RESEARCH ARTICLE

Modes of transmission of Crimean-Congo Hemorrhagic Fever in Iraq in 2023: which is more common and more serious?

Ghazwan A. Baghdadi,[a] Ihab Raqeeb Aakef,[a] Sarmad Basim Salman,[b] Raghad Ibrahim Khaleel.[c]

ABSTRACT

Introduction: Crimean-Congo hemorrhagic fever (CCHF) is a viral tick-borne zoonotic disease. CCHF virus is transmitted to humans by tick bites, contact with infected animal or human tissues or blood during and immediately after slaughtering. Since 1979, when the first case of CCHF was diagnosed, Iraq has continued to report CCHF cases on an annual or semi-annual basis.

Objective: to investigate the modes of transmission of CCHF and determine the most common and the most serious mode, determining the factors affecting mortality and case fatality rate in this period.

Methods: A cross-sectional study was conducted in Baghdad/Iraq. The study included all confirmed cases in Iraq during 2023. Outbreak investigation activities were conducted for all the confirmed cases to detect the mode of transmission. Binary logistic regression analysis was used in statistical analysis.

Results: The most common mode of transmission found was animal/ possible animal contact (67%), followed by tick/possible tick bite (32.2%) and then human contact (0.9%). Residence (P=0.043) and bleeding at presentation (P=0.000) were found to be significant predictors of fatal outcomes.

Conclusion: The most common mode of transmission identified was animal/possible animal contact. No significant difference was found between different modes of transmission in terms of fatal outcomes.

Key words: Crimean-Congo, Hemorrhagic fever, Iraq, Mode of transmission.

INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a viral tick-borne zoonotic disease. It is distributed in Africa, Asia, Southeast Europe and the Middle East. CCHF was first recognised during an outbreak in the Crimean Peninsula (1944–1945). The virus was found identical to a virus isolated from a patient in the Democratic Republic of the Congo (1956). The disease was called after these two places. [1] The causative agent is a virus belonging to the Orthonairovirus genus, Nairoviridae family. The geographic distribution and incidence have increased during the last period.[2]

The disease is asymptomatic in animals. On the other hand, it causes an acute and sometimes fatal infection in humans.[3] The symptoms include fever, myalgia, dizziness, headache, backache, abdominal pain, nausea, vomiting, diarrhoea, petechial rash, ecchymoses, and other haemorrhagic phenomena. Severely ill patients may have rapid kidney deterioration, pulmonary failure or sudden liver failure on day five of illness.[4]

CCHF virus circulates in nature between ixodid hard ticks and vertebrate hosts. It is transmitted to humans through bites from infected ticks or direct contact with the tissues or blood of infected ticks, viraemic livestock, and viraemic patients. CCHF virus is transmitted

a: MBChB, CABMS/CM. Community Physician, Communicable Diseases Control Centre (CDC Iraq), Public Health Directorate, MoH/Baghdad/Iraq. *b:* MBChB CABMS/CM, Community Physician, The National Centre for Training and Human Development, Ministry of Health, Baghdad, Iraq. *c:* BVM, Central Public Health Laboratory (CPHL), Public Health Directorate, Baghdad), Iraq.
Corresponding Author: **Ghazwan A. Baghdadi**, E mail: **ghazwancommunity2015@yahoo.com.**

among ticks transovarially, transstadially, and venereally. Transmission through co-feeding may occur. After being infected, ticks remain infective throughout their whole life. The factors contributing to CCHF infection vary among different countries. The incubation period of CCHF is shorter with high viral doses and in bloodstream infections.[5]

CCHF virus transmits in an endemic cycle between asymptomatic mammals and ticks. The genus Hyalomma appears to be the main vector of the virus. Venereal and transovarial transmission is possible for this species. Many mammalian species can transmit CCHF virus to ticks when they are viremic.[6] CCHF virus is transmitted to humans by tick bites or contact with infected animal tissues or blood during and immediately after slaughter. Many cases have occurred among slaughterhouse workers, agricultural workers, and veterinarians. The third mode of transmission from human to human can occur through close contact with infected patients' blood, organs, secretions or other body fluids. Nosocomial infections can occur through the reuse of needles and improper sterilisation of medical equipment and supplies. The length of the incubation period depends on the mode of virus transmission. Following tick bite, this period is usually one to three days (maximum nine days) and five to six days (maximum therteen days) after contact with infected tissues and blood.[4]

Since 1979, when the first case of CCHF was diagnosed in Al-Yarmouk Hospital,[7] Iraq continues to report CCHF cases annually or semi-annually. Since 2021, Iraq has witnessed a significant unpreceded outbreak that severely hit the southern provinces, with around one-half of the patients reporting contact with animals, contact with raw meat and animal slaughtering during the past 14 days.[8]

The epidemiology of CCHF in close neighbouring countries, such as Iran and Turkiye, is well recognised. From 1978 to 2021, the mortality rate of CCHF in some Arabic countries varied from 24 to 61% throughout various outbreaks. In addition, CCHF is reported throughout the Middle East, Africa, Southern and Eastern Europe, India, and other Asian countries; an estimated 10,000 to 15,000 human infections occur annually.[9]

Although the reported cases of CCHF in Iraq in the last few years were unprecedented, very few studies addressed this problem, especially the mode of transmission and their related details, nationally, regionally and globally. This study was designed to investigate the modes of transmission of CCHF and determine the most common and severe modes, as well as the factors affecting mortality and case fatality rates in Iraq during 2023.

METHODS

Setting and study design: A cross-sectional study with analytical elements was conducted at the Zoonotic Section of the Communicable Disease Control Centre (CDC Iraq), Public Health Directorate, Ministry of Health, Iraq, using data recorded in 2023 at the National Surveillance System in Iraq. (587 confirmed CCHF cases).

Ethical consideration: The research protocol of this study was approved by the research ethics committee at the public health directorate according to the code of ethics in research in the Ministry of Health in Iraq. The authors obtained acceptance from the public health directorate to use data from the National Surveillance System for this study. The personal data of the patients were kept confidential and anonymous.

Definition of cases; inclusion and exclusion criteria: We included any confirmed CCHF case defined as suspected or probable with a positive real-time polymerase chain reaction (RT-PCR) test or IgM in ELISA.[10] The test was conducted at the Central Public Health Laboratory (CPHL) in Baghdad using RT-PCR (RealStar® CCHFV RT-PCR Kit 1.0/Altona) or ELISA IgM (Human Crimean-Congo Hemorrhagic Fever Virus IgM [CCHF-IgM] ELISA Kit/abbexa) techniques which were used to determine the results as positive or negative. Records of one patient were excluded from the study because the data were incomplete.

Sampling: The study included all CCHF-confirmed cases during 2023 in Iraq from the national surveillance system in the Communicable Disease Control Center (CDC Iraq/Zoonotic Section).

Data collection, variables and data extraction form: We reviewed the registry of CCHF and extracted the following data:

1. Demographic characteristics of patients.
2. Mode of transmission.
3. Incubation period.
4. Outcome.

A team of Outbreak investigation activities routinely visits each patient's house with positive CCHF to investigate the contacts, habitat, and transmission route and then instructs the household members about proper preventive measures. This team practice considerable effort to get exact information, including those regarding the mode of transmission and then classify it according to the following categories:

1. Tick bite: if the patient mentioned a history of tick bite during the past 14 days.
2. Animal blood/tissue contact: if the patient mentioned a history of contact with blood or tissues of animals during the past 14 days.
3. Human contact: if the patient mentioned a history of contact with blood or tissues of the human case during the past 14 days.
4. Possible tick bite: if the patient did not mention a history of tick bite or animal contact or human case contact or mentioned exposure to both modes (tick bite and animal contact together) during the past 14 days, but the outbreak investigation team concluded that the case was due to possible tick bite according to the results of the investigation activity; if the patient lived or travelled to an area including contact with ticks on animals during the past 14 days and were likely to be subjected to a tick bite. (Taking in consideration the median incubation period for each mode of transmission if tick bite or animal contact).
5. Possible animal contact: if the patient did not mention a history of tick bite or animal contact or human case contact or mentioned exposure to both modes (tick bite and animal contact together) during the past 14 days, but the outbreak investigation team concluded that the case was due to possible animal contact according to the results of the investigation activity; if the patient lived in an area with no history of contact with ticks on animals and had no history of travel to an area including contact with ticks on animals during the past 14 days and were likely to be subjected to contact with raw meat. (Taking in consideration the median incubation period for each mode of transmission if tick bite or animal contact).

The national surveillance system relies on immediate data notification and routine monthly data collection from zoonotic units in various provinces, utilising yearly updated case investigation forms and Excel sheets based on the annual national zoonotic plan. The case investigation form includes data regarding socio-demographic characteristics, clinical signs, epidemiological data, and the patient's outcomes. The data was received online at the CDC Baghdad/Zoonotic Section and then analysed. The independent variables included age, gender, occupation, residence, bleeding and transmission mode. The dependent variable is patient outcomes, specifically cure or death.

Data management and analysis plan: A detailed description of each variable was created using the Statistical Package for the Social Sciences (SPSS) version 27 and Microsoft Excel 2019. Descriptive statistics were conducted for all the included variables. Only serial numbers were related to the details of the participants, and the collected data was managed daily. Data was expressed using frequency/percentage. Data were presented using tables and graphs. The chi-square test was used to determine the association between the studied variables and the patient's outcome. Following this, Binary logistic regression analysis was used to identify significant predictors of the fatal outcome.

Table 1 | Socio-demographic and clinical characteristics of the patients, Iraq, 2023.

Variables	Number	Percentage
Age group		
<15 y	17	2.9
15-24 y	135	23.0
25-44 y	265	45.1
45-64 y	137	23.3
≥65 y	33	5.6
Gender		
Male	340	57.9
Female	247	42.1
Occupation		
Housewife	216	36.8
Butcher	78	13.3
Animal breeder	48	8.2
Health worker	7	1.2
Other	238	40.5
Residence		
Rural	267	45.5
Urban	238	40.5
Semiurban	69	11.8
Slums	13	2.2
Bleeding		
Yes	303	51.6
No	284	48.4
Outcome		
Cure	504	85.9
Death	83	14.1

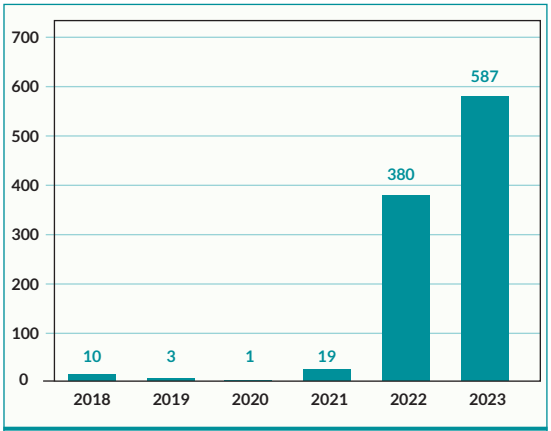

Figure 1 | Distribution of CCHF cases according to years, Iraq, 2018-2023.

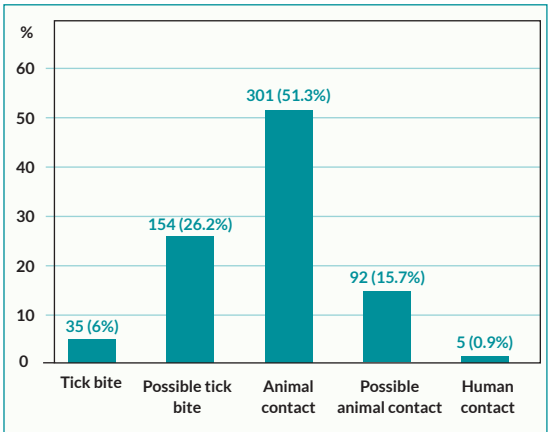

Figure 2 | Distribution of patients according to modes of transmission (5 categories), Iraq, 2023.

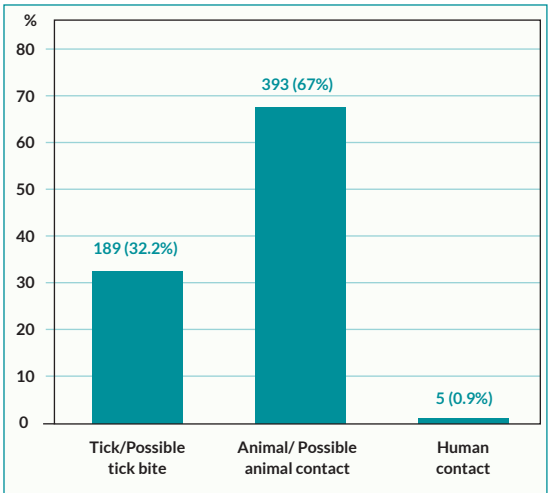

Figure 3 | Distribution of patients according to modes of transmission (3 categories), Iraq, 2023.

RESULTS

The study included 587 confirmed cases out of 2186 suspected cases in 2023. The current study showed that the most common age group category was 25-44 years, with 265 participants (45.1%), followed by 45-64 years, with 137 participants (23.3%). Males constituted 340 (57.9%) of the patients. By exclusion of other occupational groups, the most common occupational group found was housewives, at 216 (36.8%), followed by butchers, at 78 (13.3%). The study also showed that 267 (45.5%) patients lived in rural areas, while 238 (40.5%) lived in urban areas. Additionally, 51.6% of patients presented with bleeding at the time of presentation. The case fatality rate was 14.1%, as shown in **Table 1**. **Figure 1** shows the distribution of CCHF cases according to the period from 2018-2023.

Table 2 | Relationship of final outcome with socio-demographic and clinical characteristics of the patients, Iraq, 2023.

Variables	Final outcome						P value †
	Cure		Death		Total		
	N	%	N	%	N	%	
Age group							0.309
<15 y	17	3.4	0	0.0	17	2.9	
15-24 y	118	23.4	17	20.5	135	23.0	
25-44 y	222	44.0	43	51.8	265	45.1	
45-64 y	120	23.8	17	20.5	137	23.3	
≥65 y	27	5.4	6	7.2	33	5.6	
Gender							0.237
Male	287	56.9	53	63.9	340	57.9	
Female	217	43.1	30	36.1	247	42.1	
Occupation							0.627
Housewife	188	37.3	28	33.7	216	36.8	
Butcher	64	12.7	14	16.9	78	13.3	
Animal breeder	40	7.9	8	9.6	48	8.2	
Health worker	7	1.4	0	0.0	7	1.2	
Other	205	40.7	33	39.8	238	40.5	
Residence							0.039*
Rural	235	46.6	32	38.6	267	45.5	
Urban	207	41.1	31	37.3	238	40.5	
Semiurban	52	10.3	17	20.5	69	11.8	
Slums	10	2.0	3	3.6	13	2.2	
Bleeding							0.001*
Yes	246	48.8	57	68.7	303	51.6	
No	258	51.2	26	31.3	284	48.4	
Mode of transmission							0.577
Tick /possible tick bite	160	31.7	29	34.9	189	32.2	
Animal/possible animal contact	339	67.3	54	65.1	393	67.0	
Human contact	5	1.0	0	0.0	5	0.9	

*Statistically significant result. † Chi-square test was used to calculate the p values

Regarding modes of transmission, the most common category found was animal contact 301 (51.3%), followed by possible tick bite 154 (26.2%) and possible animal contact 92 (15.7%). See **Figure 2**.

When divided into three categories (tick/ possible tick bite, animal/ possible animal contact, human contact), the most common category found was animal/ possible animal contact 393 (67%), followed by tick/possible tick bite 189 (32.2%) and then human contact 5 (0.9%) as shown in **Figure 3**.

This study showed that residence and bleeding at presentation were significantly associated with fatal outcomes with p-values of 0.039 and 0.001, respectively. After doing a binary regression analysis, there is no significant difference between different modes of transmission regarding fatal outcomes (P=0.989). The same result was found regarding age group (P=0.734), gender (P=0.748) and occupation (P=0.960). Although the detailed odd ratios of the different categories were insignificant compared to the reference category (slums), residence, in general, was found to be a significant predictor of fatal

Table 3 | Predictors of CCHF fatal outcome, Iraq, 2023. †

Variables	Adjusted odd's ratio	P value
Age group		0.734
<5 y	0.000	1.000
5-14 y	0.000	0.998
15-24 y	0.459 (0.152-1.381)	0.166
25-44 y	0.631 (0.227-1.757)	0.379
45-64 y	0.471 (0.155-1.430)	0.184
≥65 y	Reference	
Gender		0.748
Male	1.239 (0.336-4.563)	0.748
Female	Reference	
Occupation		0.960
Housewife	0.929 (0.247-3.497)	0.913
Butcher	1.333 (0.638-2.786)	0.445
Animal breeder	1.144 (0.460-2.845)	0.772
Health worker	0.000	0.999
Other	Reference	
Residence		0.043*
Rural	0.583 (0.145-2.337)	0.446
Urban	0.638 (0.159-2.563)	0.527
Semiurban	1.497 (0.351-6.396)	0.586
Slums	Reference	
Bleeding		0.000*
Yes	2.598 (1.535-4.398)	0.000*
No	Reference	
Mode of transmission		0.989
Tick /possible tick bite	0.000	0.999
Animal/possible animal contact	0.000	0.999
Human contact	Reference	

*Statistically significant result. † Using binary logistic regression.

outcome (P=0.043). Moreover, bleeding at presentation was a significant predictor of fatal outcome (P=0.000), as shown in Table 2 and Table 3.

DISCUSSION

In 2023, we identified 2,186 suspected and 587 confirmed cases of CCHF, marking this year as the highest since 1979.[8] Case investigation teams have also made significant efforts to determine the exact or probable mode of transmission.

This current study shows that less than half of the patients, 265 (45.1%), were in the 25-44 years age category, and less than one-fourth, 137 (23.3%), were in the 45-64 years age category. Males represented more than half of the 340 patients (57.9%). The age and gender distribution in this study may be attributed to the fact that the majority of the workforce in the animal sector in Iraq consists of young males. By exclusion of other unspecified occupations, the most common occupational group found was housewives, at 216 (36.8%), followed by butchers, at 78 (13.3%). This considerable percentage of housewives can be due to the traditional fact in Iraq that housewives commonly deal with raw meat, especially after slaughtering, in addition to dealing with animal breeding in rural areas. The study showed nearly equal percentages of rural and urban distribution (45.5% versus 40.5%, respectively), which can be attributed to the overlap of rural and urban areas in Iraq in the current period. According to a study in Turkiye (2023), among 84 positive CCHF cases, it was found that nearly 60% of them were in the age range 26-65 years, more than 60% were males, 32.1% were housewives and farmers (for each).[11] In another study in Iran, more than half (55.4%) were in the 21-40 age range, with a male-to-female ratio of 3:1; butchers, farmers, and housewives were the most common working categories.[12] Another study from Afghanistan (2021) showed that 24 out of 34 patients were rural residents.[13]

The current study showed that more than half (51.6%) of the patients presented with bleeding. The hemorrhagic manifestations were observed among 7% and 63% of the patients in two studies in Turkiye (2021)[14] and Iran (2020),[15] respectively. The case fatality rate in this study was 14.1%. According to Blair et al. study in 2019, total deaths among confirmed cases till 2017 were found to be 177 out of 1256 in Iran, 469 out of 10,333 in Turkey, 88 out of 334 in Afghanistan and 94 out of 429 in Pakistan.[16]

The most common transmission mode identified was animal/possible animal contact (393, 67%). This finding agreed with what is observed in the Arab world and Iran; the most common mode of CCHF virus transmission was exposure to the blood or viscera of infected livestock.[17,18] On the other hand, tick bite was the primary mode of transmission in Turkiye and many other countries.[19,20]

This study found that residence and bleeding at presentation were significant predictors of fatal outcomes, with p-values of 0.043 and 0.000, respectively. According to a 2016 study in Turkiye, no significant result was observed regarding residence, with a p-value =1.000.[21] Bleeding was associated with fatal outcomes in a study in Turkiye in 2016.[21] However, a 2020 study from Iran found no significant difference. [15]

The present study found no significant difference in fatal outcomes between different modes of transmission (P = 0.989) using the binary regression analysis. The same results were found regarding age group (P = 0.734), gender (P = 0.748), and occupation (P = 0.960). This result agreed with two different studies. [21,22]

Strengths and limitations: The study's strength lies in the fact that the data were collected by an official national centre responsible for collecting CCHF cases in the country. The limitations include recall bias, and some of the data regarding the exact occupation of patients was inaccurate due to uncooperative individuals.

CONCLUSION

Since 1979, 2023 is the highest year in the number of cases of CCHF. Animal/possible animal contact was the most common transmission mode, followed by tick/possible tick bite. Residence and bleeding at presentation were found to be significant predictors of fatal outcomes. The present study found no significant difference in fatal outcomes between different modes of transmission.

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Abbreviations list: Crimean-Congo hemorrhagic fever (CCHF); real-time polymerase chain reaction (RT-PCR); Communicable Disease Control Center (CDC); Statistical Package for Social Sciences (SPSS).

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