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TICK-BORNE ENCEPHALITIS SURVEILLANCE IN KAZAKHSTAN, 2019-2021

Ulyana A. Kirpicheva[1], https://orcid.org/0000-0003-0428-113X

Zhanna Zh. Shapiyeva[1], https://orcid.org/0000-0002-7748-9436

Elmira S. Utegenova[1], https://orcid.org/0000-0003-2000-3404

[1] Scientific and Practical Centre for Sanitary-Epidemiological Expertise and Monitoring, the Branch of the National Center for Public Health, Ministry of Health, Republic of Kazakhstan, Almaty, Republic of Kazakhstan.

Abstract

Introduction. Tick-borne encephalitis is an urgent vector-borne disease, caused by Ixodidae ticks bites and consuming row goat and cow's milk infected with TBE virus. TBE incidence in Kazakhstan is cyclical, which is associated with the epidemic process and social factors affecting the foci of infection. The appearance of a new focus of infection is noted. Over the last 10 years the average long-term incidence rate amounted to 0.19 per 100000 people.

Methods. The purpose of this study was to describe and evaluate the existing surveillance system for TBE in Kazakhstan. We investigated TBE surveillance in Kazakhstan by studying the main documents of the system: official data on morbidity, case reports, guidelines and regulatory legal acts, annual reports of territorial Departments of sanitary and epidemiological control.

Results. The results of the study revealed some gaps, such as shortage or low qualification of personnel, the speed of information transfer between the levels of the system, the lack of a systematized electronic database, the low level of usage of statistical methods in the analysis and interpretation of the collected data.

Conclusion. Since the results of the study were revealed to public health makers, there was improvement of the TBE surveillance system. In last year studies have been actively conducted, forecasting of the epidemiological situation was performed, and recommendations for preventive measures were issued.

Key words: *Tick-borne encephalitis; Ixodid ticks; Public health surveillance; TBE.*

Резюме

НАДЗОР ЗА КЛЕЩЕВЫМ ЭНЦЕФАЛИТОМ В КАЗАХСТАНЕ ЗА 2019-2021 ГОДЫ

Ульяна А. Кирпичева[1], https://orcid.org/0000-0003-0428-113X

Жанна Ж. Шапиева[1], https://orcid.org/0000-0002-7748-9436

Эльмира С. Утегенова[1], https://orcid.org/0000-0003-2000-3404

[1] Научно-практический центр санитарно-эпидемиологической экспертизы и мониторинга, Филиал Национального центра общественного здоровья Министерства здравоохранения Республики Казахстан, г. Алматы, Республика Казахстан.

Введение. Клещевой энцефалит – актуальное для Казахстана острое трансмиссивное заболевание, вызываемое укусами иксодовых клещей и употреблением в пищу козьего и коровьего молока, зараженного вирусом клещевого энцефалита. В Казахстане заболеваемость носит циклический характер, что связано с эпидемическим процессом и социальными факторами, влияющими на очаги инфекции. Отмечается появление новых очагов инфекции. За последние 10 лет средний долгосрочный показатель заболеваемости составил 0.19 на 100 000 человек. Целью исследования было описать и оценить действующую систему эпиднадзора за клещевым энцефалитом в Республике Казахстан.

Методы. Мы описали систему эпиднадзора за клещевым энцефалитом в Республике Казахстан. При описании использовались основные документы системы: официальные данные о заболеваемости, отчеты о вероятных и подтвержденных случаях, нормативно-правовые акты, ежегодные отчеты территориальных департаментов санитарно-эпидемиологического контроля.

Результаты. Результаты исследования выявили некоторые пробелы, такие как нехватка или недостаточная подготовка специалистов в системе, низкая скорость передачи информации между уровнями системы, отсутствие систематизированной электронной базы данных, низкий уровень использования статистических методов при анализе и интерпретации собранных данных.

Заключение. С тех пор как результаты исследования были доведены до сведения органов общественного здравоохранения, система эпиднадзора была усовершенствована. В последний год активно проводятся исследования, осуществляется прогнозирование эпидемиологической ситуации, и выдаются рекомендации по профилактическим мерам.

Ключевые слова: *Клещевой энцефалит, Иксодовые клещи, Система эпиднадзора, ТВЕ.*

Түйіндеме

ҚАЗАҚСТАН РЕСПУБЛИКАСЫНДАҒЫ КЕНЕ ЭНЦЕФАЛИТІН ЭПИДЕМИОЛОГИЯЛЫҚ ҚАДАҒАЛАУ ЖҮЙЕСІ, 2019-2021 жж.

Ульяна А. Кирпичева[1], https://orcid.org/0000-0003-0428-113X

Жанна Ж. Шапиева[1], https://orcid.org/0000-0002-7748-9436

Эльмира С. Утегенова[1], https://orcid.org/0000-0003-2000-3404

[1] ҚР ДСМ «Қоғамдық денсаулық сақтау ұлттық орталығы» ШЖҚ РМК «Санитариялық-эпидемиологиялық сараптама және мониторинг ғылыми-практикалық орталығы» филиалы, Алматы қ., Қазақстан Республикасы.

Кіріспе. Кене энцефалиті - иксод кенелерінің шағуынан және кене энцефалиті вирусын жұқтырған ешкі мен сиыр сүтін тұтынудан туындайтын Қазақстан үшін өзекті жіті трансмиссивті ауру. Қазақстанда бұл аурудың циклдік сипаты болады, бұл эпидемиялық процеске және инфекция ошақтарына әсер ететін әлеуметтік факторларға байланысты. Инфекцияның жаңа ошақтарының пайда болуы байқалады. Соңғы 10 жылда сырқаттанушылықтың орташа ұзақ мерзімді көрсеткіші 100 000 адамға шаққанда 0.19 құрайды. Зерттеудің мақсаты Қазақстан Республикасындағы кене энцефалитін қадағалаудың қолданыстағы жүйесін сипаттау және бағалау болды.

Материалдар мен әдістер: Біз Қазақстандағы кене энцефалитін эпидқадағалау жүйесін сипаттадық. Біз жүйенің негізгі мына құжаттарын қолдандық: сырқаттанушылық туралы ресми деректер, ықтимал және расталған жағдайлар туралы есептер, нормативтік-құқықтық актілер, аумақтық санитариялық-эпидемиологиялық бақылау департаменттерінің жыл сайынғы есептері.

Нәтижелері: Зерттеу нәтижелері жүйеде мамандардың жетіспеушілігі немесе даярлығының жеткіліксіз болуы, жүйе деңгейлері арасында ақпараттың берілу жылдамдығының төмендігі, жүйеленген электрондық деректер базасының болмауы, жиналған деректерді талдау және интерпретациялау кезінде статистикалық әдістерді қолдану деңгейінің төмендігі сияқты кейбір олқылықтарды анықтады.

Қорытынды: Зерттеу нәтижелері қоғамдық денсаулық сақтау органдарына мәлімделгеннен бері эпидқадағалау жүйесі жетілдірілді. Кене энцефалитінің мониторингін бекіту туралы бұйрықтың жобасы жолданды, 2019–2021 жылдардағы расталған жағдайлар бойынша электрондық база құрылды. Соңғы жылы зерттеулер белсенді түрде жүргізіліп жатыр, эпидемиологиялық ахуалды болжау жүзеге асырылады және алдын алу шаралары бойынша ұсынымдар берілуде.

Түйінді сөздер: *Кене энцефалиті, Иксод кенелері, Эпидемиологиялық қадағалау жүйесі, ТВЕ.*

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INTRODUCTION

Tick-borne encephalitis (TBE) is a transmissible infectious disease resulting from the bite of ixodid ticks and from consuming raw goat and cow's milk infected with the TBE virus. TBE is common in forest and forest-steppe zones of temperate climates. The distribution area of the TBE virus covers a vast territory of the Eurasian continent, including Europe, Russia, Far East Asia, and Japan. About 10-12 thousand cases of TBE have registered annually in the world, but according to WHO data, the incidence may be significantly higher due to the sub-clinical course of cases in endemic areas [1-3, 6, 17, 23].

Over the last 10 years, 344 cases of TBE were registered in the Republic of Kazakhstan (hereinafter – Kazakhstan), including 3 deaths, with a maximum incidence rate of 0.27 per 100000 people in 2016 and a minimum of 0.13 per 100000 people in 2021. The average long-term incidence rate amounted to 0.19 per 100000 people. Annually 25-35 cases of TBE and 1-2 cases of mixed infection of TBE and Lyme disease are registered. TBE incidence in Kazakhstan is cyclical, which is associated with the epidemic process and social factors affecting the foci of infection [4-5, 10].

Ixodid tick species composition, virus incidence, abundance in nature, and cases of tick bites affect the level of incidence among the TBE population. The number of people exposed to tick bites coincides with the ixodid ticks' periods of activity in the foci (Figure 1). Annually the amount is up to 13 thousand people, of which 40-50% are children. Up to 70% of tick bites are registered in the East Kazakhstan and Almaty regions which are historically endemic [11, 14, 13, 24].

Recent studies indicate the spread of the TBE viral area and vectors beyond the endemic territories in Kazakhstan. There is registration of TBE cases in previously non-endemic territories: Akmola (since 2010), Kostanay (since 2015), and North Kazakhstan regions (since 2018) (Figure 2) [12, 15-16, 20-21].

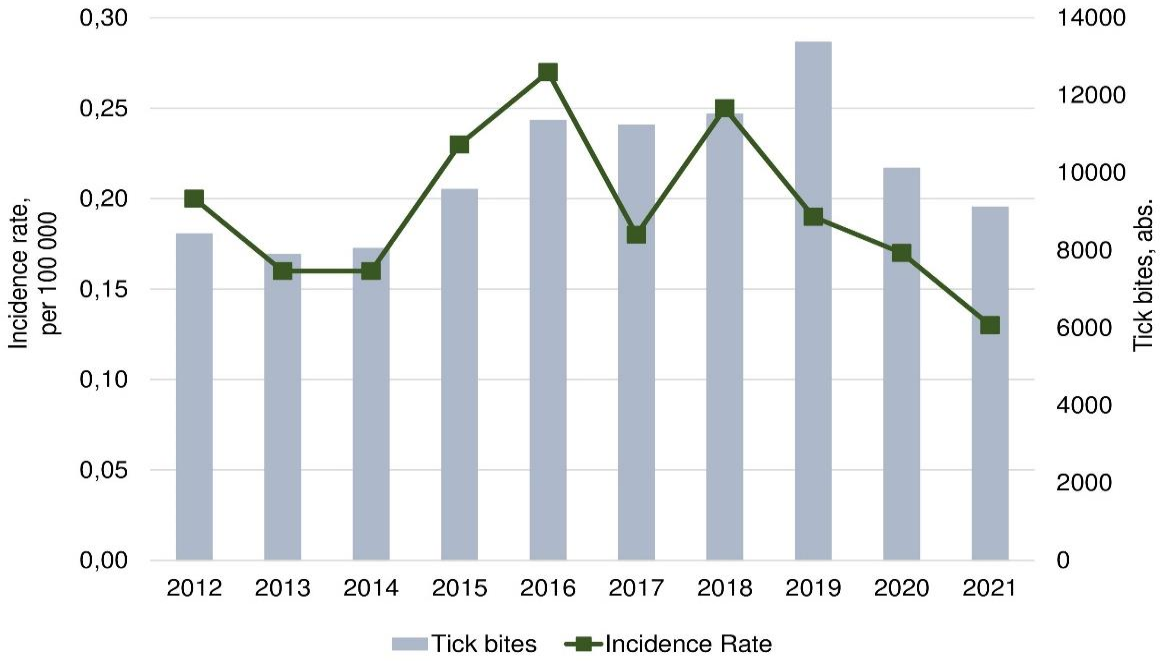


Figure 1. Tick-borne encephalitis incidence and people exposed to tick bites in an endemic area, Kazakhstan, 2012-2021.

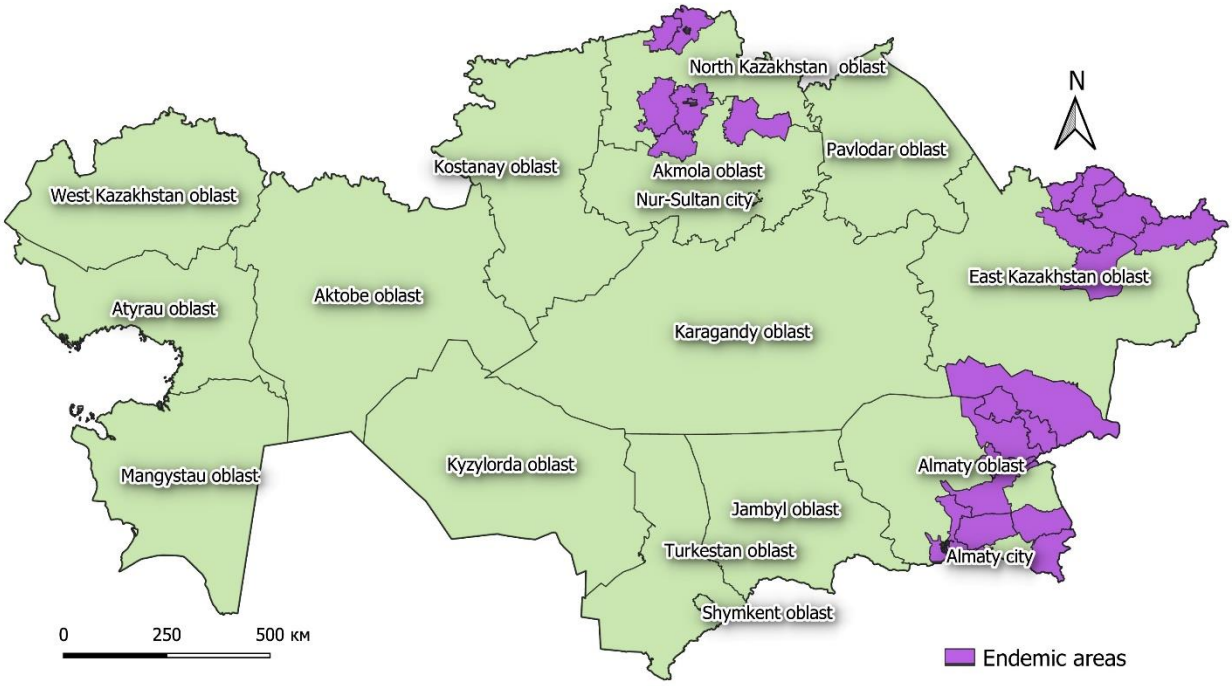


Figure 2 – Tick-borne encephalitis endemic area based on 2019-2021 morbidity data, Kazakhstan.

Based on the above, TBE is a concerning infection in Kazakhstan and is under epidemiological surveillance. The surveillance system in the country has changed significantly since 1991-1993, due to the widespread alignment and collection of data, usage of computer equipment, and modern technologies.

The main purpose of TBE surveillance is to study the spread and predict epizootic and epidemic manifestations in natural foci to implement control and preventive measures [8]. The entire population of endemic regions of the country is under supervision.

TBE cases are detected due to passive surveillance. The possible definition of a TBE case is not used. For the diagnosis of a probable TBE case corresponding clinical picture and epidemiological data is essential (bite and/or contact with a tick and/or visit an endemic region within 3-30 days before the symptoms). Healthcare worker (hereinafter – HCW) after making a preliminary diagnosis "Probable TBE case", enters

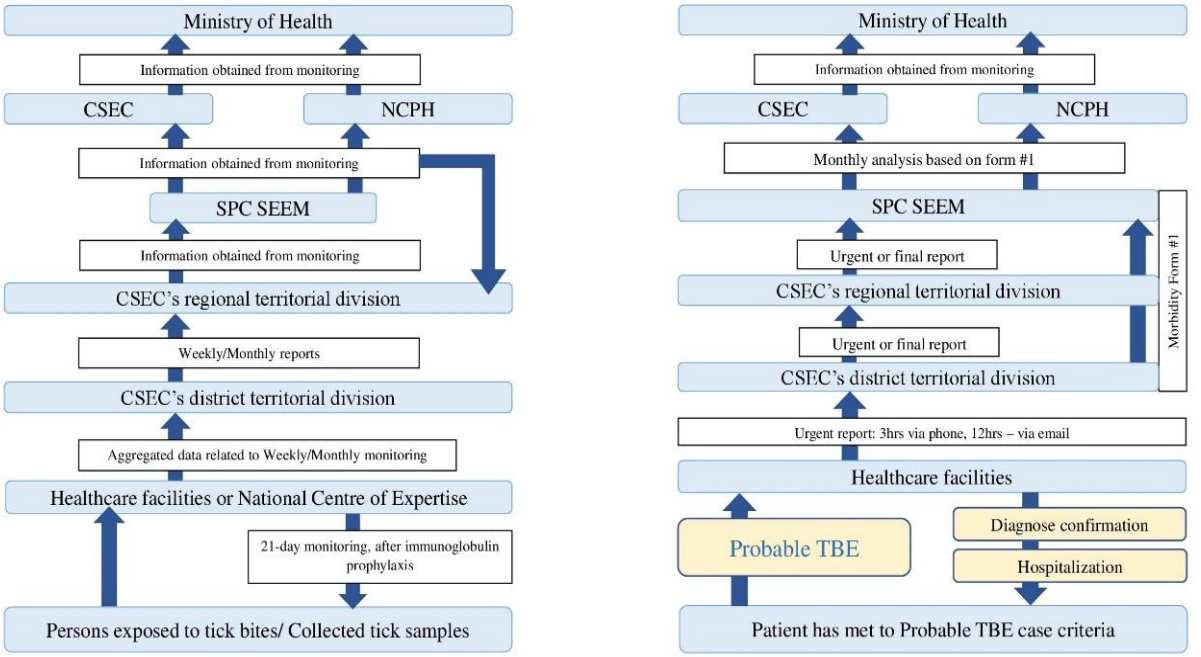
the patient's data into the medical system, and submits an emergency notification to the CSEC's district territorial division. Probable cases are required to undergo laboratory diagnostics to confirm or dismiss TBE [9].

CSEC district territorial division's specialists conduct an epidemiological investigation of each TBE case, followed by a completion examination form of infectious disease. They send an urgent and final report to the CSEC head department and SPC SEEM.

TBE is confirmed by positive laboratory results: detection of IgM antibodies to the TBE virus by ELISA in blood serum or cerebrospinal fluid; a fourfold or more increase in the IgG titer to the TBE virus; detection of the TBE virus RNA by PCR. Samples investigation is carried out in clinical diagnostic laboratories and CSEC's territorial laboratories of the "National Centre of Expertise" (hereinafter – NCE).

During the epidemic season, HCWs in endemic areas record people exposed to tick bites. Emergency prevention is carried out for persons who have reported tick bites in endemic areas, as well as in the case of a positive result of the tick for the TBE virus. Yearly data show 90% coverage of prophylactic immunoglobulin treatment in bitten individuals. Persons who do not receive immunoglobulin mostly are previously vaccinated, live in non-endemic territories, and/or have medical contraindications. There is also preventive immunization among persons living in natural foci, as well as decreed groups and people entering endemic territories.

To fulfill surveillance tasks during the epidemic season CSEC's territorial division and SPC SEEM conduct weekly and monthly monitoring. Due to weekly monitoring data are collected and analyzed on TBE cases, tick bites, and laboratory studies. Data is collected by demographic, epidemiological, clinical manifestation and preventive measures characteristics. Information is transmitted in aggregated form along the "vertical" line from the lower to upper departments of the surveillance system (Figure 3).



Notes: CSEC - Committee of Sanitary and Epidemiological Control of the Ministry of Healthcare of Kazakhstan, SPC SEEM - Scientific and Practical Centre of Sanitary Epidemiological Monitoring, NCPH - National Center of Public Health

Figure 3. Information steps in Tick-borne encephalitis surveillance system in Kazakhstan.

As part of surveillance monthly entomological monitoring is also carried out. The phenology and biology of ixodid ticks' observations and collection of ticks at stationary points in nature are carried out by CSEC's district territorial divisions and NCE laboratories' specialists. In 2012 to justify preventive measures introduced ticks collection from an exposed person. Collected ticks are examined to determine the species composition and tick virology rate. Aggregated data is sent to SPC SEEM monthly.

As part of TBE surveillance, CSEC's district territorial divisions provide data on extensive reporting forms on TBE epidemiology, clinical picture, diagnosis, entomological data, and anti-epidemic and acaricidal measures. SPC SEEM collects, analyses, interprets, and disseminates surveillance data at the national level. During supervision, a descriptive epidemiological analysis, assessment, and forecasting of the epidemiological situation are performed, and recommendations for preventive measures are issued.

The combination of socioeconomic and climatic factors, expansion of foci, and susceptible hosts actively contribute to the occurrence of TBE cases, while the natural focality of TBE creates conditions for the widespread of the disease in previously non-endemic areas. The latest published data confirm the increase in morbidity and the need for further scientific research, which is an important component of the surveillance system [28].

The purpose of this study was to describe and evaluate the existing TBE surveillance system in Kazakhstan.

Methods

We conducted an evaluation study of the TBE surveillance system in Kazakhstan following the Guidelines for Evaluating Surveillance Systems developed by the Centers for Disease Control and Prevention (hereinafter – CDC) in February-April 2022 [7].

We used 2019-2021 weekly, monthly, semi-annual, and annual reports, morbidity data, of the territorial division of the Committee of Sanitary and Epidemiological Control of the Ministry of Healthcare of Kazakhstan (hereinafter – CSEC) of the endemic area and the "Scientifical and Practical Center of Sanitary Epidemiological Monitoring", National Center of Public Health (hereinafter – SPC SEEM). We used the following normative legal acts: Order No. KR DSM-44 "Sanitary and epidemiological requirements for the organization and implementation of sanitary, anti-epidemic and preventive measures to prevent parasitic diseases", Order No. RK DSM-169/2020 "On approval of the rules for registration and investigation, record keeping and reporting of cases of infectious, parasitic diseases and (or) poisoning, adverse events after immunization", Order No. 623 "On approval of standards in areas of medical activity to identify cases of especially dangerous human infections during their registration", Order No. 9 "Clinical protocol for the diagnosis and treatment of tick-borne encephalitis". To obtain additional information, we consulted with territorial surveillance department officials.

Tests for statistical significance were not carried out. The description of the system was studied against the following attributes: simplicity, flexibility, timeliness, stability, and representativeness. Each attribute, depending on its completeness, was evaluated as good or bad.

Results

Simplicity

The TBE surveillance system in Kazakhstan is relatively complex. The usage of the TBE standard case definition is complicated by the nonspecific clinical manifestations, low alertness of medical workers both in endemic and high-potential prevalence areas, and lack of epidemiological connection to TBE foci. It is complicated to identify probable cases of tick-borne encephalitis.

The system has several reporting levels, and e-mail is used to transmit information. Data is stored locally at each level in excel format and aggregated by SPC SEEM. The Electronic Integrated Disease Surveillance System (hereinafter – EIDSS) is being implemented, but it is not currently used for TBE surveillance. In this regard, it is difficult to quickly transmit information from one to another level of the system due to absence of unified electronic database.

At the same time, there is an insufficient level of training for conducting operational and retrospective analysis using modern epidemiological methods at regional and district levels. While in shortage of parasitological and entomological specialists, their functions are performed by epidemiologists or sanitary doctors who do not have appropriate training.

Flexibility

Since TBE surveillance is fully coordinated and funded by the Ministry of Health (hereinafter - MH), all changes occur quickly and are fully implemented. In general, the TBE surveillance model is identical to other infectious disease surveillance and can be easily adapted for any health-related condition.

Data quality

Most of the information is fully provided in reports form. Specialists at different levels are well-trained in filling out the relevant forms. At the same time, there were isolated issues related to updates in data collection forms. As the analysis showed, there is no approved form for urgent reports. There was a lack of reliable information in CSEC's regional territorial divisions' urgent reports about TBE cases, such as place of tick exposure, date of onset of the symptoms, concomitant diseases, etc. Consequently, the lack of information in the reports affects the quality of the analysis.

Despite the approval of regulatory documents in the system, there have been cases of incorrect use of the standard case definition, including diagnosing a "Suspected case of tick-borne encephalitis".

Information exchange from one level of the system to another is carried out manually using paper and electronic resources. Collected information ensures the planning and adjustment of existing preventive and anti-epidemiological measures for TBE.

TBE surveillance data is used in planning preventive measures and in research projects of MH and other non-governmental organizations. MH managed to use the legal norms of the country and the penalties for non-submission and/or incomplete presentation of data to perform this task.

Representativeness

The surveillance system mainly covers the population of endemic territories of the country. TBE cases, due to the nonspecific symptoms, could be missed in non-endemic territories. Therefore, it cannot be said that the system is representative of the entire Kazakhstan population. Nevertheless, the data collection forms include demographic, epidemiological, clinical, and diagnostic data that can fully describe the affected population.

According to the 2019-2021 CSEC's regional territorial divisions' data, there was a decrease in confirmed cases (referred to as cases) of TBE: 2019 – 35 cases, 2020 – 31 cases, and 2021 – 24 cases. Similarly, during this period, there was a decrease in the number of people exposed to tick bites - from 13 to 9 thousand people.

Studies of ticks for virus transmission and determination of the species composition are carried out concerning ticks collected in nature by CSEC's district territorial divisions' specialists and NCE specialists. At the same time, determining species composition is non-systematic due to the lack of entomologists in the administrative territory. Studies for the detection of TBE virus antigen are carried out mostly using the ELISA method, to a lesser extent – PCR. In 2021, the number of PCR studies significantly increased compared to previous years up to 380 specimens collected in nature and 579 taken from exposed persons. The effectiveness of the studies conducted differs significantly in comparison to research methods and years *(Table 1)*. Determination of the species composition due to the 2019-2021 period was carried out only in the Almaty region. The species composition was represented by *Ix. persulcatus, D. marginatus, and D. reticulatus.* In other areas, species composition was not identified due to a lack of entomologists.

Table 1.

Ixodic ticks' investigation for TBE virus by ELISA and PCR methods, Kazakhstan, 2019-2021.

Year	ELISA						PCR					
	Ticks collected in nature			Ticks collected from exposed people			Ticks collected in nature			Ticks collected from exposed people		
	Total	Pos*	%	Total	Pos*	%	Total	Pos*	%	Total	Pos*	%
2019	1293	18	1,4%	454	73	16,1%	61	0	0%	62	5	8,1%
2020	7796	5	0,1%	437	4	0,9%	69	0	0%	28	3	10,7%
2021	7614	0	0%	720	32	4,4%	380	0	0%	579	5	0,9%

**Positive*

The main problem in carrying out entomological monitoring is providing the collection, species determination, and tracking by NCE laboratories' specialists, who mostly, do not have special entomology training. According to monthly data, the species' composition was not always determined. The latest phenological observation data for 2020–2021 show certain changes in the onset of the main TBE carriers, associated mainly with natural and climatic factors, which requires regular observations. However, due to the lack of entomological specialists, a potentially unfavorable situation is developing in terms of TBE incidence.

Timeliness

According to the 2019-2021 annual reports, 60% of TBE cases sought medical help 1-7 days after the onset of symptoms, third of cases sought medical help 8-10 days after the onset of symptoms. A few cases were referred to a month after the onset of symptoms. This is a consequence of the population's low alertness and the remoteness of people from medical organizations. The diagnosis of a "Confirmed case of tick-borne encephalitis" was made in 50% of cases three days after hospitalization, which indicates low alertness of HCW in identifying probable TBE cases.

In addition, during the 2019-2021 epidemic season, there were cases of delays in weekly and monthly reports from the CSEC's regional territorial divisions, which was due to the high load of specialists in implementing preventive measures against COVID-19.

Discussion

In general, we assessed TBE surveillance as a complex, flexible and acceptable system. The system detects cases among people and monitors people exposed to ticks' bites and vectors. Within surveillance, anti-epidemic and preventive measures are being implemented, data collection, interpretation, and dissemination are being carried out, and studies are being conducted. EIDSS is being implemented. However, there were some gaps.

During the assessment, we found an insufficient number of trained parasitologists and entomologists. Certain difficulties arose due to the multilevel nature of the system. When there is yet no integrated system for data entry and storage, there were delays in transferring data from one level to another, and there were differences in the transmitted data.

The nonspecific clinical manifestations and the subclinical course of TBE cases make it difficult to identify probable cases. In this regard, there may be omissions of TBE cases, especially in the high-potential prevalence areas. Registered mixed TBE and Lyme borreliosis cases indicate the combined circulation of pathogens and the necessity for mandatory confirmation of the diagnosis by molecular methods [18-19, 26-27].

Recent surveillance data for TBE in European countries noted a significant increase in incidence in the period 2020-2021. At the same time, the decrease in incidence and persons exposed to ticks' bites in Kazakhstan could be due to the influence of restrictive measures during the COVID-19 pandemic: decreased outings to nature and contact with TBE foci. There also was an increased burden on healthcare facilities (HCF), including laboratory services, when the alertness of medical, laboratory, and surveillance workers was directed against COVID-19 [22, 25].

Conclusion

Due to changing trends in the epidemic process, expansion of information resources, the emergence of new foci, and a combined circulation of tick infectious pathogens, there is a necessity for continuous improvement of the TBE surveillance system.

Special attention should be paid to strengthening the personnel potential of the surveillance system in terms of training at all levels of the system on TBE issues. It is also necessary to encourage the use of analytical epidemiology methods in the preparation of an annual report, as well as the use of geoinformation systems and interactive technologies to monitor the activity of foci of infection. The effectiveness and quality of the surveillance system are influenced by the involvement of epidemiological research institutes to conduct epidemiological seminars, conferences, and studies.

Since the results of the study were revealed to public health makers, there was improvement of the TBE surveillance system. Last year studies have been actively conducted to evaluate the risk factors and vectors of TBE in high-potential prevalence area in Kazakhstan. While surveillance forecasting of the epidemiological situation is performed, recommendations for preventive measures are issued.

As conclusion, we recommend further studying the surveillance system at the HCF and laboratory levels and expanding the active TBE surveillance in endemic and high-potential prevalence areas.

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Corresponding Author:
Kirpicheva Ulyana – (Epidemiologist) Scientific and Practical Centre for Sanitary-Epidemiological Expertise and Monitoring, the Branch of the National Center for Public Health, Ministry of Health, Republic of Kazakhstan, Almaty, Republic of Kazakhstan.
Mailing address: Republic of Kazakhstan, Abai region, Semey, str Pavlova 29/3 r 21.
E-mail: ulyana.9355@gmail.com
Mob.: ++7 771 648 29 58