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Demographic Study and Risk Factors Associated With Crimean-Congo Hemorrhagic Fever among Patients in Thi-Qar, Iraq

Zaytoon Abdulrida Ighewish Al-Khafaji [1]

Asst. Prof., DVM, PhD. Müge FIRAT [2]

Mohammed Mohsen Mohammed [3]

Rajaa Ali Moheiseen Al-Taee [4]

Amal Ali Al-Taee [5]

Ameer Kadhim Al-Humairi [6]

Falah Hasan Obayes Al-Khikan [7]

Aneeda Khraibet Abed [8]

Ali Nadhim Shndiwe Khikani [9]

Abstract

Background:

A high mortality rate is associated with Crimean-Congo hemorrhagic fever (CCHF), a viral fever that is caused by infection with Narivirus, a member of the Bunyavirus family, and is reported sporadically in Iraq.

Materials and methods:

Confirmed cases of Crimean-Congo Hemorrhagic Fever (CCHF) in Thi-Qar city, Iraq, from 2021 to 2023 were included in this study. The demographic and epidemiological characteristics of the patients were described using frequencies and percentages. The epidemic trajectory represented the duration and timing of the outbreak.

Results:

More than half of the patients, 113 (55.9%) were males. Females represent 89 (44.1%) of patients. The mean age of the patient was 36.63 ±16.23, ranging from 6 years to 78 years. Less than one-quarter of them, 21.4%, presented with age group (20-30) years. The majority of patients got an infection in the Year 2022 (N=162, 80.2%), and the majority of them got an infection during May (N=42, 20.8%) and June (N=44, 21.8%). The majority of patients (N=70, 37.6%) were housewives. Animal breeders represent (N=17, 9.1%), and butchers represent (N=19, 10.2%). Death among patients represents (N=52, 28.6%), and patients who get a complete cure represent (N=127, 69.8%). While there was no significant correlation between socio-demographic characteristics and the outcome of patients with hemorrhagic fever, there was a significant association between the year of infection and the outcome of patients with hemorrhagic fever ($P < 0.001$).

Keywords: Hemorrhagic fever, Crimean-Congo hemorrhagic fever, Iraq, Narivirus, Viral infection.

[1] Microbiology Department, College of Medicine, University of Babylon, Iraq

[2] Çankırı Karatekin University, Turkey

[3] Microbiology Department at the College of Medicine, University of Babylon, Iraq

[4] Hammurabi Medical Collage, University of Babylon, Babylon, Iraq

[5] Department of Biology, Collage of Science, University of Babylon, Babylon, Iraq

[6] Community Medical Department at the College of Medicine, University of Babylon, Iraq

[7] Department of Microbiology, Al-Shomali General Hospital, Babylon Directorate Health

[8] Ministry of Health Dhi Qar Health Department

[9] Çankırı Karatekin University

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Introduction:

The CCHF, an acute tick-borne zoonotic infection, is caused by the Crimea-Congo virus, a member of the Nairoviridae family. In 60–80% of cases, CCHF is asymptomatic; the remaining 20–40% of patients frequently experience a fever, headache, and malaise initially, which is followed by gastrointestinal symptoms. In severe cases, haemorrhage, shock, and multi-organ system failure may occur [1].

CCHF is a severe condition that has a high death rate in people. When an infected Ixodid tick (Hyalomma genus) bites an animal, the animal contracts the CCHF infection. The most common ways humans get infected are through insect bites or direct contact with infected animals' blood or other tissues. Most instances have affected people working in the cattle business, such as veterinarians, agricultural labourers, and slaughterhouse workers. However, because CCHF has frequently produced nosocomial epidemics with significant death rates, healthcare personnel—including those who work in laboratories—are gravely at risk of contracting an infection [2].

The Congo hemorrhagic virus was initially isolated and described from blood samples of patients in the Congo in 1967. In 1969, a virus known as Crimean-Congo hemorrhagic fever virus (CCHFV) was isolated in Crimea. This virus exhibited comparable antigenic characteristics [3]. CCHFV is a member of the Orthonairovirus genus, which is a subfamily of the Nairoviridae family. The spherical virions are enveloped by an envelope and are transmitted by ticks. A tri-segmented negative-sense RNA strand is present in the virus. The L segment encodes the viral RNA-dependent RNA polymerase. The M segment encodes two viral surface glycoproteins, Gn and Gc.

The nucleocapsid protein N is encoded by the S segment.[4].Since 1979, CCHF has rarely occurred in Iraq. In 1981, a small epidemic involving eight patients and two healthcare workers isolated CCHFV. From the 1980s until 2010, there were sporadic CCHF outbreaks; between 1998 and 2009, 0 and 6 verified cases were recorded. In 2010, there were 11 laboratory-confirmed cases of CCHF, bringing the total suspected cases to 28. The majority of minor epidemics stayed within the same province.

The number of CCHFV infections has increased from 33 cases in 2021 to a sixfold increase in the first half of 2022 over the past several years [5-6] . Even though it infects a wide variety of species and causes measurable viremia, CCHFV infections in animals do not cause any symptoms. Other than humans, the only animals that were vulnerable to CCHFV were newborn mice and rats. Humans were not affected by this virus. Through intracranial or intraperitoneal injection, disease symptoms and mortality may be detected in human and newborn mice and rats. As a result, newborn rodents are the first animal models for research dealing with chronic cholesteatoma of the heart (CCHF). [7].

The objective of this investigation is to assess the prevalence of the CCHF in Thi-Qar, southern Iraq, from 2021 to 2023 by detecting some risk factors that may be associated with this outbreak.

Materials and methods:

A cross-sectional study was conducted on 202 human CCH-FV cases that were reported in the Thi-Qar Governorates, Iraq. Information from all patients' medical records concerning this epidemic were retrieved and analysed. The number and proportion of infected persons are recorded over three years, 2021-2023.

All suspected patients displaying signs of CCHFV were admitted to isolated wards and Intensive Care units. All patients throughout the epidemic had blood specimens taken. The gathered specimens were promptly sent to the Central Public Health Laboratory in Baghdad. Due to the significant biohazard risk posed by CCHF specimens, they are handled under maximum biological containment settings. Active Crimean-Congo Hemorrhagic Fever Virus (CCHFV) infection was identified by amplifying CCHFV RNA or measuring IgM or IgG specific to CCHFV levels following the primary phase of infection [8-9].

To guarantee safe specimen handling, serum samples are inactivated before nucleic acid extraction and amplification. The serum was used to isolate viral RNA specimens following the manufacturer's instructions provided by Geneaid, South Korea. The WHO-validated reagent specific for Eurasian clades IV-VII was utilized to detect CCHFV genes using primer settings and oligonucleotide sequences for RT-PCR. In order to promptly identify active infection, the RT-PCR test offers the highest degree of sensitivity.[10].

SPSS version 26 was employed to conduct the statistical analysis. Frequencies and percentages were employed to represent categorical variables. Means with standard deviations (SD) were presented for continuous variables. The means of the three categories were compared using an ANOVA test. The relationship between categorical variables was determined using Fisher's Exact test. Significant was defined as a p-value of 0.05 or lower.

Results:

The distribution of patients with hemorrhagic fever according to sex is illustrated in [Figure 1]. More than half of the patients (N=113, 55.9%) were males. Females represent (N=89, 44.1%) of patients.

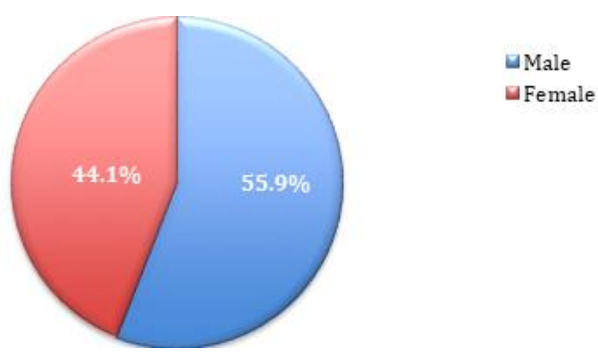

Figure 1: Distribution of patients with hemorrhagic fever according to sex (N=202).

Less than one-quarter of patients (N=43, 21.4%) presented with age group (20-30) years. The mean age of the patient was (36.63 ±16.23) with a younger patient six years and older 78 years [Table 1].

Table 1: Distribution of patients with hemorrhagic fever according to age (N=201).

Age (years)	Number	%
< 20 years	33	16.4%
20-30 years	43	21.4%
30-40 years	35	17.4%
40-50 years	40	19.9%
50-60 years	26	12.9%
60-70 years	17	8.5%
≥70 years	7	3.5%
Total	201*	100.0%

* **The age of one patient is not recorded in the database.**

The majority of patients get the infection in the year 2022 (N=162, 80.2%), and the majority of them get the infection during May (N=42, 20.8%) and June (N=44, 21.8%) [Table 2] [Figure 2 and 3].

Table 2: Distribution of patients with hemorrhagic fever according to year of infection (N=202).

Year of diagnosis	Number	%
2021	16	7.9%
2022	162	80.2%
2023	24	11.9%
Total	202	100%

Table 3: Distribution of patients with hemorrhagic fever according to month of infection (N=202).

Month of diagnosis	Number	%
January	3	1.5%
February	1	0.5%
March	3	1.5%
April	26	12.9%
May	42	20.8%
June	44	21.8%
July	27	13.4%
August	16	7.9%
September	15	7.4%
October	8	4.0%
November	15	7.4%
December	2	1.0%
Tota	202	100.0%

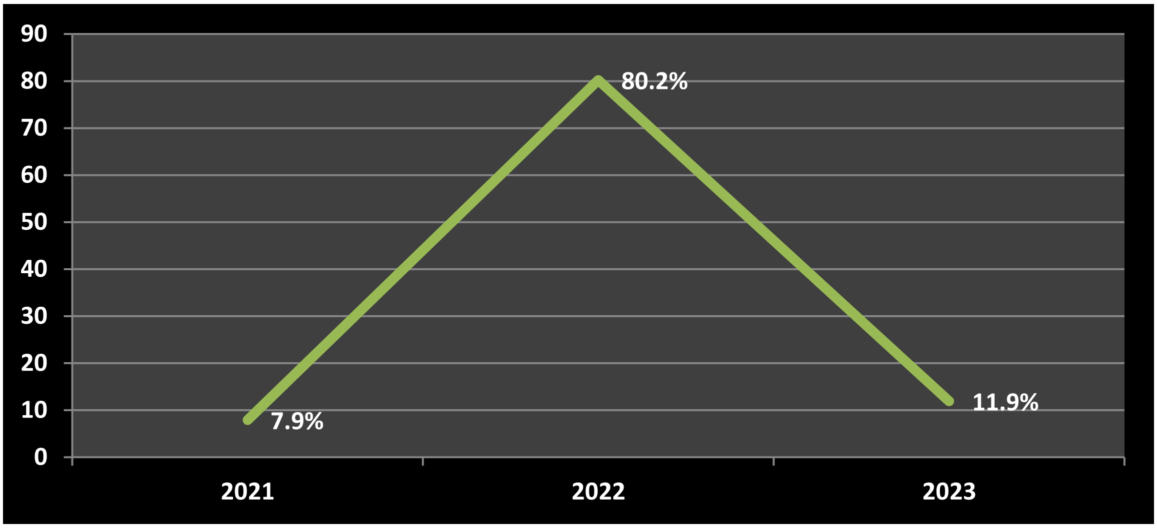

Figure 2: Distribution of patients with hemorrhagic fever according to year of infection (N=202)

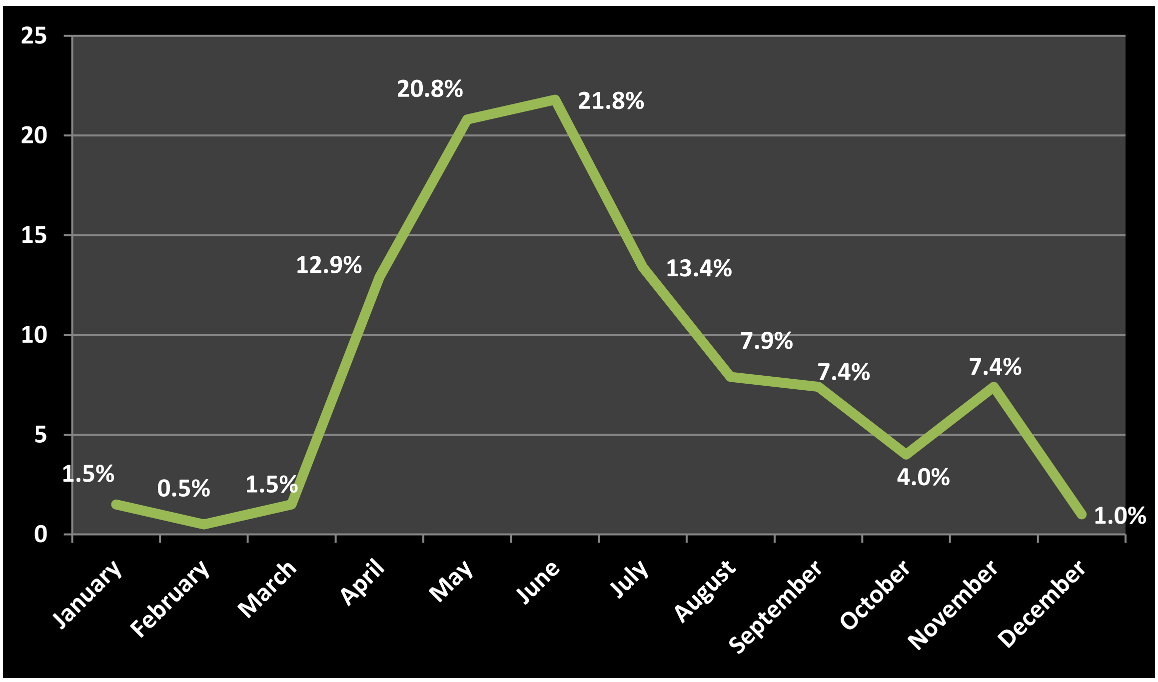

Figure 3: Distribution of patients with hemorrhagic fever according to month of infection (N=202)

The distribution of patients with hemorrhagic fever according to occupation showed that the majority of patients (N=70, 37.6%) were housewives. Animal breeders represent (N=17, 9.1%), and Butcher represent (N=19, 10.2%) [Table 3].

Table 4: Distribution of patients with hemorrhagic fever according to occupation (N=186).

Occupation	Number	%
Housewife	70	37.6%
Animal breeders	17	9.1%
Butcher	19	10.2%
Employee	18	9.7%
Free work	27	14.5%
Student	21	11.3%
Heath caregiver	1	0.5%
Child	1	0.5%

Retired	3	1.6%
No work	9	4.8%
Total	186	100.0%

*In 16 patients, the occupation was not recorded in the database.

[Figure 4] revealed the distribution of patients with hemorrhagic fever according to the outcome, including (Death, Cure and discharge on their family responsibility). Death represents (N=52, 28.6%), patients get complete cure represent (N= 127, 69.8%), and patients discharged on their family responsibility represent only three patients (1.6%) of total patients recorded in 3 years periods of data collection. Twenty patients had an unknown outcome.

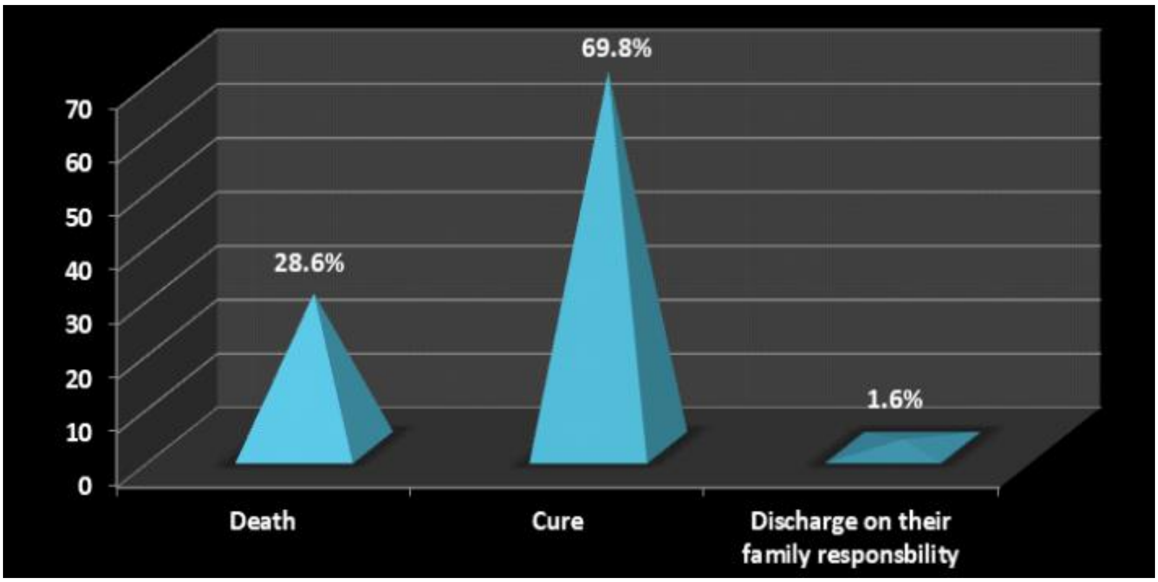

Figure 4: Distribution of patients with hemorrhagic fever according to outcome (N=182).

[Table 4] revealed the association between the outcome of patients with hemorrhagic fever, including (Death, Cure and discharge on their family responsibility) and socio-demographic characteristics, including (age, sex and occupation). There was no significant association between the outcome of patients with hemorrhagic fever and socio-demographic characteristics.

Table 5: The association between the outcome of hemorrhagic fever patients and socio-demographic characteristics.

Socio-demographic characteristics	Outcome			Total	P-value
	Death	Cure	Discharge on their family responsibility		
Age (years)	(36.40 ± 15.14)	(36.98 ± 16.52)	(38.33 ± 19.55)	(36.83 ± 16.09)	0.965
Sex					
Male	27 (51.9)	75 (59.1)	0 (0.0)	102 (56.0)	
Female	25 (48.1)	52 (40.9)	3 (100.0)	80 (44.0)	0.093
Total	52 (100.0)	127 (100.0)	3 (100.0)	182 (100.0)	
Occupation					
Housewife	19 (42.2)	41 (34.8)	3 (100.0)	63 (38.0)	
Animal breeders	6 (13.3)	11 (9.3)	0 (0.0)	17 (10.2)	
Butcher	5 (11.2)	13 (11.0)	0 (0.0)	18 (10.8)	
Other	15 (33.3)	53 (44.9)	0 (0.0)	68 (41.0)	0.407
Total	45 (100.0)	118 (100.0)	3 (100.0)	166 (100.0)	

[Table 5] illustrates the correlation between the year and month of infection and the prognosis of patients with hemorrhagic fever (Death, Cure, and discharge on their family responsibility). The prognosis of patients with hemorrhagic fever was significantly correlated with the year of infection.

Table 6: The association between the outcome of patients with hemorrhagic fever and year and month of infection

Study variables	Outcome			Total	P-value
	Death	Cure	Discharge on their family responsibility		
Year of infection					
2021	7 (43.8)	9 (56.2)	0 (0.0)	16 (100.0)	
2022	39 (24.4)	118 (73.7)	3 (1.9)	160 (100.0)	
2023	6 (100.0)	0 (0.0)	0 (0.0)	6 (100.0)	0.001*
Total	52 (28.6)	127 (69.8)	3 (1.6)	182 (100.0)	
Month of infection					
January, February and March	3 (100.0)	0 (0.0)	0 (0.0)	3 (100.0)	
April, May and June	25 (26.1)	70 (72.9)	1 (1.0)	96 (100.0)	
July, August and September	19 (32.8)	38 (65.5)	1 (1.7)	58 (100.0	
October, November and December	5 (20.0)	19 (76.0)	1 (4.0)	25 (100.0)	0.078
Total	52 (28.6)	127 (69.8)	3 (1.6)	186 (100.0)	

Discussion:

The alarming increase in the number of CCHFV infections confirmed by RT-PCR in diverse Iraqi regions is worrying. It emphasizes the necessity of taking measures to mitigate the escalating trend of CCHFV infections in order to prevent the loss of life on a global and local scale.

CCHF is prevalent in Iraq, located in Western Asia and constitutes the northeastern part of the Arab world. CCHF has been documented in Iraq since 1979, when the illness was first identified in 10 people. Between 1989 and 2009, six incidents were documented. In 2010, there were 11 cases. In 2018, three fatal cases were reported. In 2021, 33 confirmed cases were reported, including 13 fatalities (CFR 39%). Sheep and cattle farming are prevalent in Iraq. Research has shown that these animals are often infected by tick species, particularly Hylomma species, the primary carriers of CCHF. [11-12].

In the current study, the majority of patients get an infection in the Year 2022 (N=162, 80.2%), and the majority of them get an infection during May (N=42, 20.8%) and June (N=44, 21.8%).

The increased frequency of CCHF in Iraq may have resulted from several other reasons, such as rising temperatures and climate change. There have been notable variations in the temperature and climate of Iraq. Compared to other secondary hosts, H. marginatum often feeds on people with high aggression and affinity. Low humidity and high temperatures (>40°C) aggravate this tendency. People often purchase their needs from private cattle breeders who carry out the slaughtering in secret and without supervision since there is a great demand for animal sacrifices during Adha Eid. This practice is nearly universal in Iraq and might be a factor in the increased incidence of CCHF patients [13-14].

The primary difficulty in addressing this endemic is the insufficient collaboration between the animal and human sectors in disease management. The absence of tick control programmes exacerbates the spread.

There is a lack of laboratory kits for diagnosing CCHF, particularly at district levels. This may result in misdiagnosis or delayed treatment, leading to a rise in case mortality. [15].

In this study, death represents (N=52, 28.6%), patients who get complete cure represent (N= 127, 69.8%), and patients discharged on their family responsibility represent only three patients (1.6%) of total patients recorded in 3 years periods of data collection.

The WHO considers CCHFV a high-priority virus because of its high death rate, widespread vector transmission, and the lack of adequate medical prevention and treatment. [16]. The rising number of RT-PCR-confirmed CCHFV infections in most Iraqi regions is worrying, emphasising the need to implement strategies to prevent this increasing trend in CCHFV infections to save lives regionally and worldwide. The study's limitations include the absence of specific medical histories and test data for the subjects, which presents a challenge when comparing live and dying cases. Additionally, the CCHF strains of the verified cases were not provided, which could have provided additional information regarding the patient's prognostic variables and the genetic heterogeneity of CCHF in Iraq.

Conclusion:

Crimean-Congo Hemorrhagic Fever (CCHF) is a severe viral virus that poses a significant risk to public health. It is essential to comprehend the aetiology of CCHF due to its high mortality rate and the lack of a particular therapy or vaccination. The CCHF outbreak in Iraq during 2021-2023 was the largest outbreak recorded in Iraq. This rapid spreading was associated with the COVID-19 pandemic. Furthermore, it is essential to implement stringent preventative measures and increased human and vector surveillance. More investigations on ticks, which act as viral vectors, are demanded. Increased temperatures affected vector behaviour. Comprehensive laboratory investigations are necessary to determine the causes of mortality.

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