The Effect of Coinfection with Babesiosis and Lyme Disease on Novel Biomarkers

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Introduction

- The major pathogens responsible for babesiosis and Lyme disease in the US are *Babesia microti (B. microti)* and *Borrelia burgdorferi (B. burgdorgeri)* respectively, which can be transmitted simultaneously through the bite of the *Ixodes Scapularis* tick.
- The effect that coinfection with *B. microti* and *B. burgdorferi* has on human hosts has yet to be determined as human studies are limited and current literature presents conflicting results.
- The aim of this pilot study is to investigate the effect that coinfection with babesiosis and Lyme disease has on several standard and novel biomarkers markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and procalcitonin (Pc), which may assist in elucidating how these pathogens interact with each other in human hosts.

Materials and Methods

- Cases of babesiosis and coinfection with babesiosis and Lyme disease were retrospectively collected from Stony Brook University Hospital from 2012 to 2019.
- Cases of babesiosis were included if parasites were detected by peripheral blood smear and confirmed by PCR.
- Lyme disease diagnosis criteria involved 2-tier testing per CDC guidelines.
- Cases were divided into three cohorts based on whether they had CRP, ESR or Procalcitonin levels measured. Cohorts were then divided into two groups: Babesiosis monoinfection vs. coinfection with Lyme disease.
- Median values were analyzed for the following biomarkers across both groups: Max parasitemia, hemoglobin (Hgb), white blood cells (WBC), platelets, indirect bilirubin (IB), lactic acid dehydrogenase, ESR, CRP and Procalcitonin.
- Statistical analysis of data involved Fisher Exact and Wilcoxon Rank sum tests. A p-value below 0.05 was considered to be statistically significant.

Results

- ESR values trended higher in the monoinfected group compared to coinfected group (50 mm/hr vs 36 mm/hr, p=0.63, Table 1b).
- Within the ESR cohort, the coinfected group had significantly lower platelet values compared to the monoinfected group (52 K/uL vs. 75.5 K/uL, p=0.04, Table 1b).
- Within the CRP cohort, the monoinfected group had higher trends of parasitemia compared to the coinfected group (1.6% vs 0.7%, p=0.14, Table 2b).
- There was no significant difference in CRP levels between the monoinfected and coinfected groups (11.6 mg/dL vs. 12.4 mg/dL, p=0.79, Table 2b).
- Within the procalcitonin cohort, the monoinfected group had higher trends of parasitemia compared to coinfected group (1.4% vs 0.7%, p=1.0, Table 3b).
- There was no significant difference in procalcitonin levels between the monoinfected and coinfected groups (1.1 ng/mL vs 1.2 ng/mL, p=1.0, Table 3b).

Table 1a: Characteristics of Patients with Babesiosis Monoinfection vs Coinfection with Lyme Disease within ESR Cohort.

N=17	Infection Status		
	Babesiosis Monoinfection (N=10)	Coinfection with Lyme Disease (N=7)	P-value
Age, Median (IQR)	57.0 (44 – 75)	67.0 (52 – 85)	0.3285
Gender, n (%)			
Male	9 (90.0)	5 (71.43)	0.5368
Female	1 (10.0)	2 (28.57)	
Race, n (%)			
White	7 (70.0)	5 (71.43)	1.0000
Non-White	3 (30.0)	2 (28.57)	
Admitted, n (%)			
No	2 (20.0)	0 (0.0)	0.4853
Yes	8 (80.0)	7 (100.0)	
ICU Admission, n (%)			
No	9 (90.0)	6 (85.71)	1.0000
Yes	1 (10.0)	1 (14.29)	
Hypertension, n (%)			
No	8 (80.0)	6 (85.71)	1.0000
Yes	2 (20.0)	1 (14.29)	
Diabetes, n (%)			
No	9 (90.0)	7 (100.0)	1.0000
Yes	1 (10.0)	0 (0.0)	
CHF/CAD/Arrhythmias, n (%)			
No	8 (80.0)	6 (85.71)	1.0000
Yes	2 (20.0)	1 (14.29)	
Leukemia/Lymphoma, n (%)			
No	9 (90.0)	7 (100.0)	1.0000
Yes	1 (10.0)	0 (0.0)	
Cancer (Other), n (%)			
No	9 (90.0)	6 (85.71)	1.0000
Yes	1 (10.0)	1 (14.29)	
CKD, n (%)			
No	10 (100.0)	6 (85.71)	0.4118
Yes	0 (0.0)	1 (14.29)	
COPD/Asthma, n (%)			
No	8 (80.0)	5 (71.43)	1.0000
Yes	2 (20.0)	2 (28.57)	
Liver Disease, n (%)			
No	9 (90.0)	7 (100.0)	1.0000
Yes	1 (10.0)	0 (0.0)	
Autoimmune Disease, n (%)			
No	8 (80.0)	7 (100.0)	0.4853
Yes	2 (20.0)	0 (0.0)	
Immunocompromised, n (%)			
No	6 (60.0)	7 (100.0)	0.1029
Yes	4 (40.0)	0 (0.0)	
Splenectomy, n (%)			
No	9 (90.0)	7 (100.0)	1.0000
Yes	1 (10.0)	0 (0.0)	

Table 1b: Biomarkers of Patients with Babesiosis Monoinfection vs Coinfection with Lyme Disease within ESR Cohort.

N=17	Infection Status		
	Babesiosis Monoinfection (N=10)	Coinfection with Lyme Disease (N=7)	P-value
Max Parasitemia (%), Median (IQR)	1.6 (1.2 – 3.5)	1.8 (0.6 – 2.6)	0.4639
Hemoglobin (Hgb) (g/dL), Median (IQR)	10.9 (9.1 – 13.0)	11.5 (7.5 – 13.7)	0.8836
White blood cells (WBC) (K/uL), Median (IQR)	6.0 (4.7 – 7.7)	4.9 (3.5 – 5.2)	0.3055
Platelets (K/uL), Median (IQR)	75.5 (65 – 115)	52.0 (43 – 72)	0.0401
Indirect Bilirubin (IB) (mg/dL), Median (IQR)	0.8 (0.7 – 1.1)	0.8 (0.4 – 1.0)	0.5558
Lactate Dehydrogenase (LDH) (IU/L), Median (IQR) (6 values not recorded)	923 (552 – 1090)	558.5 (381 – 779)	0.3602
Erythrocyte Sedimentation Rate (ESR) (mm/hr), Median (IQR)	50.0 (28 – 88)	36.0 (9 – 71)	0.6254

Table 2a: Characteristics of Patients with Babesiosis Monoinfection vs Coinfection with Lyme Disease within CRP Cohort.

N=17	Infection Status		
	Babesiosis Monoinfection (N=12)	Coinfection with Lyme Disease (N=5)	P-value
Age, Median (IQR)	62.0 (45.5-73.0)	53.0 (52.0 – 54.0)	1.0000
Gender, n (%)			
Male	11 (91.67)	5 (100.0)	1.0000
Female	1 (8.33)	0 (0.0)	
Race, n (%)			
White	9 (75.0)	2 (40.0)	0.2801
Non-White	3 (25.0)	3 (60.0)	
Admitted, n (%)			
No	2 (16.67)	0 (0.0)	1.0000
Yes	10 (83.33)	5 (100.0)	
ICU Admission, n (%)			
No	9 (75.0)	5 (100.0)	0.5147
Yes	3 (25.0)	0 (0.0)	
Hypertension, n (%)			
No	8 (66.67)	5 (100.0)	0.2605
Yes	4 (33.33)	0 (0.0)	
Diabetes, n (%)			
No	10 (83.33)	4 (80.0)	1.0000
Yes	2 (16.67)	1 (20.0)	
CHF/CAD/Arrhythmias, n (%)			
No	9 (75.0)	4 (80.0)	1.0000
Yes	3 (25.0)	1 (20.0)	
Leukemia/Lymphoma, n (%)			
No	11 (91.67)	5 (100.0)	1.0000
Yes	1 (8.33)	0 (0.0)	
Cancer (Other), n (%)			
No	10 (83.33)	5 (100.0)	1.0000
Yes	2 (16.67)	0 (0.0)	
CKD, n (%)			
No	12 (100.0)	5 (100.0)	N.A
Yes	0 (0.0)	0 (0.0)	
COPD/Asthma, n (%)			
No	11 (91.67)	4 (80.0)	0.5147
Yes	1 (8.33)	1 (20.0)	
Liver Disease, n (%)			
No	11 (91.67)	5 (100.0)	1.0000
Yes	1 (8.33)	0 (0.0)	
Autoimmune Disease, n (%)			
No	9 (75.0)	5 (100.0)	0.5147
Yes	3 (25.0)	0 (0.0)	
Immunocompromised, n (%)			
No	9 (75.0)	5 (100.0)	0.5147
Yes	3 (25.0)	0 (0.0)	
Splenectomy, n (%)			
No	12 (100.0)	5 (100.0)	N.A
Yes	0 (0.0)	0 (0.0)	

Table 2b: Biomarkers of Patients with Babesiosis Monoinfection vs Coinfection with Lyme Disease within CRP Cohort.

N=17	Infection Status		
	Babesiosis Monoinfection (N=12)	Coinfection with Lyme Disease (N=5)	P-value
Max Parasitemia (%), Median (IQR)	1.6 (1.2 – 5.2)	0.7 (0.6 – 1.4)	0.1395
Hemoglobin (Hgb) (g/dL), Median (IQR)	10.9 (9.6 – 13.2)	12.5 (6.6 – 13.7)	1.0000
White blood cell (WBC) (K/uL), Median (IQR)	6.0 (3.8 – 6.8)	5.0 (4.1 – 5.2)	0.6353
Platelets (K/uL), Median (IQR)	72.0 (61 – 81)	72.0 (52 – 103)	1.0000
Indirect Bilirubin (IB) (mg/dL), Median (IQR)	0.8 (0.7 – 1.1)	0.8 (0.7 – 0.9)	0.5232
Lactate Dehydrogenase (LDH) (IU/L), Median (IQR) (5 values not recorded)	700.0 (505 – 1006.5)	797.5 (526.5 – 951)	1.0000
C-reactive protein (CRP) (mg/dL), Median (IQR)	11.6 (6.4 – 15.7)	12.4 (4.2 – 20.3)	0.7916

Table 3a: Characteristics of Patients with Babesiosis Monoinfection vs Coinfection with Lyme Disease within Procalcitonin Cohort.

N=12	Infection Status		
	Babesiosis Monoinfection (N=7)	Coinfection with Lyme Disease (N=5)	P-value
Age, Median (IQR)	62.0 (41 – 62)	84.0 (82 – 87)	0.0088
Gender, n (%)			
Male	6 (85.71)	4 (80.0)	1.0000
Female	1 (14.29)	1 (20.0)	
Race, n (%)			
White	2 (28.57)	2 (40.0)	1.0000
Non-White	5 (71.43)	3 (60.0)	
Admitted, n (%)			
No	7 (100.0)	5 (100.0)	N.A
Yes	0 (0.0)	0 (0.0)	
ICU Admission, n (%)			
No	4 (57.14)	3 (60.0)	1.0000
Yes	3 (42.86)	2 (40.0)	
Hypertension, n (%)			
No	6 (85.71)	4 (80.0)	1.0000
Yes	1 (14.29)	1 (20.0)	
Diabetes, n (%)			
No	5 (71.43)	5 (100.0)	0.4697
Yes	2 (28.57)	0 (0.0)	
CHF/CAD/Arrhythmias, n (%)			
No	5 (71.43)	4 (80.0)	1.0000
Yes	2 (28.57)	1 (20.0)	
Leukemia/Lymphoma, n (%)			
No	7 (100.0)	5 (100.0)	N.A
Yes	0 (0.0)	0 (0.0)	
Cancer (Other), n (%)			
No	7 (100.0)	4 (80.0)	0.4167
Yes	0 (0.0)	1 (20.0)	
CKD, n (%)			
No	7 (100.0)	5 (100.0)	N.A
Yes	0 (0.0)	0 (0.0)	
COPD/Asthma, n (%)			
No	6 (85.71)	3 (60.0)	0.5227
Yes	1 (14.29)	2 (40.0)	
Liver Disease, n (%)			
No	7 (100.0)	5 (100.0)	N.A
Yes	0 (0.0)	0 (0.0)	
Autoimmune Disease, n (%)			
No	5 (71.43)	5 (100.0)	0.4697
Yes	2 (28.57)	0 (0.0)	
Immunocompromised, n (%)			
No	6 (85.71)	5 (100.0)	1.0000
Yes	1 (14.29)	0 (0.0)	
Splenectomy, n (%)			
No	7 (100.0)	5 (100.0)	N.A
Yes	0 (0.0)	0 (0.0)	

Table 3b: Biomarkers of Patients with Babesiosis Monoinfection vs Coinfection with Lyme Disease within Procalcitonin Cohort.

N=12	Infection Status		
	Babesiosis Monoinfection (N=7)	Coinfection with Lyme Disease (N=5)	P-value
Max Parasitemia (%), Median (IQR)	1.4 (0.5 – 3.9)	0.7 (0.7 – 5.8)	1.0000
Hemoglobin (Hgb) (g/dL), Median (IQR)	11.2 (8.1 – 11.9)	11.9 (10.7 – 12.5)	0.5130
White blood cell (WBC) (K/uL), Median (IQR)	5.6 (3.9 – 12.8)	7.6 (5.4 – 8.1)	0.6837
Platelets (K/uL), Median (IQR)	65.0 (54 – 112)	46.0 (38 – 52)	0.1432
Indirect Bilirubin (IB) (mg/dL), Median (IQR)	0.7 (0.7 – 0.9)	0.9 (0.7 – 1.1)	0.8042
Lactate Dehydrogenase (LDH) (IU/L), Median (IQR) (1 value not recorded)	448 (315 – 977)	399.5 (384 – 557)	0.6358
Procalcitonin (Pc) (ng/mL), Median (IQR)	1.1 (0.4 – 1.3)	1.2 (0.5 – 1.2)	1.0000

Conclusion

- Coinfection had significantly lower platelets within the ESR cohort but this was not demonstrated in other cohorts.
- While not statistically significant, monoinfection showed greater trends of ESR.
- Max parasitemia trended lower in the coinfection group within the CRP and Procalcitonin cohorts, which is consistent with previous studies that suggest that *B. burgdorferi* may mitigate the degree of parasitemia caused by *B. microti*. [1-2]
- CRP and procalcitonin levels were similar across both groups.
- While this study was limited by its small sample size, the data presented suggests that the utility of using novel biomarkers to elucidate the interaction between *B. burgdorferi* and *B. microti* during simultaneous infection requires further study

References

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