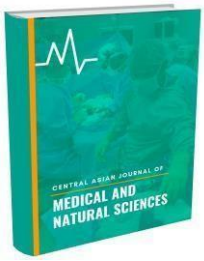

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Article

Prevalence and Case Fatality Rate Among Crimean-Congo Hemorrhagic Fever Patients in Iraq from 2021 to 2023

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Abstract: Crimean Congo Hemorrhagic Fever (CCHF), a zoonotic illness transmitted by ticks, has been present in Iraq since 1979. However, the incidence of CCHF has sharply increased since 2021, raising concerns about its public health impact. This study aims to estimate the prevalence and case fatality rate (CFR) of CCHF in Iraq for the years 2021, 2022, and 2023, and to examine the association of CFR with ribavirin administration and the interval between symptom onset and hospital admission. A retrospective cross-sectional analysis was conducted on 957 confirmed CCHF cases from across Iraq, excluding the Kurdistan region, with data provided by the Iraqi Communicable Disease Control Center. Results show a declining CFR of 47.4%, 19.5%, and 13.6% over the three years, with a statistically significant reduction in CFR (P=0.000). However, the study found no significant association between CFR and either ribavirin administration (P=0.422) or the interval from symptom onset to hospital admission (P=0.447). The findings suggest that while the CFR has significantly decreased, ribavirin administration and early hospital admission did not significantly influence patient outcomes during the study period. These results highlight the need for further investigation into other factors that may contribute to improving patient survival rates in CCHF cases.

Keywords: CFR, CCHF, Iraq, Ribavirin, Hospital admission, Symptoms onset, Prevalence.

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1. Introduction

The Crimean Congo Hemorrhagic Fever (CCHF) is endemic illness, with sporadic outbreaks and human cases according to the World Health Organization of the Eastern Mediterranean Region (WHO EMO) in a number of the nations in this region [1].

The Crimea-Congo virus, which is a member of the Nairoviridae family and causes acute tick-borne zoonotic illness, has been spreading endemically in Iraq since 1979 [2]. 60-90% of CCHF cases are asymptomatic, and the percentage of asymptomatic or subclinical cases is higher in areas where the disease is most endemic. The remaining 10– 40% will first experience fatigue, fever, and headaches before developing gastrointestinal problems. Severe cases may worsen into hemorrhage, shock, and multiorgan failure [3].

The case fatality rate (CFR) associated with disease outbreaks is generally as high as 40%, though it varies by area and even within epidemics [4].

Higher rates of CCHF disease are found in locations where hyalomma tick concentrations are abundant because hyalomma ticks are the major vector for CCHF and their geographic distribution aligns with that of the disease [5]. A sero-study to look at the disease's animal hosts was conducted in Turkey, Iran, and Iraq in 2016 and 20-30% of the

animals tested positive, according to the data, with goats having the highest rate of positive animals (50%) [6].

Ever since the first instances of CCHF were reported to Al-Yarmouk Hospital in 1979, several cases have been recorded by the health authorities. The most prominent outbreak was in 1979, with 10 cases and 7 deaths reported. In 1980, there were multiple cases reported in the Iraqi province of Sulaimani, namely in Halabja city. Published studies indicate that between the 1980s and 2009, the annual number of confirmed cases ranged from 0 to 6. In 2010, 11 confirmed cases were documented over a period of three weeks, resulting in a 36% case fatality rate [1]. Ten instances were confirmed during the 2018 epidemic and eight of these cases were fatal [7]. Four years have passed with no cases of CCHF: 2008, 2014, 2016, and 2017. After 19 cases were confirmed by laboratories in 2021, the number of patients started to increase [8].

To regulate the disease's hosts and vector, the transportation, animal health, and other sectors must work together comprehensively. Furthermore, to help in the early diagnosis and identification in order to provide better patient management and stop the disease from spreading further [9,10].

Aims of the study:

1. Estimate the change in prevalence and case fatality rate of CCHF for the years 2021, 2022, and 2023.
2. Estimating the association of CFR with ribavirin administration and the interval between symptoms onset and hospital admission.

2. Materials and Methods

Study design and patients:

A retrospective Cross-sectional study collected the data from Communicable Diseases Control Center in Baghdad, Iraq regarding confirmed CCHF patients for the years 2021,2022, & 2023.

Population of the study:

This study collected 957 confirmed CCHF human cases from all over Iraq except Kurdistan region for 3 years.

Inclusion criteria: Confirmed cases of Crimean Congo Hemorrhagic Fever disease in Iraq for the years 2021 to 2023.

Exclusion criteria: Confirmed cases of Crimean Congo Hemorrhagic Fever disease in Iraq for the years 2021 to 2023 living in Kurdistan Region.

Ethical issues:

The Ministry of Health in Iraq, Department of Public Health, Communicable Diseases Control Center in Baghdad granted permission for the collection of data that will only be used for research while protecting patient privacy.

Statistical analysis

The significance of difference between categorical (qualitative) variables was tested using Pearson's Chi-square test ($\chi 2$ test) and considered as significant difference if the P-value is less than 0.05. Otherwise, non-significant difference

3. Results

For the years 2021, 2022, and 2023, the pattern of Crimean-Congo Hemorrhagic Fever cases indicated a significant increase that began with a prevalence of 5.4 patients per 10,000,000 persons, 102.8 patients per 10,000,000 persons, and 153.4 patients per 10,000,000 persons respectively. On the other side, the case fatality rate had a marked significant

decrease as 47.4%, 19.5%, and 13.6% respectively for the study years as shown below in **Table 1,** with noticing that 7 cases were excluded in 2023 for calculating the CFR because they were discharged at their own responsibility and their fate is vague.

Table 1. Distribution of disease outcome according to study years

Patients' fate	Years						P-value
	2021		2022		2023		
	No.	%	No.	%	No.	%	
Cured	10	52.6	301	80.5	481	86.4	0.000***
Died	9	47.4	73	19.5	76	13.6	

Note: *** means a highly significant association (P<0.005) with Chi-square test

According to the 272 patients who recorded whether they have or have not administered the ribavirin in 2023 by which this antiviral was introduced to the management regimin, the disease outcome relating to ribavirin treatment administration displayed non-significant association (P = 0.422) but the case fatality rate for patients who received the mentioned drug (11.2%) is lower than those who did not receive (14.6%), as illustrated below in **Table 2**.

Table 2. Distribution of disease outcome according to ribavirin treatment administration in 2023

Patient's fate	Ribavirin treatment administration				P-value
	Yes		No		
	No.	%	No.	%	
Cured	150	88.8	88	85.4	0.422
Died	19	11.2	15	14.6	

The distribution of the patients' fate according to the interval between the onset of symptoms and their admission to hospital showed a non-significant association (P= 0.447). In addition, cured patients had interval ranged (0-15) days with a mean of 3.9 ± 2.5 days, whereas the patients who died had an interval range (0-10) days with a mean of 3.7 ± 2.2 days, as cleared in the following **Table 3,** with noticing that 12 cases were excluded as 5 had no signs and symptoms at all & 7 were discharged at their own responsibility hence, there fate is vague.

Table 3. Distribution of disease outcome according to the interval from symptoms onset to hospital admission

Interval from symptoms to hospital admission (days)	Patients Fate				P-value
	Cured		Died		
	No.	%	No.	%	
0	56	84.8	10	15.2	0.447
1	70	86.4	11	13.6	
2	113	82.5	24	17.5	
3	134	79.3	35	20.7	
4	118	81.4	27	18.6	
5	119	82.1	26	17.9	
6	69	90.8	7	9.2	
7-15	108	85.7	18	14.3	
Mean ± SD (Range)	3.9 ± 2.5 (0-15)		3.7 ± 2.2 (0-10)		

4. Discussion

This study included 957 positive RT-PCR Crimean-Congo Hemorrhagic Fever patients from whole Iraq for the years 2021, 2022, & 2023 except Kurdistan Region patients. The year 2022 recorded cases 19.0 times higher than 2021, while 2023 recorded cases 1.5 times higher than 2022, which means that the cases are increasing each year. The possible cause for the sharp rise between 2021 and 2022 is that in the spring of 2021 the veterinary department could not do their duty of spraying and dipping campaigns due to the restrictions and shortage of resources owing to COVID-19 pandemic which in turn leaded to an increase in the tick population in addition to the increased temperature and decreased humidity that leads to facilitating the molting of hyalomma tick nymphs into adults. While the increase from 2022 to 2023 may be due to the above mentioned explanation regard the weather.

Other probable cause for the sharp rise of the three years' cases compared to the previous years may be the resistance of ticks to the used insecticide or acaricide. Last but not least, the drought resulting from water scarcity in water bodies led to the migration of residents from the countryside to the city center or semi-urban areas, bringing with them their animals that carry ticks, and thus changing the nesting places of the ticks to areas more in contact with humans, so CCHF cases increased.

The case fatality rate (CFR) along the years of the present study displayed a highly significant association (P-value =0.000) as a decrease (47.4%, 19.5%, & 13.6%) respectively for the years (2021, 2022, & 2023). Other studies [8] and [11] conducted in Iraq in 2022 & 2023 reported the following CFR respectively (16.4% & 12.7%).

This decrease in the CFR along the study years could be due to good knowledge about the disease within the health system that leads to improvement in management of the patients. Other cause may be the changes that could occur to the virus -as it is RNA virus- which may decrease its virulence thus reducing the CFR. The difference between the current study results and the other two studies mentioned above is result of the difference in the duration as these studies have included specific months of the year whereas the present study covers all the months.

When the case fatality rate was linked to ribavirin treatment administration, it was noticed that a slight decrease in CFR for those who received ribavirin treatment (11.2%) and non-receivers (14.6%), although the association was non-significant (P-value= 0.422) which agrees with

[12], (8.4%) & (7.6%) CFR for ribavirin and non-ribavirin receivers with (P- value= 0.733) & this may depend on the early administration of this drug the disease course and mainly before the beginning of the hemorrhagic phase, when the viral load is higher, due to its mechanism of action that reduces the viral replication and consequently the viral effect, which is consistent with [13].

Eventually, the effectiveness of ribavirin treatment is controversially worldwide but the World Health Organization still recommend the use of ribavirin for treating CCHF patients as it is considered a wide spectrum antiviral for both, RNA and DNA viruses.

By linking the case fatality rate with the interval between symptoms onset and hospital admission, a non-significant association (P-value= 0.447) was noticed with CFR among the intervals. Additionally, the survival patients had a mean of 3.9 days while the non-survivals had 3.7 days. this result agrees with [14] who had (P-value= 0.4) with a mean of 4.9 days for survivals and 4.7 days for non-survivals. This could probably be explained depending on the base that fatal cases have a rapid disease prognosis so they deteriorate and seek medical care faster than survivals.

5. Conclusion

This study concluded that the disease prevalence has greatly increased from 2021 to 2023 compared with the previous years with the possibility of acaricides or incecticide resistance which needs further investigation in addition to the need for comprehensive campaigns and even using the social media for increasing the awareness about CCHF source of infection, mode of transmission, & the prevention and control measures for all people. It was also found that the case fatality rate has significantly decreased along the study years, while a non-significant association has been noticed for CFR with the interval from symptoms onset to hospital admission & ribavirin treatment administration, although the CFR for ribavirin receivers was slightly less than non-receivers which needs further detailed studies about these associations.

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