







## Prediction of indicators about transboundary natural plague foci in the Balkhash-Alakol depression of Kazakhstan and the Dzungarian basin of China

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### ABSTRACT

The Kazakhstan-China territorial border has vast swathes (1782.75 km), where transboundary natural plague foci are located and where the "Great Silk Road" used to pass. This road played a major role in cultural, trade and economic ties between the countries of Europe, South-West and Central Asia and China, where the operation of the transport corridor "Western Europe - Western China" has been launched. A comprehensive assessment of the spatio-temporal characteristics of the plague foci in the Balkhash-Alakol depression of Kazakhstan compared to the transboundary plague foci in the Dzungarian basin (depression) has been carried out in China in order to identify and build a chain of predictors in the search for individual predictive informative features and their subsequent integration for the formation of target tasks. The paper presents data on the results of epizootological monitoring conducted in natural plague foci of Kazakhstan in the investigated region over the past 30 years, on an area of 124.9 thousand km<sup>2</sup>, and laboratory data on the results of phenotypic and molecular-genetic properties of more than 600 strains of plague bacterium isolated in this territory. A comparative analysis was carried out from the data obtained by Chinese scientists on the characteristics of *Yersinia pestis* strains that form natural plague foci in the Dzungarian Basin of China. Improvement and organization within epidemiological monitoring for plague, study, and determination of prognostic parameters in transboundary territories is crucial, given that on the level of that, the whole complex of preventive works for preserving epidemiological stability and biological safety would greatly depend.

**Key words:** Plague, *Yersinia pestis*, Plague foci, Balkhash-Alakol depression, Dzungarian basin, The Silk Road.

**Article type:** Research Article.

### INTRODUCTION

Humanity is constantly struggling with various biological threats, which include plague, a hazardous natural focal disease with a predominantly vector-borne mechanism of infection (Chernyavskaya 2020). It is known that the

plague microbe is an etiologic factor in the existence of natural foci of this infection, and not only the epizootic activity of foci but also the level of their epidemic potential depends on its characteristics. Natural foci, where the plague pathogen constantly circulates, occupy 6.0-7.0% of the land area of the globe (Anisimov *et al.* 2004) and are practically found on all continents (except Australia and Antarctica). Epidemiologic manifestations of plague in 2012-2021 were registered in the territory of 11 countries; the number of cases amounted to 5643, of which 768 were fatal (lethality rate: 13.6%). In 2022, 626 cases (18 fatal) were registered in four countries of the world. Epidemiologic unwellness from the plague was noted in the Democratic Republic of the Congo, Madagascar, the People's Republic of China, and Mongolia. In the Commonwealth of Independent States (CIS) countries, 45 natural plague foci with a total area of more than 2160.0 thousand km<sup>2</sup> have been identified, which are located in the plain (steppe, semi-desert, desert) and highland regions of Armenia, Azerbaijan, Kazakhstan, Kyrgyzstan, Russia, Tajikistan, Turkmenistan, and Uzbekistan (Popov *et al.* 2020; Popova & Kutuyev 2022). Kazakhstan has the most active and the largest natural plague foci in the CIS (more than 51.0%). The enzootic territory of Kazakhstan for plague distribution is currently divided into 7 natural and 15 autonomous foci, within which there are more than 100 landscape-epizootological regions, where plague epizootics with different intensity and localization occur constantly or with interepizootic periods of different duration (Aikimbayev *et al.* 2004; Atshabar *et al.* 2015). The last human plague case was registered in the Republic of Kazakhstan in 2003 (Atshabar *et al.* 2015). According to the analysis of indicators, regardless of the cases of the epidemic of plague within the last 115 years (1899-2005), cases of human diseases by plague infection on average amounted to - 18.1 % of epidemic years in Kazakhstan on registration of cases of human diseases by plague infection, including regions of the country: West Kazakhstan - 38.0 %, Kyzylorda - 32.6 %, Atyrau - 17.7 %, Mangystau - 7.9 %, Aktobe - 7.4 %, Almaty - 4.76 % of epidemic years. Taking into account the epizootic situation on plague (Aikimbayev *et al.* 2004), the state institutions of Kazakhstan annually perform the necessary volume of sanitary and preventive works, where the main activities are preventive vaccination of people and camels, village disinfection and derivatization, creation of sanitary protection zones by field disinfection around temporary and permanent settlements, sanitary-educational work and others, the volume and timeliness of which ensure the reduction of the risk of human infection. The study's purpose is to comprehensively assess the spatiotemporal characterization of the plague foci of the Balkhash-Alakol depression of Kazakhstan and the transboundary Dzungarian basin (depression) of China.

## MATERIALS AND METHODS

### Epizootological monitoring and collection of field material

The research was carried out according to generally accepted methods of epizootological monitoring (Stepanov *et al.* 1990; Smolensky *et al.* 2019) using modern tools of the GPS system and GIS technology. The experimental base of the study was the Shymkent Anti-Plague Station branch and the Central Reference Laboratory of the Masgut Aikimbayev's National Scientific Center for Especially Dangerous Infections of the Ministry of Health of the Republic of Kazakhstan (NSCEDI, MoH of the RK). Field and laboratory studies were carried out on the basis of the Resolution of the Chief State Sanitary Doctor of the Ministry of Health of the Republic of Kazakhstan "On carrying out sanitary and anti-epidemic and sanitary-preventive measures on the enzootic plague territory of the Republic of Kazakhstan for 2021-2025" No 8 from 26.02.2021, in accordance with Article 36 of the Code of the Republic of Kazakhstan "On public health and healthcare system", taking into account the requirements of the International Health Regulations (2005) in order to ensure epidemiological well-being for the plague on the territory of the Republic of Kazakhstan and approved by the Bioethics Committee of the NSCEDI of the MoH of the RK. The materials are based on accumulated long-term observations (2009-2022) in the process of epizootological examination within the Turkestan region (Sozak district) and Ulytau region (Ulytau district) of Kazakhstan. The survey area in the South passed along the Shu River; in the North, it passed to the Zhideli sands. The length was about 300 km. In the West, the border was the Sarysu River, and in the East, the survey area reached the border with the Zhambyl region of Kazakhstan, about 200 km from West to East. The survey area was more than 50.0 thousand km<sup>2</sup>. 36203 mammals and 486 173 ectoparasites were studied during the analyzed period (total – 522 376 samples).

### Study of the properties of isolated strains

To study phenotypic and molecular genetic studies (PCR) of this, 49 strains of *Yersinia pestis* were used, isolated from the Betpakdala autonomous plague focus of Kazakhstan obtained from the depository and museum of living cultures of the NSCEDI. All manipulations with *Y. pestis* strains were carried out in accordance with biological

safety standards (Nekrasova *et al.* 2012) and techniques for working with pathogens (Nekrasova *et al.* 2001). DNA extraction of the *Y. pestis* strains was carried out using the QIAamp DNA Mini Kit (Qiagen, USA; Halos *et al.* 2004; Billeter *et al.* 2011). Genotyping of *Y. pestis* was carried out using whole genome sequencing. According to the manufacturer's instructions, DNA sample preparation was performed using the Nextera XT DNA Library Preparation Kit (catalog number FC-131-1024). Sequencing was performed on a high-performance MiSeq sequencer, Illumina platform, and a set of chemical reagents MiSeq Reagent Kit v3, 600 Cycles (catalog number: MS-102-3003) according to the manufacturer's instructions.

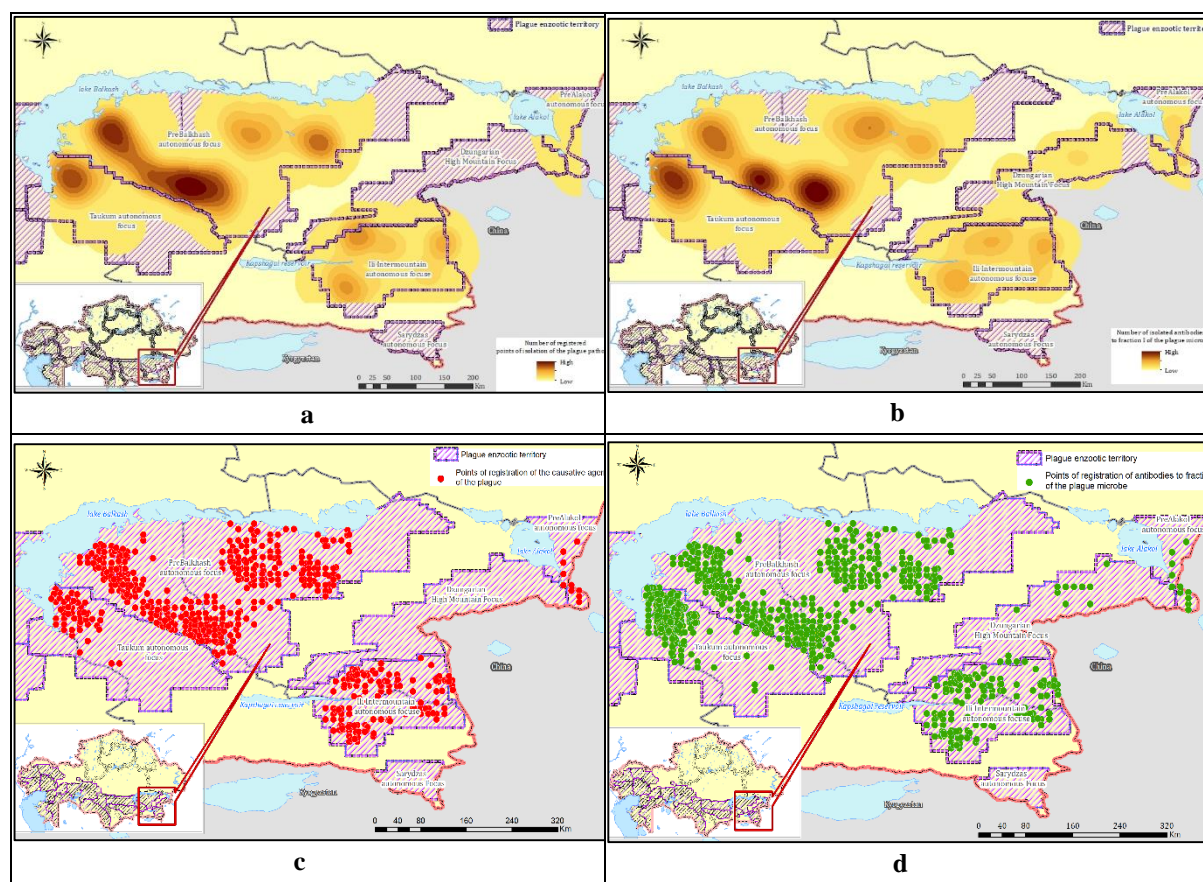
### Research quality control

Quality control was ensured by testing control strains deposited in the museum of living cultures of the NSCEDI: reference strains of *Y. pestis* from various autonomous foci of Kazakhstan, *Y. pestis* EV strain, *Y. pseudotuberculosis* strain, and fragments of loci of four well-studied strains representing the main biovars of the plague microbe were used as reference samples: Pestoides F (biovar Microtus/Antiqua), Nepal516 (biovar Antiqua), KIM10+ (biovar Mediaevalis) and CO92 (biovar Orientalis).

## RESULTS

The characterized area of the territory - Balkhash-Alakol depression (synonyms: hollow, plain, basin, lowland), is located in Southeastern Kazakhstan on the territory of two regions of Almaty (now divided into two regions - Zhetysu and Almaty and part of East Kazakhstan (Wikipedia 2022a), the approximate area (S) of which constitutes 240.0 thousand km<sup>2</sup>. The Balkhash-Alakol Depression (hereinafter - BAD) is a flat closed depression in Southeastern Kazakhstan, at 342-600 m above sea level. Total area: length 800 km, width 100-300 km. Most of the depression is occupied by Lake Balkhash, Sasykkol, and Alakol (Wikipedia 2022b). The water network is represented by rivers: Ili, Karatal, Aksu, Lepsy, Ayaguz, Urjar, Katynsu, Emel, Yrgaiti, Zhamanty, and Tentek. A certain part is occupied by sand massifs: Saryesik Atyrau, Taukum, Moyinkum, Lekkum, Zhamanzhal, Irishar, Zhamankum, Taskarakum, Sarytauikum (PaleoKazakhstan.info 2022). The territory of BAD includes the Pribalkhash (74900 km<sup>2</sup>), Ili intermountain (23900 km<sup>2</sup>), Taukum (21800 km<sup>2</sup>), Prialakol (2850 km<sup>2</sup>) autonomous foci of the Central Asian desert foci, which border the Jungar (20.1 km<sup>2</sup>) and Saryjaz (1400 km<sup>2</sup>) high-mountain plague foci of Kazakhstan. The results of epizootological (laboratory studies) surveys for the last 30 years (1990-2020) are shown in Fig. 1, where plague epizootics with different intensities and localization run continuously or with interepizootic periods of different duration. The territory of desert plague foci of BAD has a typical desert appearance by a number of landscape-geographical characteristics (climate, soils, vegetation). The climate of BAD is sharply continental with low precipitation (135-200 mm per year), with the average annual temperature: January -12-14 °C, and July +22-24 °C. Winters are cold and snowy, while summers are hot and sultry. Vegetation is peculiar to desert: saxaul, juzgun, teresken, wormwood, saltwort, etc. Soils are brown desert-steppe soils, low-carbonate gray soils, and solonchaks. Overweighed sands form semifixed ridges (up to 30 m high) with thickets of saxaul, teresken, dzhuzgun and sparse wormwood as well as saltwort vegetation on brown desert-steppe and low-carbonate sierozems (Wikipedia 2022b; PaleoKazakhstan.info 2022). The large territory and diversity of landscapes provide an opportunity for a wide range of wildlife species. The most diverse in terms of species composition is the rodent group. The biodiversity of terrestrial vertebrates includes about 50 species of mammals. Thirteen species of mammals have been recorded in the area, which participated in the plague epizootic among wild animals. Of these, 95% of the isolated plague strains are attributable to the Greater Sandpiper (GS), which, in terms of breadth of distribution and number of individuals, occupies a central place in the desert biocenosis and is the main carrier of plague. According to the results of epizootologic surveys of sandy plague foci, the share of detected infected territory was: in Pribalkhash - 47.2 %, in Ili intermountainous - 34.6 %, in Taukum - 16.4 %, and in Prialakol - 1.8 % (Atshabar *et al.* 2015). Table 1 gives characteristics of the main carrier, vectors, subspecies, and biovars of *Y. pestis*, biochemical activity, phylogenetic affiliation, virulence, and epidemic significance related to natural foci of BAD of Kazakhstan. In this area, the Greater Sandpiper (GS) practically inhabits all desert and transitional desert-semidesert areas of the locality, forming huge, diffuse settlements. The most important feature of GS distribution in the hearth is the existence of relatively isolated settlements. The main barriers to the exchange of species between settlements are geographical barriers. There are ten independent GS populations: Taukum, Saryesik-Atyrau, Lyukkum, Aralkum, Lepsy-Aguz, Dzungar, Prialatynemel, Karakum, Syugatinsk and Karadalinsk. In the last 10-18 years, there has been an active expansion of the main host in the northeastern direction with the development of new territories. The average annual fall abundance of the main

carrier in the focus is 847 species per km<sup>2</sup>, ranging from 43 to 1280 years. The density of their burrows is 100-480 per km<sup>2</sup>, and their habitability is 10.0-75.0 %. During the period of deep depression (1980-1983), GS practically disappeared over a vast territory, and the population was preserved in parcellar groups (Atshabar *et al.* 2015).



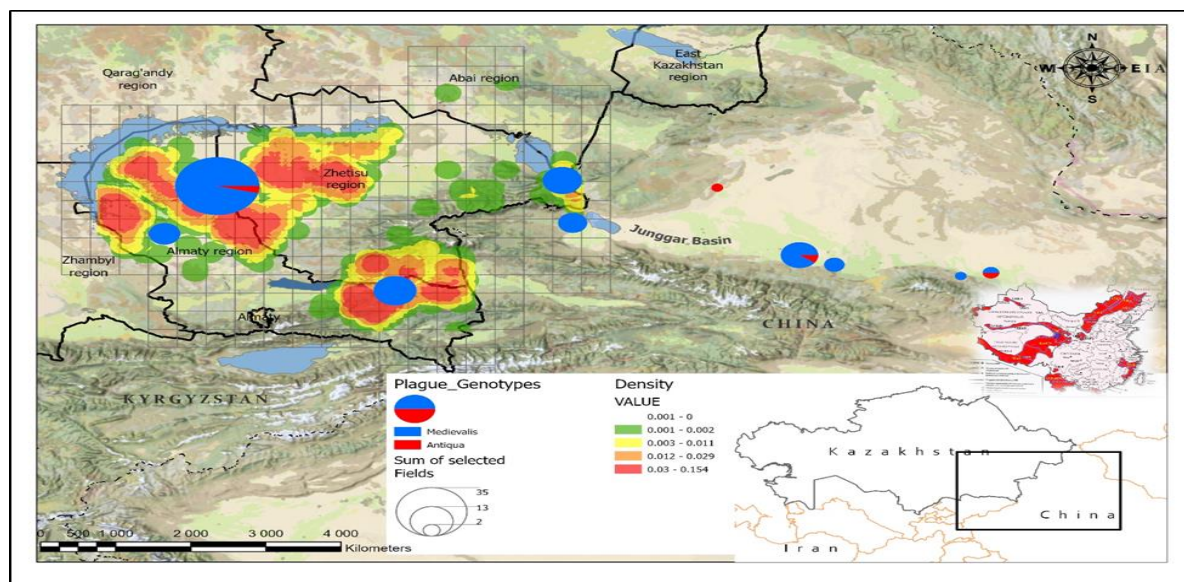
**Fig. 1.** Results of epidemiological surveys to isolate strains and identify seropositive animals for plague in natural plague foci in the Balkhash-Alakol lowland of Kazakhstan over the past 31 years (1990–2020). Subfigures: a – density according to the isolation of *Y. pestis* cultures; b – density for the detection of seropositive animals for plague; c – places of isolation of cultures of *Y. pestis*; d – places of detection of seropositive animals for plague.

By analyzing materials of long-term investigations (1990–2020) on the recurrence of epizootics for 30 years in the context of primary sectors, we have found the existence of small structural elements and nuclei of epizootics in the plague foci of the Balkhash-Alakol depression (BAD) of Kazakhstan (Fig. 2). By superimposing the places of the existence of enzootic nuclei on hydrogeological and geomorphological maps of the Ili-Karatal interfluvium, the confinement of plague pathogen reservation sites to relief features with alluvial and diluvial-pluvial deposits was established. This hypothesis about the confinement of plague pathogen reservation sites is confirmed by scientists such as V.I. Sapozhnikov (2001), O.S. Serzhanov *et al.* (1982, 1978). Notably, such soil-edaphic indicators create favorable conditions for a full annual cycle of fleas than in aeolian sands with monotonous relief. For this reason, ephemeral epizooty occurs on the latter for one or two seasons in each epizootic cycle (Xueqin *et al.* 2003). In desert plague foci, the main vectors are fleas of the great Sandpiper belonging to the genus *Xenopsylla* (Medvedev *et al.* 2023). Thus, in the sands of Saryishik-Atyrau *X. skrjabini* dominates, and within the Ili ancient delta *X. gerbilli minax*. The total abundance of fleas of the genus *Xenopsylla* ranges from 580–170690 specimens per km<sup>2</sup> (average 43412; Atshabar *et al.* 2015). As a result of long-term analysis, 30.0 % of strains of the plague pathogen were isolated from mammals and 70.0% from ectoparasites.

The plague pathogen is an etiologic factor in the existence of natural foci of this infection and its characteristics determine not only the epizootic activity of foci, but also the level of epidemic potential (Atshabar *et al.* 2015). Over the period 2011–2020, we studied phenotypic and molecular genetic properties of more than 647 strains of plague microbe circulating in BAD plague foci of Kazakhstan (Table 2).

**Table 1.** Characteristics of the main carrier, main vectors, subspecies, and biovars of *Y. pestis*, biochemical activity, phylogenetic branch, virulence, and epidemic significance related to natural foci of the Balkhash-Alakol depression of Kazakhstan.

Natural focus, type of the focus	Main carrier	Main vectors	The main properties of the causative agent of the plague		
			Subspecies, biovar, phylogenetic branch	Biochemical signs of the pathogen	Virulence, epidemic significance
Balkhash, Ili intermountain, Taukum, Prialakol deserts gerbils	<i>Rhombomys opimus</i> , <i>Meriones meridianus</i> , <i>M. tamariscinus</i> , <i>M. erythrorus</i>	Fleas of the genus <i>Xenopsylla</i> ( <i>X. gerbilli minax</i> , <i>X. hirtipes</i> , <i>X. Sckrjabini etc.</i> ), <i>Echidnophaga</i> , <i>Coptopsylla</i> , <i>Ceratopsyllus</i> , <i>Paradoxopsyllus</i> , <i>Ctenophthalmus</i>	Main subspecies, medieval biovar 2.MED1	Does not ferment rhamnose, do not recover nitrates, fermentes arabinose and glycerin	Virulent, epidemically significant
Sarydzhas highmountain, marmot	<i>Marmota baibacina</i>	<i>O. silantiewi</i> & <i>R. li ventricosa</i> .	Main subspecies, antique biovar 0. ANT5	Does not ferment rhamnose, do not recover nitrates, fermentes arabinose and glycerin	Virulent, epidemically significant
Dzhongar highmountain, mixed	<i>Microtus arvalis</i> , <i>Myodes</i> , <i>Apodemus uralensis</i> , <i>Spermophilus erythrogenus</i> , <i>Urocitellus undulatus</i> , <i>M. baibacina</i>	<i>Citellophyllus tesquorum</i> , <i>Ct. arvalis</i> , <i>C. ullus</i> , <i>Ct. assimilis</i> , <i>Fr. alata</i> , <i>O. silantiewi</i> .	Not detected	–	–



**Fig. 2.** Frequency of detection of seropositive animals and strains of *Y. pestis*, indicating the number of identified biovars circulating in natural plague foci of the Balkhash-Alakol lowland (basin) of Kazakhstan for the period of 1990-2020.

Most isolated strains are typical for the representatives of the Central Asian desert foci regarding cultural, morphological, and biochemical properties (Fatima *et al.* 2019). The strains are sensitive to plague and pseudotuberculosis phages and ferment glycerol, maltose, glucose, arabinose, and mannitol with acid formation without gas; they do not ferment lactose and rhamnose. Cultures cannot reduce nitrate to nitrite. They produce pesticin I, but are not sensitive to it. The strains are susceptible to levomycetin, streptomycin, doxycycline, gentamicin, and tetracycline (Kiljunen *et al.* 2011). The strains are pigment-sorbing on Jackson-Burrows medium with hemin (psb+); the number of psb+ cells in different strains ranges from 92.0 to 100.0 %. The population of

freshly isolated cultures is dominated by calcium-dependent (Ca-) cells with negligible calcium-independent (Ca+) cells. Most strains grow on a basic medium supplemented with methionine, phenylalanine, threonine, and cysteine.

**Table 2.** Results of laboratory studies of *Yersinia pestis* strains isolated from natural plague foci of Kazakhstan on the territory of the Balkhash-Alakol lowland and transboundary high-mountain foci for the period of 2011-2020.

Name of the autonomous plague center (NAPC)	Total strains (%)	Of these by phenotypic properties (%)		Of these by molecular genotypic properties (%)	
		Typical	Atypical	Typical	Atypical
Pribalkhash	49.8	85.7	14.3	93.7	6.3
Ili intermountain	29.9	96.4	3.6	100.0	–
Taukum	16.8	97.2	2.8	100.0	–
Prialakol	1.7	100.0	–	100.0	–
Sarydzhaz highmountain	1.8	100.0	–	100.0	–
Dzhongar highmountain	–	–	–	–	–
Total (in %)	100	91.3	8.7	96.9	3.1

At the same time, over the years of the survey, cultures that were atypical in some properties were identified. In the Pribalkhash autonomous foci, strains with reduced ability to synthesize fraction 1, dependent on arginine and tryptophan, unable to degrade maltose and mannitol, not fermenting glycerol, with reduced virulence for laboratory animals and altered sensitivity to antibiotics are found. The most frequent changes in typical properties are observed in strains isolated in Bakanassky ancient Dedelt Plain and in the sands of Saryishik-Atyrau. Detection of strains with altered properties is mostly independent of the phase of the epizootic process. A selective study of more than 60 strains of plague microbe isolated in 2002 using molecular diagnostic methods showed that 82.0% of strains had all three plasmids (110, 70, 9.5 kb) characteristic of plague microbe. Meanwhile, 17.9% of strains did not have any of these plasmids. When polymerase chain reaction was used to search for several genes (F1, Rep, Pst), all three genes were observed in all examined strains. The Balkhash-Alakol basin has significant recreational and tourist potential, which is based on natural and cultural-historical attractions and plague epidemic potential. The population constitutes - 2,077,656 people. Population density on average (per 1 km<sup>2</sup> of territory) is 7.1 people. The region's administrative center until April 2001 was Alma-Ata, and now it is a city of republican significance with a population of 2,147,113 people (2022) and a density of 2899 people/km<sup>2</sup>. In agricultural lands, the predominant position is occupied by pasture lands, which total 24072,76 thousand hectares, or 90.5 % of all lands. The main part of agricultural land is designated for agricultural plots and farms. The rural population is dispersed in 987 settlements with a population of 100 to 5,000 or more people, with a prevalence (about 40%) of settlements having a population of more than 1,000. Noteworthy, the epidemic potential for plague includes the presence of camels kept in a plague-enzootic area. Camels occupy a special place in plague epidemiology. The diversity of camel use and the considerable population of camels result in close contact with them by people engaged in agriculture (Abdeliev *et al.* 2022). Historically, epidemic complications caused by diseased and dead camels in Kazakhstan caused maximum threat to human life and were associated with huge economic expenses. There are 9471 camels in the natural foci of BAD plague, distributed in 19 districts and 99 rural districts and settlements. Notably, if in 2012, the total number of camels in our country amounted to 164.8 thousand heads, by the end of 2022, there will be 254.6 thousand heads. For the last 11 years, there has been an increase in the number of camels by 89.8 thousand heads, which indicates the possibility of camel breeding in Kazakhstan as one of the promising components of the livestock sector of agriculture. At present, the anti-plague stations, sanitary-epidemiological service organizations, and medical and preventive organizations of Kazakhstan carry out constant epidemiological monitoring and protective measures for especially dangerous infections, including regular epizootological monitoring in plague focal areas to prevent outbreaks of plague infection among people and camels.

## DISCUSSION

In 2018, Chinese scientists published a detailed article on phenotypic and molecular genetic characteristics of *Yersinia pestis* strains forming natural plague foci of the Dzungarian Basin in China (Zhang *et al.* 2018), transboundary with BAD natural plague foci. According to the data published by Zhang *et al.* in 2005-2006, 25 strains of *Y. pestis* were isolated in 6 counties of the Dzungarian Basin in the territories of two natural foci, the

Dzungarian sandy focus ( $S = 160.0$  thousand  $\text{km}^2$ ) and the Tien Shan natural focus ( $S = 47.4$  thousand  $\text{km}^2$ ), where their phenotypic, virulent and molecular genetic properties (MLVA and CRISPR typing) were studied (Zhang *et al.* 2018). Researchers in China found that *Y. pestis* strains of the Medievalis biovar 2.MED1 genovariant circulates in sandy areas, while the Antiqua biovar strains belong to the phylogenetic branches of 0.ANT1 and 0.ANT3 circulates in mountainous areas (Zhang *et al.* 2018). The connecting link of the analyzed plague foci is the Dzungarian Gate - which connects the Balkhash-Alakol Depression of Kazakhstan and the Jungar Plain of China; through these gates passed the "Great Silk Road" (Wikipedia 2022c). This road played a major role in developing economic and cultural ties between the peoples of the Caucasus, West Asia, Central Asia, and China. For instance, it served as a conductor for the spread of technology and innovation, including art, religion, and technology (Wikipedia 2022d). In 2008, Russia and Kazakhstan signed a memorandum on developing the transport corridor "Western Europe - Western China", where this international transport and trade and economic corridor China - Kazakhstan is already functioning (Wikipedia 2022e). The State border between Kazakhstan and China is 1,782.75 km long. The border between Kazakhstan and China contains two checkpoints - Khorgos and Dostyk. In 2012, the Government of the Republic of Kazakhstan and the Government of the People's Republic of China agreed on checkpoints across the Kazakhstan-China state border (Resolution of the Government of the Republic of Kazakhstan dated June 5, 2012 No. 750), which function permanently and currently, in order to further strengthen and develop friendly relations between the two countries and the traditional friendship of the two nations, to stimulate bilateral trade and economic cooperation, based on the principles of equality and mutual benefit. According to the above-mentioned agreement (paragraph 1 of art. 5) in the event of a threat to national security, public order or the danger of the spread of quarantine and infectious diseases of humans, animal diseases included in the list of the Office International des Epizooties (OIE) (now – The World Organization for Animal Health), or quarantine pests and plant diseases, agreed upon by a separate bilateral international treaty, one of the parties may temporarily close checkpoints, delay their opening or restrict access through checkpoints, notifying the other party through diplomatic channels 5 days before taking appropriate measures (in an emergency, do not in less than 24 hours). Studying the phenotypic and molecular genetic properties of *Y. pestis*, the bacterium that causes plague, presents many challenges. These include sample collection and preservation, biosafety, strain variability, a wide range of genetic variations, the cost of research, and more. Despite these challenges, technological advances have led to significant progress in studying *Y. pestis* in recent years, and research continues to be relevant. The study of phenotypic properties and variability of the plague microbe has been validated by numerous scientific studies (Serzhanov *et al.* 1982). Phenotypic studies of plague microbe strains from the Balkhash-Alakol Basin have shown that *Y. pestis* has different characteristics, such as growth patterns, colony morphology, and resistance. *Y. pestis* has various characteristics, such as growth patterns, colony morphology, antibiotic resistance, and virulence factors, which are crucial for understanding its biology and pathogenesis. Variability in the phenotypic properties of *Y. pestis* has been observed among different strains, which may affect its virulence and transmission potential. This variability may be related to genetic diversity or environmental factors, and it is important to understand how it affects the spread and severity of disease outbreaks (Serzhanov *et al.* 1978). In addition, phenotypic studies have also shown that *Y. pestis* can adapt to different host environments, which is important for understanding its survival strategies and virulence. Molecular genetic studies have provided a better understanding of the structure and organization of the genome of *Y. pestis*, leading to a better understanding of its evolution, virulence mechanisms, and the molecular basis of antibiotic resistance. In addition, molecular techniques have identified specific *Y. pestis* markers critical for diagnosing and monitoring plague outbreaks. The study of phenotypic and molecular genetic properties of *Y. pestis* is crucial for understanding the biology of the plague microbe and developing strategies to control and prevent plague outbreaks, epidemics, and pandemics in general. During the observation period, spatial and biocenotic variability of the geographical landscape structure of the study area was observed. We considered cause-and-effect relationships of such phenomena as changes in the population structure of the parasitic system of the plague microbe, peculiarities of distribution and dynamics of plague morbidity among wild animals, as well as the influence of climatic and anthropogenic factors on the epizootic process in natural foci of plague BAD.

## CONCLUSION

Comparative analysis of the two transboundary plague foci showed the identity of the desert and highland foci in terms of landscape-geographical, epizootic, and epidemic indicators, including the circulation of plague microbe

strains with the same phenotypic and molecular-genetic properties. If in the desert plague, the Jungar basin focuses on circulating strains of *Y. pestis* biovar Medievalis genovariant - 2.MED1, then in the foci of the Balkhash-Alakol depression circulate as strains of *Y. pestis* biovar Medievalis, and in the mountain foci circulate strains of biovar Antiqua of the primary subtype. The basis for the implementation of epidemiological monitoring of plague, including the epizootological potential of natural foci, on the level of which the whole complex of preventive measures is in direct dependence. Given that a certain group of factors is affecting the dynamics of the plague epizootic process, which were predictors and prerequisites for planning and conducting scientific research. Based on the above, the following will be carried out: study of epizootological characterization of the territory of the country on camel plague and development of veterinary and sanitary measures to improve their effectiveness; conducting microbiological and molecular genetic studies on plague, introduction of modern methods of laboratory research and training of young specialists; determination of genetic diversity of the plague pathogen circulating in plague enzootic areas of the country using the method of full-genome sequencing and creation of a genomic biorepository; elucidation of the reasons for the preservation of the plague microbe within the enzootic and interepizootic period nuclei in plague for targeted prophylactic (anti-plague) measures.

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