

Supplementary Material

Table S1. A summary of clinical, hematological, biochemical, blood gas, acid base and endocrine data in the whole group of babesia-infected dogs and the sub-groups collapsed versus non-collapsed and survivors versus non-survivors. The level of significance between the medians of the groups is noted.

| Parameter | Normal range | Whole group (n; IQR) | Not collapsed (n; IQR) | Collapsed (n; IQR) | P value | Survived (n; IQR) | Died (n; IQR) | p value |
|--|--------------|-------------------------|------------------------|-----------------------|---------|-------------------------|-----------------------|---------|
| Clinical | | | | | | | | |
| Rectal Temperature (°C) | 37.5-39.5 | 39.6 (320; 39-40.1) | 39.7 (248; 39.2-40.1) | 38.5 (72; 37-39.7) | <0.001 | 39.7 (287; 39-40.1) | 38.7 (32; 37.5-39.7) | <0.001 |
| Pulse (bpm) | 60-160 | 128 (316; 116-148) | 128 (245; 112-148) | 132 (71; 120-150) | 0.099 | 128 (286; 116-147) | 132 (29; 120-152) | 0.415 |
| Respiratory rate (bpm) | 15-30 | 44 (287; 32-60) | 44 (217; 32-60) | 44 (70; 36-60) | 0.433 | 44 (258; 32-60) | 40 (28; 32-60) | 0.748 |
| Age (months) | | 20 (319; 9-48) | 12 (247; 9-36) | 24 (72; 10-48) | 0.891 | 20 (286; 9-48) | 22 (32; 9-49) | 0.76 |
| Weight (kg) | | 15.6 (307; 7.8-26.7) | 16.2 (238; 8.6-27.50) | 14.6 (69; 5.7-26) | 0.646 | 15.5 (277; 8-26.2) | 20.2 (29; 8-33.2) | 0.421 |
| Haematology | | | | | | | | |
| Hematocrit (L/L) | 0.37-0.55 | 0.19 (317; 0.12-0.31) | 0.22 (247; 0.145-0.33) | 0.11 (70; 0.08-0.16) | <0.001 | 0.19 (285; 0.13-0.31) | 20 (31; 0.105-0.31) | 0.425 |
| Reticulocytes ($\times 10^9/L$) | | 82.58 (113; 44.4-170.9) | 80 (91; 42.7-80) | 89.1 (22; 57.4-226.2) | 0.709 | 82.85 (100; 46.3-170.9) | 82.2 (13; 32.4-110.9) | 0.55 |
| Total white cell count ($\times 10^9/L$) | 6-15 | 6.35 (320; 4.53-11.15) | 5.82 (247; 4.3-8.52) | 10.5 (69; 5.58-15.7) | <0.001 | 6.21 (287; 4.43-9.97) | 9.27 (32; 5.03-16.17) | .031 |
| Band cell count ($\times 10^9/L$) | 0-0.5 | 0.41 (291; 0.17-0.99) | 0.32 (225; 0.14-0.69) | 1.245 (66; 0.53-2.51) | <0.001 | 0.365 (260; 0.15-0.875) | 1.015 (30; 0.53-2.18) | <0.001 |
| Platelet count ($\times 10^9/L$) | 200-500 | 20 (316; 5.9-47) | 18 (247; 5.8-40) | 23 (69; 4.3-56) | 0.331 | 18 (287; 5.4-45) | 22.5 (32; 10.3-54) | 0.224 |
| Biochemistry | | | | | | | | |
| Lactate (mmol/L) | <2 | 2.2 (209; 1.4-4.2) | 2 (166; 1.3-3) | 9 (43; 3.65-11) | <0.001 | 2.2 (186; 1.4-3.4) | 4.3 (23; 1.7-10.8) | 0.006 |
| Glucose (mmol/L) | 3.3-5.5 | 4.7 (317; 3.6-5.6) | 4.7 (246; 3.8-5.5) | 4 (71; 2.3-5.6) | 0.065 | 4.7 (285; 3.7-5.5) | 3.9 (31; 1.8-5.6) | 0.079 |
| Bilirubin ($\mu\text{mol/L}$) | 1-6.8 | 8.8 (230; 4.8-24.3) | 7.3 (181; 4.6-11.8) | 51 (49; 16.2-103.4) | <0.001 | 8.2 (206; 4.8-18.9) | 29.4 (24; 9.8-93.3) | 0.001 |
| ALP (U/L) | 20-165 | 104 (293; 73.5-147) | 95 (226; 68-128) | 147 (67; 102-221) | <0.001 | 100.5 (262; 74-143) | 125 (30; 73-194) | 0.242 |

| | | | | | | | | |
|--------------------------------|------------|--------------------------|-------------------------|-------------------------|--------|-------------------------|-------------------------|--------|
| ALT U/L) | 9-73 | 32 (294; 23-61) | 28 (226; 21-48) | 76 (68; 44-172) | 0.005 | 30 (263; 22-54) | 63 (30; 24-102) | 0.014 |
| Bile acids (μmol/L) | 0-8 | 9.84 (280; 2.64-28.95) | 7 (214; 2.2-24.5) | 26.7 (66; 7-59.8) | 0.044 | 9.8 (252; 2.6-28.3) | 8 (27; 4-54.7) | 0.316 |
| Albumin (g/L) | 28-41 | 23.3 (294; 20.3-27.9) | 23.9 (226; 21.1-28.3) | 20.7 (68; 17.5-23.5) | <0.001 | 23.4 (263; 20.5-27.9) | 22.4 (30; 19.5-25.9) | 0.235 |
| Urea (mmol/L) | 2.3-8.9 | 8.05 (188; 5.6-18.28) | 6.8 (145; 5.2-11.1) | 22 (43; 14.9-28.2) | <0.001 | 7.5 (167; 5.5-14.4) | 25.5 (21; 16.8-31.5) | <0.001 |
| Creatinine (μmol/L) | 59-109 | 66.5 (320; 50-92) | 64 (248; 50-89) | 71.5 (72; 54-119.5) | 0.075 | 64 (287; 50-87.5) | 126 (32; 49-165) | 0.001 |
| SIP (mmol/L) | 0.7-2.1 | 1.46 (184; 1.22-1.92) | 1.4 (132; 1.2-1.6) | 2 (52; 1.5-2.7) | <0.001 | 1.43 (168; 1.2-1.82) | 3.58 (15; 2.05-4.35) | <0.001 |
| Na ⁺ (mmol/L) | 142-151 | 141 (262; 138.2-143) | 141 (100; 138.8-143) | 141 (30; 137-143) | 0.786 | 141 (120; 138.9-143) | 137.95 (12; 133-143) | 0.228 |
| K ⁺ (mmol/L) | 3.6-5.1 | 3.8 (262; 3.5-4.1) | 3.87 (100; 3.58-4.09) | 3.67 (30; 3.27-4.1) | 0.282 | 3.83 (120; 3.55-4.09) | 4.01 (12; 3.32-4.71) | 0.436 |
| Cl ⁻ (mmol/L) | 107-117 | 113 (260; 109.9-116.5) | 113 (99; 110-116.2) | 111.8 (30; 108-119) | 0.727 | 113 (119; 110-116.9) | 107.2 (12; 98.1-114.2) | 0.009 |
| Ca ⁺⁺ (mmol/L) | 1.22-1.46* | | 1.24 (153; 1.17-1.29) | 1.17 (48; 1.09-1.22) | <0.001 | 1.22 (195; 1.16-1.28) | 1.1 (17; 1.01-1.22) | 0.001 |
| Blood gas and acid base | | | | | | | | |
| pO ₂ (mmHg) | 81-103 | 91.4 (98; 81-101.2) | 91.6 (71; 82.2-101.3) | 91.3 (27; 70.1-100.1) | 0.616 | 91.6 (87; 81.8-101.2) | 89.1 (11; 56.6-101.7) | 0.54 |
| pCO ₂ (mmHg) | 31-43 | 25.4 (252; 21.8-29.5) | 26,7 (97; 23.3-30) | 19.5 (29; 14.2-25.9) | <0.001 | 25.4 (115; 21.9-29.30) | 26.3 (11; 19.1-31.1) | 0.966 |
| pH | 7.35-7.46 | 7.429 (253; 7.378-7.467) | 7.433 (97; 7.402-7.471) | 7.36 (29; 7.306-7.439) | <0001 | 7.43 (116; 7.389-7.469) | 7.36 (11; 7.332-7.441) | 0.049 |
| HCO ₃ (mEq) | 18-26 | 16.6 (255; 13.7-19.3) | 17.3 (98; 14.9-19.4) | 11.9 (29; 7-15.8) | <0.001 | 16.6 (117; 13.8-19.2) | 14.2 (11; 11-18.9) | 0.586 |
| Anion Gap (mmol/L) | 8-16 | 14.8 (258; 12.5-17.8) | 13.87 (99; 12.3-16.5) | 18.8 (30; 14.4-25.9) | <0.001 | 14.6 (118; 12.5-17.2) | 19.4 (11; 16.3-26.5) | 0.009 |
| Endocrine | | | | | | | | |
| Total thyroid hormone (nmol/L) | 13-45 | 11.4 (245; 4.04-17.18) | 13.87 (180; 8.7-18.1) | 2.24 (63; 0.2-5.1) | <0.001 | 12.3 (219; 5.1-17.4) | 2.77 (24; 1.16-5.13) | <0.001 |
| Cortisol (nmol/L) | 10-160 | 159.87 (244; 83.6-382.3) | 112 (179; 70.4-204.5) | 485.2 (63; 368.5-695.5) | <0.001 | 141.5 (218; 79.7-303.2) | 551.3 (25; 472.5-695.5) | <0.001 |

Table S2. Summary of the 10 most common macroscopic lesions in babesia-infected dogs that presented for post mortem examination.

| Macroscopic lesions | Proportion of necropsied cases in which each lesion was observed (number of dogs evaluated by post mortem (percent)) |
|---|---|
| Splenomegaly due to red pulp hyperplasia | 25 (100%) |
| Hepatitis | 25 (100%) |
| Visceral hemorrhages (excluding GIT, lung and brain) | 22 (88%) |
| Anemia | 20 (80%) |
| Icterus | 17 (68%) |
| Acute interstitial pneumonia ('shock lung') | 16 (64%) |
| GIT hemorrhage | 6 (24%) |
| Pericardial effusion | 9 (36%) |
| Thoracic effusion | 4 (16%) |
| Abdominal effusion | 3 (12%) |
| Pericardial and thoracic effusion Abdominal and thoracic | 2 each (16%) |
| Cerebral babesiosis | 4 (16%) |
| Acute kidney injury (nephrosis) | 4 (16%) |

Table S3. Clinico-pathological abnormalities identified in this cohort of *Babesia rossi* infected dogs ranked from most to least common.

| Abnormality | Proportion (percentage) | Abnormality | Proportion (percentage) |
|--|-------------------------|---|-------------------------|
| Mixed acid-base disorder (metabolic acidosis with respiratory alkalosis) | 86 | Increased urea (> 8.9 mmol/L) | 43.6 |
| Hemoglobinuria (macroscopic and dip stick) | 84.1 | Increased bile acids (>15 umol/L) | 42 |
| Anemia (hematocrit < 0.37L/L) | 83 | Increased serum inorganic phosphate (>1.6 mmol/L) | 32.6 |
| Hypoalbuminemic (<27 g/L) | 72.8 | Hypoglycemia (glucose < 3.3mmol/L) | 19.2 |
| Identified as having the systemic inflammatory response syndrome | 60.5 | Arterial hypoxia (pO ₂ < 60 mmHg) | 18 |
| Lactate > 2 mmol/L | 55.5 | Icterus | 16.25 |
| Hypercortisolemic (> 160 nmol/L) | 50% | Warm in saline agglutination positive | 13 |
| Hypocapnoeic (pCO ₂ < 25.19 mmHg) | 49.2 | Increased creatinine (>133 umol/L) | 9.6 |
| Reduced HCO ₃ (< 16.29 mEq/L) | 47.7 | Hemoconcentration (hematocrit > 0.55L/L) | 1 |
| Total T4 < 13 pmol/L | 44.5 | | |

Table S4 A and B. The number of cases that satisfied the various criteria for the diagnosis of SIRS (A) and the number of cases that were positive for the number of SIRS criteria (B) (SIRS: Systemic inflammatory response syndrome)

A)

| White cell criteria | Band cell count | Temperature | Pulse rate | Respiratory rate |
|----------------------------------|------------------|-------------------|-------------------------|------------------------|
| WCC>12 or <4 x10 ⁹ /L | count≥10% of WCC | ≤37.8 or ≥39.7 °C | ≥160 breaths per minute | ≥40 breaths per minute |
| 126 | 92 | 172 | 50 | 184 |

(B)

| One SIRS criteria | Two SIRS criteria | Three SIRS criteria | Four SIRS criteria |
|-------------------|-------------------|---------------------|--------------------|
| 70 | 101 | 51 | 9 |