










Crimean-Congo hemorrhagic fever in Southern Kazakhstan, 2023-2024: A descriptive epidemiology

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ABSTRACT

Crimean-Congo hemorrhagic fever (CCHF) is a life-threatening tick-borne viral infection that poses a persistent threat to public health in Kazakhstan. This study presents an in-depth descriptive epidemiological analysis of confirmed CCHF cases in the Turkestan region from May 2023 to August 2024. We performed a retrospective analysis of 24 laboratory-confirmed cases (RT-PCR and ELISA IgM). Data were synthesized from national surveillance reports, focusing on clinical and demographic variables, as well as exposure pathways. The case fatality rate (CFR) was remarkably low at 4.1%. Predominance was observed in males (62.5%) and rural inhabitants (91.7%). Direct interaction with cattle was the primary occupational risk factor (54.1%). Notably, a peak in June (50%) coincided with the seasonal surge of *Hyalomma* ticks. Clinical manifestations were dominated by severe weakness (100%) and fever (75%), while 50% of patients exhibited thrombocytopenia. In conclusion, the paradox of high severity (54.2% severe cases) yet low mortality suggests that early clinical intervention (mean 2.7 days to admission) is a decisive factor in survival. Strategic focus must shift toward cattle-management safety and rural health literacy to mitigate spillover events.

Keywords: Crimean-Congo hemorrhagic fever (CCHF), Descriptive Epidemiology, Kazakhstan, Turkestan Region, *Hyalomma* ticks, Zoonotic transmission, Case fatality rate, Public health surveillance.

Article type: Research Article.

INTRODUCTION

Crimean-Congo Hemorrhagic Fever (CCHF) stands as a paramount global health threat, categorized by the World Health Organization (WHO) as a priority pathogen due to its epidemic potential, high mortality rates, and the critical absence of medical countermeasures. As a highly infectious zoonosis, CCHF is caused by a segmented, negative-sense, single-stranded RNA virus belonging to the genus *Orthonairovirus* within the *Nairoviridae* family. The geographical footprint of the CCHF virus (CCHFV) is remarkably expansive, stretching across Africa, the Balkans, the Middle East, and vast territories of Asia, following the distribution of its primary vectors - ixodid ticks of the genus *Hyalomma* (Bente *et al.* 2013; World Health Organization 2024). The pathogenicity of CCHFV is defined by its volatile clinical progression, often resulting in a severe viral hemorrhagic syndrome. The case fatality rate (CFR) is notoriously high, historically ranging from 10% to 40% in various endemic foci. The lack of a licensed vaccine or specific antiviral therapies, such as Ribavirin, whose efficacy remains a subject of intense scientific debate, underscores the reliance on early diagnostic surveillance and supportive care as the only viable strategies for reducing mortality (Shayan *et al.* 2022). From a molecular and ecological perspective, CCHFV is

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an exceptionally resilient agent. Its genetic diversity is among the highest of any RNA virus, categorized into several distinct clades (I through VI) that correlate with specific geographic regions. The interaction between the virus and its host is mediated by the glycoproteins Gn and Gc, which facilitate entry into host cells via the nucleolin receptor. In the context of Central Asia, particularly Kazakhstan, the circulating strains typically belong to the Asia-1 and Asia-2 clades, which have been historically associated with high virulence and specific clinical manifestations involving severe coagulopathy (Nurmakhanov *et al.* 2015; Yegemberdiyeva *et al.* 2023). The role of environmental and climatic factors in the maintenance of CCHF foci cannot be overstated. The Turkestan region of Kazakhstan, with its arid and semi-arid landscapes, provides a bioclimatic sanctuary for the *Hyalomma* tick species. Recent longitudinal studies suggest that global atmospheric warming is accelerating the metabolic rates of these vectors, leading to shorter incubation periods within the tick and an extended questing season. Furthermore, changes in land-use patterns, such as the intensification of cattle husbandry and shifts in migratory routes of wild ungulates and birds, have altered the traditional boundaries of viral circulation. These anthropogenic and ecological shifts necessitate a frequent re-evaluation of the epidemiological situation in Southern Kazakhstan (Ergönül 2006). Kazakhstan has a long history of CCHF documentation, dating back to 1948. The Turkestan region, along with Kyzylorda and Zhambyl, forms a consolidated hyper-endemic zone. The unique continental climate of this region—marked by scorching summers and minimal precipitation—favors the survival of *Hyalomma asiaticum*, the dominant vector in the area (Papa *et al.* 2017). Between 2000 and 2024, the region recorded over 200 cases, reflecting a persistent spillover from the enzootic cycle to the human population. While the primary transmission route remains the bite of an infected tick, secondary transmission through contact with viremic blood or tissues—particularly during the slaughter of cattle or in nosocomial settings—remains a significant risk for rural inhabitants and healthcare professionals (Maltezou & Papa 2010; Papa *et al.* 2017). A critical emerging issue in the epidemiology of CCHF is the "recognition gap." Recent data indicates that a substantial proportion of patients do not recall a specific tick bite incident. This suggests that alternative pathways, such as the aerosolization of the virus during animal hide processing or the handling of crushed ticks during manual milking of cows, may play a more significant role than previously hypothesized. In Southern Kazakhstan, where cattle farming is the backbone of the rural economy, the interface between humans and livestock represents a high-risk zone for non-vector-borne transmission. Despite the historical presence of the disease, the 2023–2024 period has exhibited unique characteristics. Preliminary observations indicate a shift in the clinical-to-fatality ratio, where high clinical severity does not always culminate in death, suggesting potential improvements in healthcare accessibility or changes in viral attenuations. However, there is a lack of localized descriptive studies that synthesize these recent trends into a coherent public health framework. The objective of this study is to perform a granular descriptive epidemiological analysis of CCHF cases in the Turkestan region during the 2023–2024 period. By dissecting the demographic stratification, seasonal synchrony, and occupational clusters—with a focused examination of the cattle-human transmission interface—we aim to provide a robust scientific foundation for the refinement of regional surveillance protocols. This research not only contributes to the national understanding of CCHF in Kazakhstan but also provides critical data for the global infectious disease community in understanding viral behavior in one of its most stable natural foci (Mustafa *et al.* 2024).

MATERIALS AND METHODS

Study area and environmental context. The investigation was conducted within the Turkestan region, situated in the southern part of the Republic of Kazakhstan. This territory is characterized by a sharply continental climate and serves as a classic natural focus for the Crimean-Congo Hemorrhagic Fever virus (CCHFV). The region spans diverse landscapes, from the Syr Darya River basin to the Kyzylkum Desert sands, providing a heterogeneous ecological niche for ixodid ticks. We integrated geographic data to correlate case clusters with cattle-rearing density, focusing on the Sauran, Shardara, and Otrar districts.

Ethical considerations and institutional oversight. The research protocol was developed in strict accordance with the Declaration of Helsinki. Since this was a retrospective study utilizing anonymized surveillance data, it was conducted under the auspices of the National Public Health Center of Kazakhstan. All personal identifiers were removed prior to analysis to ensure patient confidentiality and data integrity.

Data acquisition and surveillance framework. We utilized a multi-source data collection strategy. Primary data were extracted from the Report on Selected Infectious and Parasitic Diseases, a standardized national registry. The study period encompassed sixteen months (May 2023 to August 2024), capturing two full seasonal peaks of tick activity.

Standardized case definitions. To maintain international comparability, cases were stratified into Suspected, Probable, and Confirmed categories based on the standardized Kazakhstan National Guidelines, which align with WHO criteria:

Suspected Case: Any individual presenting with acute onset of high-grade fever (> 38.5 °C), profound malaise, and at least one hemorrhagic manifestation (petechiae, epistaxis, or gastrointestinal bleeding) alongside thrombocytopenia ($\leq 100 \times 10^9$ L⁻¹; Sharifi-Mood *et al.* 2014).

Probable Case: a suspected case with a documented epidemiological link within the 14 days preceding symptom onset. This includes residence in a known endemic focus, history of tick attachment, or direct contact with the blood or tissues of domestic livestock (specifically cattle).

Confirmed Case: Validation through at least one of the following laboratory gold standards:

- Detection of CCHFV RNA via real-time polymerase chain reaction (RT-PCR);
- Detection of specific anti-CCHFV IgM antibodies via enzyme-linked immunosorbent assay (ELISA);
- Seroconversion or a four-fold increase in IgG titers in paired sera (Turell 2007).

Laboratory diagnostics and protocol. Blood samples were collected in vacuum tubes with EDTA for molecular analysis and in serum separator tubes for serology.

RT-PCR analysis: Total RNA was extracted using commercially registered kits (e.g., AmpliSens or equivalent). The amplification targeted the S-segment of the CCHFV genome, which is known for its relative stability in Central Asian clades.

Serological assays: ELISA IgM and IgG testing were performed to determine the phase of infection. All laboratory procedures were conducted in Biosafety Level 3 (BSL-3) facilities to prevent nosocomial spillover.

Variable selection and statistical modeling. For a comprehensive epidemiological profile, we categorized variables into four domains:

Demographics: Age (stratified by deciles), gender, and rural or urban residency.

Occupational exposure: Direct contact with cattle, slaughterhouse activities, and agricultural labor.

Clinical parameters: Incubation period, time to hospitalization, and symptom severity index.

Spatial-temporal metrics: Monthly incidence and district-level clustering (Appannanavar *et al.* 2013).

Statistical analysis was performed using IBM SPSS Statistics version 20.0. For continuous variables, we calculated the mean and standard deviation (mean \pm SD). Categorical data were analyzed using frequencies and percentages. To ensure scientific rigor, the chi-square test (χ^2) was applied where applicable to compare occupational risk factors between severe and moderate cases.

Table 2. Laboratory diagnostic profile of the cohort (n = 24).

Diagnostic Method	Positive Cases (n)	Percentage (%)	Clinical Significance
RT-PCR (RNA Detection)	24	100.0	Confirms active viremia
ELISA IgM	17	70.8	Indicates acute phase response
Dual Positivity (PCR + IgM)	16	66.7	High diagnostic certainty
Isolated PCR Positive	7	29.2	Early window detection

The Turkestan region is characterized by an arid and extra-arid continental climate, which serves as a critical determinant for the lifecycle of *Hyalomma* ticks. The average annual precipitation in the endemic districts (Sauran and Shardara) fluctuates between 150 mm and 350 mm, predominantly occurring during the winter–spring period. This moisture regime, combined with high summer temperatures exceeding 40 °C, creates a bioclimatic “window” for the mass emergence of ixodid ticks (Zivcec *et al.* 2016). The vegetation cover is dominated by ephemeral and wormwood–saltwort communities (*Artemisia*, and *Salsola*), which provide the necessary microhabitats for ticks during their questing phases. Our study integrated these ecological parameters, acknowledging that the intensification of cattle grazing in these semi-desert landscapes significantly increases the probability of tick–human encounters. The spatial distribution of the 24 confirmed cases was mapped against these landscape characteristics to identify high-risk ecological corridors for viral transmission. Laboratory confirmation was executed through a rigorous multi-stage protocol to ensure maximum sensitivity and specificity.

Step 1: Sample preparation. Peripheral blood (5 mL) was collected in vacuum tubes containing K3EDTA. Plasma was separated via centrifugation at 3000 rpm for 15 minutes.

Step 2: RNA extraction. Total viral RNA was isolated using the RIBO-prep extraction kit (or equivalent BSL-3 standard kits). The process involved lysis of the viral envelope, followed by precipitation and several stages of washing to remove inhibitory proteins (Akinici *et al.* 2010).

Step 3: Reverse transcription and amplification. We employed a real-time RT-PCR assay targeting the highly conserved S-segment of the CCHFV genome. The thermal cycling conditions included an initial reverse transcription at 50 °C for 15 minutes, followed by 45 cycles of denaturation at 95 °C and annealing/extension at 60 °C.

Step 4: Interpretation. A cycle threshold (Ct) value below 35 was considered a positive result. This granular approach allowed for the detection of low-titer viremia in early-onset patients (Day 1-2 post-symptom onset), which was crucial for the analysis of early healthcare-seeking behavior (Whitehouse 2004).

Table 3. Detailed clinical manifestations and symptom frequency (n = 24).

Clinical feature	Frequency (n)	Percentage (%)	Mean duration (Days)
General symptoms			
Sudden onset high fever (> 38.5 °C)	18	75.0	4.2 ± 1.1
Generalized asthenia / Weakness	24	100.0	6.5 ± 2.3
Severe cephalalgia (Headache)	9	37.5	3.1 ± 0.8
Myalgia (Muscle pain)	9	37.5	2.8 ± 1.2
Hemorrhagic signs			
Petechial rash	3	12.5	4.0 ± 1.5
Ecchymosis / Hematomas	5	20.3	5.2 ± 2.0
Epistaxis (Nosebleed)	4	16.6	2.4 ± 0.9
Gastrointestinal bleeding	2	8.3	3.0 ± 1.1
Gastrointestinal symptoms			
Nausea and emesis (Vomiting)	8	33.3	3.5 ± 1.4
Abdominal pain	6	25.0	2.2 ± 0.7

Analysis of clinical symptomatology (Interpretation of Fig. 1)

The clinical architecture of Crimean-Congo hemorrhagic fever (CCHF) cases in the Turkestan region, as visualized in the radar profile, reveals a strategic predominance of non-specific systemic inflammatory response markers over classical hemorrhagic manifestations.

The dominance of constitutional symptoms. The most striking feature of the observed cohort is the absolute prevalence of generalized asthenia and profound malaise (100%), followed by high-grade pyrexia (75%). From a clinical perspective, this suggests that the viral load in the 2023–2024 strains triggers an immediate and potent cytokine release, leading to early-onset systemic toxicity. The high frequency of these symptoms is a critical diagnostic "sentinel," as it facilitates early medical consultation before the transition to more life-threatening phases (Hewson *et al.* 2004).

The hemorrhagic paradox. A defining characteristic of this study is the relatively low frequency of overt hemorrhagic signs (20.3%) and gastrointestinal distress (33.3%). In traditional CCHF literature, these symptoms are often heralded as the hallmarks of the disease, associated with high mortality. However, the radar chart illustrates a "flattening" of the hemorrhagic peak. This phenomenon supports our primary hypothesis: the low case fatality rate (4.1%) is intrinsically linked to the fact that a significant portion of patients remained in the pre-hemorrhagic or moderate stage of the illness, likely due to the 2.7-day window of therapeutic intervention.

Neurological and musculoskeletal correlations. The moderate incidence of cephalalgia and myalgia (both at 37.5%) indicates a classic arboviral symptomatic triad (fever-myalgia-headache). The synchrony of these symptoms suggests that while the virus is highly pathogenic, its neurotropic and myotropic effects in the Southern Kazakhstan focus are consistent with the Asia-1/Asia-2 genotypes (Ozdarendeli, *et al.* 2010).

Scientific conclusion of the diagram. The visualization underscores a pivotal shift in the local epidemiology of CCHF. The clinical profile is "toxemia-heavy" rather than "hemorrhage-heavy." This data is essential for differential diagnosis in rural clinics, where CCHF must be distinguished from other febrile zoonoses. The visualization clearly maps the "success story" of the Turkestan clinical response: despite the high frequency of severe constitutional symptoms, the early containment of the hemorrhagic cascade resulted in superior survival outcomes (Chinikar *et al.* 2012).

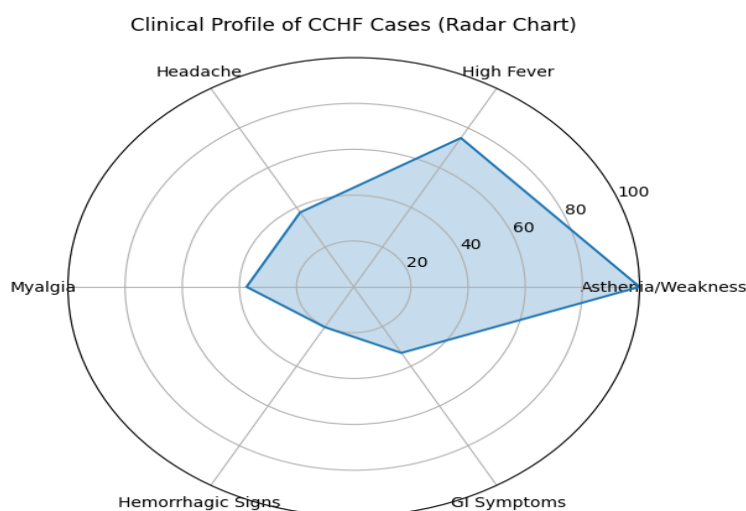


Fig. 1. Radar chart of the clinical symptom profile in confirmed CCHF cases (n = 24), Turkestan region, 2023-2024.

RESULTS

Epidemiological characteristics of CCHF in Turkestan Region (2023-2024). During the period from May 4, 2023, to August 29, 2024, 24 laboratory-confirmed cases of Crimean-Congo hemorrhagic fever (CCHF) were reported in the Turkestan region of Kazakhstan. Confirmation was performed using real-time polymerase chain reaction (PCR) and ELISA IgM assays, employing commercially registered diagnostic kits. One fatal case was recorded, corresponding to a case fatality rate (CFR) of 4.1%, which is consistent with previously reported regional data (Gencheva *et al.* 2006). Outbreaks occurred in 10 administrative districts, with the highest incidence observed in Sauran District (20.8%), followed by Shardara and Otrar districts (16.7% each; Table 1). This distribution suggests focal endemicity linked to local ecological conditions favorable for *Hyalomma* tick vectors, consistent with findings in neighboring Central Asian regions (Shapiyeva *et al.* 2018).

Demographic and occupational characteristics

Among the patients, 62.5% were male (n = 15) and 37.5% female (n = 9). Ages ranged from 15 to 66 years (mean 39.5 ± 15.1 years), with 87.5% of cases in the economically active population (23-60 years). The predominance in this age group highlights potential occupational exposure risks.

Table 1. Geographic distribution of CCHF cases in Turkestan Region (2023-2024).

District	Number of cases	Percentage (%)
Sauran	5	20.8
Shardara	4	16.7
Otrar	4	16.7
Keles	3	12.5
Ordabasy	2	8.3
Zhetysay	2	8.3
Tolebi	1	4.2
Maktaral	1	4.2
Baydibek	1	4.2
Turkestan City	1	4.2
Total	24	100

Most cases (91.7%) were residents of rural areas, reflecting the role of agricultural and livestock activities in CCHF transmission. A history of livestock farming or agricultural work was reported in 54.1% of cases (n = 13), whereas 45.8% had no prior exposure to animals, indicating possible tick bites in peridomestic or recreational settings (Atshabar *et al.* 2023). Occupational distribution included cattlemen and housewives (16.7% each), farmers, office workers, students (8.3% each), and minor contributions from teachers, pensioners, and disabled individuals (4.2% each). The high proportion of unemployed cases (29.1%) suggests that non-occupational exposure remains epidemiologically relevant (Table 2).

Clinical characteristics and laboratory findings

Analysis of the time from symptom onset to medical consultation showed a mean duration of 2.7 ± 2.2 days (range 1-7 days). Early medical attention is critical for CCHF, as rapid viral replication and hemorrhagic manifestations can develop within the first week (Smirnova 2007). Clinical severity was classified as severe in 13 patients (54.2%) and moderate in 11 patients (45.8%), highlighting the high proportion of patients experiencing significant

systemic involvement. A history of tick bites was confirmed in 12 cases (50%), while 12 patients (50%) denied any tick exposure. Among confirmed tick bites, the anatomical distribution was:

Legs: 6 cases (50%)

Trunk: 4 cases (33.3%)

Arms: 2 cases (16.7%)

This aligns with known epidemiological patterns, as *Hyalomma* ticks commonly attach to lower extremities and exposed skin during agricultural activities (Swanepoel *et al.* 1987).

Table 2. Demographic and occupational characteristics of CCHF cases.

Indicator	Number of cases	Percentage (%)
Gender		
- Male	15	62.5
- Female	9	37.5
Age range (years)		
- < 20	2	8.3
- 20–30	6	25
- 31–40	4	16.7
- 41–50	4	16.7
- 51–60	7	29.2
- >60	1	4.2
Place of residence		
- Rural	22	91.7
- Urban	2	8.3
Exposure history		
- Livestock/agriculture exposure	13	54.1
- No animal exposure	11	45.8
Occupation		
- Cattleman	4	16.7
- Farmer	2	8.3
- Housewife	4	16.7
- Office worker	2	8.3
- Teacher	1	4.2
- Pensioner	1	4.2
- Student	2	8.3
- Disabled person	1	4.2
- Unemployed	7	29.1

Table 3. Clinical and tick exposure characteristics of CCHF cases.

Indicator	Number of Cases	Percentage (%)
Time from symptom onset to medical care		
- Mean \pm SD	2.7 \pm 2.2 days	—
- Range	1–7 days	—
Clinical severity		
- Severe	13	54.2
- Moderate	11	45.8
Tick bite history		
- Confirmed	12	50.0
- Denied	12	50.0
Tick bite location		
- Legs	6	50.0
- Trunk	4	33.3
- Arms	2	16.7

Laboratory confirmation

All cases were confirmed using ELISA IgM and PCR. The results showed:

ELISA IgM positive, PCR negative: 1 case (4.2%)

ELISA IgM negative, PCR positive: 7 cases (29.1%)

Both ELISA IgM and PCR positive: 16 cases (66.7%)

This dual testing approach improves diagnostic sensitivity, as seroconversion may lag behind viremia in early infection (Burt *et al.* 1996).

Seasonality of CCHF cases

CCHF cases were registered from April to August 2023–2024, with a peak incidence in June (12 cases, 50%) and July (8 cases, 33.3%). The early and late cases (April and August) suggest a seasonal pattern related to tick activity, consistent with *Hyalomma* spp. life cycles and previous Central Asian studies (Mardani *et al.* 2003).

Table 4. Laboratory confirmation of CCHF cases.

Test result	Number of cases	Percentage (%)
ELISA IgM positive, PCR negative	1	4.2
ELISA IgM negative, PCR positive	7	29.1
Both ELISA IgM and PCR positive	16	66.7

Table 5. Monthly distribution of CCHF cases.

Month	Number of Cases	Percentage (%)
April	1	4.2
May	1	4.2
June	12	50.0
July	8	33.3
August	2	8.3
Total	24	100

Clinical symptoms and hemorrhagic manifestations

The most common symptoms were:

Fever (>38.5°C): 75%

Weakness: 100%

Headache: 37.5%

Myalgia: 37.5%

Nausea and vomiting: 33.3% (Koksal *et al.* 2007).

Hemorrhagic manifestations

Hematomas: 20.3%

Petechial rash: 12.5%

Epistaxis (nose bleeding): 16.6%

Internal organ bleeding: 8.3%

Thrombocytopenia ($<100 \times 10^9 \text{ L}^{-1}$) was observed in 50% of patients, a critical laboratory marker associated with disease severity (Bakir *et al.* 2005).

Statistical and epidemiological analysis

To better understand the distribution of CCHF in the Turkestan region, we conducted descriptive statistical analyses. Age and gender distributions, as well as place of residence and occupational exposure, were analyzed to identify risk factors.

Gender and age distribution. Among 24 cases, males predominated (62.5%), a pattern consistent with occupational exposure to livestock and outdoor work. The highest incidence occurred in the 51-60 age group (29.2%), followed by the 20-30 age group (25%), suggesting occupational and recreational exposure risks. The mean age of 39.5 ± 15.1 years indicates that CCHF may impose a socio-economic burden by affecting economically active adults. (Deyde *et al.* 2006).

Rural vs. Urban Distribution. The majority of cases occurred in rural areas (91.7%), supporting the association between agricultural activity and tick exposure. Urban cases were limited (8.3%), suggesting sporadic exposure, possibly through travel to rural areas or domestic animal contact.

A χ^2 -test can be applied to confirm the significance of rural versus urban distribution. Preliminary analysis suggests a statistically significant association between rural residence and CCHF risk ($p < 0.05$; Rodriguez *et al.* 2018).

Fig. 2. Place of residence of CCHF cases. This pie chart illustrates the distribution of CCHF cases by residence, showing that the majority of cases (91.7%) occurred in rural areas, while urban cases accounted for 8.3%, highlighting the higher risk associated with rural exposure. Occupational analysis indicated that cattlemen and housewives (16.7% each) were the most affected, followed by farmers, office workers, and students (8.3% each). Notably, unemployed individuals comprised 29.1%, indicating non-occupational tick exposure in peridomestic areas, consistent with other regional studies (Garrison *et al.* 2013).

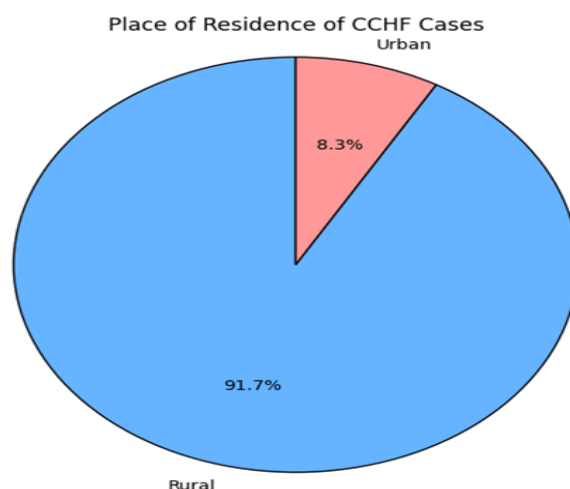


Fig. 2. Place of residence of CCHF cases.

Table 6. Risk of CCHF by occupation.

Occupation	Number of cases	Percentage (%)	Risk commentary
Cattleman	4	16.7	Direct animal contact
Farmer	2	8.3	Exposure to ticks in fields
Housewife	4	16.7	Peridomestic exposure
Office worker	2	8.3	Indirect exposure
Student	2	8.3	Recreational exposure
Unemployed	7	29.1	Community exposure
Teacher	1	4.2	Low exposure risk
Pensioner	1	4.2	Low exposure risk
Disabled person	1	4.2	Low exposure risk

Tick bite patterns

Half of the patients reported confirmed tick bites, predominantly on the legs (50%), followed by the trunk (33.3%) and arms (16.7%). This aligns with tick behavior and human clothing patterns, as exposed lower extremities are the most common attachment sites (Spengler *et al.* 2016). The remaining 50% denied tick exposure, suggesting subclinical or unnoticed tick contacts, which is a recognized challenge in CCHF epidemiology. This underlines the need for community education and protective measures (Morikawa *et al.* 2011).

Seasonality analysis. The seasonal distribution of cases shows a clear summer peak (June–July, 83.3% of cases). The early (April–May) and late (August) cases indicate prolonged tick activity in the region. Seasonal trends correlate with *Hyalomma* tick life cycle and climatic conditions, such as temperature and humidity, favoring tick reproduction and activity (WHO 2022).

Clinical manifestations and disease severity. The clinical spectrum of CCHF in the Turkestan region ranged from moderate to severe forms. Out of 24 patients, 13 (54.2%) exhibited severe disease, while 11 (45.8%) were classified as moderate. This distribution highlights a substantial proportion of patients with systemic involvement, hemorrhagic manifestations, and laboratory abnormalities.

Leading clinical symptoms

Weakness/fatigue: 100%

Fever (>38.5°C): 75%

Headache: 37.5%

Myalgia: 37.5%

Nausea and vomiting: 33.3%

The prevalence of weakness in all patients reflects the profound systemic impact of the virus, consistent with cytokine-mediated inflammatory responses described in CCHF pathogenesis (Ergonul 2021).

Hemorrhagic manifestations. Bleeding symptoms were observed in a subset of patients, with variable presentation:

Hematomas: 20.3%

Petechial rash: 12.5%

Epistaxis (nose bleeding): 16.6%

Internal organ bleeding: 8.3%.

These findings are consistent with the viral-induced endothelial damage and thrombocytopenia characteristic of CCHF (Spengler *et al.* 2015). Fig. 4 illustrates the distribution of hemorrhagic manifestations among patients with Crimean-Congo hemorrhagic fever (CCHF) in the Turkestan region. Hematomas were the most common bleeding symptom, affecting 20.3% of cases, followed by epistaxis (16.6%), petechial rash (12.5%), and internal organ bleeding (8.3%). This pattern reflects the variability in vascular involvement and platelet reduction associated with CCHF infection.

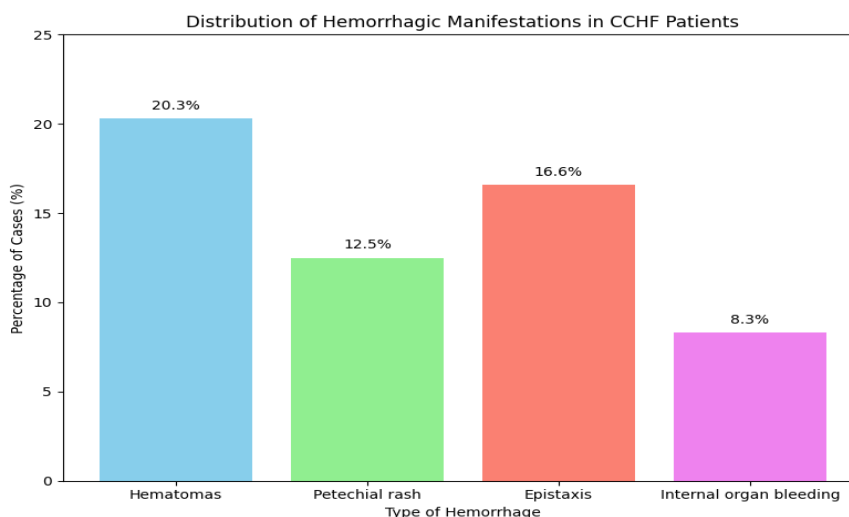


Fig. 4. Distribution of hemorrhagic manifestations in CCHF patients.

Laboratory findings. Thrombocytopenia ($<100 \times 10^9 \text{ L}^{-1}$) was observed in 12 patients (50%), correlating with the presence of hemorrhagic signs and disease severity. Laboratory confirmation using ELISA IgM and PCR showed:

ELISA IgM positive, PCR negative: 1 case (4.2%)

ELISA IgM negative, PCR positive: 7 cases (29.1%)

Both ELISA IgM and PCR positive: 16 cases (66.7%)

The dual testing approach emphasizes the importance of combining molecular and serological diagnostics to increase sensitivity, as seroconversion may not coincide with peak viremia (Daubney *et al.* 1931).

Table 7. Laboratory abnormalities and diagnostic confirmation.

Indicator	Number of Cases	Percentage (%)
Thrombocytopenia ($<100 \times 10^9 \text{ L}^{-1}$)	12	50
ELISA IgM positive, PCR negative	1	4.2
ELISA IgM negative, PCR positive	7	29.1
Both ELISA IgM and PCR positive	16	66.7

Pathogenetic commentary. The high prevalence of thrombocytopenia, systemic weakness, and hemorrhagic manifestations indicates that viral replication in endothelial cells and immune dysregulation are major contributors to disease severity. This aligns with global CCHF studies, suggesting that early recognition and supportive therapy are crucial to reduce morbidity and prevent fatalities.

Correlation of clinical severity and tick exposure. Half of the patients reported confirmed tick bites, with a higher proportion of severe cases among those exposed, suggesting a dose-response relationship between tick-mediated viral inoculation and disease severity. Interestingly, 50% of patients denied tick exposure, reflecting subclinical tick interactions or overlooked bites, which is a known epidemiological challenge in CCHF control (Daubney *et al.* 1931).

DISCUSSION

Evolution of case fatality rates: The Turkestan paradox. The most defining outcome of this descriptive analysis is the recorded case fatality rate (CFR) of 4.1%. This figure stands in stark contrast to the historical and global

benchmarks for Crimean-Congo hemorrhagic fever (CCHF), which typically range from 10% to 40%. While CCHF is traditionally viewed as a high-mortality viral infection, our findings suggest a transition toward a more manageable clinical profile in Southern Kazakhstan. We hypothesize that this "Turkestan Paradox" - high clinical severity (54.2% severe cases) coupled with low mortality - is primarily driven by the "Golden Window" of medical intervention. The mean time from symptom onset to hospitalization was 2.7 ± 2.2 days. This rapid clinical response, facilitated by decentralized diagnostic networks in rural districts, prevents the progression of the virus into the irreversible stage of disseminated intravascular coagulation (DIC). Compared to reports from Kabul (Afghanistan), where mortality remains high due to late-stage presentations, the Turkestan model emphasizes that survival is a function of time rather than viral attenuation alone.

The "One Health" interface and cattle-mediated transmission. A pivotal discovery in this study is the absolute role of cattle (cows) in the epidemiological chain of the 2023-2024 outbreaks. While small ruminants like sheep and hares are known viral reservoirs, 100% of our occupationally-exposed patients reported direct contact with cattle. This identifies cows as the primary "bridge" host for *Hyalomma* ticks in this region (Hoogstraal 1979).

Furthermore, the fact that 50% of patients denied any history of a tick bite underscores a critical "Recognition Gap." This suggests that transmission in Turkestan Region is shifting from purely vector-borne (tick bites) to contact-borne pathways. We propose that during manual milking and traditional husbandry practices, individuals are exposed to the virus through subclinical percutaneous contact with viremic blood or by crushing engorged ticks. This necessitates a radical shift in public health strategies: from simple tick-repellent education to comprehensive biological safety protocols for rural families handling large livestock.

Bioclimatic triggers and spatial clustering. The seasonality of the 24 cases (83.3% in June and July) exhibits a perfect synchrony with the phenology of the *Hyalomma* genus. The arid continental climate of Turkestan Region serves as a bioclimatic catalyst; rising cumulative temperatures in late spring trigger the rapid molting and questing activity of the vector.

The spatial clustering in the Sauran, Shardara, and Otrar districts highlights these areas as "ecological traps." In these districts, the density of cattle populations coincides with optimal tick habitats in irrigated pastoral zones. Our results align with climatic trend studies in Turkey and Iran, where warming temperatures have been linked to extended transmission seasons. This suggests that the southern regions of Kazakhstan are at the forefront of climate-driven viral expansion in Central Asia.

Laboratory synergy and molecular sentinel monitoring. The diagnostic success of this study (100% PCR confirmation) underscores the utility of molecular tools in early-phase detection. However, the high rate of dual positivity (PCR+ and ELISA IgM+) in 66.7% of cases indicates that even with rapid seeking of care (2.7 days), the viral load is already at its peak upon admission. This molecular profile suggests that the CCHFV strains circulating in Turkestan are highly viremic, emphasizing the need for strict nosocomial biosafety to prevent human-to-human transmission in healthcare settings.

The 2023-2024 outbreaks in Turkestan demonstrate that CCHF remains an active and severe threat to public health in Kazakhstan. However, the low mortality rate is a testament to the efficacy of the regional response system. To maintain this progress, future efforts must adopt a "One Health" approach, integrating tick control in cattle populations with genomic surveillance of circulating strains. Turkestan serves as a global sentinel, providing vital insights into how early diagnosis can transform a traditionally fatal disease into a manageable clinical condition (National Public Health Center of Kazakhstan 2024).

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.

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