Procalcitonin as a Potential Biomarker in the Study of Human Babesiosis

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Introduction

- *Babesia microti* causes acute febrile hemolytic anemia by invading and destroying erythrocytes [1].
- Multiple cases of babesiosis have reported concurrent elevations in procalcitonin [2-4].
- We examined the correlation between parasitemia, procalcitonin level, and the latter's potential as a prognostic biomarker for babesiosis [1].

Materials and Methods

- **Retrospective study:** Babesia cases were identified from the Stony Brook University Hospital and Stony Brook South Hampton Hospital electronic health record systems from 2012 to 2019.
- **Inclusion criteria:** having babesia symptoms, including but not limited to fevers and evidence of hemolytic anemia; a procalcitonin level; and parasites detected by peripheral blood smear with Giemsa stain (later confirmed by *B. microti* DNA RT-PCR).
- **Data collected:** Maximum parasitemia, defined as largest parasite percentage detected on peripheral smear, was recorded and median values calculated. Procalcitonin values were also ordered and median values were calculated.
- **Statistical Analysis.**

✓Cases were cross referenced for the presence of severe disease, defined as need for admission to the intensive care unit (ICU).

✓Correlation between maximum parasitemia and procalcitonin values were examined with the nonparametric Spearman rank correlation.

✓Fractional polynomials were used to assess the functional form of the correlation (i.e. linear vs. non-linear). Receiver-operator characteristic (ROC) curve analyses were used to identify cutoff points for procalcitonin and maximum parasitemia as markers for prediction of ICU admission.

Table 1: Demographics and characteristics of patients with acute babesiosis who had procalcitonin values measured

Patient Characteristics (total n=33)	Number Of Cases	% of Cohort
Gender		
Male	21	63.6%
Female	12	36.4%
Ethnicity		
Caucasian	19	57.6%
Hispanic	13	39.4%
Asian	1	3.0%
Comorbidities		
Immunocompromised	8	24.2%
Splenectomy	1	3.0%
Hypertension	13	39.4%
Diabetes	7	21.2%
Cardiac disease	8	24.2%
Cancer	4	12.1%
Chronic kidney disease	2	6.1%
Chronic lung disease	6	18.2%
Liver disease	1	3.0%
Autoimmune disease	3	9.1%
Admission Status		
Inpatient admission	29	87.9%
ICU admission	8	24.2%

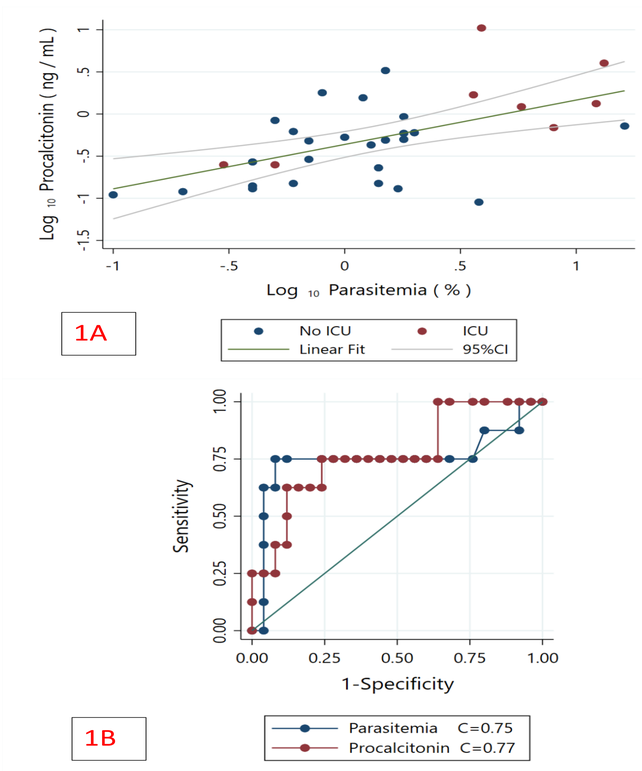

Figure 1A. Linear correlation between $\log_{10}$-parasitemia and $\log_{10}$- procalcitonin levels. The linear correlation of the log-transformed variables was r=0.556 (P=0.001), similar to the nonparametric (Spearman) correlation coefficient (ρ=0.567). The red dots represent patients who were admitted to the intensive care unit.

Figure 1B. Receiver-operator characteristic curve of parasitemia for prediction of intensive care unit admission (0.75; 95%CI: 0.58—0.89; P=0.005); optimal cut-off is 3.6%. Receiver-operator characteristic curve of procalcitonin for prediction of intensive care unit admission (C=0.77; 95%CI: 0.58–0.89; P=0.005); optimal cut-off is 1.2 ng/mL.

Results

- Maximum parasitemia and procalcitonin levels demonstrated a positive correlation, ρ= 0.567 (P=0.0006).
- In fractional polynomial analysis, log-transformed procalcitonin levels had a linear correlation with log-transformed maximum parasitemia, r=0.556 (P=0.001, Fig 1A).
- In ROC curve analysis, a cut off level of ≥ 1.2 ng/mL for procalcitonin had optimal prediction characteristics for ICU admission (sensitivity 62.5%, specificity 88%; correct classification 82%). A cut off level of ≥ 3.6% for maximum parasitemia had optimal prediction characteristics for ICU admission (sensitivity 75%, specificity 92%, correct classification 88%) (1B).
- Comparison of AUC for procalcitonin and parasitemia yielded no significant difference (P=0.81).

Conclusion and Clinical Implications

- Our data suggest that procalcitonin and parasitemia percentages may be directly proportional, and that a certain level of procalcitonin may predict severity of disease given the similarities in AUC for both biomarkers. If confirmed, procalcitonin may prove helpful adjunct to trend disease progression.
- Studies of procalcitonin have evaluated its adjunctive role in antibiotic cessation during bacterial infections of the lower respiratory tract and in identifying bacterial sepsis [5,6]. Our findings suggest that the biomarker may be elevated during infections with parasites such as *B. microti* and further study is required to elucidate if the biomarker has similar potential during protozoal diseases.
- Future study is required to determine if procalcitonin can be used to provide adjunctive diagnostic value as well. Evidence suggests that babesiosis is expanding into areas with low clinical awareness and automated hematology analyzers may miss parasitic forms [7-9]. This highlights the need for new biomarkers to assist in raising index of suspicion as delay in diagnosis of babesia is known to have worse outcomes [9].

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