

## Research Article

# Children with Lyme Arthritis in Slovenia: Demographic, Clinical and Laboratory Characteristics

Maša Vovk<sup>1\*</sup>, Eva Ružič-Sabljič<sup>2</sup>, and Maja Arnež<sup>3</sup><sup>1</sup>Health Center Trebnje, Golievtrg 3, Slovenia<sup>2</sup>Institute of Microbiology and Immunology, Slovenia<sup>3</sup>Department of Infectious Diseases, University Medical Centre Ljubljana, Slovenia

## \*Corresponding author

Maša Vovk, Health Center Trebnje, Golievtrg 3, 8210 Trebnje, Slovenia, Email: masa.vovk@gmail.com

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## Keywords

• Lyme arthritis; Lyme borreliosis; Pediatrics; Endemic area

## Abstract

**Introduction:** Lyme borreliosis is an infectious disease caused by *B. burgdorferi sensu lato* and transmitted by a tick. In Slovenia it is highly endemic and common in children. A clinical sign of early disseminated and late disease is Lyme arthritis (LA). The aim of the study was to define demographic, clinical and laboratory characteristics of children with Lyme arthritis.

**Methods:** The retrospective clinical study was carried out at the Department of Infectious Diseases, University Medical Center Ljubljana, Slovenia, from 2006 to 2013. The study comprised patients with Lyme arthritis younger than 15 years old. Lyme arthritis was defined by the clinical standards for the diagnosis of Lyme borreliosis in Slovenia. The data was acquired from medical records via a questionnaire, and the infection was proven through microbiological testing of serum and synovial fluid. The patients were being followed up for six months.

**Results:** 37 children were diagnosed with Lyme arthritis, their average age was 8.7 years; girls were affected more frequently; cases were evenly distributed throughout the year; most patients come from Central Slovenia; less than one third of them recall a tick bite; less than half of the patients have the associated general symptoms of a borrelial infection; the knee is the most commonly affected joint, with pain being the most common local symptom. Confirmed and probable Lyme arthritis were diagnosed in 24% and 76% of the patients.

**Conclusion:** As Slovenia is endemic for borreliosis, a prospective study of children with LA is required to understand the natural course of the disease, and shorten time to treatment.

## ABBREVIATIONS

LB: Lyme Borreliosis; USA: United States of America; LA: Lyme Arthritis; ESR: Erythrocyte Sedimentation Rate; PCR: Polymerase Chain Reaction; CRP: C-reactive Protein; IgM: Immunoglobulin M; IgG: Immunoglobulin G; IFA: Immuno Fluorescent Assay; DNA: Deoxyribonucleic Acid; EM: Erythema Migrans

## INTRODUCTION

Lyme borreliosis (LB) is a tickborne infectious disease caused by a subspecies of *Borrelia burgdorferi sensu lato* [1]. In Slovenia the vector is the *Ixodes ricinus* tick and the most common species of the spirochete are *B. afzelii* and *B. garinii* [2,3]. Slovenia is a highly endemic region for LB where approximately 41 % of ticks are infected with borrelia [4,5]. The incidence of the disease in 2012 was 239.8 cases per 100,000 persons and is reported to be growing [6]. One of the highest rates of incidence is in the age group from 5 to 14 years [7].

LB affects various organs, and arthritis is a clinical sign of early disseminated and late disease [8]. In the United States of America (USA) arthritis occurs in 60 % of untreated children, while it is much less frequent in Europe. Reports from Germany estimate that less than 25 % of LB patients have arthritis [8,9]. This discrepancy can be explained by different strains of borrelia

and tick vectors among continents [10]. In the USA, only *B. burgdorferi sensu stricto* has been found [3].

Clinically, monoarticular arthritis predominates, although symmetric and unilateral oligoarticular arthritis is not rare [11]. In 90 % of the patients, the most frequently affected joint is the knee, which can be swollen, erythematous, warm and painful [12,13]. Joint inflammation is accompanied by fever and/or other general symptoms and signs of Lyme arthritis (LA) and can be preceded by flu-like symptoms and migratory joint pain [14,15]. In comparison to adults, LA in children progresses more acutely. Most patients do not recall a tick bite.

Laboratory findings in patients with LA are nonspecific. Erythrocyte sedimentation rate (ESR) may be elevated and liver enzymes were also found to be elevated in 20 % of the patients during the early disseminated phase of the disease in Europe [3,16]. In the USA, the liver is affected in 35 % of the patients. The number of leukocytes found in synovial fluid can be elevated up to 5000 cells/mm<sup>3</sup> and protein concentration levels are also found to be above normal values [3,16,17].

Some patients experience acute LA, which presents as a brief episode of joint inflammation that subsides in a couple of days, while in others the course of the disease is intermittent with short relapsing episodes and can be chronic [8]. The proportion

of persistent synovitis lasting more than 6 months in American children is estimated to be 39 % [18]. After antibiotic treatment, synovial membranes can still demonstrate spirochetes, which may be responsible for long term disease course [19]. However, with treatment the outcome in children is still excellent [20].

The criteria for diagnosing of LA in Slovenian children classify patients into three categories – confirmed, probable and possible LA [21]. In order to establish the diagnosis, serological testing, combined with polymerase chain reaction (PCR) assays of blood and synovial fluid help to differentiate LA from septic arthritis, juvenile idiopathic arthritis, reactive arthritis and other joint affecting diseases [22-24].

Antibiotic treatment is initiated as soon as the patient meets the diagnostic criteria for confirmed or probable LA [25]. Recommendations regarding the initial choice of antibiotics vary between clinicians in the USA, Slovenia and other European countries. In Slovenia, antibiotic guidelines for LB management are based on our own clinical studies and vary from other European recommendations. Our guidelines for the treatment of LA in children recommend a fourteen day course of IV ceftriaxone, followed by one month of antibiotic therapy if unsuccessful. The mainstay in the treatment of LA in children is the first regimen of fourteen days' parenteral application of ceftriaxone, which is followed by one month antibiotic therapy if unsuccessful [3,25,26].

## MATERIALS AND METHODS

All patients included in our retrospective clinical study were presented to the Department of Infectious Diseases, University Medical Center Ljubljana, Slovenia from January 2006 to December 2013. Thirty seven children fulfilled the following inclusion criteria: age < 15 years old, hospitalization and diagnosis of LA according to the Slovenian definition [21].

### Data collection

Medical records were obtained from the archives of the Department of Infectious Diseases, and the Pediatric Clinic, University Medical Center Ljubljana. A structured data collection sheet was used for collection of demographical, clinical and laboratory characteristics. Information on previous tick bites, the time of the disease onset, joint status, and treatment were obtained. Arthritis was evaluated as acute if a child presented with one episode of joint inflammation, intermittent when there were multiple episodes that lasted less than 6 months, and chronic when arthritis persisted for more than 6 months. The questionnaire also contained information about arthrocentesis and laboratory findings. The presence of symptoms and clinical status were obtained at the initial visit and then after two weeks, six weeks and six months after the beginning of antibiotic treatment. Confirmed LA was defined by the presence of arthritis and one of the following: solitary or multiple EM rash or strain identification of *B. burgdorferi* from serum or synovial fluid samples and/or sero conversion of specific serum antibodies. Probable arthritis was defined by the presence of arthritis and the presence of serum IgM and/or IgG antibodies [21].

### Laboratory analysis

Basic hematologic and biochemical testing were performed

in all patients. Microbiological tests for indirect and/or direct evidence of infection with *B. burgdorferisensulato* were processed at the Institute of Microbiology and Immunology at the Faculty of Medicine, University of Ljubljana.

### Serology

Blood samples from all patients and synovial fluid samples from 4 children were analyzed for specific IgM and IgG antibodies against *B. burgdorferisensulato*. In a seven-year period between 2006 and 2012, antibodies were detected by immuno fluorescent assay (IFA) without absorption, using *B. afzelii* antigen. Titers  $\geq 256$  were interpreted as positive [27,28]. In 2013, an indirect chemiluminescence immunoassay with recombinant antigens, using outer surface protein C-Osp C and variable major protein-like sequence expressed-VlsE was used for IgM detection and VlsE for IgG detection of *B. burgdorferisensulato*. IgM titers  $\geq 22$  E/ml and IgG titers  $\geq 15$  E/ml were evaluated as positive.

### Cultivation

Citrated plasma samples and synovial fluid were inoculated in modified Kelly-Pettenkofer medium. Samples were incubated for 12 weeks at 33°C and sub cultivated weekly. Every two weeks they were checked for the presence of spirochetes using dark field microscopy. Strain identification was done by pulsed-field gel electrophoresis [22].

### PCR Assay

Strains of *B. burgdorferisensulato* were identified by PCR in some of synovial fluid and serum samples.

**Statistical analysis:** Statistical analyses were performed using statistical program SPSS 20.0. Descriptive statistical methods were applied to evaluate characteristics of collected data. The frequency of variable distribution was assessed through a nonparametric chi-squared test and the degree of association between nominal variables through phico efficient. For both tests,  $p < 0.05$  was statistically significant.

## RESULTS

In a eight-year period, 37 children, 18 (48.6 %) boys and 19 (51.4 %) girls were diagnosed with LA in Slovenia. Their average age was 8.7 years, with a range from 1.9 to 14.3 years. LA was confirmed in 9 (24.3 %) patients and was probable in 28 (75.7 %) patients, as depicted in Table 1. Arthrocentesis was performed in 17 of 37 (45.9 %) patients. An attempt of DNA strain isolation by PCR from synovial fluid was performed in 14 of 37 (37.8 %) patients. Confirmed LA was diagnosed as statistically significant more frequently in patients who had arthrocentesis than in patients who had not had the procedure ( $\phi = 0.489$ ;  $p = 0.003$ ). Cultivation of synovial fluid samples was performed in 10 patients, but it was negative. Only *B. afzelii* was isolated from the blood in one of 19 (5.3 %) patients. Positive borrelial serum antibody IgM titers were identified in five of 37 (13.5 %) patients, and positive IgG titers in thirty-three of 37 (89.2 %) patients with LA.

**Demographics.** Fourteen of 37 (37.8 %) children were referred to our clinic from their primary pediatrician, sixteen (43.2 %) were formerly treated at the Unit of Allergy, Rheumatology and Clinical Immunology, Pediatric Clinic of Ljubljana, others were

**Table 1:** Case definitions for diagnosis of Lyme arthritis in 37 patients administered at Department of Infectious Diseases, University Medical Center Ljubljana, Slovenia.

Case definition for diagnosis of Lyme arthritis	Confirmed	Probable
Number of patients (%)	9 (24.3)	28 (75.7)
<i>B.burgdorferisensulato</i> DNA strain confirmed in synovial fluid with PCR assay	1 (2.7)	
<i>B.burgdorferisensulato</i> DNA strain confirmed in synovial fluid with PCR assay + IgG serum antibodies	3 (8.1)	
<i>B.burgdorferisensulato</i> DNA strain confirmed in synovial fluid with PCR assay + IgG serum antibodies + IgG synovial fluid antibodies	2 (5.4)	
Multiple EM	1 (2.7)	
IgG serum antibodies		22 (59.5)
IgM serum antibodies		1 (2.7)
IgG and IgM serum antibodies		4 (10.8)
IgG serum antibodies + IgG synovial fluid antibodies		1 (2.7)
History of solitary EM	1 (2.7)	
Solitary EM + <i>B. burgdorferisensulato</i> from blood sample cultivation + IgG serum antibodies	1 (2.7)	

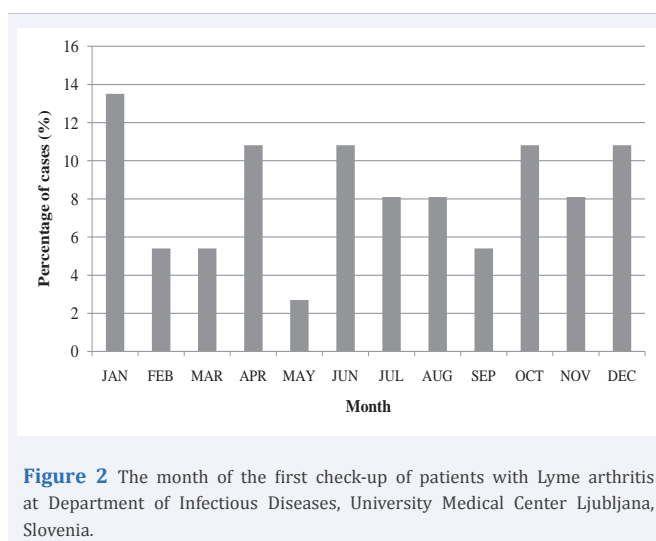
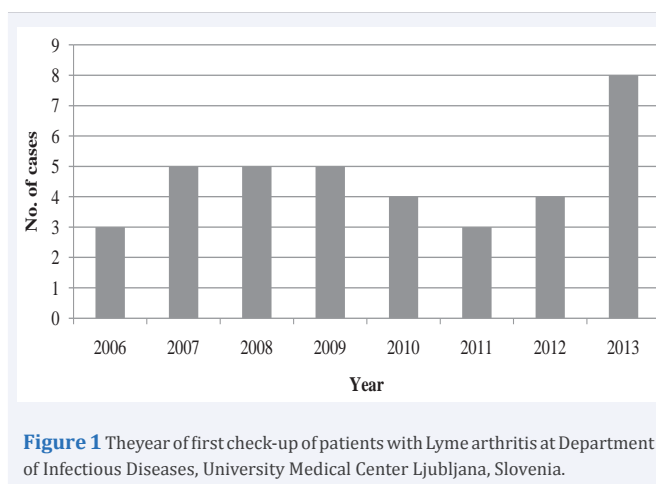
**Abbreviation:** EM: Erythema Migrans

accepted from secondary hospitals across Slovenia. The month and year of the first check-up of patients with LA are shown in Figure 1&2). Children with LA came from seven of twelve statistical regions of Slovenia; 62 % of them came from Central Slovenia region, 16 % of patients were residents of the Gorenjska region, 8 % lived in South-east Slovenia, 5 % in the Goriška region, and 3 % in Zasavska, Spodnje-posavska and Notranjska-Karst regions.

Eleven of 37 (29.7 %) of patients recalled a tick bite or/and other insect bite. Mean duration from tick or/and insect bite to first symptom presentation was 126 days with a span from 2 to 198 days.

First symptoms and/or clinical signs that children reported were arthralgia (64.9 %), general symptoms (24.3 %), a solitary EM (5.4 %), soft watery stool (2.7 %) and redness at the site of the tick bite (2.7 %). The accompanying general symptoms, namely flu, higher body temperature, vertigo, fatigue, malaise, headache, vertigo, sleep disturbances and other symptoms in children are presented in Table 2. Among other symptoms loss of appetite, abdominal pain, vomiting, mild generalized arthralgia and chest pain were listed. Median duration of symptoms in patients with LA before the start of treatment was 21 days, with a range from 1 to 98 days. The accompanying clinical signs are shown in Table 3.

Median duration of arthritis in children presenting with LA before start of treatment was 20 days, with a range from 1 to 238 days. Seventy eight percent of children had one joint involved at the time of presentation at the clinic, 2 joints were affected in 19 % of patients and only one child had arthritis of more than 4 joints. The knee was more frequently affected than other joints ( $\chi^2 = 52.080$ ;  $p < 0.001$ ) as 22 children reported knee arthritis. The second most commonly affected joint was the hip, with 16 % of cases, followed by the ankle (14 %), the wrist (8 %), and small joints of the fingers and toes (8 %). Two patients had elbow arthritis, and 2 shoulder arthritis, only one had back pain. The



**Table 2:** Accompanying general symptoms in children presenting with Lyme arthritis.

	No. of cases at presentation (%) (n=37)	No. of cases after two weeks (%) (n=28)	No. of cases after six weeks (%) (n=26)	No. of cases after six months (%) (n=15)
General symptoms	18 (48.6)	6 (21.4)	8 (30.8)	4 (26.7)
Higher body temperature	8 (21.6)	3 (10.7)	1 (3.8)	0 (0)
Flu	6 (16.2)	1 (3.6)	1 (3.8)	1 (6.7)
Headache	4 (10.8)	0 (0)	4 (15.4)	2 (13.3)
Other	4 (10.8)	2 (7.1)	8 (30.8)	2 (13.3)
Vertigo	2 (5.4)	0 (0)	0 (0)	1 (6.7)
Fatigue	2 (5.4)	1 (3.6)	1 (3.8)	1 (6.7)
Malaise	1 (2.7)	0 (0)	0 (0)	0 (0)
Fever	1 (2.7)	0 (0)	0 (0)	0 (0)
Sleep disturbances	0 (0)	0 (0)	1 (3.8)	0 (0)
Myalgia	0 (0)	0 (0)	1 (3.8)	0 (0)

**Abbreviation:** n: Number of Cases

**Table 3:** Clinical findings in children presenting with Lyme arthritis.

	No. of cases at presentation (%) (n=28)	No. of cases after two weeks (%) (n=19)	No. of cases after six weeks (%) (n=26)	No. of cases after six months (%) (n=16)
Clinical findings	11 (93.3)	4 (21.2)	5 (19)	1 (6.3)
Enlarged lymph nodes	9 (32.4)	2 (10.6)	4 (15.2)	0 (0)
Pharyngeal erythema	3 (10.8)	0 (0)	3 (11.4)	0 (0)
Systolic murmur	1 (3.6)	3 (15.9)	0 (0)	0 (0)
Nasal congestion	1 (3.6)	0 (0)	1 (3.8)	0 (0)
Conjunctivitis	1 (3.6)	0 (0)	0 (0)	0 (0)
Abdominal pain on palpation	0 (0)	1 (5.3)	0 (0)	0 (0)
Enlarged spleen	0 (0)	0 (0)	0 (0)	1 (6.3)

**Table 4:** Laboratory synovial fluid characteristics in children presenting with Lyme arthritis.

	n	$\bar{X} \pm S$	M (range)
Albumins (g/L)	4	27.8 ± 3	27 (25–32)
Uric acid (µmol/L)	1	276 ± 0	276 (276)
Proteins (g/L)	8	52.9 ± 7.4	53.5 (44–64.4)
Leukocytes (x 10 <sup>9</sup> /L)	7	20.4 ± 8.3	23.9 (9–31)
Glucose (mmol/L)	8	4.4 ± 1.8	4.5 (2.1–7.5)
LDH (µkat/L)	4	15.1 ± 15.6	7.7 (6.5–38.4)
Relative thickness	6	1.032 ± 0.005	1.031 (1.027–1.038)
pH	3	7.53 ± 0.05	7.5 (7.5–7.58)

**Abbreviations:**  $\bar{X}$  arithmeticmean; S: Standard deviation; M: Median; n: Number of Cases; LDH: Lactate Dehydrogenase

main clinical characteristic of the affected joint was pain on any movement that strained the joint, in 86.5 %; joint flexibility was reduced in 78.4 % of patients, and joint swelling was present in 73 % of cases. Locally elevated temperature (29.7 %), pain within activity (24.3 %) and redness of skin above the joint (2.7 %) were a little less common.

Twenty (54.1 %) children presented with acute arthritis, five (13.5 %) had intermittent symptoms, and eight (21.6 %) patients suffered from chronic arthritis. The data was insufficient to determine the course of arthritis in 4 (10.8 %) cases. Six months after antibiotic treatment arthritis persisted in three (8.1 %) patients.

At the presentation at the clinic, 5 of 18 (28 %) children had elevated serum levels of aspartate amino transferase. In some patients elevated values of inflammatory markers were found. Median value of ESR was 9 mm/h with a range from 2 to 98 mm/h and median value of CRP was 8 mg/L, with a range from 0 to 110.4 mg/L. The white cell counts were within normal limits. Laboratory synovial fluid characteristics are presented in Table (4).

Thirty-five of 37 (94.6 %) patients were treated with ceftriaxone intravenously. Median duration of antibiotic therapy was 14 days with a range from 8 to 28 days. Four (10.8 %) children required antihistamines because of an allergic reaction to the medication. Fourteen (37.8 %) patients with LA concurrently received non steroidal anti-inflammatory drugs. Two patients were not treated with antibiotics, as the diagnosis was reactive arthritis in one child, and the other child had a positive serology for *B. burgdorferi* sensu lato but the arthritis was felt to be due to an injury.

All children who presented with LA were admitted to the hospital, but continued antibiotic therapy in an outpatient clinic. Average duration of hospital stay was one day with a range from one to seven days.

## DISCUSSION

In our study of 37 children, there was a slight female predominance (51.4 %) of patients. A similar trend was described in another small European study, while American authors observed quite the contrary [29, 30]. It is not clear yet whether the variability of tick and borrelia species among continents influences this observation [1]. With the median age of 8.7, the patients with LA in Slovenia are slightly older than children in Slovenia who present with multiple EM rashes, another clinical picture of early disseminated LB [31]. Other European and American studies confirm our findings [12,32]. Most of our patients live in the Central Slovenia region where the incidence of LB has been the highest [6].

Arthritis is a common disease in children, but with many overlapping features with both septic and non septic non-Lyme arthritis, it can also be a real challenge to confirm LA [14]. Almost half of involved patients were initially examined at the Unit of Allergy, Rheumatology and Clinical Immunology, Pediatric Clinic of Ljubljana, and only after excluding other diagnoses were they referred to our clinic. In the diagnostic process orthopedic surgeons were also consulted, which emphasizes the importance of team work in the management of LA.

A diagnosis of confirmed arthritis was proved in one quarter of all patients (Table 1). In a Norwegian study the number of LA cases in adult patients was three times higher, but the reason for such a difference is most probably a wider definition of confirmed arthritis used in Norway [33]. Although reports of species identification of borrelia from a blood sample in patients with LA are rare, the confirmed LA of a hip was defined with identification of *B. afzelii* and simultaneously presents solitary EM in one girl [34]. Two other patients also reported a history of EM rashes and in six (16 %) patients the diagnosis was proven by PCR analysis of synovial fluid. Despite the fact that European and American studies report up to an 85 % and 70 % rate of

successful direct proof of borrelia species in synovial fluid, respectively, only fourteen (38 %) of the patients in our study had diagnostic arthrocentesis of the affected joint, attempting to confirm a strain directly by PCR [35,36]. Our study shows that confirmed LA was diagnosed more frequently in patients who had arthrocentesis than in children, who did not have the procedure, and this was statistically significant. These findings indicate that arthrocentesis and an attempting to get direct proof of a spirochetal infection in synovial fluid are important for children with suspected LA. Probable LA was diagnosed in 28 patients with specific antibodies IgM/IgG in blood samples. However, sero conversion after six months was observed neither in our patients, nor in Haugeberg's study. Contrary to reports on adult patients with LA, 3 children from our study did not have positive serum antibody titers [31].

Most patients were seen in 2013 (Figure 1), which can be explained by the higher incidence rates of LB in recent years in Slovenia [6]. Particularly, the increased LB rate that year might be explained by using a new indirect chemiluminescence immunoassay with recombinant antigens, which is more sensitive and equally specific, with respect to IFA [28]. Even though ticks are more active during spring, summer and fall in Slovenia, children with LA presented to the clinic throughout the entire year. Similar reports have come from other parts of Europe [32,37]. One explanation is that arthritis is both an early and late manifestation of LB, and can present even months after the initial tick bite [11]. In contrast, the USA notices the highest rate of LA during the late spring and summer months as a result of an effective cycle of *B. burgdorferi* transmission between larval and nymphal ticks [3].

As in previous studies, only one third of the patients recalled a tick bite and/or insect bite in the previous year [9,13,32]. Mean duration until presentation of the first symptoms was 126 days, which confirms the findings of an American study where the observation period was 4.3 months [12].

Arthralgia was reported as an initial symptom by 64.5 % of patients, and only 5 % of children had a history of an EM. Early American studies showed a higher incidence of EM rashes (72.5 %) in comparison to our findings or the recent studies where only 6 % of patients presented initially with skin changes [15,20]. Early recognition and treatment of LB has heavily reduced the appearance of EM as a prior sign to arthritis [20,30].

Early disseminated LB is usually accompanied by general symptoms, and in our study 49 % of patients reported fever, flu-like symptoms and headache, as the most common symptoms. Tory et al. came to similar conclusions with a retrospective study where 30 % of children had fever and 28 % of patients complained of flu-like symptoms [20]. In comparison to adult patients, children have less fatigue, but headache occurs at equal rates [38]. Lyme endocarditis was excluded in a patient with chest pain.

Eleven of 28 (39.3 %) patients with LA had other clinical signs of infection besides arthritis (Table 3). Enlarged lymph nodes were found in more patients (32.4 %) than in the American study. On the other hand, pharyngeal erythema, conjunctivitis and nasal congestion were less frequent in Slovenia [30]. Patients

were followed for six months, and at the last check-up one patient presented with an enlarged spleen and knee arthritis, possibly representing an associated tick-borne infection. Although coinfection rates after tick bites are very high in endemic areas they were not excluded in this case [39]. It would be important to address that problem in further studies.

LA presents as periodic inflammatory episodes of a joint or persistent mono-, oligo- or polyarthritis [3]. More than three quarters of our patients developed monoarticular arthritis, 19 % had oligoarthritis and only one patient had polyarthritis. Huppertz et al., report that 26 % of patients had two to four joints involved. Even more cases of oligoarthritis were found in the USA, where reported number reached approximately 33 %. In adults and children the knee is the most frequently affected joint in the case of LA, which was confirmed in our study, where 44 % of the patients had knee arthritis [13,32]. Coxitis was observed in 16 %, ankle arthritis in 14 %, and other joint arthritis in 26 % of patients. In a 1977 study, Steere et al., found coxitis to be a rare presentation of LA in children (18.5 %) [40]. This finding was later confirmed by American studies [12,14,38]. A German study also showed the predominance of knee arthritis, followed by ankle and elbow arthritis. All studies were quite small, and generalization is therefore limited [29].

The major clinical manifestations of LA have been reported to be swelling, pain and limited joint motion that were also predominant in our patients [32]. One third of Slovenian children also reported localized warmth of the affected joints, arthralgia during inactivity, whereas only one child had erythema over the joint. Other studies reported similar symptoms [12,32].

In comparison to Huppertz et al., and Steere et al., the course of LA in our patients was primarily acute [17, 32]. Only 21.6 % of patients presented with chronic disease. Researchers have reported genetic variability between *B. burgdorferi* among continents, and showed that strains from the USA induced greater inflammatory response than *B. burgdorferi* from Europe, differing in clinical manifestations [41]. Thus, we believe that genetic diversity explains the shorter course of LA in Slovenia.

Six months after completing antibiotic treatment, three patients still had clinical signs of arthritis. American studies report antibiotic refractory LA is associated with the HLA-DRB molecules that bind an epitope of *B. burgdorferi* outer surface protein A. This mechanism applies only to American patients because European strains do not have this epitope. Further research is needed to answer the pathogenesis of refractory arthritis [42].

The results of CBC's and biochemistry profiles in most of our patients were in the normal reference range. Only CRP and ESR were elevated in some children, which correlate with data from European and American studies [14,33]. One quarter of our patients had elevated liver enzymes, which has already been reported [43,44].

A synovial fluid analysis is both diagnostic and therapeutic in suspected LA. Of all age groups tested in Europe and the USA, elevated leukocytes and predominance of neutrophil granulocytes are found to be higher in children than adults [13,32,33,40]. The same situation exists with septic arthritis [14,17]. Proteins are

frequently elevated, with glucose values in the normal range [40]. Even though our results match the mentioned findings, careful interpretation is required as the number of samples in our study is low (Table 4).

Mean duration of general symptoms and arthritis in our study before treatment was 21 and 20 days, respectively. Gerber and colleagues reported symptoms lasting twice as long, while Tory et al., marked median symptom duration of 14 days prior to treatment [12,20].

Although there is a possibility that symptoms disappear without intervention, patients are treated with antibiotics because the goal is to prevent progress to chronic LB [3,15]. As Slovenian recommendations differ from the American guidelines, children were treated with ceftriaxone intravenously for 14 days, some of them getting extra non steroidal anti-inflammatory drugs upon the rheumatologist's advice [25]. Two patients did not get antibiotics despite positive serology and a diagnosis of probable LA. The presence of IgG serum antibodies was believed to be an incidental finding in a patient with a concomitant injury of the knee. In an endemic area, it is necessary to interpret laboratory results with extra care [3,45].

## CONCLUSION

As the study is retrospective, it has its weaknesses. One limitation is the incomplete patient documentation, laboratory tests and follow-ups were not planned in advance and therefore they were not carried out in all patients. The number of children included in the study is relatively small due to LA being a rare disease in Slovenia. A prospective study of children with LA would be beneficial. More attention to taking a thorough history, and ordering comprehensive laboratory tests would prove beneficial, especially when combined with more accurate data about demographic, clinical and laboratory characteristics in children with LA. This will result in a better understanding of the course of the disease in children, and decrease the time between disease presentation and treatment.

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