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Lyme Neuroborreliosis in Children Hospitalized in Children's Clinical University Hospital in 2018–2022: Epidemiology, Diagnostics and Treatment

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Summary

Introduction. Lyme disease is the most common tick-borne infection in Europe. Neuroborreliosis is seen in approximately 10–12 % of all Lyme disease cases in children. Nevertheless, there are very few studies regarding Lyme neuroborreliosis especially concerning the paediatric population.

Aim of the study. The aim of this study is to determine the most common symptoms, diagnostic and treatment strategies of Lyme neuroborreliosis in pediatric population.

Materials and methods. A retrospective study was made including 49 patients 28 days to 18 years of age with diagnosis A69.2 (Lyme disease according ICD10) and neurologic symptoms admitted to the Children's Clinical University Hospital from 2018 to 2022. Data was collected from Andromeda hospital database and analysed using IBM SPSS Statistics version 29.0 ($p < 0.05$).

Results. During the study period 158 children with Lyme disease were diagnosed in Latvia. 69 patients were hospitalized in Children's Clinical University hospital with Lyme disease diagnosis, of which 71 % presented with neurological symptoms (n = 49). The median age of patients was 7 (Q_1; Q_3 4,75–13,25) years, 47 % were females (n = 23) and 53 % were males (n = 26). 22 % were identified as "definite" Lyme neuroborreliosis (n = 11), while 49 % (n = 24) were identified as "possible" Lyme neuroborreliosis and 29 % were identified as "not confirmed" Lyme neuroborreliosis according to diagnostic criteria. The most common clinical manifestation of neuroborreliosis was facial paresis, which was diagnosed in 39 % (n = 19) followed by meningitis, which was diagnosed in 35 % of the cases (n = 17). Both meningitis and facial paresis simultaneously were diagnosed in 12 % of the cases (n = 6). Ceftriaxone was used in 69 % of the cases (n = 34), in 12 % of the cases doxycycline was used (n = 6). Both drugs were used in 12 % (n = 6), while in 6 % of the cases none of these drugs were used (n = 3).

Conclusions. Most common clinical presentations of Lyme neuroborreliosis in children were facial paresis and meningitis, which corresponds well with the literature. Management of Lyme neuroborreliosis remains challenging and a more definite diagnostic algorithm should be emphasized among different specialists.

Keywords: Borrelia burgdorferi infection, Lyme disease, facial palsy, meningitis, children.

Introduction

Lyme disease is the most common tick-borne infection in Europe and its neurological form is the second most common manifestation of Lyme disease surpassed only by *Erythema migrans*. The incidence of the neurological manifestations of Lyme disease in Europe ranges from 0.6–2.4 per 100 000 in Sweden to 5.8–10.0 per 100 000 in Germany. Lyme neuroborreliosis can be seen in both children and adults but it is more common in paediatric population. Lyme neuroborreliosis is caused by a group of bacteria called *Borrelia burgdorferi sensu lato* (*B.burgdorferi s.l.)* complex, which includes more than 20 *Borrelia spp.* species from which 6 species are considered pathogenic to human. In Europe as well as Latvia the most common species of *B.burgdorferi s.l.* complex are *B.burgdorferi sensu stricto, B.garinii, B.afzeli* and *B.bavariensis* (4, 11). Studies have found that the clinical manifestation of the disease might be affected by the specie causing the disease, for example, *B.garinii* is thought to be associated with neurological manifestations, *B.burgdorferi sensu stricto* is associated with Lyme arthritis etc. (4).

The first case of Lyme disease in Latvia was registered in 1986 (4). Since then, the incidence of Lyme disease has grown both in Latvia and the whole Northern hemisphere due to climate change, because as the winters get warmer, it is easier for the ticks to survive during winter which increases the tick-borne infection incidence (4, 6). The incidence of the neurologic manifestations of Lyme disease or neuroborreliosis is thought to be from 3 % up to 16 % of all Lyme disease cases (8, 12).

The course of Lyme disease can be divided into 2 phases – early localised and disseminated, which can be further divided as early disseminated (symptoms < 6 months) and late disseminated phase (symptoms > 6 months) (3; 5; 6). Neuroborreliosis can occur in both disseminated stages and can impact both the peripheral and the central nervous system. The neurologic symptoms typically appear a few weeks to months after the tick bite (3). The most common clinical forms of neuroborreliosis in children are cranial nerve, especially *N.facialis* neuritis and meningitis (1, 2, 6, 8, 10). In some cases *N.facialis* neuritis and aseptic meningitis can occur simultaneously. Most commonly neuroborreliosis affects the peripheral nervous system but it can involve the central nervous system in about 4 % of all cases. In these cases, the most common clinical manifestations are acute myelitis, hemiparesis, opsoclonus-myoclonus, ataxia or encephalitis.

To diagnose Lyme disease, it is necessary to detect the specific anti-*Borrelia* IgM and IgG antibodies in serum. It is usually done by 2-tier testing – first a screening test is done using ELISA methodology. If this test is positive or borderline, then a second test – *WesternBlot* is done to confirm the screening test results as there can be false positive results using ELISA (3). This test should be evaluated in context with the clinical manifestations as up to 20 % of healthy individuals living in the endemic zones can have positive serum anti-*Borrelia* antibodies (5; 8; 9). At the same time the specific anti-*Borrelia* antibodies can be negative in serum at the early stages of the disease as the IgM antibodies can be detected only starting from the 3rd week of the disease while the IgG antibodies can be detected only starting from the 6th week (8). The gold standard for the diagnosis of neuroborreliosis is the detection of the specific anti-*Borrelia* antibody production intrathecally (3, 5, 8). To confirm the intrathecal antibody synthesis, it is necessary to detect the specific anti-*Borrelia* IgM and IgG antibodies in cerebrospinal fluid (CSF) as well as in serum and afterwards calculate the antibody index (AI) which is the ratio of antibody titre in CSF vs in serum (3, 12).

The main treatment of Lyme neuroborreliosis is antibiotic treatment. The most used and recommended treatment according to EFNS guidelines is ceftriaxone i/v or doxycycline p/o, however it is acceptable to use also cefotaxime or penicillin G i/v (5). The length of the treatment should be 14–21 days (5, 7, 8). Many studies have shown that there are no significant differences in efficacy between the treatment with doxycycline p/o and ceftriaxone i/v, therefore it is recommended to use ceftriaxone i/v for children up to 8/9 years of age as doxyxycline p/o in many countries is not registered for use in children younger than 8/9 years due to the side effects. For children older than 9 years doxyxycline p/o should be used as it is more convenient for the patient, reduces the length of hospital stay and the risk of complications. However, in case of CNS involvement ceftriaxone i/v should be used at any age.

Aim of the study

The aim of this study is to gather and analyse all existing data about diagnostics, clinical characteristics and therapy of Lyme neuroborreliosis in Children's Clinical university hospital from 1st January 2018 to 31st December 2022.

Materials and methods

Participants of this study were selected using the Children's clinical university hospital system Andromeda, where all patients between 1st January 2018 and 31st December 2022 with the diagnosis of Lyme disease (coded according to the ICD-10 classifications – A69.2) were found. Afterwards the patients were enrolled in the study according to the inclusion criteria:

1. At the time of admission patient was 28 days to 17 years old.
2. Patients' final diagnosis was Lyme disease (A69.2).
3. Patient had neurologic symptoms.

In total 49 patients were selected, the data from the patient records were obtained, anonymized and coded to carry out statistical analysis.

All patients were divided into 3 groups based on whether the diagnosis of neuroborreliosis was definite, possible or not-confirmed based on the EFNS guidelines. The criteria for a definite neuroborreliosis diagnosis were:

1. Neurological symptoms suggestive of neuroborreliosis without other obvious reasons.
2. CSF pleocytosis.
3. Intrathecal *B.burgdorferi* antibody production.

The case was sorted into the possible neuroborreliosis group if only 2 of these criteria were fulfilled (11).

Statistical analysis was carried out using IBM SPSS Statistics v29.0.

Results

In total 49 patients were enrolled in the study, from which 53% (26) were boys and 47% (23) were girls. The median age was 7.0 years (5.0–13.5). The largest age group (18; 37%) was 4–6 years.

All patients were divided into 3 groups – definite, possible and not-confirmed neuroborreliosis according to EFNS guidelines. Definite neuroborreliosis group consisted of 11 (22%) patients, possible neuroborreliosis group had 24 (49%) patients, but 14 (29%) patients were included in the not confirmed neuroborreliosis group.

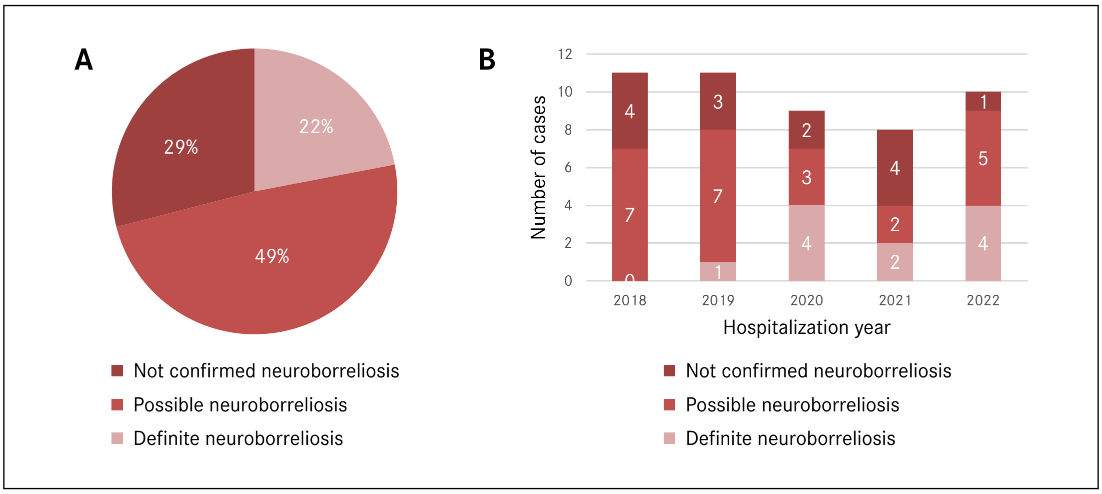

Figure 1. A Proportion of definite, possible and not confirmed neuroborreliosis cases in the study. **B** The number of definite, possible and not confirmed neuroborreliosis cases per year.

Most cases in this study fell into the possible neuroborreliosis category (Fig.1) and over the years, except for the year 2021, the number of cases of not confirmed neuroborreliosis lowers. Unfortunately, there are still cases of not confirmed neuroborreliosis, for example, in 2022 not confirmed neuroborreliosis was seen in 1 patient. Most common reason for a case to be sorted into the not confirmed neuroborreliosis group, is the lack of CSF analysis, which makes it impossible to sort this patient into definite or possible neuroborreliosis group.

From all patient records data regarding serum laboratory testing (specific anti-*Borrelia* IgM and IgG antibodies, CRP level), CSF laboratory testing (Leu and Ly count, specific anti-*Borrelia* IgM and IgG antibodies, antibody index and PCR testing) as well as symptoms and treatment, were collected.

In 44 (90%) patients *B.burgdorferi* specific IgM antibodies in serum were measured using ELISA methodology. 27 (61%) patients had positive IgM antibodies; 11 (25%) patients had negative IgM antibodies while 6 (14%) patients had borderline result in this test. *WesternBlot* was carried out for only 19 (39%) patients and only 10 patients had positive test results. From those who had positive screening test (n = 27), only 8 (33%) patients had *WesternBlot* done, which was positive in 63% (5) of the cases, while 3 patients (38%) had negative *WesternBlot* results. From definite neuroborreliosis group all patients had the screening test for IgM antibodies carried out and it was positive in all cases, while *WesternBlot* was carried out in 5 cases, and it was positive in only 40% (2) of the cases.

The screening test for IgG antibodies was carried out in 45 (92%) patients (all patients in definite neuroborreliosis group, 92% (22) of the patients in the possible neuroborreliosis group and 86% (12) of the patients in the not confirmed neuroborreliosis group). It was positive in 35 (78%) patients, negative in 8 (20%) patients and borderline in 1 (2%) patient. *WesternBlot* was done in 18 (37%) patients, and it was positive in 14 (78%) patients, negative in 3 (17%) patients and borderline in 1 (6%) patient. In total 31 (63%) patients did not have the *WesternBlot* test done.

C-reactive protein (CRP) level in serum was measured in 45 (92%) patients, and it was elevated in 9 (20%) patients. In definite neuroborreliosis group the test was done in 10 (91%) patients and it was in the normal range in all cases, in possible neuroborreliosis group it was measured in 23 (96%) patients, and it was elevated in 9 patients (39%). However, in the not confirmed neuroborreliosis group the test was done in 12 (83%) patients and for all patients it was in the normal range. In the not confirmed neuroborreliosis group the CRP level was statistically significantly lower than in the possible neuroborreliosis group (Kruskal-Wallis tests, $H = -13.726$, $p = 0.010$).

Lumbar puncture and CSF analysis was done in 36 (74%) of the cases. The analysis was carried out for only 1 patient in the not confirmed neuroborreliosis group, but all the tested parameters were within the normal range in this patient, therefore it was sorted into the not confirmed neuroborreliosis group. In 35 (97%) patients for whom the lumbar puncture and CSF testing was done, the WBC (white blood cell) and Ly (lymphocyte) count was elevated. Protein level in the CSF was measured in 36 (74%) patients and it was elevated in all cases.

IgM anti-*Borrelia* antibodies in CSF were measured in 27 (55%) patients, and they were positive in 23 (85%) patients, while in 1 (4%) case they were borderline and in 3 (11%) cases they were negative. In the definite neuroborreliosis group they were measured in 17 (91%) patients, and they were positive in all cases. In the possible neuroborreliosis group they were measured in 17 (71%) patients, and they were positive in 77% (13) of the patients, and borderline in 6% (1) of the patients. IgG anti-*Borrelia* antibodies in CSF were measured in 28 (57%) patients, and they were positive in 21 (75%) patients. In the definite neuroborreliosis group IgG antibodies were measured in all cases, and they were positive in all patients. In the possible neuroborreliosis group IgG antibodies were measured in 17 (71%) patients, and they were elevated in 10 (59%) patients.

Antibody index was calculated in only 12 (24%) patients, and it was positive in 10 (91%) patients. In possible neuroborreliosis group the AI index was calculated in only 2 patients, and it was negative in both cases. 8 (16%) patients had their CSF tested using PCR to detect *B.burgdorferi* in the CSF, and for 1 patient it was positive, therefore the patient was sorted into the definite neuroborreliosis group.

The most common symptom was facial paresis, which was seen in 25 (51%) patients. It was followed by fever – 24 (49%) patients; headache – 21 (43%) patients and meningeal symptoms as well as nausea and vomiting both in 11 (22 %) patients. (Fig. 2) There were statistically significant differences between the groups in the frequency of meningeal symptoms (Fisher exact test, $x^2=6.499$; $p=0.032$), nausea and vomitting (Fisher exat test, $x^2=9.432$, $p=0.007$) and facial paresis (Chi square test, $x^2(2; N=49)=9.428$, $p=0.009$).

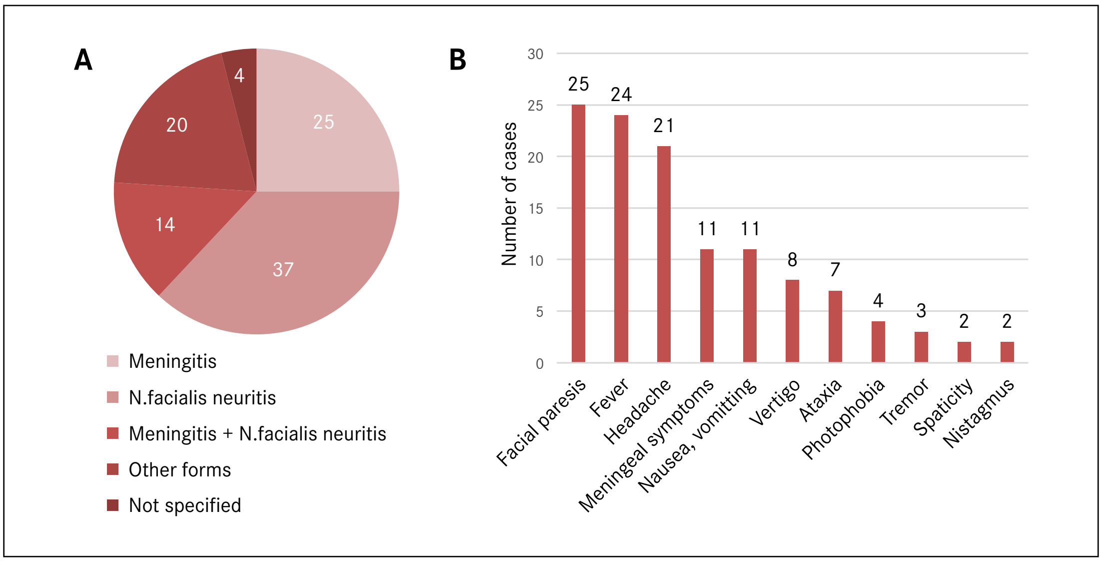

Figure 2. A The percentage of different clinical forms in all groups.
B The most common symptoms of neuroborreliosis in study population.

The most common clinical forms in definite neuroborreliosis group were *N.facialis* neuritis (4 (36 %) patients) and concurrent meningitis and *N.facialis* neuritis (2 (18 %) patients). In possible neuroborreliosis group the most common clinical form was meningitis (11 (46 %) patients), followed by concurrent meningitis and *N.facialis* neuritis (5 (21 %) patients). In 1 (4 %) case in this group the clinical form was not specified. In the not confirmed neuroborreliosis group the most common clinical form was *N.facialis* neuritis (11 (79 %) patients), followed by other cranial nerve neuritis (2 (14 %) patients). Also, in this group in 1 (7 %) case the clinical form was not specified. The differences in the frequency of different clinical forms between the groups were statistically significant (Fisher exats test, $x^2=32.805$; $p=<0.001$).

In this study mainly 2 antibiotics were used to treat the neuroborreliosis – ceftriaxone and/or doxycycline. Ceftriaxone was used more frequently as it was used in 32 (65 %) patients. Doxycycline was used in 7 (14 %) patients but in 6 (12 %) patients both drugs were used. In 4 (8 %) patients neither drug was used. In 3 (6 %) patients under the age of 8 years doxycycline was used and in 2 (4 %) patients both ceftriaxone and doxycycline were used which is in contradiction to the guidelines as doxycycline is recommended only for children over the age of 8/9 years depending on the country (8 years in Latvia). Both in the definite and possible neuroborreliosis groups ceftriaxone was used more frequently (8 (73 %) and 19 (79 %) patients) while in the not confirmed neuroborreliosis group ceftriaxone and doxycycline were used with an equal frequency (7 (36 %) patients). Amoxycillin was used only in the not confirmed neuroborreliosis group. The drug used in therapy differed statistically significantly between the groups (Fisher exact test, $x^2=17.590$; $p=0.001$). Glucocorticoids were used in 14 (29 %) patients from which 13 patients had *N.facialis* neuritis. In the definite neuroborreliosis group 1 (18 %) patients used glucocorticoids, in possible neuroborreliosis group – 3 (13 %) patients, while in the not confirmed neuroborreliosis group they were used in 9 (64 %) patients. The differences in glucocorticoid usage among the groups were statistically significant (Fisher exact test, $x^2=10.804$; $p=0.003$).

Discussion

From the whole study population 11 (22%) patients were sorted into the definite neuroborreliosis group, 24 (49%) patients — into the possible neuroborreliosis group, while 14 (29%) patients were included in the not confirmed neuroborreliosis group. The main reason why patients had to be included into the not confirmed neuroborreliosis group, was the lack of lumbar puncture and therefore analysis of the CSF as the analysis were essential for the diagnostic criteria for the patient to be included in either definite or possible neuroborreliosis diagnostic group. In total only 74% of the patients had undergone lumbar puncture and CSF testing which means that in 26% of the patients the diagnosis of neuroborreliosis can neither be confirmed nor excluded. Across different studies the distribution of patients can differ. For example, in van Gorkom et al. study from 156 patients 6.4% were included in the definite neuroborreliosis group while 4.5% were included in the possible neuroborreliosis group (12). However, in a study by Backman and Skogman from 295 patients 23% fell into the definite neuroborreliosis group while 12% were included in the possible neuroborreliosis group (1). In this study compared to other studies the possible neuroborreliosis group was significantly larger (49%; n = 24) than in other studies which might be because even though these patients had undergone lumbar puncture and there was some CSF testing done, unfortunately the antibody index had not been calculated which is one of the inclusion criteria for definite neuroborreliosis group.

The serum analysis was carried out for all the patients, but not in all cases the two-tier testing algorithm was used. From the patients included in this study 3 (6%) patients had *WesternBlot* done without the screening test. However, from the patients who had positive anti-*Borrelia* IgM antibody screening test, the confirmatory test using *WesternBlot* was done in only 8 (30%) patients. From the patients who had positive anti-*Borrelia* IgG antibody screening test, the *WesternBlot* was done in 11 (31%) patients. In the definite neuroborreliosis group the screening test for both anti-*Borrelia* IgM and IgG antibodies was positive in all cases, however the *WesternBlot* test for both anti-*Borrelia* IgM and IgG antibodies was positive in only about 40% of the cases, which emphasises the fact that antibodies against *B.Burgdorferi* can be within the normal range and it is absolutely necessary to do the lumbar puncture and CSF testing whenever there is a clinical possibility of neuroborreliosis.

In 97% of the patients who had CSF testing done, there was pleocytosis with mononuclear dominance, which corresponds well with the data from other studies where mononuclear cell dominated in 99% of the patients with definite neuroborreliosis and 77% of the patients in possible neuroborreliosis group (1; 9).

The main diagnostic criterion for definite neuroborreliosis diagnosis is confirmation of intrathecal antibody synthesis, where antibody index is used. In this study from the 36 patients who had CSF testing done the antibody index was calculated in only 31% of the patients. All the patients who had undergone lumbar puncture and CSF testing but did not have the antibody index calculated were included in the possible neuroborreliosis group which might cause some deviations in the results as it is not possible to exclude definite neuroborreliosis diagnosis in these patients. From the patients who had the antibody index calculated, 11 (91%) patients had positive antibody index and therefore were included in the definite neuroborreliosis group.

The most common form of neuroborreliosis was *N.facialis* neuritis in 37% of the patients, followed by meningitis (25%). In 14% of the patients concurrent *N.facialis* neuritis and meningitis was diagnosed. These results correspond well with other studies carried out in Europe where *N.facialis* neuritis and meningitis are mentioned as the 2 most common forms of neuroborreliosis (5; 6; 8). However, in some of these studies the percentage of *N.facialis* neuritis cases exceeded 50% which was not seen in this study (5; 8). In the not confirmed neuroborreliosis group the only clinical forms were *N.facialis* neuritis and other cranial nerve neuritis, which might be one of the reasons why these patients did not have lumbar puncture and CSF testing done.

The 2 main antibiotics used to treat neuroborreliosis in this study were ceftriaxone (i/v) and doxycycline (p/o). According to guidelines the efficacy of these drugs is equal therefore it is recommended that ceftriaxone should be used in patients under 8 or 9 years of age (depending on the country's legislature) because of the doxycycline's side effects (5; 8). However, afterwards doxycycline should be used as it is perorally administered, is much easier to use, reduces hospitalization length, costs and the risk of side effects. In this study 32 (65 %) patients were treated with ceftriaxone while 7 (14 %) patients were treated with doxycycline. 6 (12 %) patients were given ceftriaxone to start and afterwards they were switched to doxycycline. From the study population 3 patients younger than 8 years of age were given doxycycline and 2 more patients under 8 years of age were give ceftriaxone to start and then switched to doxycycline. At the same time 10 patients over 8 years of age were given ceftriaxone although doxycycline should be the first line treatment for these patients. The differences in the choice of the drug between the groups were statistically significant and it was seen that ceftriaxone was chosen much more frequently in the definite and possible neuroborreliosis group compared to not confirmed neuroborreliosis group. The reason might be that the therapy with ceftriaxone might seem more effective based on the broader spectrum and way of administration, however it has been shown in multiple studies that the efficacy of both drugs is equal (5; 8).

The main limitation of this study might be the small study population. Another limitation might be the short time period of the study as well as the lack of data about the clinical outcome. In the future a broader study should be carried out over a larger period of time, including more patients and sending out questionnaires to the already included patients to evaluate the long-term outcomes of neuroborreliosis.

Conclusions

A total of 49 patients were enrolled in the study, from which 35 patients were included in the definite or possible neuroborreliosis groups while 14 patients were included in the not confirmed neuroborreliosis group due to the lack of appropriate testing. These results emphasize the need for a diagnostic algorithm for neuroborreliosis.

The data analysed in the study about IgM and IgG antibodies against *B.burgdorferi* un the serum and CSF show that negative antibody testing in the serum does not exclude the possibility of neuroborreliosis and underline the need for CSF testing if the neuroborreliosis diagnosis is likely.

The most common symptoms are *N.facialis* neuritis, headache, fever and nausea and vomiting. The most common clinical forms of neuroborreliosis is *N.facialis* neuritis, lymphocytic meningitis and the combination of both.

The most used antibiotics in the treatment of neuroborreliosis in this study were ceftriaxone and doxycycline, but they were not always used according to guidelines, which emphasises the need for an adequate treatment algorithm for neuroborreliosis.

References

1. Backman, K., Skogman, B. H. Occurrence of erythema migrans in children with Lyme neuroborreliosis and the association with clinical characteristics and outcome – a prospective cohort study. BMC Pediatrics, 2018, N18.
2. Dersch, R., Hottenrott, T., Schmidt, S., et al. Efficacy and safety of pharmacological treatments for Lyme neuroborreliosis in children: a systematic review. BMC Neurology, 2016, N16.
3. Garcia-Monco, J. C., Benach, J. L. Lyme Neuroborreliosis: Clinical Outcomes, Controversy, Pathogenesis, and Polymicrobial Infections. Annals of Neurology, 2019, N85, p. 21–31.
4. Kovalchuka, L., Cvetkova, S., Trofimova, J., et al. Immunogenetic Markers Definition in Latvian Patients with Lyme Borreliosis and Lyme Neuroborreliosis. International Journal of Environmental Research and Public Health, 2016, N13, p. 1194.
5. Mygland, Å., Ljøstad, U., Fingerle, V., et al. EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis. European Journal of Neurology, 2009, N17, p. 8.
6. Myszkowska-Torz, A., Frydrychowicz, M., Tomaszewski, M., et al. Neuroborreliosis and Post-Treatment Lyme Disease Syndrome: Focus on Children. Life, 2023, N13, p. 900.

7. Nguala, S., Baux, E., Patrat-Delon, S., et al. Methodological Quality Assessment with the AGREE II Scale and a Comparison of European and American Guidelines for the Treatment of Lyme Borreliosis: A Systematic Review. Pathogens, 2021, N10, p. 972.
8. Rauer, S., Kastenbauer, S., Hofmann, H. Guidelines for diagnosis and treatment in neurology – Lyme neuroborreliosis. German medical science, 2020, Vol. 18.
9. Skogman, B. H., Croner, S., Nordwall, M., et al. Lyme Neuroborreliosis in Children. A Prospective Study of Clinical features, Prognosis, and Outcome. Pediatric Infectious Disease Journal, 2008, N27, p. 1089–1094.
10. Skogman, B. H., Wilhelmsson, P., Atallah, S., et al. Lyme neuroborreliosis in Swedish children – PCR as a complementary diagnostic method for detection of Borrelia burgdorferi sensu lato in cerebrospinal fluid. European Journal of Clinical Microbiology & Infectious Diseases, 2021, N40, p. 1003–1012.
11. Strnad, M., Hönig, V., Růžek, D., et al. Europe-Wide Meta-Analysis of Borrelia burgdorferi Sensu Lato Prevalence in Questing Ixodes ricinus Ticks. Applied and Environmental Microbiology, 2017, N83.
12. van Gorkom, T., Voet, W., van Arkel, G. H. J., et al. Retrospective Evaluation of Various Serological Assays and Multiple Parameters for Optimal Diagnosis of Lyme Neuroborreliosis in a Routine Clinical Setting. Microbiology Spectrum, 2022, N10.