting the neurological signs. (B) Improvement in body condition after therapy

Neurological findings during the course of therapy in dogs with cerebral babesiosis are summarized in Table 1. In general, there was a gradual clinical improvement in the various neurological manifestations with progression of therapy and follow-up. However, there were no statistically significant differences in the frequency of individual neurological signs between observation periods (p>0.05). The most frequent neurological abnormality was ataxia, observed in 72.72% of dogs on day 0, rising to 77.77% on day 3, and falling to 62.50%, 50.00% and 50.00% on days 7, 14 and 28, respectively (p=0.826). The hind limb stiffness followed a similar pattern. The paddling was observed initially in 63.63% of dogs, increasing to 77.77% on day 3 and 75.00% on day 7, then markedly decreasing to 25.00% on day 14 and complete resolution by day 28 (p=0.130). Opisthotonus and hind limb twitching were present in 54.54% of dogs at day 0, increased slightly to 62.50% at day 7, decreasing to 25.00% at day 14 and disappearing by day 28 (p=0.448). Twitching of hind limbs increased to 66.66% in day 3 and then decreased gradually to 0% (p=0.344). Seizures were observed in 54.54% of the dogs on days 0 and 3, and reduced to 37.50% on day 7, but still present in 50.00% of the remaining dogs on days 14 and 28 (p=0.951). Moreover, a progressive reduction was observed for several severe neurological manifestations (p>0.05), like head pressing, stupor, decerebellate & decerebrate rigidity (Table 1). Rotations and nystagmus were comparatively infrequent. Blindness increased slightly from 18.18% at baseline to 25.00% on days 7 and 14 but was absent by day 28 (p=0.949). Paraplegia decreased from 18.18% on day 0 to 12.50% on day 7 and was not observed from day 14 onward (p=0.813). Most neurological abnormalities showed an overall trend toward resolution by the later follow up periods, but none of the observed changes was statistically significant (p>0.05). The lack of statistical significance may be partly explained by the steadily decreasing number of dogs available for follow-up. However, the clinical course suggests a gradual neurological recovery after treatment, especially in hind-limb stiffness, paddling, opisthotonus, hind-limb twitching, stupor, head pressing, circling, nystagmus and paraplegia.

The post-therapeutic haematological profile of dogs with cerebral babesiosis is shown in Table 2. There were significant differences in apparently healthy dogs and different post therapeutic observation periods for haemoglobin, TLC, lymphocyte, eosinophil, monocyte percentages, and absolute lymphocyte, eosinophil and monocyte counts. However, TEC, PCV, MCV, MCH, MCHC, neutrophil percentage, absolute neutrophil count and platelet count did not differ significantly between groups. The concentration of haemoglobin was significantly lower in affected dogs on day 0 (10.21±0.18 g/dL) as compared with apparently healthy dogs (13.03±0.42 g/dL; p=0.001). There was progressive correction of anaemia as haemoglobin increased progressively on days 7, 14 and 28 after therapy. But values in the later observation period were still intermediate compared to the healthy group. The PCV and TEC also increased numerically from day 0 to day 28, approaching the apparently healthy values, however the differences were not significant. MCV, MCH and MCHC were

Table 2: Post-therapeutic assessment of haematological parameters in dogs with cerebral babesiosis (Mean ± SE)

Parameters	Apparently healthy dogs (n=10)	Post-therapeutic days of observation				P-value
		0th day (n=11)	7th day (n=8)	14th day (n=4)	28th day (n=2)	
Haemoglobin (g/dL)	13.03±0.42^{a}	10.21±0.18^{b}	11.02±0.80^{b}	11.91±0.04^{ab}	12.22±0.02^{ab}	0.001**
TEC (×10^{6}/µL)	6.51±0.19^{a}	5.09±0.08^{b}	5.51±0.66^{ab}	5.69±0.62^{ab}	6.10±0.03^{ab}	0.051*
PCV (%)	39.29±2.14	31.23±2.10	33.01±2.65	34.03±1.12	36.41±1.34	0.101
MCV (fL)	60.35±4.26	61.35±3.69	59.90±4.22	59.80±4.32	59.68±3.28	0.999
MCH (pg)	20.01±0.92	20.16±0.82	20.00±2.32	20.93±1.72	20.03±2.01	0.996
MCHC (g/dL)	33.16±2.54	32.69±2.14	33.38±0.32	34.99±0.32	33.56±0.32	0.978
TLC (×10^{3}/µL)	9.33±0.81^{a}	14.32±1.22^{b}	13.79±1.39^{ab}	11.08±0.78^{ab}	9.27±0.08^{ab}	0.012*
Neutrophils (%)	73.67±1.20	71.18±0.54	76.11±2.81	74.31±1.80	73.91±0.71	0.270
Lymphocytes (%)	20.43±0.85^{b}	17.02±0.75^{ac}	15.09±0.66^{a}	19.97±0.52^{bc}	21.04±0.09^{bc}	<0.001**
Eosinophils (%)	3.81±0.23^{b}	6.72±0.65^{a}	5.08±0.31^{ab}	2.87±0.09^{b}	3.01±0.01^{b}	<0.001**
Monocytes (%)	2.09±0.27^{c}	5.08±0.01^{a}	3.72±0.01^{b}	2.89±0.01^{bc}	2.04±0.01^{c}	<0.001**
Absolute neutrophil count (×10^{3}/µL)	6.89±1.23	10.19±1.09	10.49±1.13	8.24±0.89	6.85±0.70	0.134
Absolute lymphocyte count (×10^{3}/µL)	1.90±0.09^{a}	2.44±0.09^{b}	2.09±0.08^{ab}	2.21±0.10^{ab}	1.95±0.04^{ab}	0.001**
Absolute eosinophil count (×10^{3}/µL)	0.35±0.07^{c}	0.96±0.03^{a}	0.70±0.02^{b}	0.32±0.03^{c}	0.28±0.01^{c}	<0.001**
Absolute monocyte count (×10^{3}/µL)	0.19±0.01^{d}	0.73±0.01^{a}	0.51±0.01^{b}	0.31±0.01^{c}	0.19±0.01^{d}	<0.001**
Platelet count (×10^{3}/µL)	2.71±0.07	1.94±0.24	2.01±0.31	2.11±0.31	2.28±0.02	0.110

Means bearing different superscripts within each row differ significantly (p<0.05) by Tukey-Kramer post-hoc test.

relatively stable throughout the period of observation and no significant differences were observed among groups (p>0.05). There was evidence of significant leukocytic response after therapy. TLC was significantly increased on day 0 (14.32±1.22 ×103/µL) as compared to apparently healthy dogs (9.33±0.81 ×103/µL) and then showed a gradual decline on days 7, 14 and 28 respectively (p=0.012; Table 2). The fall in TLC toward normal value shows the resolution of inflammatory or stress related leucocytic response with clinical recovery.

Differential leukocyte profile showed significant changes in lymphocytes, eosinophils and monocytes (Table 2). The percentage of lymphocytes was lowest on day 7 compared with healthy dogs and then increased on days 14 and 28 (p<0.001). In contrast, the eosinophils and monocytes percentages were significantly increased on day 0 compared with apparently healthy dogs and then progressively declined on days 7, 14 and 28, respectively (p<0.001). The absolute lymphocyte, eosinophil, & monocyte counts also varied significantly among groups (p=0.001) and followed the pattern of percentage values. Neutrophil percentage however showed a relative stability during the study period, ranging from 71.18±0.54% to 76.11±2.81%, with no significant difference between observation periods (p=0.270). Similarly absolute neutrophil count decreased numerically from 10.19±1.09 ×10^{3}/µL on day 0 to 6.85±0.70 ×10^{3}/µL on day 28 (p=0.134). Platelet counts did not differ significantly (p=0.110) although they increased numerically from 1.94±0.24 ×10^{3}/µL at baseline to 2.28±0.02 ×10^{3}/µL on day 28. The haematological findings in general showed a gradual return of the erythrocytic parameters to normal and the leukocytic changes normalized after therapy. The most significant recovery was observed in the profiles of haemoglobin, TLC, lymphocytes, eosinophils and monocytes, particularly by day 28. The improvement of several parameters toward the values observed in apparently healthy dogs supports the progressive haematological recovery that occurs with clinical improvement in dogs affected with cerebral babesiosis.

The post-therapeutic biochemical profile of cerebral babesiosis in dogs in relation to healthy controls is presented in Table 3. Significant differences were observed between the apparently healthy dogs and the different post-therapeutic observation periods for albumin, ALT, ALP, total bilirubin, direct bilirubin and BUN. Conversely, total protein, globulin, A/G ratio, indirect bilirubin, creatinine, glucose and magnesium concentrations were not significantly different between groups. Total protein concentration was comparatively lower in affected dogs on day 0 (5.08±0.91 g/dL) than in healthy dogs (6.81±0.22 g/dL), and gradually increased on days 7, 14 and 28 (p=0.255). The globulin concentration remained relatively constant over the period of observation. Likewise, the A/G ratio displayed

Table 3: Post-therapeutic assessment of biochemical changes in dogs with cerebral babesiosis (Mean ± SE)

Parameters	Healthy dogs (n=11)	Post-therapeutic days of observation				P-value
		0th day (n=11)	7th day (n=8)	14th day (n=4)	28th day (n=2)	
Total protein (g/dL)	6.81±0.22	5.08±0.91	5.48±0.21	6.01±0.31	6.23±0.09	0.255
Albumin (g/dL)	3.25±0.04^{a}	1.84±0.11^{c}	2.12±0.09^{b}	2.43±0.21^{bc}	2.79±0.08^{ab}	<0.001**
Globulin (g/dL)	3.56±0.08	3.24±0.41	3.36±0.38	3.58±0.42	3.44±0.17	0.945
A/G ratio	0.91±0.20	0.58±0.22	0.63±0.07	0.68±0.03	0.81±0.08	0.707
ALT (IU/L)	18.71±1.56^{a}	44.86±11.30^{ab}	53.00±8.20^{b}	43.12±7.10^{ab}	38.08±6.60^{ab}	0.049*
ALP (IU/L)	87.05±6.31^{a}	281.90±7.08^{b}	139.50±34.83^{a}	127.60±22.08^{a}	96.80±8.08^{a}	<0.001**
Total bilirubin (mg/dL)	0.84±0.05^{a}	1.27±0.09^{b}	0.96±0.12^{ab}	1.02±0.03^{ab}	0.89±0.01^{ab}	0.007**
Direct bilirubin (mg/dL)	0.44±0.02^{a}	0.76±0.04^{b}	0.49±0.03^{a}	0.61±0.12^{ab}	0.47±0.23^{ab}	<0.001**
Indir. bilirubin (mg/dL)	0.40±0.03	0.51±0.05	0.47±0.08	0.41±0.07	0.42±0.08	0.562
BUN (mg/dL)	16.56±0.95^{a}	28.81±0.63^{b}	25.67±2.55^{b}	24.77±2.02^{b}	23.08±0.08^{ab}	<0.001**
Creatinine (mg/dL)	0.91±0.07	1.47±0.37	1.37±0.14	1.08±0.22	1.06±0.02	0.465
Glucose (mg/dL)	102.27±0.56^{a}	91.08±4.09^{b}	96.27±1.56^{ab}	95.08±2.08^{ab}	99.03±0.41^{ab}	0.051*
Magnesium (mg/dL)	1.94±0.20	2.72±0.44	2.39±0.03	2.08±0.41	2.33±0.52	0.427

Means bearing different superscripts within each row differ significantly (p<0.05) by Tukey-Kramer post-hoc test.

a gradual numerical improvement from 0.58±0.22 on day 0 to 0.81±0.08 on day 28, approaching the healthy value of 0.91±0.20, but the difference was non-significant (p=0.707). There was a significant difference in albumin concentration between the groups (p<0.001). On day 0, the albumin concentration observed in affected dogs was lowest (1.84 ± 0.11 g/dL) compared to healthy dogs (3.25 ± 0.04 g/dL), which increased gradually on days 7, 14 and 28, respectively, after therapy indicating a gradual improvement of the hypoalbuminaemic state associated with cerebral babesiosis, although the value on day 28 was still slightly lower than that of the healthy dogs.

Of the hepatic enzymes, ALT was significantly different (p=0.049) and ALP was highly significantly different (p<0.001) between groups and period post-treatment. The activity of ALT and ALP increased significantly (p<0.01) on day 0 in cerebral babesiosis affected dogs. The ALT activity reached the maximum level with 53.00±8.20 IU/L on day 7, and thereafter, a gradual improvement in hepatocellular enzyme activity occurred after therapy with decrease in ALT on day 14 and 28. Post-treatment ALP values however decreased gradually and markedly on day 7, day 14 and day 28, reaching close to the healthy value. Bilirubin concentrations were also significantly altered, being significantly (p=0.007) increased from 0.84±0.05 mg/dL in healthy dogs to 1.27±0.09 mg/dL on day 0, and later it decreased gradually on days 7, 14 and 28 reaching close to the value in healthy dogs. Direct bilirubin showed the same trend and was significantly different between the groups (p<0.001). Conversely, indirect bilirubin was relatively constant during the study and was not significantly different (p=0.562, Table 3).

Renal biochemical parameters significantly improved after therapy. In affected dogs BUN was significantly increased on day 0 (p<0.001) and was still high on day 7 and day 14, but was back to 23.08±0.08 mg/dL on day 28 (Table 3). The fall indicates progressive improvement in the azotaemic status following treatment. No significant difference was observed in creatinine among the groups (p=0.465), but a numerical increase from 0.91±0.07 mg/dL in healthy dogs to 1.47±0.37 mg/dL on day 0, then a reduction by day 28 was observed. Blood glucose showed a numerical decrease from 102.27±0.56 mg/dL in healthy dogs to 91.08±4.09 mg/dL on day 0 and gradually increased to 99.03±0.41 mg/dL on 28 (p=0.051). Magnesium concentrations were similar during the observation period and were not significantly different between the groups (p=0.427). In general, the biochemical data showed progressive improvement of hepatic, haemolytic and renal-related biochemical abnormalities after therapy. The most important alterations were a decrease in elevated ALP, ALT, total and direct bilirubin, BUN and a progressive normalization of the albumin concentration. By day 28 several of the biochemical parameters had approached the values in apparently healthy dogs.

Biochemical changes in serum also supported the multisystemic nature of *B. gibsoni* infection. Albumin decreased significantly in the beginning and improved progressively after therapy. Hypoalbuminaemia had been reported previously in dogs infected with *B. gibsoni* and may be associated with inflammation, altered hepatic protein synthesis and increased protein loss during systemic disease. The progressive rise in albumin level in this study might suggest improvement in systemic inflammation and liver function during recovery (Bilwal *et al.,* 2017). The early stage rise of ALT and ALP in cerebral babesiosis may be related to secondary hepatocellular and hepatobiliary

changes associated with severe haemolysis, tissue hypoxia, systemic inflammation and altered hepatic perfusion. ALT and ALP levels gradually decreased after therapy, which could be due to resolution of hepatocellular stress and cholestatic changes after control of parasitaemia and haemolysis. The parallel decrease in total and direct bilirubin concentrations further supports progressive improvement of haemolytic and hepatobiliary alterations (Sai *et al.,* 2023). Therefore, normalization of ALT and, in particular ALP, during follow-up may be considered an indicator of the recovery of hepatic and biliary function after successful therapeutic intervention. Increased BUN has been reported in canine *B. gibsoni* infection and may represent altered renal perfusion, dehydration, tissue hypoxia or systemic effects of severe babesiosis (Reddy *et al.,* 2024). However, in the present study, no significant difference was found for creatinine between groups, suggesting that the observed increase in BUN was not accompanied by a similar persistent increase in creatinine (Chan *et al.,* 2025). The progressive improvement in neurological, haematological and biochemical parameters following therapy indicates an overall favourable clinical and systemic response to treatment in dogs with cerebral babesiosis.

Azithromycin every 24 h combined with atovaquone every 8 h for 10 days is the current recommended treatment for *Babesia gibsoni* (Birkenheuer *et al.*, 2004; Baneth, 2018). Diminazene diaceturate, along with other supportive medications such as probiotic and prebiotic capsules, iron supplements, 20% mannitol, doxycycline, prednisolone, furosemide, and kidney and liver cleanser. For 21 days, a single dose of diminazene aceturate at 3.5 mg/kg body weight deep i/m was administered along with an oral combination of doxycycline, enrofloxacin, and metronidazole @ 5, 3, and 10 mg/kg body weight. Clindamycin-metronidazole-doxycycline has been shown in some studies to be effective; however, this regimen is time-consuming and frequently necessitates supportive therapy. The combination of imidocarb, diminazene, and clindamycin is another alternate treatment plan (Lin *et al.,* 2012). Antibiotics (doxycycline) can reduce the disease's clinical symptoms, but they cannot totally eradicate piroplasms. Although the prognosis for dogs with cerebral babesiosis appears to be grave, An *et al.* (2019) reported full neurological recovery of a dog with cerebral babesiosis after treatment with imidocarb dipropionate.

Conclusions

To conclude, canine cerebral babesiosis is a rare, yet serious neurological complication associated with high mortality, caused by *Babesia gibsoni*. Overall, post-therapeutic clinical, haematological and biochemical findings suggested a favourable response to treatment and progressive recovery in dogs with cerebral babesiosis. The serial clinical and laboratory monitoring is useful in assessing therapeutic response and prognosis of cerebral babesiosis as evidenced by the improvement in neurological manifestations, normalization of haematological parameters and biochemical abnormalities. The declining number of dogs available at later follow-up periods should however be considered when interpreting the statistical results. Nevertheless, the prognosis was still poor given the high mortality rate observed in the study.

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