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 LB are considered endemic in the southern region of Kazakhstan [1, 2], where it is estimated that 60-70% of the population of Almaty city and Jambyl oblast, and also reveal seropositive samples in residents of Turkistan oblast, the endemic areas.

**ABSTRACT**

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 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, 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. havigesi* [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 multiformal 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 diagnostics 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 Almaty oblast is not officially recognized as endemic for LB, ticks of the *Ixodes* spp. inhabit the region, and seropositive samples have been previously detected in residents [22]. Notably, in 2022, a case of Lyme neuroborreliosis and tick-borne encephalitis co-infection was identified in a patient from Jambly 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 or inaccurate diagnoses, untreated 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 (Jambly oblast), and Shymkent city (Turkistan oblast).

**MATERIALS AND METHODS**

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**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 (Jambly 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 performed according to the manufacturer’s instructions. Serum samples were collected.
The current research aimed to investigate the 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 (Turkmekent oblast). The study employed an enzyme-linked immunosorbent assay (ELISA) method, with the cut-off values of the Cutoff Calibrator being considered positive, values of test sera above OD 1.9 being considered negative, and those equal to OD 1.9 being considered questionable. 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 intervals (CI). The Fisher’s exact (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 proportion 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% (5/114, 95% CI: 2.3-8.6%) (Table 1).

In a prior study [19], the seroprevalence of 5.6% was identified in Almaty city. The higher seropositivity rate detected in 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 (Turkmekent oblast).

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

The average age of individuals with IgG seropositivity was 33.9 ± 12.2, compared to 34.5 ± 17.5 for seronegative donors. This analysis revealed no significant difference in seroprevalence across different age groups (Table 1). Nevertheless, there were no seropositive results observed in individuals aged 65 years and older. Although not statistically significant, a relatively higher seropositivity 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 mouthing of *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. are 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.

### 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 higher seropositivity rate in residents of Shymkent (Turkmekent oblast). Thus, our research provides new data on the LB incidence among residents of the southern region of Kazakhstan, underlining the imperative need for future LB-endemic areas.

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### LITERATURE

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Original Article

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СЕРОЛОГИЧЕСКОЕ ИССЛЕДОВАНИЕ ЛАЙМ-БОРРЕЛИОЗА В ЮЖНОМ РЕГИОНЕ КАЗАХСТАНА

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АННОТАЦИЯ

Лайма-боррелиоз (ЛБ) – инфекционное заболевание, вызываемое группой спирохет Borrelia burgdorferi sensu lato. Зарожение происходит через укусы твердых клещей рода Ixodes. на территории южного Казахстана регистрируются случаи лихорадки неизвестной этиологии, однако распространенность 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. Тюрукская область также относится к неэндемичному региону. Целью данного исследование было изучение серопревалентности IgG антител к Borrelia burgdorferi в Южном регионе Казахстана.

Ключевые слова: Лайма-боррелиоз, Borrelia burgdorferi sensu lato, южный Казахстан, серонегативность, ИФА.

КАЗАХСТАНСКИЙ АНТИСЕПТИЧЕСКИЙ НАЦИОНАЛЬНЫЙ ЦЕНТР МОЛЕКУЛЯРНОЙ БИОЛОГИИ И БИОХИМИИ ИМ. М.А. АЙТЖОХИНА, г. АЛМАТЫ

ТУВИЙ

Лайма боррелиоза (ЛБ) – Borrelia burgdorferi sensu lato спирохетария болезнь токсична якутская журавль вуру. Инфекция Ixodeś тексту кать эпидемия шамшы сары армавор болып. Офундит Казахстанда эпидемология белгісін қабылдайды.
жағдайлары тіркелген, бірақ бұл аймақта ЛБ таралуы әлі зерттелген. Иксодид кене векторлары Жамбыл облысында да өмір сүреді, мұнда тұрғындар арасында ЛБ қоздырғышына антиденелер бүрін анықталған, бірақ ол эндемиялық емес болып саналады. Туркістан облысы да эндемиялық емес аймаққа жатады. Бұл зерттеудің мақсаты IgG антиденелерінің B. burgdorferi s.l. Алматы к., Жамбыл облысының Тараз к. және Туркістан облысының Шымкент к. салыстырмалы түрде дені сау тұрғындары арасында. Екі мың жиырым 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% СI: 3,3-7,6%), ал нақтырақ айтсақ, Алматы каласының тұрғындарының 9,3% (11/118, 95% СI: 4,7-16,1%, p=0,03), 4,5% – Тараз (11/242, 95% СI: 2,3-8,0%) және 1,9% – Шымкент (2/105, 95 % СI: 0,2-6,7%). Зерттеу нәтижелері Алаты каласында және Жамбыл облысында ЛБ қоздырғышының таралуын растайды, сондай-ақ Түркістан облысының тұрғындарынан алғаш рет эндемиялық аймақтарға барған кезде жұқтыру мүмкіндігін корсетеді, серопозитивті сынамаларды анықтайды. Эндемиялық және күдікті эндемиялық аймақтарда ЛБ мониторингін жалғастыру әдісінен және эндемиялық емес аймақтардағы медицина қызметкерлері мен жалпы жұртшылық арасында инфекция туралы хабарлардың артықшылығы мен жаңа жұптыйрлық серологиялық қызметтерге әкімшілік, серопреваленттілік, иммуно-ферменттік талдау.

Herizti сөздер: Лайм-боррелиоз, Borrelia burgdorferi sensu lato, оңтүстік Қазақстан, серопреваленттілік, иммуно-ферменттік талдау.