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Clinical and Laboratory Factors Associated with Mortality in Crimean-Congo Emorrhagic Fever: A Retrospective Study of 100 PCR-Confirmed Cases in Nasiriyah, Iraq

Riyadh Khion Abdulah[1], Haider Shaheed Mohammed[2]*, Imad H. Tahir[3], Abdul-Hassan Mahdi Salih[4]

[1] Department of Pharmacognosy and Medical Plants, College of Pharmacy, University of Thi-Qar, Thi-Qar 64001, Iraq.
[2] Department of Internal Medicine, Faculty of Medicine, University of Thi-Qar, Thi-Qar, Iraq.
[3] Department of Internal Medicine, College of Medicine, University of Thi-Qar, Thi-Qar, Iraq.
[4] Department of Physiology, College of Medicine, University of Thi-Qar, Thi-Qar 64001, Iraq.
*Corresponding author: Haider Shaheed Mohammed
Email: Hayder.Sh@utq.edu.iq, ORCID: https://orcid.org/0000-0003-1010-800X
Other ORCID identifiers
Riyadh Khion Abdulah: https://orcid.org/0009-0002-1118-3175
Imad H. Tahir: https://orcid.org/0000-0002-2206-0931
Abdul-Hassan Mahdi Salih: https://orcid.org/0009-0009-8866-9190

ABSTRACT:

Background: Crimean-Congo hemorrhagic fever (CCHF) is a severe tick-borne viral zoonosis that can progress to hemorrhage, multiorgan dysfunction, and death. Local data on clinical and laboratory correlates of fatal outcome remain limited.

Objective: To describe the clinical and laboratory profile of PCR-confirmed CCHF and identify factors associated with in-hospital mortality in patients treated at a tertiary hospital in Nasiriyah, Iraq.

Methods: This retrospective observational study included 100 symptomatic patients with PCR-confirmed CCHF admitted to the isolation ward of Al-Hussein Teaching Hospital between February 2022 and April 2023. Demographic characteristics, animal-contact history, bleeding manifestations, hematologic indices, coagulation parameters, alanine aminotransferase (ALT), C-reactive protein (CRP), renal function, hospital course, complications, and outcomes were abstracted from medical records.

Results: Among 100 patients, 55 were male and 45 were female; 75 patients recovered and 25 died, giving an in-hospital mortality of 25%. Thrombocytopenia was present in 94%, CRP was elevated in 76%, ALT in 64%, white blood cell counts were outside the reference range in 72%, D-dimer was elevated in 38%, activated partial thromboplastin time was prolonged in 37%, and acute kidney injury was documented in 15%. Mortality was significantly associated with abnormal white blood cell counts, prolonged coagulation parameters, elevated D-dimer, elevated ALT, elevated CRP, impaired renal function, animal-contact history, and bleeding-status category. All 25 deaths occurred among patients with recorded complications and intensive care unit admission. Platelet status and hemoglobin category were not significantly associated with outcome in the

original analysis.

Conclusion: Hematologic dysregulation, coagulation abnormalities, systemic inflammation, and hepatic and renal dysfunction were associated with mortality in this cohort. Because the study was retrospective and the analyses were unadjusted, these findings should be interpreted as clinical risk signals rather than independent prognostic effects and should be validated in larger multicenter cohorts.

1. INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a potentially fatal viral zoonosis transmitted primarily through Hyalomma ticks and through exposure to blood or body fluids from infected animals or humans. The disease is endemic across parts of Africa, Asia, the Middle East, and southeastern Europe, and its geographic distribution is closely linked to the ecology of competent tick vectors [1–3]. Outbreaks continue to impose substantial clinical and public-health burdens because of the potential for severe disease, nosocomial transmission, and rapid progression in a subset of infected patients [3,5–7].

Iraq has experienced recurrent CCHF activity, including marked outbreaks in recent years [4,8,9]. In outbreak settings, early recognition and appropriate infection-control precautions are particularly important for both patient management and protection of healthcare workers. However, the initial clinical presentation may be nonspecific, and patients can progress from a febrile illness to bleeding, shock, organ dysfunction, and death [3,6].

The pathophysiology of severe CCHF is complex and involves endothelial injury, immune dysregulation, inflammatory activation, coagulation disturbance, and progressive multiorgan involvement [3,16,17]. Previous studies have examined laboratory markers associated with severe or fatal disease, including leukocyte abnormalities, thrombocytopenia, liver injury, renal dysfunction, coagulation abnormalities, elevated D-dimer, and inflammatory markers [11–15]. These parameters may help clinicians identify patients who require intensified surveillance and supportive care.

The present study was undertaken to characterize the demographic, clinical, and laboratory features of patients with PCR-confirmed CCHF admitted to Al-Hussein Teaching Hospital in Nasiriyah and to evaluate factors associated with in-hospital mortality. The analysis focused on routinely available bedside and laboratory variables that may assist early clinical risk stratification in resource-constrained outbreak settings.

2. MATERIALS AND METHODS

2.1 Study design and setting

A retrospective observational study was conducted using medical-record data from patients admitted to the isolation ward of the infectious diseases service at Al-Hussein Teaching Hospital in Nasiriyah, Iraq. The study period extended from February 2022 through April 2023.

2.2 Study population

The study included 100 symptomatic patients with confirmed CCHF. Diagnosis was established by detection of CCHF viral nucleic acid using polymerase chain reaction (PCR). Symptomatic PCR-positive patients were eligible. Patients who were PCR-positive but asymptomatic and patients with hemorrhagic manifestations who tested negative for CCHF RNA were excluded.

2.3 Data collection

Data were abstracted from patient case files using a structured data-collection form reviewed by three experts: a community medicine specialist, a physician, and a statistician. The form covered three domains: (1) demographic and exposure information, including age, sex, residence, occupation, and animal contact; (2) laboratory data, including complete blood count parameters, coagulation studies, liver and renal indices, D-dimer, and inflammatory markers; and (3) clinical data, including bleeding manifestations, duration and location of hospitalization, complications, and final outcome.

2.4 Variable definitions

Age was categorized as 10–45 years, 46–65 years, and >65 years. Clinical presentation was categorized according to whether bleeding manifestations were documented. The white blood cell reference range was 4,500–11,000 cells/μL; values below and above this range were categorized as leukopenia and leukocytosis, respectively. Thrombocytopenia was defined as a platelet count <150,000 cells/mm³. Hemoglobin was categorized using sex-specific reference ranges (13–18 g/dL for males and 12–16 g/dL for females). Activated partial thromboplastin time (aPTT) was considered prolonged when >35 seconds. ALT was considered elevated above 63 U/L in males or 54 U/L in females. CRP was considered elevated at >1 mg/dL. D-dimer was categorized as elevated above 0.5 according to the threshold used in the source dataset; the measurement unit was not reported. Renal impairment was categorized as acute kidney injury according to the criteria used in the clinical records. A hospital stay >7 days was classified as prolonged.

Recorded complications included acute respiratory distress syndrome, multiorgan dysfunction syndrome, acute kidney injury requiring renal replacement therapy, acute liver failure, shock, and life-threatening hemorrhage. Final outcome was categorized as discharged/recovered or in-hospital death.

2.5 Statistical analysis

The original analysis was performed using IBM SPSS Statistics version 25. Categorical variables were summarized as frequencies and percentages. Associations between categorical clinical or laboratory variables and patient outcome were evaluated using contingency-table tests, with statistical significance defined as $p<0.05$. The present manuscript reports the p values provided in the source analysis and standardizes values reported as 0.000 to $p<0.001$.

2.6 Ethical considerations

The source manuscript states that ethical authorization was obtained from the relevant administrative authorities at Al-Hussein Teaching Hospital and that informed consent was obtained from participants. An ethics committee name and approval/reference number were not reported in the source document.

3. RESULTS

3.1 Participant characteristics

A total of 100 patients with PCR-confirmed CCHF were included. Fifty-five (55%) were male and 45 (45%) were female. Most patients were aged 10–45 years (60%), lived in rural areas (77%), and had a documented history of animal contact (90%). Bleeding manifestations were recorded in 40% of patients. Seventy-five patients recovered and were discharged, whereas 25 died, corresponding to an in-hospital mortality of 25%.

Laboratory abnormalities were common. Seventy-two percent had a white blood cell count outside the reference range (58% below and 14% above the range), 94% had thrombocytopenia, 64% had elevated ALT, 76% had elevated CRP, 38% had elevated D-dimer, 37% had prolonged aPTT, and 15% had acute kidney injury. Most patients (71%) had a hospital stay shorter than 7 days (Table 1).

Table 1. Demographic, clinical, and laboratory characteristics of the cohort (N=100)

Characteristic	Category	Male, n	Female, n	Total, n (%)
Age, years	10–45	39	21	60 (60%)
	46–65	11	19	30 (30%)
	>65	5	5	10 (10%)
Residence	Rural	41	36	77 (77%)
	Urban	14	9	23 (23%)

Characteristic	Category	Male, n	Female, n	Total, n (%)
Occupation	Government-employed	7	5	12 (12%)
	Self-/non-government employed	43	0	43 (43%)
	Retired	4	4	8 (8%)
	Housewife	1	36	37 (37%)
Animal contact	No	6	4	10 (10%)
	Yes	49	41	90 (90%)
Bleeding manifestations	Present	22	18	40 (40%)
	Absent	33	27	60 (60%)
White blood cell count	Within range	19	9	28 (28%)
	Below range	27	31	58 (58%)
	Above range	9	5	14 (14%)
Platelet count	Within range	5	1	6 (6%)
	Below range	50	44	94 (94%)
Hemoglobin	Within sex-specific range	36	19	55 (55%)
	Below range	19	26	45 (45%)
aPTT	Within range	34	29	63 (63%)
	Prolonged	21	16	37 (37%)
ALT	Within range	21	15	36 (36%)
	Elevated	34	30	64 (64%)
CRP	Within range	13	11	24 (24%)
	Elevated	42	34	76 (76%)
Renal function	Normal	46	39	85 (85%)
	Acute kidney injury	9	6	15 (15%)

Characteristic	Category	Male, n	Female, n	Total, n (%)
D-dimer	Within range	36	26	62 (62%)
	Elevated	19	19	38 (38%)
Hospital stay	<7 days	42	29	71 (71%)
	≥7 days	13	16	29 (29%)

3.2 Demographic, exposure, and clinical factors associated with outcome

Age, sex, residence, and occupation were not significantly associated with outcome in the source analysis. Animal-contact history was associated with outcome (reported p=0.014). Importantly, the direction of this association requires cautious interpretation: 6 of 10 patients without documented animal contact died compared with 19 of 90 patients with animal contact. Bleeding status was also associated with outcome (reported p=0.001); 3 of 40 patients with documented bleeding died compared with 22 of 60 patients without documented bleeding (Table 2).

Complications were documented in 29 patients. All 25 patients who died had recorded complications, compared with 4 of 75 patients who recovered. Similarly, all deaths occurred among patients admitted to the intensive care unit (ICU); only 3 survivors required ICU care. These variables therefore represent strong markers of severe disease during hospitalization, although their temporal relationship to death limits interpretation as baseline prognostic factors (Table 4).

Table 2. Demographic and exposure characteristics according to in-hospital outcome

Characteristic	Category	Recovered, n	Died, n	Mortality within category, %	Reported p value
Age, years	10–45	44	16	26.7	0.875
	46–65	23	7	23.3	
	>65	8	2	20.0	
Sex	Male	41	14	25.5	0.548
	Female	34	11	24.4	
Residence	Rural	58	19	24.7	0.544
	Urban	17	6	26.1	
Occupation	Government-employed	9	3	25.0	0.860
	Self-/non-government employed	32	11	25.6	
	Retired	7	1	12.5	

Characteristic	Category	Recovered, n	Died, n	Mortality within category, %	Reported p value
	Housewife	27	10	27.0	
Animal contact	No	4	6	60.0	0.014
	Yes	71	19	21.1	
Bleeding manifestations	Present	37	3	7.5	0.001
	Absent	38	22	36.7	

Note: p values are reproduced from the original analysis. Percentages in the mortality column were calculated from the reported cell counts.

3.3 Hematologic and coagulation factors associated with outcome

White blood cell category was significantly associated with outcome (reported p<0.001). Mortality was highest among patients with leukocytosis: 10 of 14 patients with above-range white blood cell counts died, compared with 7 of 28 patients with counts within range and 8 of 58 with below-range counts. Thrombocytopenia was highly prevalent but was not significantly associated with mortality (reported p=0.169). Hemoglobin category was also not significantly associated with outcome (reported p=0.066).

Coagulation abnormalities showed strong associations with mortality. Twenty of 37 patients with prolonged aPTT died compared with 5 of 63 patients with aPTT within range (reported p=0.001). Likewise, 21 of 38 patients with elevated D-dimer died compared with 4 of 62 patients whose D-dimer was within range (reported p=0.001) (Table 3).

Table 3. Hematologic and coagulation parameters according to in-hospital outcome

Parameter	Category	Recovered, n	Died, n	Mortality within category, %	Reported p value
White blood cell count	Within range	21	7	25.0	<0.001
	Below range	50	8	13.8	
	Above range	4	10	71.4	
Platelet count	Within range	6	0	0.0	0.169
	Below range	69	25	26.6	
Hemoglobin	Within range	45	10	18.2	0.066
	Below range	30	15	33.3	
aPTT	Within range	58	5	7.9	0.001
	Prolonged	17	20	54.1	
D-dimer	Within range	58	4	6.5	0.001
	Elevated	17	21	55.3	

3.4 Hepatic, inflammatory, renal, and hospital-course factors

Elevated ALT was associated with mortality (reported p=0.003): 22 of 64 patients with elevated ALT died compared with 3 of 36 patients with ALT within range. CRP was elevated in 76 patients; all 25 deaths occurred in this group, whereas none of the 24 patients with CRP within range died (reported p=0.001). Acute kidney injury was documented in 15 patients, of whom 11 died; by contrast, 14 of 85 patients with normal renal function died (reported p<0.001).

Hospital-stay duration itself was not reported as significantly associated with outcome. In contrast, the occurrence of complications and admission to the ICU were strongly associated with death (both reported p<0.001) (Table 4).

Table 4. Biochemical, inflammatory, renal, and hospital-course factors according to outcome

Parameter	Category	Recovered, n	Died, n	Mortality within category, %	Reported p value
ALT	Within range	33	3	8.3	0.003
	Elevated	42	22	34.4	
CRP	Within range	24	0	0.0	0.001
	Elevated	51	25	32.9	
Renal function	Normal	71	14	16.5	<0.001
	Acute kidney injury	4	11	73.3	
Hospital stay	<7 days	54	17	23.9	Not reported
	≥7 days	21	8	27.6	
Complications	Absent	71	0	0.0	<0.001
	Present	4	25	86.2	
Care location	General ward	72	0	0.0	<0.001
	ICU	3	25	89.3	

4. DISCUSSION

This retrospective cohort of 100 PCR-confirmed CCHF cases had an in-hospital mortality of 25%. The principal findings were the significant associations between mortality and abnormal white blood cell counts, coagulation abnormalities, elevated D-dimer, elevated ALT, elevated CRP, and acute kidney injury. These findings are clinically coherent with the recognized pattern of severe CCHF, in which dysregulated inflammation, endothelial injury, coagulation disturbance, and progressive organ dysfunction can accompany fatal disease [3,16,17].

The observed mortality is comparable with reports from other affected settings. Rasikh and colleagues described substantial mortality among fatal CCHF cases in Kabul, and other clinical series have emphasized liver dysfunction and multiorgan complications as markers of severe disease [11,12]. In the present cohort, elevated ALT was common and was substantially more frequent among patients who died. Although ALT elevation alone is not specific for CCHF severity, its association with outcome supports close monitoring of hepatic injury as part of serial clinical assessment.

Coagulation abnormalities were among the clearest mortality-associated findings. Prolonged aPTT and elevated D-dimer were both strongly associated with death, consistent with previous work identifying coagulation disturbance among important severity indicators in CCHF [13]. The combination of endothelial injury, inflammatory activation, and altered hemostasis provides a plausible pathophysiological basis for these findings [3,16,17]. Thrombocytopenia, despite being present in 94% of the cohort, was not significantly associated with outcome in the original analysis. This illustrates an important distinction between a common diagnostic feature and a variable that discriminates between survivors and nonsurvivors within an already affected cohort. Inflammatory and renal abnormalities also distinguished patients with poor outcomes. All deaths occurred among patients with elevated CRP, and acute kidney injury carried a high mortality proportion. Previous CCHF studies have similarly identified renal dysfunction and laboratory evidence of systemic injury as adverse prognostic signals [14,15]. White blood cell abnormalities were also associated with outcome, with particularly high mortality among the small subgroup with leukocytosis, consistent with previous observations that deviation in leukocyte indices may accompany severe disease [15].

Two clinical associations require careful interpretation. First, animal-contact history was statistically associated with outcome, but the mortality proportion was higher among patients without documented animal contact than among those with documented contact. This pattern may reflect the small number of patients in the no-contact group, exposure misclassification, or other unmeasured factors and should not be interpreted as evidence that animal contact is protective. Second, patients without documented bleeding had higher mortality than those with bleeding manifestations. This may indicate that overt hemorrhage was not a reliable standalone indicator of impending death in this cohort and that severe disease can occur through organ dysfunction and systemic deterioration without prominent bleeding. Finally, complications and ICU admission were strongly associated with death, with all deaths occurring in these groups. These variables are best regarded as markers of established severe disease rather than independent baseline predictors because they may occur after clinical deterioration. For prognostic modeling, future studies should prioritize variables available early in the disease course and use multivariable approaches that account for confounding and timing.

4.1 Strengths and limitations

A strength of this study is the inclusion of 100 PCR-confirmed cases treated during a defined outbreak period at a single referral hospital, allowing clinically relevant comparison of routinely available variables. However, several limitations should be considered. The retrospective single-center design limits generalizability and depends on the completeness and accuracy of medical records. Laboratory variables were analyzed largely as categorical values rather than as continuous measurements or longitudinal trends. Viral load and detailed timing of laboratory abnormalities relative to symptom onset were not reported. The analysis was univariable; therefore, independent prognostic effects cannot be established. Some source tables and narrative descriptions contain inconsistencies in reported p values or cell descriptions, and the original statistical output should be verified before journal submission. The epidemiologic characterization of exposure and transmission patterns was also limited.

5. CONCLUSIONS

In this cohort of 100 patients with PCR-confirmed CCHF, in-hospital mortality was 25%. Abnormal white blood cell counts, prolonged aPTT, elevated D-dimer, elevated ALT, elevated CRP, and acute kidney injury were associated with death, while thrombocytopenia and hemoglobin category were not significantly associated with outcome in the original analysis. Complications and ICU admission characterized the most severe disease course. These findings support early, repeated assessment of coagulation, inflammatory, hepatic, renal, and hematologic parameters in patients with CCHF. Larger multicenter studies using standardized measurements and multivariable prognostic models are needed before these variables can be used as independent predictors of mortality.

DECLARATIONS

Funding: The study was self-funded.

Conflict of interest: The authors reported no conflict of interest.

Ethics approval and consent to participate: The source manuscript reports that ethical authorization was obtained from the relevant administrative authorities at Al-Hussein Teaching Hospital and that informed consent was obtained from all participants. No ethics committee name or approval/reference number was provided in the source document.

Data availability: A data-availability statement was not provided in the source manuscript.

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