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Introduction

- Previous studies have shown that many patients referred to academic centers for Lyme disease (LD) did not have *Borrelia burgdorferi* (Bb) infection.
- We compared characteristics of patients and prior treatment history as to whether they had illness compatible with LD.

Methods

We retrospectively reviewed 950 patients referred between 2000 and 2013 for a presumptive diagnosis or concern for LD. Persons age 12 years or greater were included. Subjective and objective findings were abstracted from electronic medical charts to obtain demographics, clinical and laboratory information, treatments and clinical outcomes. Diagnosis of Lyme disease followed CDC criteria. Statistical analysis performed by Fisher's exact test.

Results

Of the total 950 patients, 249 (26.2%, 112 active LD, 104 prior LD, and 33 post treatment Lyme syndrome) met criteria for Lyme disease. The 112 active LD were categorized as 38 early localized LD, 41 early disseminated LD, 28 late disseminated LD, and 5 persistent Lyme arthritis, while 688/950 (72.4%) did not meet Lyme disease criteria, and 13/950 (1.4%) were diagnosed with possible LD. Significantly less associated with having LD were patients with symptoms more than 6 months (OR=0.23, [95% CI: 0.16-0.32]), those who have previously received 3 or more anti-infective medications (OR=0.50, [CI:0.33-0.78]), patients who have received these medications for more than 6 months (OR = 0.25, [CI: 0.12-0.51]), those who have been diagnosed with tick-borne co-infections (OR = 0.43, [CI: 0.24-0.75]), and female gender (OR=0.51, [CI: 0.38-0.69]). In 741 patients referred for symptoms greater than 6 months, 589/741 (79.5%) had neither serologic nor objective clinical evidence implicating Bb infection. Patients with a history of unvalidated testing are also less likely to have LD (OR=0.14, [CI: 0.05-0.34]). For these 589 patients without evidence of LD, 496/589 (84.2%) had previously received treatment for LD. Mean treatment duration in patients without LD was 102 days (p<0.05) compared to mean duration in patients with LD was 70.5 days. Of those with LD, 31 individuals took 28 non-IDSA guideline recommended anti-infectives compared to 148 non-LD patients who took 43 different anti-infectives including antibacterial, antifungal, antiviral and anti-parasitic agents (OR=0.43, [CI: 0.28-0.66]).

Conclusions

Among referred patients, symptom duration of more than 6 months, female gender, history of unvalidated testing for *B. burgdorferi*, previous use of ≥ 3 anti-infectives, duration of therapy ≥ 6 months, and history of tick-borne co-infection are all less likely to suggest LD as an explanation for presenting symptoms. Most patients referred without evidence of LD received unnecessary and extensive anti-infective therapy. Even patients with LD, many received inappropriate medications and were treated longer on average than the 2-4 weeks of treatment recommended in CDC and IDSA guidelines.

Figure 1 Lyme Status

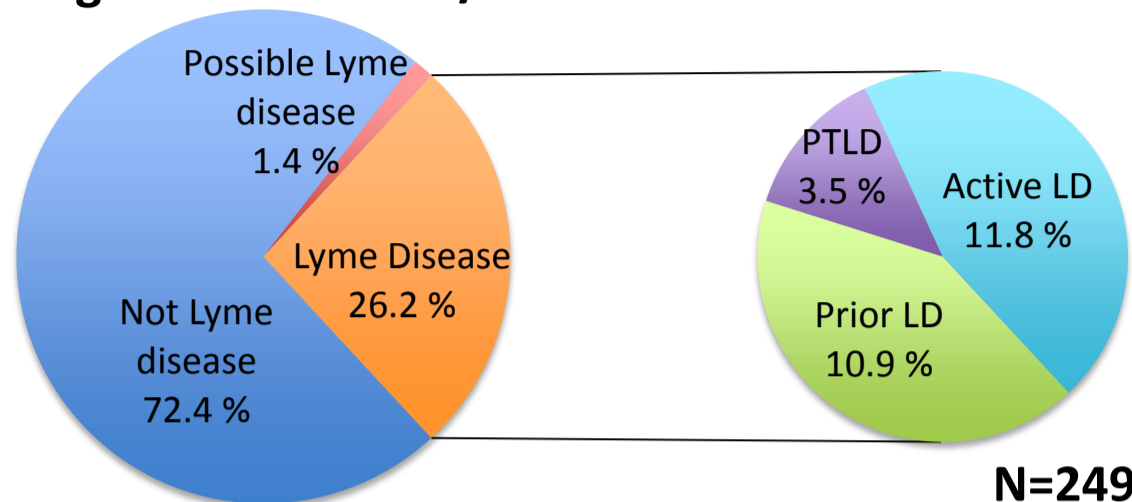
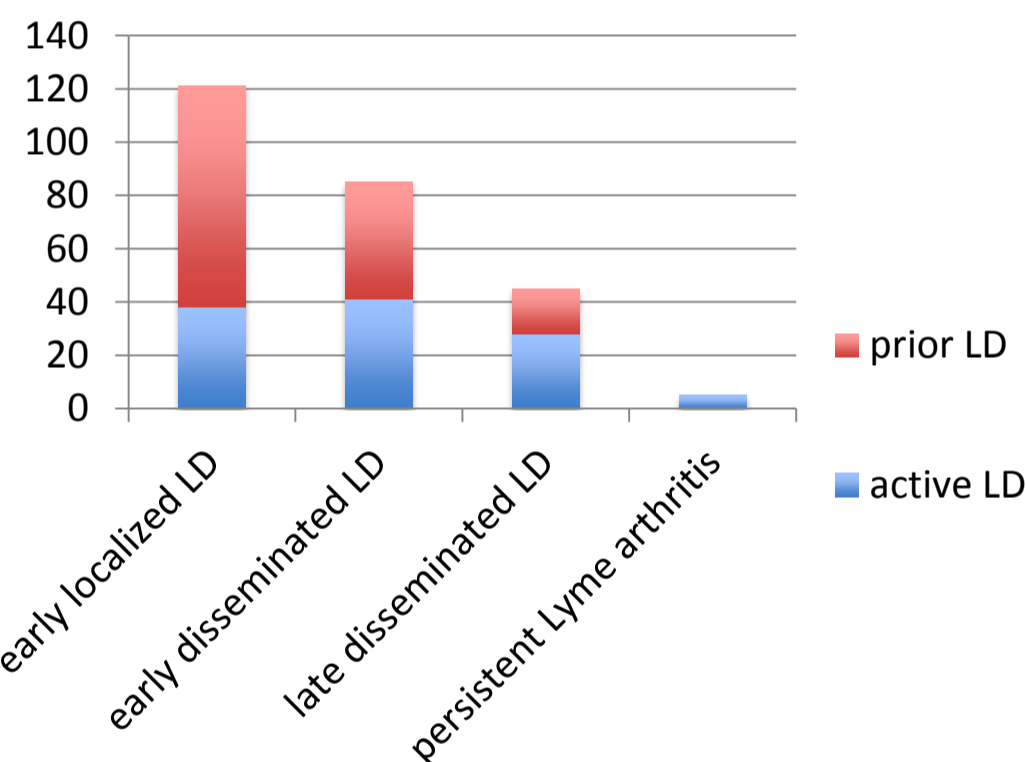


Figure 2 Lyme diagnosis



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Table: Demographics, Symptoms, Treatment

| | Lyme 249 (26.2%) | Not Lyme 688 (72.4%) |
|--|-------------------|----------------------|
| Age | | |
| Range (Median) | 13-88 (47.3) | 14-90 (44.5) |
| Gender | Number (%) | Number (%) |
| Male | 123 (49.4) | 230 (33.4) |
| Female | 126 (50.6) | 458 (66.6)* |
| Race | | |
| White/Caucasian | 229 (92.0) | 632 (91.9) |
| Other/Unknown | 20 (0.8) | 56 (8.2) |
| Home residence | | |
| Mid-Atlantic | 238 (95.6) | 645 (93.8) |
| Other | 11 (4.4) | 43 (6.3) |
| Co-infection history (dx by prior physicians) | | |
| Yes | 15 (6.0) | 90 (13.1)* |
| No | 234 (94.0) | 598 (86.9) |
| Duration of symptoms | | |
| ≥ 6 months | 144 (57.8) | 589 (85.7)* |
| < 6 months | 105 (42.2) | 98 (14.3) |
| Presenting symptoms | | |
| Arthralgia | 163 (65.5) | 511 (74.3)* |
| Fatigue/Malaise | 146 (58.6) | 480 (69.8)* |
| Myalgia | 90 (36.1) | 292 (42.4) |
| Headache | 90 (36.1) | 291 (42.3) |
| Erythema Migrans | 58 (23.3) | 16 (2.3)* |
| Sleep Disturbance | 56 (22.5) | 249 (36.2)* |
| Joint Swelling | 43 (17.3) | 113 (16.4) |
| Paresthesia | 42 (16.9) | 154 (22.4) |
| Fever | 31 (12.4) | 75 (10.9) |
| Number of anti-infective medications used prior to referral | | |
| ≤ 2 | 219 (87.9) | 560 (81.4) |
| ≥ 3 | 30 (12.0) | 128 (18.6)* |

| | Lyme 249 | Not Lyme 688 |
|---|-------------------------|-------------------------|
| Treatment duration prior to referral | Number (%) | Number (%) |
| 0 day | 12 (4.8) | 114 (16.6)* |
| 1-30 days | 99 (39.8) | 203 (29.5)* |
| 31-90 days | 102 (41.0) | 212 (30.8)* |
| 91-182 days | 25 (10.0) | 74 (10.8) |
| ≥ 183 days | 9 (3.6) | 78 (11.3)* |
| unknown | 2 (0.8) | 7 (1.0) |
| Range days | 0-2555 | 0-1440 |
| Mean (median) days, all | 67.1 (40.0) | 84.9 (40.0) |
| Mean (median) days, those who took ABX | 70.5 (42.0) | 102.0 (50.0)* |
| Received anti-infectives prior to referral | Total 237 (95.2) | Total 574 (83.4) |
| Doxycycline | 209 (88.2) | 464 (80.8)* |
| Ceftriaxone | 49 (20.7) | 130 (22.6) |
| Amoxicillin | 49 (20.7) | 88 (15.3)* |
| Cefuroxime | 14 (5.9) | 67 (11.7)* |
| Azithromycin | 8 (3.4) | 63 (11.0)* |
| Non-IDSA guideline anti-infectives | 31 (13.1) | 148 (25.8)* |
| unknown | 7 (3.0) | 18 (3.1) |
| Number of validated lab tests performed per individual | | |
| 0 | 10 (4.0) | 41 (6.0) |
| 1 | 87 (34.9) | 224 (32.6) |
| 2 | 73 (29.3) | 190 (27.6) |
| ≥3 | 79 (31.7) | 233 (33.9) |
| Mean (median) | 2.1 (2.0) | 2.2 (2.0) |
| Number of unvalidated lab tests⁺ performed per individual | | |
| 0 | 244 (98.0) | 598 (86.9)* |
| 1 | 3 (1.2) | 33 (4.8)* |
| 2 | 2 (0.8) | 48 (7.0)* |
| ≥3 | 0 (0.0) | 9 (1.3) |
| Mean (median) | 0 (0.0) | 0.2 (0.0) |

* Statistically significant (p < 0.05)

⁺ Unvalidated lab testing: tests other than CDC 2-tiered LD, Bb PCR, CSF Bb ab or Bb C6 serology