West Kazakhstan Medical Journal
Volume 66, Issue 3, DOI 10.18502/wkmj.v66i3.16571
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Research Article

Crimean-Congo Hemorrhagic Fever in the Zhambyl Region: Epidemiological Features of the Occurrence of Infection in 2023

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Abstract

Crimean-Congo hemorrhagic fever (CCHF) is an acute tick-borne viral infection with a high fatality rate. The main vector of the CCHF virus is ticks of the genus *Hyalomma*. Humans get infected through tick bites or by direct contact with the blood of infected humans or domestic animals. The endemic regions of CCHF in Kazakhstan are Kyzylorda, Turkestan, and Zhambyl. In the Zhambyl region, the first evidence of human cases was reported in 1982. In the following years, cases of CCHF were annually registered in two districts (Sarysu and Moiynkum) of the Zhambyl region. The study goal is twofold: 1) to provide a retrospective review of CCHF cases reported through the surveillance system in the Zhambyl region from 1991 to 2023 and 2) to analyze epidemiological features of CCHF cases in the Zhambyl region in 2023. Surveillance data on CCHF during the 1991–2023 period in the Zhambyl region were extracted from the "Report on selected infectious and parasitic diseases". Incidence (per 100,000 population) was defined as the number of annual new cases divided by the total population each year. Descriptive analysis was performed on case characteristics, time, and place of CCHF cases in the Zhambyl region in 2023. In total, 216 cases of CCHF were reported from 1991 to 2023. The incidence increased sharply with peak activity in 1995 and has declined since 2002. The natural foci of the disease have shifted from the Sarysu and Moiynkum districts to the Shu, Bayzak, and Zhambyl districts. Overall, 12 cases of CCHF were reported in the Zhambyl region in 2023, mainly in nonendemic (Shu, Bayzak, Zhambyl) districts. An analysis of epidemiological data for 2023 showed that the first peak of CCHF incidence was in March-June, with another peak from October to November. We observed dynamic distribution of CCHF in the Zhambyl region from 1991 to 2023, wherein Sarysu and Moiynkum endemic districts foci tended to increase by expanding to the Shu, Bayzak, Zhambyl districts. The disease trend is seasonal, and the life cycle of ticks can indirectly influence morbidity rates. Additional research is needed to elucidate the environmental, meteorological, and social factors associated with CCHF incidence in different decades.

Keywords: virus, Crimean-Congo hemorrhagic fever, tick-borne infections

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Received: 10 March 2024
Accepted: 23 May 2024
Published: 26 September 2024

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1. Introduction

Crimean-Congo hemorrhagic fever (CCHF) is an acute tick-borne viral infection that is characterized by a high fatality rate during outbreaks. It is asymptomatic in infected livestock. Humans get infected through tick bites or by direct contact with the blood of infected humans or domestic animals [1]. The main vector of the CCHF virus is ticks of the genus *Hyalomma*. Recently, the disease has been mostly distributed in more than 30 countries across Asia, the Middle East, Africa, and some parts of Europe [2]. CCHF is endemic in Kazakhstan. Every year, averages of 15-20 cases are registered in natural foci of CCHF among the population. In some years, the infection is characterized by outbreaks and nosocomial infections among medical workers [3, 4]. The main endemic regions of CCHF in Kazakhstan are the Kyzylorda, Turkestan, and Zhambyl regions. The high population density in the southern part of Kazakhstan, the favorable climate for virus-carrying vectors, and the migration of infected ticks by animals and wild birds endemic to the CCHF virus create favorable conditions for the spread of CCHF in the region [4].

The first reported human cases were registered in 1982 in the Zhambyl region. However, evidence of CCHF virus circulation was detected in animal serosurveillance studies in 1974 [5, 6]. In the Zhambyl region, the majority of CCHF cases were registered in the Sarysu, Moiynkum, and Talas districts. Moreover, CCHF cases in the Zhambyl region were considered the most active in Kazakhstan until 2001, characterized by numerous outbreaks of the disease among the population; for instance, in 1989, it reached 80 cases [6,7]. In total, 270 cases of CCHF were registered in the Zhambyl region from 1982 to 2013, with 73% of cases in the Sarysu district and 27% in the Moiynkum district. There were several CCHF outbreaks in the 1990s and 2000s [6]. Currently, cases are reported in the Zhambyl region annually.

The Zhambyl region is located in the southern part of Kazakhstan (44°-00'N, 72°-00'E) and covers 144,200 square kilometers. It is administratively divided into ten districts and the city of Taraz. The dominant climate in the Zhambyl region is arid and continental, with the annual average temperature being 11.2 degrees Celsius and annual average precipitation being 420mm [8]. The northern and southwestern parts of the Zhambyl region are located in zones with significantly different climatic characteristics. The climate and landscape strongly impact the timing of the epidemic processes. The onset of the epidemic process in the northern part is noted at an earlier date and at lower air temperatures than in its southwestern part [6, 9, 10].

The study aimed to: 1) provide a retrospective review CCHF cases reported through surveillance system in the Zhambyl region from 1991 to 2023 and 2) analyze epidemiological features of CCHF cases in the Zhambyl region in 2023.

2. Materials and Methods

2.1. Data collection and source

The data on CCHF cases were obtained from the "Report on selected infectious and parasitic diseases", prepared by the Scientific and Practical Center for Sanitary and Epidemiological Expertise and Monitoring of the National Public Health Center, a branch of the Ministry of Health in the Republic of Kazakhstan, in accordance with Appendix 1 to the order of the Ministry of Health of the Republic of Kazakhstan dated December 22, 2020, No. MoH RK -313/2020. For retrospective analysis the approval of the Ethics Committee was not needed.

According to the health standard for determining particularly dangerous infections in the Republic of Kazakhstan, CCHF cases were classified as follows: (I) suspected case, (II) probable case and (III) confirmed case. (I) A patient with acute severe illness accompanied by high fever and hemorrhagic syndrome characterized by one of the following signs: petechial rash; hemorrhages; bleeding (nasal, uterine, gastrointestinal, gingival, less often - others); thrombocytopenia ($\leq$100 x10^9/L) was defined as a suspected case of CCHF. (II) A probable case of CCHF is diagnosed when the definition of suspected case is met and at least one of the following factors is present: 1) the person stayed for two weeks before illness or residence in the territory natural outbreak (where cases of disease in humans or animals with CCHF are recorded) and one of the following occurred: tick bite; contact with a tick or blood from the tick; contact with the blood of a CCHF patient; contact with the blood of animals, possible carriers of the virus (hares and others); 2) there is an epidemiological link to a confirmed case of CCHF. (III) A confirmed case must fit one of the following criteria: isolation of the CCHF virus from the patient's blood, CCHF RNA virus positive in PCR, detection of antibodies of the IgM or IgG by ELISA, detection of antigen in pathological material by immunohistochemistry method.

2.2. Statistical analysis

To analyze changes in CCHF incidence in the Zhambyl region, we included all case data from 1991 to 2023. Incidence (per 100,000 population) was defined as the number of new cases annually divided by the total population each year. We performed a descriptive analysis of case characteristics, time, and place of CCHF cases in the Zhambyl region in 2023.

3. Results

A total of 216 cases and 18 deaths from CCHF were reported from 1991 to 2023 in the Zhambyl region: 136 cases in the Sarysu district, 50 cases in the Moiynkum district, six cases in the Talas district. In

non-endemic districts of CCHF six cases were found in the Bayzak district, eight in the Zhambyl and Shu districts, and two in Taraz city (Figure **1**).

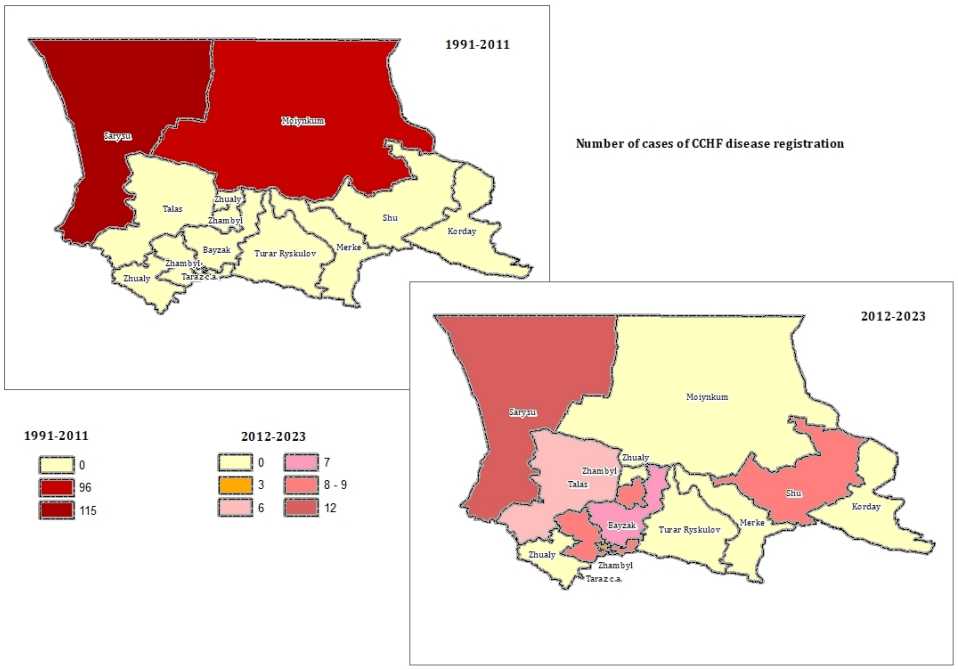

Figure 1: Dynamics of CCHF cases in Zhambyl region from 1991 to 2011 comparable from 2012 to 2023.

Between 1991 and 2023, there were periods of sharp increase with peak activity in 1995 (35 cases, 3.41 per 100,000), 1998 (12 cases, 1.2 per 100,000), 1999 (27 cases, 2.74 per 100,000), 2000 (33 cases, 3.35 per 100,000), and 2001 (22 cases, 2.24 per 100,000). A period of decline in the incidence of CCHF has been observed since 2002, with the number of registered cases as follows: 2002 (four cases, 0.41 per 100,000), 2003 (six cases, 0.61 per 100,000), 2004 (one case), 2005 (one case), and 2006 (one case, 0.1 per 100,000). The period between 2007 to 2010 is considered to be of epidemiological well-being, characterized by the complete absence of CCHF cases among the the Zhambyl region population. In the years between 2011 to 2022, the number of CCHF cases in Zhambyl region is seen to have sharply decreased. (Figure **2**).

While analyzing this period, it was found that clinical cases among people began to be registered in areas that are not endemic for CCHF. In the Talas district, cases were registered in in 2012, 2013, and 2020. In the Bayzak district, they were registered in 2016, 2017, and in 2022-2023. In the Zhambyl district, cases were documented between 2016 to 2018, and again in 2023. In the Shu district, the first case was registered in 2021 and 2023.

A characteristic feature of the 2023 period was that 12 cases of CCHF were registered in non-endemic areas, namely the Shu, Bayzak, and Zhambyl districts, with one case in the endemic Sarysu district. Eight cases were registered in the Shu district (including one fatal case), two cases in the Bayzak district (including one fatal case), one case in the Jambyl district, and one case in the Sarysu district (including

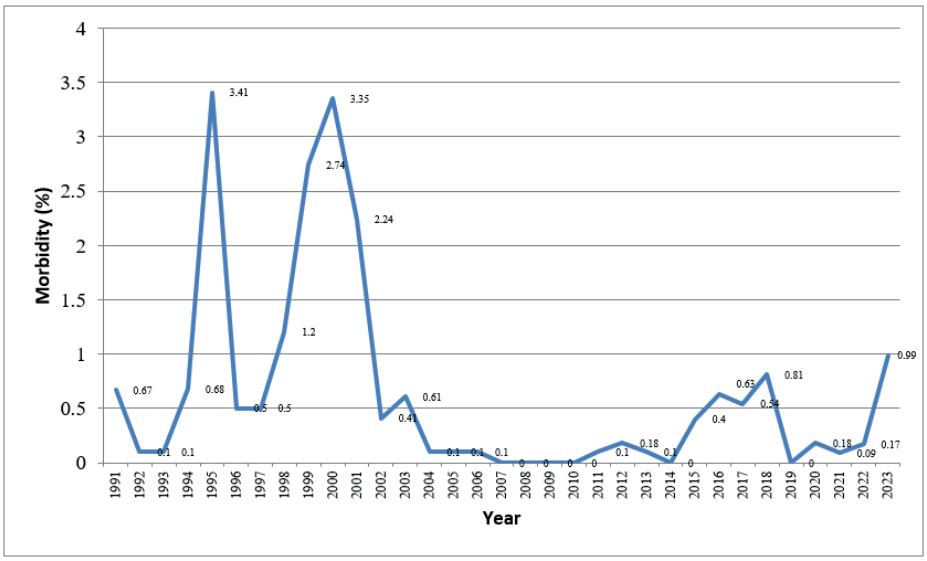

Figure 2: Long-term dynamics of CCHF morbidity in Zhambyl region (1991-2023) per 100, 000 population.

one fatal case). A total of 37 cases of CCHF meeting the definitions of “suspected case of CCHF” and “probable case of CCHF” were recorded and categorized into a table for data analysis. The data were arranged in chronological order as sick people were admitted throughout the year. (Table 1).

Table 1: Epidemiologic data on registration of CCHF cases in 2023 in Zhambyl region.

N°	District, village	The Date of Illness	Date of Hospitalization	Preliminary Diagnosis	Final Diagnosis
1	Taraz city	07.03.2023	10.03.2023	Suspected case of CCHF	Enterovirus infection
2	Moiynkum district, Saryozek	14.03.2024	15.03.2023	Suspected case of CCHF	Enterovirus infection
3	Zhambyl district, Grodikovo	02.04.2023	02.04.2023	Suspected case of CCHF	Hemorrhagic fever of unspecified etiology
4	Shu district, Shu	20.04.2023	27.04.2023	Probable case of CCHF	Confirmed case of CCHF
5	Taraz city	27.04.2023	27.04.2023	Probable case of CCHF	Thrombocytopenia
6	Moiynkum district, Kumozek	05.05.2023	07.05.2023	Probable case of CCHF	Enterovirus infection
7	Shu district, Shu	07.05.2023	13.05.2023	EI enterovirus infection, Idiopathic thrombocytopenic purpura	Confirmed case of CCHF
8	Taraz city	13.05.2023	16.05.2023	Probable case of CCHF	Enterovirus infection
9	Shu district, Tolebi	13.05.2023	16.05.2022	Probable case of CCHF	Idiopathic thrombocytopenic purpura
10	Shu district, Shu	17.05.2023	17.05.2022	Suspected case of CCHF	Acute respiratory viral infection
11	Bayzak district, Talas	17.05.2023	20.05.2022	Probable case of CCHF	Confirmed case of CCHF
12	Bayzak district, Tuimekent	21.05.2023	22.05.2023	Suspected case of CCHF	Acute respiratory viral infection

Table 1: Continued.

N°	District, village	The Date of Illness	Date of Hospitalization	Preliminary Diagnosis	Final Diagnosis
13	Shu district, Shu	22.05.2024	25.05.2023	Probable case of CCHF	Acute respiratory viral infection
14	Sarysu district, Zhanatas	26.05.2023	31.05.2023	Probable case of CCHF	Enterovirus infection
15	Shu district, Shu	06.06.2023	07.06.2023	Probable case of CCHF	Confirmed case of CCHF with fatality
16	Shu district, Shu	08.06.2023	08.06.2023	Probable case of CCHF	Thrombocytopenia
17	Zhambyl district, Grodikovo	08.06.2023	09.06.2023	Suspected case of CCHF	Acute respiratory viral infection
18	Taraz city	12.06.2023	12.06.2023	Probable case of CCHF	Enterovirus infection
19	Zhambyl district, Ornek	16.06.2023	23.06.2023	Probable case of CCHF	Confirmed case of CCHF
20	Zhambyl district, Grodikovo	23.06.2023	24.06.2023	Probable case of CCHF	Enterovirus infection
21	Moiynkum district, Kylyshbay	22.06.2023	24.06.2023	Probable case of CCHF	Enterovirus infection
22	Shu district, Shu	23.06.2023	26.06.2023	Probable case of CCHF	Confirmed case of CCHF
23	Zhambyl district, Birlesu-Yenbek	30.06.2023	30.06.2023	Suspected case of CCHF	Hemorrhagic fever of unspecified etiology
24	Zhualy district, Tasbastau	27.06.2023	29.06.2023	Suspected case of CCHF	Acute brucellosis
25	Shu district, Baluan Sholak	07.07.2023	12.07.2023	Probable case of CCHF	Confirmed case of CCHF
26	Zhambyl district, Togyztarau	12.07.2023	14.07.2023	Probable case of CCHF	Enterovirus infection
27	Taraz city	18.07.2023	20.07.2023	Probable case of CCHF	Enterovirus infection
28	Zhambyl district, Ornek	03.08.2023	03.08.2023	Probable case of CCHF	Enterovirus infection
29	Moyinkum district, Kushaman	09.08.2023	12.08.2023	Probable case of CCHF	Hemorrhagic fever of unspecified etiology
30	Shu district, Konaev	23.08.2023	31.08.2023	Probable case of CCHF	Confirmed case of CCHF
31	Shu district, Moiynkum	30.09.2023	04.10.2023	Probable case of CCHF	Confirmed case of CCHF
32	Sarysu district, Igilik	26.09.2023	07.10.2023	Probable case of CCHF	Confirmed case of CCHF with fatality
33	Zhuali district, Shakpak	10.09.2023	17.10.2023	Suspected case of CCHF	Thrombocytopenia
34	Sarysu district, Saudakent	16.10.2023	16.10.2023	Probable case of CCHF	Eclampsia, 36-week pregnancy
35	Bayzak district, Abay	19.10.2023	19.10.2023	Probable case of CCHF	Confirmed case of CCHF with fatality
36	Bayzak district, Myrzatai	30.10.2023	30.10.2023	Suspected case of CCHF	Acute respiratory viral infection
37	Shu district, Baidibek	24.11.2023	29.11.2023	Probable case of CCHF	Confirmed case of CCHF

The following regularity was observed in the seasonality of CCHF incidence in 2023: the first clinical symptoms in patients admitted for medical care with suspected or probable cases of CCHF were reported in March, with a gradual increase in cases in May and June, and a further rise from October to November (Figure **3**).

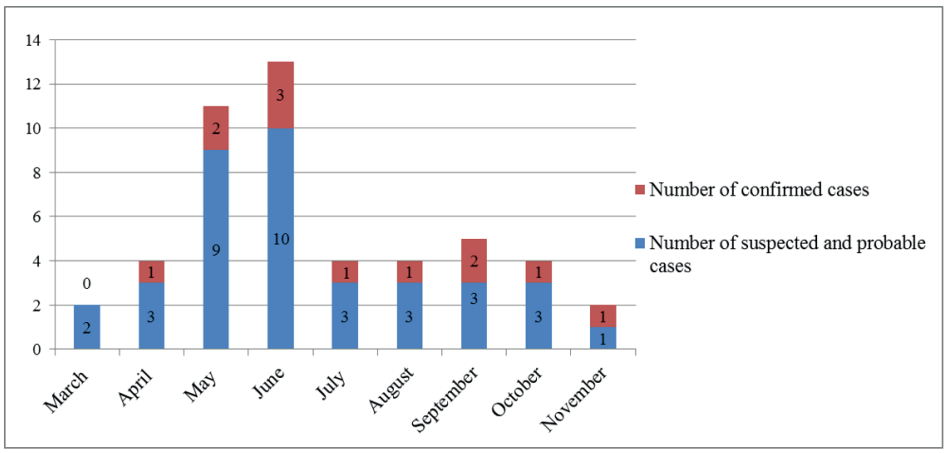

Figure 3: Number of suspected, probable and confirmed cases of CCHF in Zhambyl region in 2023.

The majority of patients (73%) visited the hospital within 3 days after the first symptoms of the disease. At the time of hospitalization, a suspected case of CCHF was diagnosed in 10 cases, a probable case of CCHF was diagnosed in 25 cases. In one instance, Enterovirus infection and idiopathic thrombocytopenia were diagnosed initially, with subsequent confirmation of CCHF.

4. Discussion

The retrospective analysis on the incidence of CCHF in the Zhambyl region over a 33-year period provide valuable information for understanding the disease's dynamics and the effectiveness of control measures. The retrospective analysis showed that CCHF foci in the Sarysu and Moiynkum districts were the most active until 2007, with large outbreaks reported annually (e.g., 35 cases in 1995, 27 cases in 1999, 33 cases in 2000, and 22 cases in 2001) [6]. From 2007 to 2014, only one case of CCHF was reported in these districts, while the first reported cases of CCHF in the Talas district began in 2012 and tended to increase, expanding to the Shu, Bayzak, Zhambyl districts.

The detection of CCHF-positive tick samples in areas where the incidence of CCHF among the population has been observed in recent years indicates the expansion of CCHF areas in the Zhambyl region and their activation. The frequency of CCHF cases among the population, characterized by an undulating pattern, is primarily due to the periods of activity of adult stages of vectors — ticks. The seasonality of disease manifestation depends on the life cycle of certain tick species. In regions dominated by *H. a. asiaticum*, activity occurs from March to July and September to October, whereas

in areas where *H. anatolicum* predominates, it occurs from July to August. With the presence of *D. niveus* ticks in natural foci, human disease is possible almost throughout the year [6, 11, 12]. Climate, especially temperature and humidity, is one of the major factors influencing tick distribution, potentially extending the active season of ticks and increasing the survival of non-parasitic stages (such as eggs and egg-laying females) in the environment [13]. In some cases, this facilitates the establishment of tick populations in new areas that become more suitable for tick survival and development [6, 14]. This conclusion is supported by epidemiological data showing a significant positive correlation between CCHF cases and temperature in the Zhambyl region.

Fatal cases were registered among residents of rural areas. The fatality rate for CCHF was 25% (three fatal cases out of 12 confirmed cases), with deaths mainly occurring on days three and ten of the disease [15]. Despite patients being admitted early to the hospital and medical professionals' awareness of the disease, suspected and probable cases of CCHF were confirmed in 12 out of 37 cases. The final diagnoses for non-confirmed cases were: 11 cases had Enterovirus infections, five cases had acute respiratory viral infections, three cases had thrombocytopenia, and three cases had idiopathic thrombocytopenic purpura, acute brucellosis, and eclampsia respectively. Three patients were diagnosed with hemorrhagic fever of unspecified etiology. These data indicate similarities in clinical manifestations with CCHF.

Early medical attention and alertness among health care professionals are important factors in controlling the spread of the disease. This demonstrates the need for further education and awareness of the population and health care personnel on the signs and methods of preventing CCHF.

It is necessary to conduct annual monitoring of infection in both focal and non-focal areas with natural and climatic conditions conducive to the habitat of potential vector species of the CCHF virus. The study of tick infestation with the CCHF virus in two regions, which differ in landscape, climatic conditions, and species diversity of these ectoparasites, has allowed for the identification of the main dominant species. This information is crucial for implementing preventive measures in CCHF foci. In conclusion, the discussion of the study's results emphasizes not only the dynamics of disease incidence, but also the importance of control and prevention measures, as well as additional research to elucidate the environmental, meteorological, and social factors associated with CCHF incidence at different times.

Declarations

Conflict of Interests

The authors confirm that there is no conflict of financial/nonfinancial interests related to the writing of the article.

Authors' Contribution

All authors participated in conceptualizing and writing the article. The final version of the manuscript was checked and approved by all authors. The authors did not receive an honorarium for the article.

Funding

This study was funded by the Committee of Science of the Ministry of Science and Higher Education of the Republic of Kazakhstan, monitoring of the epidemiological and epizootological situation, external and priority internal sources of threats to biological safety 2023-2025 (BR 218004/0223).

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