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**PART A. NATURAL SCIENCES**

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Daugavpils Universitātē docētāju un studējošo zinātniskās konferences notiek kopš 1958. gada. Konferencēm ir starpdisciplinārs raksturs un tajās piedalās gan studējošie, gan docētāji, gan arī zinātnieki no dažādām pasaules valstīm. Daugavpils Universitātes 67. starptautiskās zinātniskās konferences pētījumu tematika bija ļoti plaša – dabas, veselības aprūpes, humanitāro un mākslas un sociālo zinātņu jomās.

Zinātnisko rakstu krājumā *Daugavpils Universitātes 67. starptautiskās zinātniskās konferences rakstu krājums = Proceedings of the 67<sup>th</sup> International Scientific Conference of Daugavpils University* apkopoti 2025. gada 10.–11. aprīlī konferencē prezentētie materiāli.

The annual scientific conferences at Daugavpils University have been organized since 1958. The themes of research presented at the conferences cover all spheres of life. Due to the facts that the conference was of interdisciplinary character and that its participants were students and outstanding scientists from different countries, the subjects of scientific investigations were very varied – in the domains of natural sciences, health care science, the humanities and art, and social sciences.

The results of scientific investigations presented during the conference are collected in the collection of scientific articles *Proceedings of the 67<sup>th</sup> International Scientific Conference of Daugavpils University*.

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*Elizabete Markova,  
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**LYME BORRELIOSIS IN AMBULATORY PRACTICE**

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# VESELĪBAS APRŪPES ZINĀTNE / HEALTH CARE SCIENCE

## LYME BORRELIOSIS IN AMBULATORY PRACTICE

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### Abstract

#### Lyme borreliosis in ambulatory practice

**Key Words:** *Lyme disease, Lyme borreliosis, Borrelia burgdorferi, erythema migrans, serological diagnostics*

Each year, several hundred cases of Lyme borreliosis are registered in Latvia. Diagnosis is based on clinical presentation, epidemiological history, and serological testing. Relying solely on positive serological results may lead to false-positive or false-negative conclusions.

**Objective:** To evaluate whether the diagnosis of Lyme borreliosis in Latvia is overestimated and whether there is a correlation between clinical symptomatology and laboratory findings.

**Materials and methods:** A retrospective analysis of 188 cases at the Latvian Centre of Infectology (2020–2023) was performed. Demographic, epidemiological, clinical and laboratory data, treatment and its duration were assessed.

**Key results:** 70% were female; average age – 51.7 years. In 64% of cases, a tick bite was confirmed. 21% had no characteristic erythema; 68% had no joint symptoms, and 24% reported pain in multiple joints. Serological results: IgM ELISA positive in 60%, IgG ELISA 52%, IgM IB 20%, IgG IB 23%. *Borrelia* DNA was negative in 34% of cases. Treatment duration was 21 days in 30% of cases. Doxycycline was used in 94% of cases.

**Conclusions:** The analysis of the relationship between clinical symptoms and laboratory test results indicates a weak correlation between clinical presentation (erythema, joint symptoms, other manifestations) and laboratory findings (IgM, IgG ELISA, immunoblot and *Borrelia* DNA).

### Kopsavilkums

#### Laima borelioze ambulatorajā praksē

**Atslēgvārdi:** *Laimas slimība, laimborelioze, Borrelia burgdorferi, migrējošā eritēma, seroloģiskā diagnostika*

Katru gadu Latvijā tiek reģistrēti vairāki simti laimboreliozes gadījumu. Diagnostika balstās uz klīnisko ainu, epidemioloģisko anamnēzi un seroloģiskiem izmeklējumiem. Diagnostika balstoties tikai uz pozitīviem seroloģiskajiem rezultātiem var radīt kļūdaini pozitīvus vai kļūdaini negatīvus rezultātus.

**Darba mērķis:** izvērtēt vai Latvijā laimboreliozes diagnoze nav pārvērtēta, un vai pastāv korelācija starp klīnisko simptomātiku ar laboratoriskajiem izmeklējumiem.

**Materiāli un metodes:** analizētas 188 pacientu ambulatorās kartes ar laimboreliozes diagnozi Latvijas infektoloģijas centrā (2020–2023). Izvērtējot demogrāfiskos, epidemioloģiskos, klīniskos un laboratoros datus, terapiju, tās ilgumu.

**Nozīmīgākie rezultāti:** 70% sievietes, vidējais vecums – 51.7 gadi. 64% gadījumu apstiprina ērces kodumu. 21% nav raksturīgā apsārtuma, 68% nav locītavu simptomi, 24% sūdzējās par sāpēm vairākās locītavās. Seroloģiskie rezultāti: IgM ELISA 60% pozitīvs, IgG ELISA 52%, IgM IB 20%, IgG IB 23% pozitīvs. *Borrelia* DNS 34% rezultāts ir negatīvs. Terapijā doksiciklīns nozīmēts 94% pacientu. Ārstēšanas ilgums 30% 21 diena.

**Secinājumi:** Sakarību izpēte starp klīnisko simptomātiku un laboratoro izmeklējumu rezultātiem pierāda, ka pastāv nenozīmīga (vāja) sakarība starp klīnisko simptomātiku (apsārtums, locītavu simptomi, citi simptomi) un laboratorajiem izmeklējumiem (IgM, IgG ELISA, IB un *Borrelia* DNS).

### Introduction

Lyme disease is currently the most common tick-borne disease, caused by the bacterium *Borrelia burgdorferi*. It is widespread in North America and Europe. It is estimated that more than 14% of the global population may have been infected with Lyme disease (Dong et al., 2022). According to data from the Centre for Disease Prevention and Control of Latvia, an average of 295 cases of Lyme disease per year were registered in Latvia between 2020 and 2022 (SPKC, 2023).

The causative agent of Lyme disease is the spirochaete *Borrelia burgdorferi*, transmitted by infected Ixodes ticks (Mead, 2015). Lyme borreliosis is a complex multisystem disease that most commonly affects the skin, nervous system, heart or joints (IDSA et al., 2020). Three clinical stages of Lyme borreliosis are distinguished: early localised, early disseminated and late-stage disease (Wasiluk et al., 2011).

The diagnosis of Lyme borreliosis worldwide remains incompletely clarified and challenging. The literature frequently reports false-positive serological test results, often caused by cross-reactivity, which complicates accurate diagnosis.

In this retrospective study, outpatient medical records of patients diagnosed with Lyme borreliosis were analysed. The correlation between clinical symptomatology and laboratory test results was assessed.

The aim of the study was to evaluate whether the diagnosis of Lyme borreliosis in Latvia is overestimated and whether there is a correlation between clinical symptoms and laboratory test results.

## **Materials and Methods**

A retrospective study was conducted in 2023 using archival data from the Latvian Centre of Infectology. The study included 188 patients with a diagnosis of Lyme borreliosis who were treated on an outpatient basis at the Latvian Centre of Infectology between 2020 and 2023. The analysed data included demographic variables (sex, age, region of residence), epidemiological data (history of tick bite) and clinical symptomatology.

Clinical variables included erythema migrans, joint-related symptoms and non-specific symptoms such as elevated body temperature, fatigue and headache. Serological testing included the detection of IgM and IgG antibodies using enzyme-linked immunosorbent assay (ELISA) and immunoblot (IB) methods, as well as testing for *Borrelia burgdorferi* DNA. Treatment-related data, including the prescribed medication and duration of therapy, were also analysed.

Data were compiled using Microsoft Excel, and statistical analysis was performed using IBM SPSS Statistics version 26.0. Pearson's chi-square test was applied for comparative statistical analysis, with a statistical significance level of 95% ( $\alpha = 0.05$ ).

## **Results**

The study included 188 patients with a confirmed diagnosis of Lyme borreliosis; 70% ( $n = 131$ ) were female and 30% ( $n = 57$ ) were male. The mean age of the patients was 51.7 years. Sixty per cent of patients ( $n = 113$ ) were residents of the Riga region.

Epidemiological analysis showed that a history of tick bite was documented in 64% of patients ( $n = 121$ ).

Analysis of clinical manifestations revealed that erythema with a diameter of up to 5 cm was observed in 19% of patients, erythema measuring 5–10 cm in 12%, and erythema larger than 10 cm in 16%. Multiple erythematous lesions of varying size were identified in 4% of patients, while in 10% of cases erythema progressed in size. Other erythema-related findings showed that 21% of patients did not present with erythema characteristic of Lyme borreliosis, and in 18% of outpatient records the size of erythema was not documented.

Evaluation of joint-related symptoms demonstrated that 68% of patients had no joint symptoms. In contrast, 24% of patients reported pain in two or more joints, most commonly in the age group of 45–64 years. Symptoms such as pain in a single joint, morning stiffness, tingling sensation, joint swelling, erythema and combinations of these symptoms were reported in fewer than 8% of the study participants.

Comparison across age groups showed that the majority of patients (59–79%) did not report other symptoms. In the age group of 30–44 years, headache was more frequently reported, whereas in the age group of 18–29 years, elevated body temperature and headache were more common.

Serological testing revealed IgM ELISA positivity in 60% of cases ( $n = 112$ ) and IgG ELISA positivity in 52% ( $n = 97$ ). Immunoblot testing showed IgM positivity in 20% of cases ( $n = 37$ ) and IgG positivity in 23% ( $n = 43$ ). Testing for *Borrelia* DNA was negative in 34% of patients ( $n = 64$ ), while in 65% of cases data were unavailable or the test had not been performed.

Across all age groups, the most frequently prescribed medication was doxycycline. Treatment duration of 21 days was prescribed in 30% of patients, 20 days in 20%, 14 days in 16%, less than 20 days in 4%, and longer than 21 days in 9% of cases. No treatment was prescribed in 7% of patients, while in 14% of cases non-standard combinations of treatment duration were documented.

## **Discussion**

In the present study, 30% of participants were male ( $n = 57$ ) and 70% were female ( $n = 131$ ). The mean age was 51.7 years ( $SD = 16.3$ ); 49.8 years ( $SD = 15.1$ ) for men and 52.6 years ( $SD = 16.8$ ) for women. According to the literature, a study conducted in the United States analysing patients between 1992 and 2016 reported a higher prevalence of Lyme borreliosis among men than women. Over time, the mean age of patients increased, with the highest incidence observed among individuals born between 1950 and 1964, corresponding to an age range of 57–71 years (Kugeler et al., 2022).

In the present study, 79 patients belonged to the 45–64-year age group, with a mean age of 55.4 years ( $SD = 5.9$ ), while 42 patients were aged 65 years or older, with a mean age of 73.3 years ( $SD = 6.33$ ). Together, these two age groups comprised 121 patients, representing the majority of the 188 study participants. These findings indicate that the age distribution observed in this study is consistent with results reported in other studies.

Demographic analysis of patient residence showed that 60% (n = 113) of patients were from the Riga region, whereas only 1% (n = 1) were from the Kurzeme region. According to data from the Centre for Disease Prevention and Control of Latvia, during the period from 2020 to 2022 the highest number of Lyme borreliosis cases was registered in the Kurzeme region, with 106 cases in 2020 and 67 cases in 2021. In contrast, 42 cases were reported in the Riga region in 2020 and 66 cases in 2021 (SPKC, 2023). Therefore, based on the present study, no conclusions regarding the regional distribution of Lyme borreliosis in Latvia can be drawn, as the choice of outpatient treatment location may be influenced by proximity to the Latvian Centre of Infectology.

The findings related to erythema migrans as a clinical manifestation largely correspond with conclusions reported by other authors. Erythema with a diameter of up to 5 cm was observed in 19% of cases (n = 35), while in 18% of cases (n = 33) the size of erythema was not documented in outpatient records. The literature indicates that erythema typically exceeds 5 cm in diameter, although it may initially be small and subsequently enlarge (Stanek et al., 2011). As epidemiological data, such as the timing of tick bite, are not always recorded in outpatient documentation, it is not possible to accurately determine the incubation period. It is therefore possible that the documented erythema reflects only the early stage of the disease and continued to progress in size.

Joint-related symptoms were not observed in 68% of cases (n = 127). In contrast, 24% of patients (n = 45) reported pain in two or more joints, predominantly in the 45–64-year age group. In the literature, Lyme arthritis in Europe and North America is described as synovitis, most commonly affecting the knee (Stanek et al., 2011), with reported prevalence of up to 60% in the United States and 3–15% in Europe (Wasiluk et al., 2011). The findings of the present study also suggest that Lyme arthritis is a relatively rare clinical manifestation, as the majority of patients did not report joint symptoms. Among the remaining participants, outpatient records indicated pain in more than two joints (24%, n = 45), morning stiffness (2%, n = 3) and tingling sensation (1%, n = 1), which, according to the literature, may suggest the possibility of rheumatological disease. Only 5% of patients (n = 3) reported synovitis-related symptoms such as arthralgia, joint swelling and erythema, while 2% (n = 3) reported pain in a single joint, which is more characteristic of Lyme borreliosis.

Across all age groups, the majority of patients (59–79%, n = 141) did not present with other symptoms. However, 47 patients reported additional symptoms, including elevated body temperature (2%, n = 3), fatigue and weakness (9%, n = 16), headache (4%, n = 8), as well as various combinations of symptoms. The literature indicates that systemic symptoms such as fever, headache and fatigue are commonly observed during the early stage of Lyme disease (IDSA et al., 2020).

According to the literature, serological diagnosis of Lyme borreliosis is conducted in two stages: following a positive IgM/IgG ELISA result, an immunoblot test is performed, and *Borrelia* DNA analysis may also be used (Waddell et al., 2016). The aim of this study was to evaluate whether

the diagnosis of Lyme borreliosis in Latvia is overestimated. In the section on serological results, graphical representations illustrate IgM and IgG ELISA, IgM and IgG immunoblot, and *Borrelia* DNA results as positive, negative or equivocal, as well as cases where data were unavailable in outpatient records.

In the subsection analysing the relationship between clinical symptoms and laboratory test results, data on IgM and IgG ELISA, IgM and IgG immunoblot, and *Borrelia* DNA were examined in relation to the type and size of erythema, joint symptoms, other symptoms and epidemiological factors. The results of the chi-square ( $\chi^2$ ) test indicated that, in most cases, the associations between the analysed variables were statistically insignificant (weak).

The results demonstrate that both positive and negative serological findings were observed across different clinical manifestations of Lyme borreliosis. This suggests that serological diagnostics may be imprecise both in patients with characteristic symptoms and in those without them, largely due to cross-reactivity. The literature indicates that serological methods continue to pose challenges because of false-positive and false-negative results (CDC, 2024). A previously conducted meta-analysis in the United States, which compiled data from 48 studies, reported that serological test results in patients who do not meet clinical criteria should be used only to exclude the disease, as positive results in such cases are likely to be false positives. Consequently, the excessive use of these tests in Lyme borreliosis diagnostics remains a subject of ongoing debate and challenge among specialists and clinicians (Maraspin et al., 2011).

False-positive IgM antibody results are frequently observed in patients whose immune response is stimulated by *Borrelia* antigens that are also present in other microorganisms, leading to cross-reactivity with *Treponema pallidum*, *Ehrlichia* species and herpes viruses. Such results may also be associated with musculoskeletal disorders or hypergammaglobulinaemia. False-negative results may occur when serological testing is performed too early, in patients with immunodeficiency, or when antibacterial therapy is initiated at an early stage of the disease (Wasiluk et al., 2011).

Across all age groups, doxycycline was the most commonly used medication for the treatment of Lyme borreliosis. The most frequently prescribed treatment duration was 21 days (30% of cases). No treatment was prescribed in 7% of cases; 20% received therapy for 20 days, 16% for 14 days, 4% for less than 20 days and 9% for more than 21 days, while 14% of cases involved non-standard treatment durations. The literature describes antibiotic regimens ranging from 5 to 30 days. In Slovenia, a study conducted at the University Medical Centre Ljubljana between July 3, 2017 and October 2, 2018 analysed 300 patients with erythema migrans to evaluate shortening doxycycline therapy from 14 to 7 days, as recommended in European guidelines. The study concluded that reducing therapy to 7 days did not reduce treatment efficacy compared to 14 days, although concerns regarding the potential development of late-stage disease were raised (Stupica et al., 2023). According

to clinical recommendations published by the Centre for Disease Prevention and Control of Latvia, the recommended duration of doxycycline therapy for erythema migrans in adults is 14–21 days, and the results of the present study are consistent with these recommendations (SPKC, 2023).

Analysis of epidemiological data showed that 64% of patients reported a confirmed tick bite, 19% denied a tick bite, and in 16% of cases information regarding tick bite was not documented. The literature indicates that patients do not always recall a tick bite, and when evaluating these parameters, the potential region and season of infection should be considered (Skar & Simonsen, 2023).

### **Conclusions**

The analysis of the relationship between clinical symptomatology and laboratory test results (IgM, IgG ELISA, immunoblot and *Borrelia* DNA) demonstrates that, in most cases, the association is statistically insignificant (weak).

Erythema as a clinical manifestation was observed more frequently than joint-related symptoms, which proved to be less significant as diagnostic indicators. Notable differences in symptom presentation were identified across different age groups, with joint involvement more commonly documented in older patients.

In Latvia, there is a tendency to overestimate the diagnostic significance of serological testing for Lyme borreliosis, particularly ELISA IgM results. This often does not correspond with the clinical presentation and may lead to false-positive diagnoses. IgM antibodies more frequently indicate recent exposure to *Borrelia burgdorferi*, whereas IgG antibodies confirm previous exposure and completed seroconversion.

Doxycycline was the most commonly used medication in therapy. However, treatment duration varied considerably among patients, indicating differences in clinical practice regarding therapeutic strategies.

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