Original Article

SEROLOGICAL SURVEY OF LYME BORRELIOSIS IN THE SOUTH REGION OF KAZAKHSTAN

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ABSTRACT

Lyme borreliosis (LB) is an infectious disease caused by spirochetes of the *Borrelia burgdorferi* sensu lato complex. Transmission occurs through the bites of hard ticks within the genus *Ixodes*. Cases of fever of unknown origin are recorded in southern Kazakhstan, however, the prevalence of LB in this area remains unstudied. Almaty oblast is recognized as an endemic area for LB. Ixodid tick vectors also inhabit Jambyl oblast, where antibodies to LB agent were previously detected among residents, while it is classified as non-endemic. Turkistan oblast is also considered non-endemic for LB. The purpose of this study was to investigate the seroprevalence of IgG antibodies to *B. burgdorferi* s.l. among apparently healthy residents of Almaty city (Almaty oblast), Taraz city (Jambyl oblast), and Shymkent city (Turkistan oblast). A total of 465 human serum samples were collected from March 2022 to September 2023. Using the ELISA method, we detected the presence of IgG antibodies to the LB agent in 5.4% of the entire study group (24/465, 95% CI: 3.3-7.6%), and specifically in 9.3% of residents of Almaty city (11/118, 95% CI: 4.7-16.1%, p=0.03), 4.5% – Taraz city (11/242, 95% CI: 2.3-8.0%) and 1.9% – Shymkent city (2/105, 95% CI: 0.2-6.7%). The results of the study confirm the seroprevalence of IgG antibodies to *B. burgdorferi* s.l. among the population of Almaty city and Jambyl oblast, and also reveal seropositive samples in residents of Turkistan oblast, suggesting possible infection during travel to endemic regions. It is important to continue LB surveillance in endemic and emerging regions, as well as to raise awareness of the infection among healthcare workers and the general public in non-endemic areas.

Keywords: Lyme borreliosis, *Borrelia burgdorferi* sensu lato, south Kazakhstan, seroprevalence, ELISA.

INTRODUCTION

Lyme borreliosis (LB) is a prevalent multicomplex infectious disease usually reported in North America and Europe, but also observed in regions of Asia [1, 2]. The manifestations of Lyme borreliosis exhibit variability; nevertheless, approximately 70-80% of individuals develop a skin rash called erythema migrans (usually appears within 3 to 30 days after infection) that may, albeit not universally, take the form of a characteristic round red rash with a partial central clearing, reminiscent of a «bull's-eye» or a "target" [3, 4]. People with LB may also experience some equivocal symptoms like fever, chills, fatigue, muscle and joint aches, and headache. In the absence of timely intervention, untreated LB may progress to more severe manifestations, including joint pain and swelling, particularly in large joints such as the knees (Lyme arthritis) [5]. In some cases, the infection can affect the nervous system (Lyme neuroborreliosis), leading to symptoms such as facial paralysis, tingling or numbness in the limbs, and cognitive impairments affecting memory or concentration [6]. Although less common, LB can exert an impact on the cardiovascular system, precipitating irregular heart rhythms and chest pain (Lyme carditis) [7]. Additionally, LB has the potential to induce ocular inflammation, distinguished by redness and visual disturbances. The disease progression typically unfolds in three stages, commencing with an early localized infection of the skin, often evidenced by the aforementioned erythema migrans, and culminating in late-stage infection, characterized by acrodermatitis chronica atrophicans, a dermatological condition marked by a skin rash that progresses to widespread skin atrophy [8].

The etiological agents of LB are spirochetes belonging to the *Borrelia burgdorferi* sensu lato complex that comprises over 20 distinct genospecies, with the majority demonstrating pathogenicity in humans. [9]. Literary sources mainly mention four prevailing genospecies responsible for causing LB in humans: *B. burgdorferi* sensu stricto, *B. afzelii, B. garinii*, and *B. bavariensis* [10, 11]. However, occasional cases of causing LB by other genospecies are described [12, 13]. *B. burgdorferi* s.l. is transmitted to both humans and animals through the bite of hard ixodid ticks belonging to the genus *Ixodes* [2]. In Eurasia, *I. persulcatus* and *I. ricinus* are two prevalent species, with *I. persulcatus* being particularly common in Kazakhstan [2, 14]. Existing literature highlights the significance of the duration of tick attachment in facilitating effective transmission of the pathogen to humans [15]. Small rodents, serving as reservoir hosts for *Borreliae*, actively contribute to the natural circulation of spirochetes [1].

Formerly, it was believed that identifying the presence of erythema migrans was sufficient to diagnose LB, however, due to the infrequent and multiform manifestation of this symptom and its potential inaccurate association with other diseases, a laboratory test, such as the enzyme-linked immunosorbent assay (ELISA) method, is deemed necessary in all cases [4]. In addition, insights into a patient's epidemiological anamnesis and exposure to ticks can aid in the diagnosis of LB, but approximately 50% of patients with LB are unaware of whether they have experienced a tick bite [16, 17].

Lyme borreliosis achieved official recognition in Kazakhstan in 2013 [17, 18]. Almaty and East-Kazakhstan oblasts are considered endemic for LB [16, 18]. In Almaty oblast, the period from March to October marks the seasonal activity of ticks, reaching its peak in May for *I. persulcatus* [19]. Natural foci of Lyme borreliosis (LB) are primarily localized in forest and mountainous landscapes within the temperate climate zone, aligning with the habitat of ixodid ticks [20]. In addition to that, most of the territory of the southern region of Kazakhstan is characterized by relatively mild winter conditions and large amounts of rainfall. The number of reported tick bites increases annually, accompanied by frequent reports of fevers of unknown origin in the southern region of Kazakhstan [21]. Surveillance data for LB in Almaty oblast remains insufficient. Although Jambyl oblast is not officially recognized as endemic for LB, ticks of the *Ixodes* spp. inhabit the region, and seropositive samples have been previously detected among residents [22]. Notably, in 2022, a case of Lyme neuroborreliosis and tick-borne encephalitis co-infection was identified in a patient from Jambyl oblast [23]. Despite Turkistan oblast being considered non-endemic for LB, individuals may travel to endemic areas where they risk tick bites. Upon returning, these people may fall ill, and due to a lack of awareness among doctors in non-endemic areas regarding the possibility of LB infection, patients are often misdiagnosed and do not receive appropriate medical care [24, 25].

Insufficient awareness of LB among medical professionals and the general public in non-endemic areas, coupled with the variability in its clinical presentation and the latent persistence of the pathogen in the body, can result in delayed and/or inaccurate diagnoses, untimely treatment, and consequently, the development of chronic conditions and disabilities. It is crucial to note that LB is just one among several tick-borne diseases prevalent in Kazakhstan, and comprehending its status contributes to broader research on the prevalence of multiple tick-borne illnesses [26].

Considering the importance of LB surveillance, we conducted a serological study to assess the prevalence of IgG antibodies to *B. burgdorferi* s.l. among apparently healthy residents of the cities of the southern region of Kazakhstan, namely Almaty city (Almaty oblast), Taraz city (Jambyl oblast), and Shymkent city (Turkistan oblast).

MATERIALS AND METHODS

Ethics statement

This study was approved by the local ethics committee of the National Center for Biotechnology, Astana, Kazakhstan.

Sample collection

For serological examination for IgG antibodies to *B. burgdorferi* s.l., serum samples were collected from clinically healthy residents of the cities of Almaty (Almaty oblast), Taraz (Jambyl oblast), and Shymkent (Turkistan oblast) (Figure 1), from March 2022 to September 2023. Serum samples were stored at − 20 ◦C. Before examination, serum samples were thawed and inactivated at 56 ◦C for 20 min. Overall, 465 samples were collected.

ELISA

IgG antibodies against *B. burgdorferi* s.l. were detected using the "LymeBest – IgG" (Vector Best, Russia) ELISA kit that utilizes the VlsE recombinant antigen. The analysis was

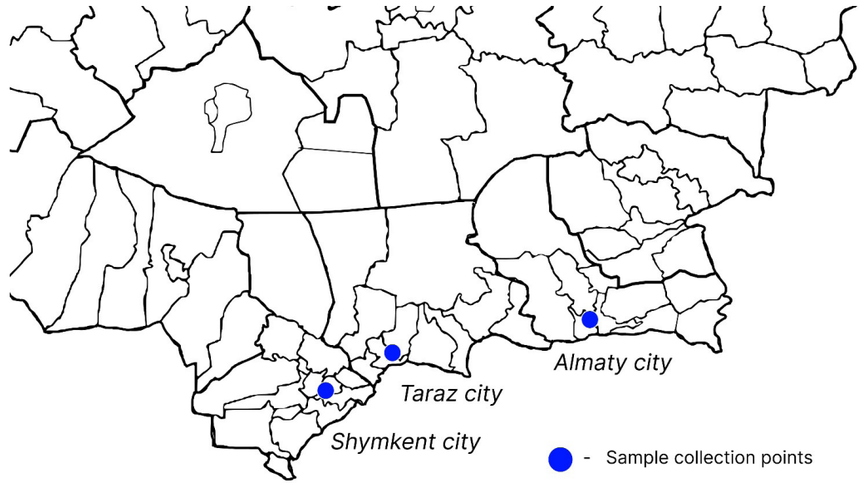

Figure 1. Sample collection area

performed according to the manufacturer's instructions. Indicators of optical density (OD) values of test sera above OD values of the Cutoff Calibrator were considered positive, values below were considered negative, and those equal to OD values of the Cutoff Calibrator ± 10 % were considered questionable.

Statistics

The exact Clopper-Pearson method, which is quite conventional and tends to produce wider intervals than necessary, was used based on the beta distribution to calculate the 95% confidence interval (CI). The odds ratio (OR) calculation was used to estimate the *p*-value and an association between seropositivity and donors' age and sex. Differences were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

IgG antibodies to *B. burgdorferi* s.l. were detected in 5.4% (24/465, 95% CI: 3.3-7.6%) of the samples (Table 1). The percentage of anti-*B.burgdorferi* s.l. IgG seropositive samples exhibited regional variations, with a higher prevalence among residents of Almaty city (11/118, 9.3%, 95% CI: 4.7-16.1%, p=0.03) in comparison to residents of Shymkent city (2/105, 1.9%, 95% CI: 0.2-6.7%). Meanwhile, the percentage of anti-*B. burgdorferi* s.l. IgG seropositive samples among residents of Taraz city was 4.5% (11/242, 95% CI: 2.3-8.0%) (Table 1).

In a prior study [19], the seroprevalence of 5.6% was identified in Almaty city. The higher seropositivity rate detected in the present research may indicate an increased exposure of the city residents to *B. burgdorferi* s.l over time. Consequently, the obtained results confirm the endemicity of LB in Almaty city [19, 27]. Furthermore, residents of Jambyl and Turkistan oblasts are also exposed to *B. burgdorferi* s.l. Given the presence of the LB vector in Jambyl oblast, where seroprevalence was previously documented [22], this region should be regarded as an emerging area for LB. The detection of IgG antibodies to *B. burgdorferi* s.l. among the population of Shymkent city (Turkistan oblast) can sustain our assumption regarding the movement of individuals between endemic and non-endemic areas for LB. Similar cases are often described in the literature [24, 25, 28]. Unfortunately, our study was limited by the absence of data on tick bite history, epidemiological anamnesis, and the medical and travel history of donors.

The average age of individuals with IgG seropositivity was 33.9 ± 12.2, compared to 34.5 ± 17.5 for seronegative donors. Our analysis revealed no significant difference in seroprevalence across different age groups (Table 2). Nevertheless, there were no seropositive results observed in individuals aged 65 years and older. Although not statistically significant, a relatively higher seroprevalence was noted in the age groups 15–24 (10.5%) and 35–44 years (9.1%). The reasons for these findings may be attributed to the mobility of young and middle-aged individuals between areas considered endemic and non-endemic for LB [28]. Additionally, the likelihood of frequent mountain hiking, a popular activity, especially among residents and visitors of Almaty oblast where ixodid ticks are prevalent, could contribute to the observed pattern [20]. Although there was also no statistically significant difference in seroprevalence among age groups specifically for Almaty city (data not shown), it is noteworthy that a previous study [19] reported a higher level of antibodies to *B. burgdorferi* s.l. in the older age group of 55-64 years (17.1%), with no seropositive results found among children under 14 years. The serological survey conducted in the Netherlands [29] reported a seroprevalence of 4.4% (n = 5592) and demonstrated an increase in seroprevalence with age, ranging from 2.6% in the age group 0–19 years to 7.7% in the age group 60-88 years. Similarly, a study in Kalmar County, Sweden [30], with a seroprevalence of 23% (n = 273), indicated a significant difference ($p < 0.01$) in seropositive rates between the age group 60-70 years (47%) and all other age groups (18-59 years; 10-23%). The studies in Germany likewise stated a growth in seroprevalence with age [31, 32]. The age-dependent distribution of seroprevalence, possibly indicative of cumulative population exposure to *B. burgdorferi* s.l., underscores the dynamic nature of exposure patterns. These variations in seroprevalence across age groups emphasize the significance of considering demographic factors in comprehending the dynamics of LB within specific populations. Nevertheless, the results of our research can be explained by the scarce sample of donors.

The seroprevalence did not exhibit a significant association with sex. Generally, the odds of exposure to *B. burgdorferi* s.l. were similar for males and females (Table 2). However, other studies demonstrated higher exposure to the LB agent in men as compared to women [29-32]. Our research faced limitations due to the absence of sex and age data for a subset of the study population.

Table 1. Seroprevalence of IgG antibodies against *B. burgdorferi* s.l. in apparently healthy residents of the cities of Almaty (Almaty oblast), Taraz (Jambyl oblast), and Shymkent (Turkistan oblast).

City	No. of examined samples	Positive (%)	Negative (%)	Odds ratio (95% CI; *p*-value)
Almaty	118	11 (9.3)	107 (90.7)	5.3 (1.1-24.5; 0.03)
Shymkent	105	2 (1.9)	103 (98.1)	1
Taraz	242	11 (4.5)	231(95.5)	2.5 (0.5-11.3; 0.25)
Total:	**465**	**24 (5.4)**	**441 (94.6)**	

Table 2. Distribution of anti-*Borrelia burgdorfe*ri s.l. seroprevalence by sex and age of donors.

	Total (%)	Positive (%)	Negative (%)	Odds ratio (95% CI; *p*-value)
Sex:				
Female	208 (44.7)	14 (6.7)	194 (93.3)	1.5 (0.6-3.4; 0.4)
Male	213 (45.8)	10 (4.7)	203 (95.3)	1
No data	44 (9.5)	-	44 (100)	-
Age group:				
≤14	47 (10.1)	1 (2.1)	46 (97.9)	1
15-24	57 (12.3)	6 (10.5)	51 (89.5)	5.4 (0.6-46.7; 0.1)
25-34	104 (22.4)	6 (5.8)	98 (94.2)	2.8 (0.3-24.1; 0.3)
35-44	66 (14.2)	6 (9.1)	60 (90.9)	4.6 (0.5-39.6; 0.2)
45-54	76 (16.3)	3 (4.0)	73 (96.0)	1.9 (0.2-18.7; 0.6)
55-64	37 (8.0)	1 (2.7)	36 (97.3)	1.3 (0.1-21.1; 0.9)
≥65	12 (2.6)	-	12 (100)	-
No data	66 (14.2)	1 (1.5)	65 (98.5)	-

CONCLUSION

The results of this serological study confirm the seroprevalence of IgG antibodies to *B. burgdorferi* s.l. among the population of Almaty city and Jambyl oblast, as well as reveal the presence of IgG antibodies to *B. burgdorferi* s.l. in residents of Shymkent (Turkistan oblast). Thus, our research provides new data on the LB incidence among residents of the southern region of Kazakhstan, underscoring the imperative to sustain LB surveillance efforts and investigate the prevalence of *B. burgdorferi* s.l. among ticks in both endemic and emerging regions. The findings also emphasize the necessity for disease monitoring initiatives among residents of Turkistan oblast, who may contract the infection during travel in LB-endemic areas. It is important to inform medical practitioners and citizens of non-endemic regions regarding the potential for LB infection. Therefore, the implementation of public health measures, including LB awareness campaigns for residents of both endemic and non-endemic areas, the formulation of effective tick control strategies, and the emphasis on early diagnosis and treatment play crucial roles in mitigating the impact of LB.

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LITERATURE

1. Steere, A. C., Strle, F., Wormser, G. P., Hu, L. T., Branda, J. A., Hovius, J. W., Li, X., Mead, P. S. Lyme borreliosis // Nature reviews. Disease primers. – 2016. – Vol. 2. – P. 16090. https://doi.org/10.1038/nrdp.2016.90

2. Ji, Z., Jian, M., Yue, P., Cao, W., Xu, X., Zhang, Y., Pan, Y., Yang, J., Chen, J., Liu, M., Fan, Y., Su, X., Wen, S., Kong, J., Li, B., Dong, Y., Zhou, G., Liu, A., Bao, F. Prevalence of *Borrelia burgdorferi* in Ixodidae Tick around Asia: A Systematic Review and Meta-Analysis // Pathogens (Basel, Switzerland). – 2022. – Vol. 11, No 2. – P. 143. https://doi.org/10.3390/pathogens11020143

3. Centers for Disease Control and Prevention (CDC). Lyme disease. Available online: https://www.cdc.gov/lyme/index.html. (accessed: 02.12.2023)

4. Schotthoefer, A. M., Green, C. B., Dempsey, G., Horn, E. J. The Spectrum of Erythema Migrans in Early Lyme Disease: Can We Improve Its Recognition? // Cureus. – 2022. – Vol. 14, No 10. – P. e30673. https://doi.org/10.7759/cureus.30673

5. Steere, A. C., Schoen, R. T., Taylor, E. The clinical evolution of Lyme arthritis // Annals of internal medicine. – 1987. – Vol. 107, No 5. – P. 725–731. https://doi.org/10.7326/0003-4819-107-5-725

6. Ogrinc, K., Lusa, L., Lotrič-Furlan, S., Bogovič, P., Stupica, D., Cerar, T., Ružić-Sabljić, E., Strle, F. Course and Outcome of Early European Lyme Neuroborreliosis (Bannwarth Syndrome): Clinical and Laboratory Findings // Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. – 2016. – Vol. 63, No 3. – P. 346–353. https://doi.org/10.1093/cid/ciw299

7. Centers for Disease Control and Prevention (CDC). Three sudden cardiac deaths associated with Lyme carditis - United States, November 2012-July 2013 // MMWR. Morbidity and mortality weekly report. – 2013. – Vol. 62, No 49. – P. 993–996.

8. Asbrink, E., Brehmer-Andersson, E., Hovmark, A. Acrodermatitis chronica atrophicans--a spirochetosis. Clinical and histopathological picture based on 32 patients; course and relationship to erythema chronicum migrans Afzelius // The American Journal of dermatopathology. – 1986. – Vol. 8, No 3. – P. 209–219. https://doi.org/10.1097/00000372-198606000-00005

9. Margos, G., Vollmer, S. A., Ogden, N. H., Fish, D. Population genetics, taxonomy, phylogeny and evolution of *Borrelia burgdorferi* sensu lato // Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases. – 2011. – Vol. 11, No 7. – P. 1545–1563. https://doi.org/10.1016/j.meegid.2011.07.022

10. Stanek, G., Strle, F. Lyme borreliosis-from tick bite to diagnosis and treatment // FEMS microbiology reviews. – 2018. – Vol. 42, No 3. – P. 233–258. https://doi.org/10.1093/femsre/fux047

11. Margos, G., Wilske, B., Sing, A., Hizo-Teufel, C., Cao, W. C., Chu, C., Scholz, H., Straubinger, R. K., Fingerle, V. *Borrelia bavariensis* sp. nov. is widely distributed in Europe

and Asia // International journal of systematic and evolutionary microbiology. – 2013. – Vol. 63, No 11. – P. 4284–4288. https://doi.org/10.1099/ijs.0.052001-0

12. Stanek, G., Reiter, M. The expanding Lyme Borrelia complex--clinical significance of genomic species? // Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. – 2011. – Vol. 17, No 4. – P. 487–493. https://doi.org/10.1111/j.1469-0691.2011.03492.x

13. Fingerle, V., Schulte-Spechtel, U. C., Ruzic-Sabljic, E., Leonhard, S., Hofmann, H., Weber, K., Pfister, K., Strle, F., Wilske, B. Epidemiological aspects and molecular characterization of *Borrelia burgdorferi* s.l. from southern Germany with special respect to the new species *Borrelia spielmanii* sp. nov. // International journal of medical microbiology : IJMM. – 2008. – Vol. 298, No 3-4. – P. 279–290. https://doi.org/10.1016/j.ijmm.2007.05.002

14. Bissenbay A.O., Zhigailov A.V., Perfilyeva Y.V., Naizabayeva D.A., Neupokoyeva A.S., Berdygulova Z.A., Ostapchuk Y.O., Maltseva E.R., Kuatbekova S.A., Nizkorodova A.S., Dmitrovskiy A.M., Skiba Y.A., Mamadaliyev S.M. Epidemiology and molecular genetic characteristics of Lyme borreliosis pathogens circulating in tick's population in the Almaty oblast of the Republic of Kazakhstan // Journal of microbiology, epidemiology and immunobiology. – 2020. – Vol. 97, No 6. – P. 535-545. https://doi.org/10.36233/0372-9311-2020-97-6-4 (in Russian)

15. Cook M. J. Lyme borreliosis: a review of data on transmission time after tick attachment // International journal of general medicine. – 2014. – Vol. 8. – P. 1–8. https://doi.org/10.2147/IJGM.S73791

16. Yegemberdieva R.A., Toksanbaeva K.N., Duĭsenova A.K., Ermukhanova N.T. Clinical manifestations of chronic forms tickborne borreliosis in the East Kazakhstan area // Vestnik Kazakhskogo natsional'nogo meditsinskogo universiteta. – 2013. – Vol. 2. – P. 89–92. (in Russian)

17. Egemberdieva R.A. Clinical and epidemiological manifestations of some natural focal vector-borne infections in Kazakhstan // Diss. Alma-Ata. – 2011. (in Russian)

18. Egemberdieva R.A., Ermukhanova N.T., Dmitrovskiy A.M., Shapieva Zh.Zh., Kyraubaev K.K., Lavrenyuk V.I. Epidemiological characteristics of some tick-borne vector-borne infections in Kazakhstan // Natsional'nye prioritety Rossii. – 2013. – Vol. 2. – P. 92–4. (in Russian)

19. Ostapchuk, Y. O., Perfilyeva, Y. V., Zhigailov, A. V., Maltseva, E. R., Neupokoyeva, A. S., Bissenbay, A. O., Berdygulova, Z. A., Naizabayeva, D. A., Nizkorodova, A. S., Shapiyeva, Z. Z., Yegemberdiyeva, R. A., Kuznetsova, T. V., Kuatbekova, S., Akanova, A., Ismagulova, G. A., Mamadaliyev, S. M., Dmitrovskiy, A. M., Skiba, Y. A. Monitoring of pathogenic *Borrelia burgdorferi* sensu lato in the Almaty oblast, Kazakhstan // Ticks and tick-borne diseases. – 2021. – Vol. 12, No 4. – P. 101725. https://doi.org/10.1016/j.ttbdis.2021.101725

20. Filippova, N.A. Ixodid Ticks of the Subfamily Ixodinae, Fauna of USSR // Nauka Publishing House, St. Petersburg. – 1997. – P. 393. (in Russian)

21. Bekshin Zh.M., Yesmagambetova A.S., Akhmetov V.N. Sanitary and Epidemiological Situation in the Republic of Kazakhstan in 2018 // Almaty. – 2019. – P. 111–8. (in Russian)

22. Head, J. R., Bumburidi, Y., Mirzabekova, G., Rakhimov, K., Dzhumankulov, M., Salyer, S. J., Knust, B., Berezovskiy, D., Kulatayeva, M., Zhetibaev, S., Shoemaker, T., Nicholson, W. L., Moffett, D. Risk Factors for and Seroprevalence of Tickborne Zoonotic Diseases among Livestock Owners, Kazakhstan // Emerging infectious diseases. – 2020. – Vol. 26, No 1. – P. 70–80. https://doi.org/10.3201/eid2601.190220

23. Ostapchuk, Y. O., Dmitrovskiy, A. M., Pak, E. A., Perfilyeva, Y. V. A Case of Combined Infection with Tick-Borne Encephalitis and Lyme Borreliosis with Severe Meningoencephalitis and Complete Recovery // Journal of global infectious diseases. – 2023. – Vol. 15, No 2. – P. 81–83. https://doi.org/10.4103/jgid.jgid_76_22

24. Jorge, L. M., Lupi, O., Hozannah, A. R., Bernardes Filho, F. Lyme disease in a Brazilian traveler who returned from Germany // Anais brasileiros de dermatologia. – 2017. – Vol. 92, No 1. – P. 148–149. https://doi.org/10.1590/abd1806-4841.20175584

25. Subedi, S., Dickeson, D. J., Branley, J. M. First report of Lyme neuroborreliosis in a returned Australian traveller // The Medical journal of Australia. – 2015. – Vol. 203, No 1. – P. 39–40. https://doi.org/10.5694/mja14.01592

26. Perfilyeva, Y. V., Shapiyeva, Z. Z., Ostapchuk, Y. O., Berdygulova, Z. A., Bissenbay, A. O., Kulemin, M. V., Ismagulova, G. A., Skiba, Y. A., Sayakova, Z. Z., Mamadaliyev, S. M., Maltseva, E. R., Dmitrovskiy, A. M. Tick-borne pathogens and their vectors in Kazakhstan - A review // Ticks and tick-borne diseases. – 2020. – Vol. 11, No 5. – P. 101498. https://doi.org/10.1016/j.ttbdis.2020.101498

27. Zhigailov, A. V., Neupokoyeva, A. S., Maltseva, E. R., Perfilyeva, Y. V., Bissenbay, A. O., Turebekov, N. A., Frey, S., Essbauer, S., Abdiyeva, K. S., Ostapchuk, Y. O., Berdygulova, Z. A., Aimbetov, R. S., Naizabayeva, D. A., Dmitrovskiy, A. M., Skiba, Y. A., Mamadaliyev, S. M. The prevalence of *Borrelia* in *Ixodes persulcatus* in southeastern Kazakhstan // Ticks and tick-borne diseases. – 2021. – Vol. 12, No4. – P. 101716. https://doi.org/10.1016/j.ttbdis.2021.101716

28. Donohoe, H., Pennington-Gray, L., Omodior, O. Lyme disease: Current issues, implications, and recommendations for tourism management // Tourism management. – 2015. – Vol. 46. – P. 408–418. https://doi.org/10.1016/j.tourman.2014.07.006

29. Hoeve-Bakker, B. J. A., van den Berg, O. E., Doppenberg, H. S., van der Klis, F. R. M., van den Wijngaard, C. C., Kluytmans, J. A. J. W., Thijsen, S. F. T., Kerkhof, K. Seroprevalence and Risk Factors of Lyme Borreliosis in The Netherlands: A Population-Based Cross-Sectional Study // Microorganisms. – 2023. – Vol. 11, No 4. – P. 1081. https://doi.org/10.3390/microorganisms11041081

30. Johansson, M., Manfredsson, L., Wistedt, A., Serrander, L., Tjernberg, I. Significant variations in the seroprevalence of C6 ELISA antibodies in a highly endemic area for Lyme borreliosis: evaluation of age, sex and seasonal differences // APMIS : acta pathologica, microbiologica, et immunologica Scandinavica. – 2017. – Vol. 125, No 5. – P. 476–481. https://doi.org/10.1111/apm.12664

31. Wilking, H., Fingerle, V., Klier, C., Thamm, M., Stark, K. Antibodies against *Borrelia burgdorferi* sensu lato among Adults, Germany, 2008-2011 // Emerging infectious diseases. – 2015. – Vol. 21, No 1. – P. 107–110. https://doi.org/10.3201/eid2101.140009

32. Dehnert, M., Fingerle, V., Klier, C., Talaska, T., Schlaud, M., Krause, G., Wilking, H., Poggensee, G. Seropositivity of Lyme borreliosis and associated risk factors: a population-based study in Children and Adolescents in Germany (KiGGS) // PloS one. – 2012. – Vol. 7, No 8. – P. e41321. https://doi.org/10.1371/journal.pone.0041321

REFERENCES

1. Steere, A. C., Strle, F., Wormser, G. P., Hu, L. T., Branda, J. A., Hovius, J. W., Li, X., Mead, P. S. Lyme borreliosis // Nature reviews. Disease primers. – 2016. – Vol. 2. – P. 16090. https://doi.org/10.1038/nrdp.2016.90

2. Ji, Z., Jian, M., Yue, P., Cao, W., Xu, X., Zhang, Y., Pan, Y., Yang, J., Chen, J., Liu, M., Fan, Y., Su, X., Wen, S., Kong, J., Li, B., Dong, Y., Zhou, G., Liu, A., Bao, F. Prevalence of *Borrelia burgdorferi* in Ixodidae Tick around Asia: A Systematic Review and Meta-Analysis // Pathogens (Basel, Switzerland). – 2022. – Vol. 11, No 2. – P. 143. https://doi.org/10.3390/pathogens11020143

3. Centers for Disease Control and Prevention (CDC). Lyme disease. Available online: https://www.cdc.gov/lyme/index.html. (accessed: 02.12.2023)

4. Schotthoefer, A. M., Green, C. B., Dempsey, G., Horn, E. J. The Spectrum of Erythema Migrans in Early Lyme Disease: Can We Improve Its Recognition? // Cureus. – 2022. – Vol. 14, No 10. – P. e30673. https://doi.org/10.7759/cureus.30673

5. Steere, A. C., Schoen, R. T., Taylor, E. The clinical evolution of Lyme arthritis // Annals of internal medicine. – 1987. – Vol. 107, No 5. – P. 725–731. https://doi.org/10.7326/0003-4819-107-5-725

6. Ogrinc, K., Lusa, L., Lotrič-Furlan, S., Bogovič, P., Stupica, D., Cerar, T., Ružić-Sabljić, E., Strle, F. Course and Outcome of Early European Lyme Neuroborreliosis (Bannwarth Syndrome): Clinical and Laboratory Findings // Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. – 2016. – Vol. 63, No 3. – P. 346–353. https://doi.org/10.1093/cid/ciw299

7. Centers for Disease Control and Prevention (CDC). Three sudden cardiac deaths associated with Lyme carditis - United States, November 2012-July 2013 // MMWR. Morbidity and mortality weekly report. – 2013. – Vol. 62, No 49. – P. 993–996.

8. Asbrink, E., Brehmer-Andersson, E., Hovmark, A. Acrodermatitis chronica atrophicans--a spirochetosis. Clinical and histopathological picture based on 32 patients; course and relationship to erythema chronicum migrans Afzelius // The American Journal of dermatopathology. – 1986. – Vol. 8, No 3. – P. 209–219. https://doi.org/10.1097/00000372-198606000-00005

9. Margos, G., Vollmer, S. A., Ogden, N. H., Fish, D. Population genetics, taxonomy, phylogeny and evolution of *Borrelia burgdorferi* sensu lato // Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases. – 2011. – Vol. 11, No 7. – P. 1545–1563. https://doi.org/10.1016/j.meegid.2011.07.022

10. Stanek, G., Strle, F. Lyme borreliosis-from tick bite to diagnosis and treatment // FEMS microbiology reviews. – 2018. – Vol. 42, No 3. – P. 233–258. https://doi.org/10.1093/femsre/fux047

11. Margos, G., Wilske, B., Sing, A., Hizo-Teufel, C., Cao, W. C., Chu, C., Scholz, H., Straubinger, R. K., Fingerle, V. *Borrelia bavariensis* sp. nov. is widely distributed in Europe and Asia // International journal of systematic and evolutionary microbiology. – 2013. – Vol. 63, No 11. – P. 4284–4288. https://doi.org/10.1099/ijs.0.052001-0

12. Stanek, G., Reiter, M. The expanding Lyme Borrelia complex--clinical significance of genomic species? // Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. – 2011. – Vol. 17, No 4. – P. 487–493. https://doi.org/10.1111/j.1469-0691.2011.03492.x

13. Fingerle, V., Schulte-Spechtel, U. C., Ruzic-Sabljic, E., Leonhard, S., Hofmann, H., Weber, K., Pfister, K., Strle, F., Wilske, B. Epidemiological aspects and molecular characterization of *Borrelia burgdorferi* s.l. from southern Germany with special respect to the new species *Borrelia spielmanii* sp. nov. // International journal of medical microbiology : IJMM. – 2008. – Vol. 298, No 3-4. – P. 279–290. https://doi.org/10.1016/j.ijmm.2007.05.002

14. Bissenbay A.O., Zhigailov A.V., Perfilyeva Y.V., Naizabayeva D.A., Neupokoyeva A.S., Berdygulova Z.A., Ostapchuk Y.O., Maltseva E.R., Kuatbekova S.A., Nizkorodova A.S., Dmitrovskiy A.M., Skiba Y.A., Mamadaliyev S.M. Epidemiology and molecular genetic characteristics of Lyme borreliosis pathogens circulating in tick's population in the Almaty oblast of the Republic of Kazakhstan // Journal of microbiology, epidemiology and immunobiology. – 2020. – Vol. 97, No 6. – P. 535-545. https://doi.org/10.36233/0372-9311-2020-97-6-4 (in Russian)

15. Cook M. J. Lyme borreliosis: a review of data on transmission time after tick attachment // International journal of general medicine. – 2014. – Vol. 8. – P. 1–8. https://doi.org/10.2147/IJGM.S73791

16. Egemberdieva R.A., Toksanbaeva K.N., Duĭsenova A.K., Ermukhanova N.T. Clinical manifestations of chronic forms tickborne borreliosis in the East Kazakhstan area // Vestnik Kazakhskogo natsional'nogo meditsinskogo universiteta. – 2013. – Vol. 2. – P. 89–92. (in Russian)

17. Egemberdieva R.A. Clinical and epidemiological manifestations of some natural focal vector-borne infections in Kazakhstan // Diss. Alma-Ata. – 2011. (in Russian)

18. Yegemberdieva R.A., Ermukhanova N.T., Dmitrovskiy A.M., Shapieva Zh.Zh., Kyraubaev K.K., Lavrenyuk V.I. Epidemiological characteristics of some tick-borne vector-borne infections in Kazakhstan // Natsional'nye prioritety Rossii. – 2013. – Vol. 2. – P. 92–4. (in Russian)

19. Ostapchuk, Y. O., Perfilyeva, Y. V., Zhigailov, A. V., Maltseva, E. R., Neupokoyeva, A. S., Bissenbay, A. O., Berdygulova, Z. A., Naizabayeva, D. A., Nizkorodova, A. S., Shapiyeva, Z. Z., Yegemberdiyeva, R. A., Kuznetsova, T. V., Kuatbekova, S., Akanova, A., Ismagulova, G. A., Mama-

daliyev, S. M., Dmitrovskiy, A. M., Skiba, Y. A. Monitoring of pathogenic *Borrelia burgdorferi* sensu lato in the Almaty oblast, Kazakhstan // Ticks and tick-borne diseases. – 2021. – Vol. 12, No 4. – P. 101725. https://doi.org/10.1016/j.ttbdis.2021.101725

20. Filippova, N.A. Ixodid Ticks of the Subfamily Ixodinae, Fauna of USSR // Nauka Publishing House, St. Petersburg. – 1997. – P. 393. (in Russian)

21. Bekshin Zh.M., Yesmagambetova A.S., Akhmetov V.N. Sanitary and Epidemiological Situation in the Republic of Kazakhstan in 2018 // Almaty. – 2019. – P. 111–8. (in Russian)

22. Head, J. R., Bumburidi, Y., Mirzabekova, G., Rakhimov, K., Dzhumankulov, M., Salyer, S. J., Knust, B., Berezovskiy, D., Kulatayeva, M., Zhetibaev, S., Shoemaker, T., Nicholson, W. L., Moffett, D. Risk Factors for and Seroprevalence of Tickborne Zoonotic Diseases among Livestock Owners, Kazakhstan // Emerging infectious diseases. – 2020. – Vol. 26, No 1. – P. 70–80. https://doi.org/10.3201/eid2601.190220

23. Ostapchuk, Y. O., Dmitrovskiy, A. M., Pak, E. A., Perfilyeva, Y. V. A Case of Combined Infection with Tick-Borne Encephalitis and Lyme Borreliosis with Severe Meningoencephalitis and Complete Recovery // Journal of global infectious diseases. – 2023. – Vol. 15, No 2. – P. 81–83. https://doi.org/10.4103/jgid.jgid_76_22

24. Jorge, L. M., Lupi, O., Hozannah, A. R., Bernardes Filho, F. Lyme disease in a Brazilian traveler who returned from Germany // Anais brasileiros de dermatologia. – 2017. – Vol. 92, No 1. – P. 148–149. https://doi.org/10.1590/abd1806-4841.20175584

25. Subedi, S., Dickeson, D. J., Branley, J. M. First report of Lyme neuroborreliosis in a returned Australian traveller // The Medical journal of Australia. – 2015. – Vol. 203, No 1. – P. 39–40. https://doi.org/10.5694/mja14.01592

26. Perfilyeva, Y. V., Shapiyeva, Z. Z., Ostapchuk, Y. O., Berdygulova, Z. A., Bissenbay, A. O., Kulemin, M. V., Ismagulova, G. A., Skiba, Y. A., Sayakova, Z. Z., Mamadaliyev, S. M., Maltseva, E. R., Dmitrovskiy, A. M. Tick-borne pathogens and their vectors in Kazakhstan - A review // Ticks and tick-borne diseases. – 2020. – Vol. 11, No 5. – P. 101498. https://doi.org/10.1016/j.ttbdis.2020.101498

27. Zhigailov, A. V., Neupokoyeva, A. S., Maltseva, E. R., Perfilyeva, Y. V., Bissenbay, A. O., Turebekov, N. A., Frey, S., Essbauer, S., Abdiyeva, K. S., Ostapchuk, Y. O., Berdygulova, Z. A., Aimbetov, R. S., Naizabayeva, D. A., Dmitrovskiy, A. M., Skiba, Y. A., Mamadaliyev, S. M. The prevalence of Borrelia in Ixodes persulcatus in southeastern Kazakhstan // Ticks and tick-borne diseases. – 2021. – Vol. 12, No4. – P. 101716. https://doi.org/10.1016/j.ttbdis.2021.101716

28. Donohoe, H., Pennington-Gray, L., Omodior, O. Lyme disease: Current issues, implications, and recommendations for tourism management // Tourism management. – 2015. – Vol. 46. – P. 408–418. https://doi.org/10.1016/j.tourman.2014.07.006

29. Hoeve-Bakker, B. J. A., van den Berg, O. E., Doppenberg, H. S., van der Klis, F. R. M., van den Wijngaard, C. C., Kluytmans, J. A. J. W., Thijsen, S. F. T., Kerkhof, K. Seroprevalence and Risk Factors of Lyme Borreliosis in The Netherlands: A Population-Based Cross-Sectional Study // Microorganisms. – 2023. – Vol. 11, No 4. – P. 1081. https://doi.org/10.3390/microorganisms11041081

30. Johansson, M., Manfredsson, L., Wistedt, A., Serrander, L., Tjernberg, I. Significant variations in the seroprevalence of C6 ELISA antibodies in a highly endemic area for Lyme borreliosis: evaluation of age, sex and seasonal differences // APMIS : acta pathologica, microbiologica, et immunologica Scandinavica. – 2017. – Vol. 125, No 5. – P. 476–481. https://doi.org/10.1111/apm.12664

31. Wilking, H., Fingerle, V., Klier, C., Thamm, M., Stark, K. Antibodies against *Borrelia burgdorferi* sensu lato among Adults, Germany, 2008-2011 // Emerging infectious diseases. – 2015. – Vol. 21, No 1. – P. 107–110. https://doi.org/10.3201/eid2101.140009

32. Dehnert, M., Fingerle, V., Klier, C., Talaska, T., Schlaud, M., Krause, G., Wilking, H., Poggensee, G. Seropositivity of Lyme borreliosis and associated risk factors: a population-based study in Children and Adolescents in Germany (KiGGS) // PloS one. – 2012. – Vol. 7, No 8. – P. e41321. https://doi.org/10.1371/journal.pone.0041321

СЕРОЛОГИЧЕСКОЕ ИССЛЕДОВАНИЕ ЛАЙМ-БОРРЕЛИОЗА В ЮЖНОМ РЕГИОНЕ КАЗАХСТАНА

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АННОТАЦИЯ

Лайм-боррелиоз (ЛБ) – инфекционное заболевание, вызываемое группой спирохет *Borrelia burgdorferi* sensu lato. Заражение происходит через укусы твердых клещей рода *Ixodes*. На территории южного Казахстана регистрируются случаи лихорадки неизвестной этиологии, однако распространённость ЛБ в этом регионе остается неизученной. Алматинская область признана эндемичной по ЛБ. Иксодовые клещи-переносчики обитают и в Жамбылской области, где ранее у жителей были выявлены антитела к возбудителю ЛБ, однако она считается неэндемичной. Туркестанская область также относится к неэндемичному региону. Целью данного исследование было изучение серопревалентности IgG антител к *B. burgdorferi* s.l. среди условно здоровых жителей г. Алматы, г. Тараз и г. Шымкент. Всего было собрано 465 образцов сыворотки крови людей с марта 2022 г. по сентябрь 2023 г. Методом ИФА было выявлено наличие IgG антител к *B. burgdorferi* s.l. у 5,4% всей исследуемой группы (24/465, 95% CI: 3,3-7,6%), а конкретно у 9,3% жителей г. Алматы (11/118, 95% CI: 4,7-16,1%, *p*=0.03), 4.5% – г. Тараз (11/242, 95% CI: 2,3-8,0%) и 1,9% – г. Шымкент (2/105, 95% CI: 0,2-6,7%). Результаты исследования подтверждают серопревалентность IgG антител к *B. burgdorferi* s.l. среди населения г. Алматы и Жамбылской области, а также впервые выявляют сероположительные образцы у жителей Туркестанской области, что позволяет предположить возможное заражение во время поездок в эндемичные регионы. Важно продолжать эпиднадзор за ЛБ в эндемичных и предполагаемых эндемичных регионах, а также повышать осведомленность об инфекции среди медицинских работников и широкой общественности в неэндемичных регионах.

Ключевые слова: Лайм-боррелиоз, *Borrelia burgdorferi* sensu lato, южный Казахстан, серопревалентность, ИФА.

ҚАЗАҚСТАННЫҢ ОҢТҮСТІК АЙМАҚЫНДАҒЫ ЛАЙМ-БОРРЕЛИОЗЫН СЕРОЛОГИЯЛЫҚ ЗЕРТТЕУ

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ТҮЙІН

Лайма боррелиозы (ЛБ) – *Borrelia burgdorferi* sensu lato спирохеталарының тобынан туындаған жұқпалы ауру. Инфекция *Ixodes* тектес қатты кенелердің шағуы арқылы болады. Оңтүстік Қазақстанда этиологиясы белгісіз қызба

жағдайлары тіркелген, бірақ бұл аймақта ЛБ таралуы әлі зерттелмеген. Алматы облысы ЛБ үшін эндемикалық болып танылған. Иксодид кене векторлары Жамбыл облысында да өмір сүреді, мұнда тұрғындар арасында ЛБ қоздырғышына антиденелер бұрын анықталған, бірақ ол эндемиялық емес болып саналады. Түркістан облысы да эндемиялық емес аймаққа жатады. Бұл зерттеудің мақсаты IgG антиденелерінің *B. burgdorferi* s.l. Алматы қ., Жамбыл облысының Тараз қ. және Түркістан облысының Шымкент қ. салыстырмалы түрде дені сау тұрғындары арасында. Екі мың жиырма екі жылдың наурызынан 2023 жылдың қыркүйегіне дейін барлығы 465 адам сарысуы сынамалары жиналды. ELISA әдісі *B. burgdorferi* s.l.-ге IgG антиденелерінің болуын анықтады. барлық зерттеу тобының 5,4% (24/465, 95% CI: 3,3-7,6%), ал нақтырақ айтсақ, Алматы қаласының тұрғындарының 9,3% (11/118, 95% CI: 4,7-16,1%, p=0,03), 4,5% – Тараз (11/242, 95% CI: 2,3-8,0%) және 1,9% – Шымкент (2/105, 95 % CI: 0,2-6,7%). Зерттеу нәтижелері Алматы қаласында және Жамбыл облысында ЛБ қоздырғышының таралуын растайды, сонымен қатар Түркістан облысының тұрғындарынан алғаш рет эндемиялық аймақтарға барған кезде жұқтыру мүмкіндігін көрсететін серопозитивті сынамаларды анықтайды. Эндемиялық және күдікті эндемиялық аймақтарда ЛБ мониторингін жалғастыру және эндемиялық емес аймақтардағы медицина қызметкерлері мен жалпы жұртшылық арасында инфекция туралы хабардарлықты арттыру маңызды.

Негізгі сөздер: Лайм-боррелиоз, *Borrelia burgdorferi* sensu lato, оңтүстік Қазақстан, серопревалеттілік, иммуноферменттік талдау.