

# Clinical Spectrum of Powassan Virus Infection in Patients Presenting with Suspected Acute Tick-borne Illness from a Lyme-endemic Focus in the Midwest

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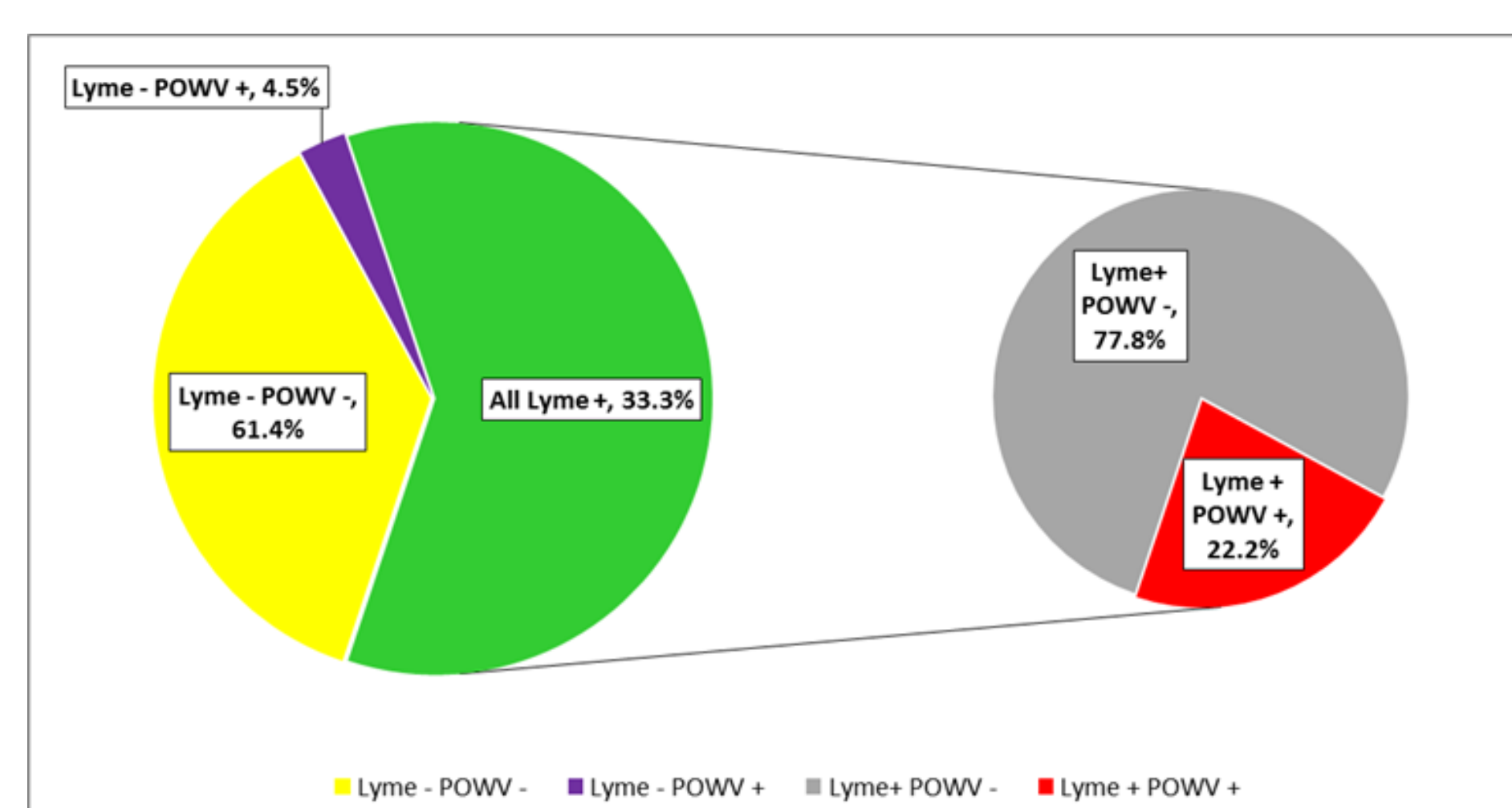
## ABSTRACT - Revised

**Background:** Powassan virus (POWV) is the North American member of the tick-borne encephalitis complex of viruses. The potential for concurrent transmission with other tick-borne pathogens, particularly the Lyme disease agent *Borrelia burgdorferi*, is under studied. To better understand the clinical spectrum of POWV infection patient health records were reviewed and laboratory studies performed to evaluate the frequency of tick-borne pathogen exposure in patients presenting with suspected acute tick-borne illness (TBI) from a Lyme-endemic focus in the Midwest.

**Methods:** 135 samples selected from patients seen at Gundersen Health System presenting during 2016 with Lyme-like symptoms were tested for Anaplasmosis, Babesiosis, Lyme disease and POWV. PCR testing was performed for Anaplasma and Babesia. Serologic testing for *B. burgdorferi* was performed using two-tier serologic testing. POWV infection was confirmed by POWV-EIA/IFA (Coppe Laboratories). IRB approval was obtained.

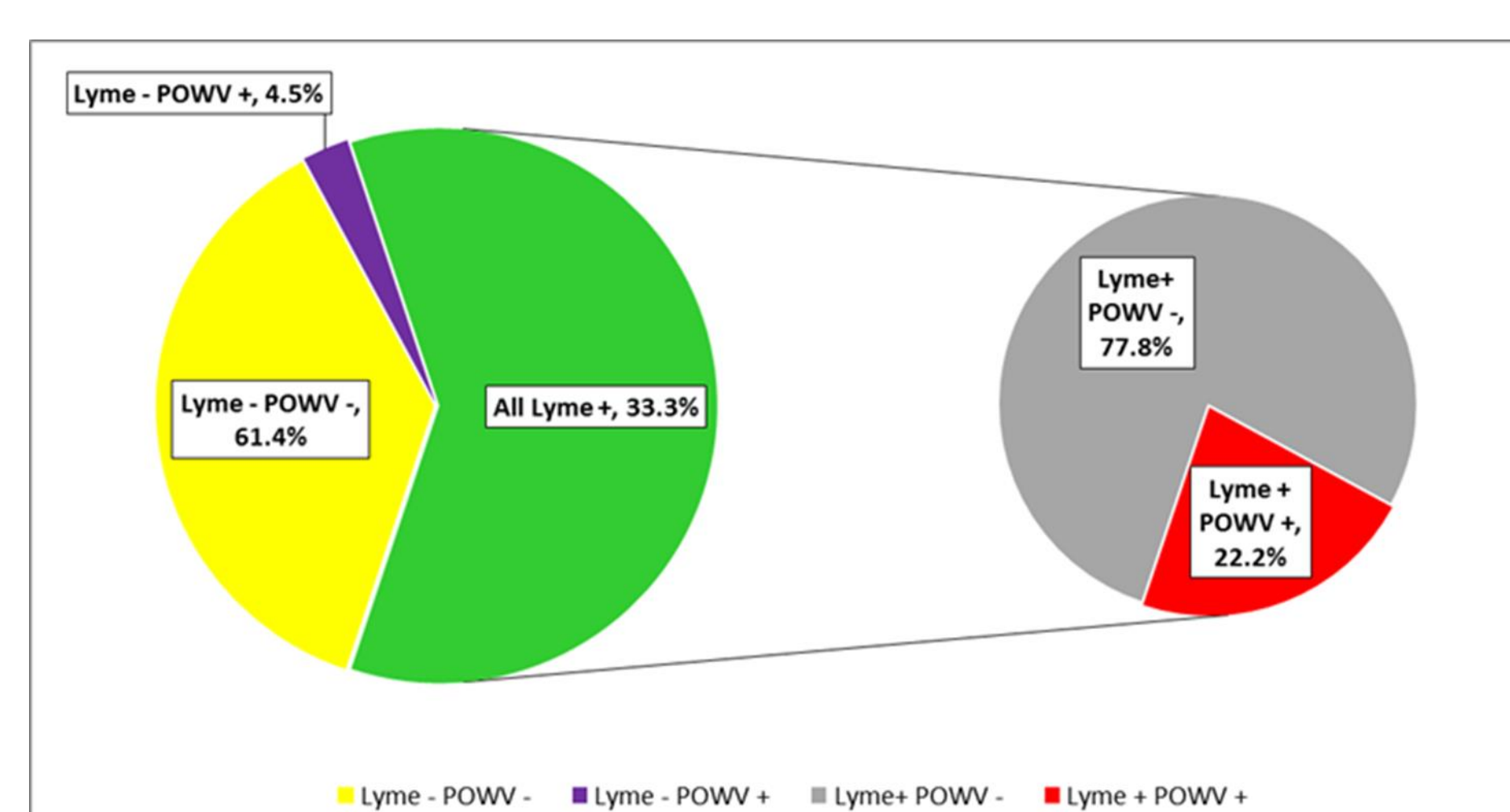
**Results:** Anaplasma infection was seen in 44/88 (50%), Babesia infection in 5/67 (7.5%), Lyme disease in 45/135 (33.3%) and POWV infection in 16/132 (12.1%) patients. Co-infections were seen in 21/135 (15.5%) patients. Patients with Babesia more often presented with anemia, myalgia and decreased appetite. Patients with Anaplasma presented with fever, chills/sweats, nausea/vomiting, no rash, elevated liver function tests, thrombocytopenia, leukopenia, and remembered the tick exposure. Lyme disease patients complained of fatigue, rash, chills/sweats, headache and remembered the tick exposure. Co-infection with both Lyme and Powassan virus was seen in 10/45 (23%) of patients. Patients with Lyme, Powassan virus or co-infection had no other significant difference in symptoms.

**Conclusions:** POWV infection is more prevalent in the Midwest than previously appreciated. Clinical data suggests that symptoms of POWV infection may be indistinguishable from those of Lyme disease, requiring laboratory testing for proper TBD diagnosis and avoidance of unnecessary antibiotic use. The high rate of POWV co-occurrence with Lyme disease may have relevance for patient outcomes and warrants further investigation.



## INTRODUCTION

*Borrelia burgdorferi* is endemic in areas of the Midwest, particularly northwestern Wisconsin. It, along with other species of *Borrelia*, *Anaplasma*, *Babesia* and Powassan virus (POWV) are transmitted by the black-legged tick, *Ixodes scapularis*. Recent studies have reported the ticks to be co-infected with multiple pathogens with the potential for transmission of multiple agents. The prevalence of POWV in ticks is increasing as is the tick territory, thus posing an increasing risk to humans. Patient health records were reviewed and laboratory studies performed to better understand the clinical symptoms of patients with POWV infection and the role of co-infection in disease.



## METHODS

- Samples: 135 frozen serum, plasma or whole blood samples from selected patients seen at Gundersen Health System during 2016 and presenting with Lyme-like symptoms. Health records were reviewed for presenting symptoms, including fever, chills/sweats, rash, fatigue, myalgia, arthralgia, gastrointestinal complaints, decreased appetite, headache, anemia, neutropenia, thrombocytopenia, altered liver enzymes, and tick exposure.
- Laboratory Studies: Testing was performed for Anaplasma, Babesia, West Nile virus, POWV and *B. burgdorferi*. Anaplasma was detected using an in-house developed PCR assay performed on serum. Babesia was detected using an in-house developed PCR assay performed on whole blood. *B. burgdorferi* was detected using IgM and IgG EIA and Lyme immunoblot. (Euroimmu US) Results were interpreted using CDC two-tier criteria. POWV was detected using POWV IgM and IgG EIA (Coppe Laboratories).
- Chi-Square analysis was performed.

## RESULTS

Patients ranged in age from 2 – 87 years old, with a median age of 53 year. 60% of patients were male. Eighty-eight patients were tested for Anaplasma, with 44(50%) positive. Sixty-seven patients were tested for Babesia, with 5 (7.5%) positive. 135 patients were tested for Lyme with 45 (33.3%) positive. 132 patients were tested for POWV with 16 (12.1%) positive. Co-infections were seen in 21 (15.5%) patients (Table 1).

Table 1. Serology results

	No. Pos	Anaplasma	Babesia	Borrelia	POWV
<b>Anaplasma</b>	44		0	5	4
<b>Babesia</b>	5			1	
<b>Borrelia</b>	44	8	1		10
<b>POWV</b>	16	4		10	

3 patients had Anaplasma, Lyme and POWV

## RESULTS

Table 2. Number (percent) with symptom.

	Anaplasma (44)	Babesia (5)	Borrelia (45)	POWV (16)
Anemia	4 (9)	3 (60)	4 (9)	2 (13)
Arthralgia	10 (23)	1 (20)	16 (36)	5 (31)
Chills/Sweats	21 (49) *	0	11(25)	5 (31)
Decreased appetite	5 (11) *	3 (60)	3 (7)	0
Increased LFT	6 (14) *	1 (20)	0	0
Fatigue	16 (36)	1 (20)	21 (48) *	3 (19)
Fever	33 (75) *	4 (90)	14 (32)	5 (31)
Headache	16 (36)	4 (90)	16 (36)	4 (25)
Leukopenia	10 (23) *	1 (10)	2 (5)	2 (13)
Myalgia	9 (20)	3 (60)	4 (9)	1 (6)
Nausea/Vomiting	11 (25) *	3 (60)	5 (11)	3 (19)
Rash	1 (2)	0	19 (43) *	5 (31)
Thrombocytopenia	19 (41) *	0	2 (5)	0
Documented Tick Exposure	20 (45) *	0	11 (25) *	3 (19)

\* Significant difference (p <0.05) as compared to subjects with no infection.

Patients with Anaplasma alone were more likely to have increased LFT, fever, and neutropenia than patients with Lyme alone and more likely to have fever than patients with POWV alone.

Patients with Lyme alone were more likely to have fatigue and rash than patients with Anaplasma alone.

No significant difference in symptoms was seen between patients with Lyme alone, POWV alone or Lyme and POWV co-infection.

## CONCLUSIONS

**In this selected cohort of patients presenting with suspected tick-borne infection:**

- Co-infections were seen in 16%
- Patients with serologic evidence of *Borrelia* infection had a 22% likelihood of POWV coinfection.
- Symptoms of patients with POWV are not significantly different from patients with Lyme.

**Laboratory testing is required for proper tick-borne disease diagnosis.**