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Original Article

Early clinical management of CCHF in resource-limited rural settings: a case series from a secondary hospital in Türkiye

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Abstract

Introduction: Crimean-Congo hemorrhagic fever (CCHF) remains a major public health concern in endemic regions such as Türkiye. Early triage and management of patients presenting to secondary-level hospitals, where most cases seek care initially, are insufficiently documented.
Methodology: This retrospective case series study was conducted at Kelkit State Hospital, a secondary-level healthcare facility in northeastern Türkiye. Eighteen patients with confirmed CCHF admitted between 8 August 2022 and 30 November 2023 were included. Demographic characteristics, clinical presentation, laboratory findings, treatment, and referral status were reviewed. Referral decisions were primarily based on severe thrombocytopenia (platelet count < 50,000/mm³) due to limited local resources. Clinical and laboratory characteristics were compared between referred and non-referred patients. Chi-square or Fisher's exact test was used for categorical variables, and the Mann–Whitney U test was used for continuous variables.
Results: The patients had a mean age of 44 ± 18 years and 72% were male. Most were engaged in animal husbandry (66%) and 56% had a history of tick exposure. Two-thirds of the patients were referred to tertiary care; all of them had platelet counts below 50,000/mm³. Polymerase chain reaction (PCR) positivity was more frequent among referred patients. The length of stay at the secondary-level hospital was longer among non-referred patients ($p = 0.01$), while total hospitalization duration was greater in the referred group. No deaths occurred.
Conclusions: Selected patients with mild to moderate CCHF can be safely managed at secondary-level hospitals, potentially reducing unnecessary tertiary referrals and healthcare system burden.

Key words: CCHF; referral; thrombocytopenia; rural; secondary.

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Introduction

Crimean-Congo Hemorrhagic Fever (CCHF) is a tick-borne zoonotic disease caused by an RNA virus of the Nairoviridae family, and is primarily transmitted to humans through *Hyalomma* species ticks [1]. It was first identified in Türkiye in 2002, and the disease has since become endemic, particularly in regions such as Central Anatolia, Eastern Black Sea, and Eastern Anatolia [2]. Clinical manifestations range from non-specific symptoms such as fever, myalgia, and headache; to severe hemorrhagic complications, which may lead to multi-organ failure and death [3–5]. Individuals living in rural areas and engaged in livestock farming represent a high-risk population due to their frequent exposure to ticks [3]. Consequently, many patients initially present to secondary healthcare institutions, where diagnosis and early management are typically initiated.

However, in most published studies the clinical course and management of CCHF have predominantly been reported from tertiary referral centers where access to intensive care units (ICUs), blood products, and advanced therapeutic options is more readily available [5–7]. In endemic resource-limited settings, patients with suspected CCHF often first seek care at secondary-level hospitals located in rural regions where healthcare systems are frequently burdened. Despite this, there is limited evidence regarding the real-world management, referral dynamics, and clinical outcomes of CCHF cases treated in secondary healthcare facilities in such settings. Addressing this gap is essential to better understand the early phase of disease management, optimize triage strategies, and improve health system efficiency in resource-constrained environments.

Therefore, this study aimed to describe the early clinical management of laboratory-confirmed CCHF cases in a secondary-level rural hospital, to examine real-world referral practices and deviations from guideline-based recommendations, and to compare clinical characteristics and outcomes between referred and non-referred patients. This study sought to contribute evidence on the potential role of secondary healthcare facilities in the safe management of selected mild to moderate CCHF cases by focusing on a resource-limited setting.

Methodology

Study design and setting

This retrospective study was conducted at the Infectious Diseases Department of Gümüşhane Kelkit State Hospital, an 81-bed secondary-level public healthcare facility located in a rural district of northeastern Türkiye. The hospital includes a total of 10 ICU beds (6 second-level and 4 first-level), but does not have a third-level ICU unit. Access to blood products is limited, and advanced therapeutic modalities such as plasmapheresis are not available. The hospital primarily serves populations engaged in agriculture and livestock farming, reflecting a typical resource-limited, rural healthcare setting.

Patient selection and case definition

Patients aged 18 years and older, who were hospitalized with a confirmed diagnosis of CCHF between 8 August 2022 and 30 November 2023, were included in the study. Diagnosis was established based on clinical and laboratory criteria in accordance with the national guideline of the General Directorate of Public Health of Türkiye [8].

CCHF confirmation was achieved through detection of viral RNA by polymerase chain reaction (PCR) or the presence of virus-specific IgM antibodies. Following the national diagnostic protocols, serological testing for IgM was not routinely performed when PCR was positive, whereas IgM testing was performed in PCR-negative cases [8]. All PCR analyses were conducted at the Erzurum Public Health Laboratory, the regional reference center, via the provincial health directorate.

Routine hematological and biochemical parameters were measured using standardized automated analyzers at the hospital laboratory, in accordance with institutional protocols.

Data collection and definitions

Patient data were retrieved from the hospital information management system. Age, gender, occupation, history of tick exposure, presenting symptoms, platelet and leukocyte counts on admission, CCHF PCR results, length of hospital stay, referral status to a tertiary center, and final outcomes were recorded.

Bleeding manifestations were identified based on clinical documentation in medical records. No standardized bleeding severity score was applicable due to the study's retrospective design.

There were no missing data for key clinical and laboratory variables included in the comparative analyses.

Referral criteria and patient grouping

According to the national CCHF management guideline, referral to tertiary care is recommended in the presence of one or more predefined clinical or laboratory risk factors, including advanced age, clinical deterioration, altered mental status, coagulation abnormalities, or comorbid conditions that may worsen the disease course [8].

In the present study, most patients were clinically stable at presentation and during early hospitalization, with no signs of rapid clinical deterioration. Therefore, patients without severe thrombocytopenia were managed and closely monitored at the secondary-level hospital, even when other guideline-defined risk factors were present.

Referral decisions were primarily driven by the presence of severe thrombocytopenia (platelet count < 50,000/mm^3). This approach reflected limited and delayed access to blood products in the rural setting, concerns regarding the ability to provide timely transfusion support if bleeding developed, and the need to ensure patient safety under resource-constrained conditions. This referral approach was applied consistently during the study period based on shared institutional practice among attending clinicians.

Clinical and laboratory parameters, PCR positivity, and hospitalization duration were compared between referred and non-referred patients.

Statistical analysis

All data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation or median (minimum–maximum) depending on data distribution. Categorical variables were presented as frequencies and percentages. When comparing between groups, the Mann–Whitney U test was used for non-parametric continuous variables, while the Chi square test or Fisher's exact test was applied for categorical data where appropriate. A two-tailed p value < 0.05 was considered statistically significant.

Results

Demographic characteristics

A total of 27 patients were hospitalized with suspected CCHF during the study period, of whom 18 were laboratory-confirmed and included in the final

analysis (Figure 1). Among the 18 patients, 72% (n = 13) were male and 28% (n = 5) were female. The mean age was 44 ± 18 years, with a range of 21 to 79 years. All patients were found to reside in rural areas.

A total of 66% (n = 12) of the patients were engaged in livestock farming, and 56% (n = 10) reported a history of active tick exposure. Regarding tick removal practices, 7 patients reported removing the ticks themselves. In two cases, removal was performed by a healthcare professional in a hospital setting, and in another by a family member. Two patients reported that exposure occurred during tick collection activities. One patient, a nurse, reported a recent history of needlestick injury.

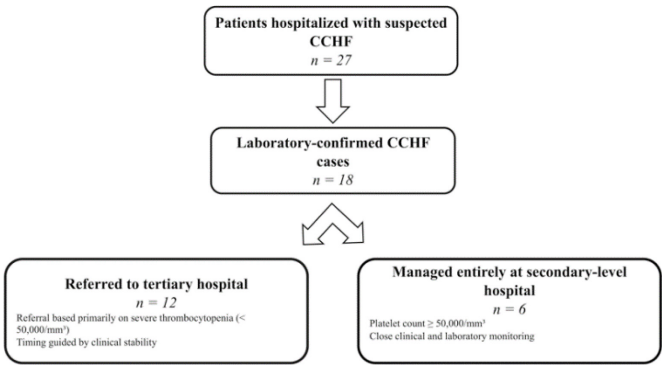
All cases presented during the summer months, between May and September. The majority of patients (83%, n = 15) were admitted through the emergency department. The median duration of symptoms before admission was 4 days (range: 2–8). Additionally, 22% (n = 4) of the patients had at least 1 comorbid condition. The most frequently reported symptoms were chills/shivering (100%), fever (94%), myalgia (77%), and conjunctival redness (77%). The most common gastrointestinal symptoms included nausea (50%) and abdominal pain (44%).

Table 1. Demographic and clinical characteristics of patients diagnosed with CCHF (n = 18).

Variables	All Patients (n=18)
Mean age (years) (± SD)	44 (± 18)
Gender, n (%)	
Male	13 (72%)
Female	5 (28%)
Occupation, n (%)	
Livestock	12 (66%)
Healthcare worker	1 (5%)
Other	5 (28%)
History of tick exposure, n (%)	10 (56%)
Presence of comorbidities, n (%)	4 (22%)
Median duration of symptoms, days (min–max)	4 (2–8)
Symptoms, n (%)	
Chills and shivering	18 (100%)
Fever	17 (94%)
Myalgia	14 (77%)
Conjunctival injection	14 (77%)
Headache	11 (61%)
Nausea/vomiting	9 (50%)
Diarrhea	9 (50%)
Abdominal pain	8 (44%)
Rash	8 (44%)
Bleeding	5 (27%)
Cough	2 (11%)
Laboratory findings at admission (mean, min–max) *	
White blood cell count (cells/mm³)	3126 (1400–8000)
Neutrophils (cells/mm³)	2096 (600–4000)
Lymphocytes (cells/mm³)	730 (100–4500)
Platelets (cells/mm³)	90,000 (49,000–137,000)
PT (s)	13.6 (10.8–19)
aPTT (s)	29.8 (23.4–35.7)
INR	1.12 (0.88–1.6)
ALT (U/L)	84.2 (15–292)
AST (U/L)	134 (26–503)
CK (U/L)	836 (79–3229)
CRP (mg/L)	11.5 (1–40)
Referral to tertiary care center, n (%)	12 (66%)

*Laboratory measurements were interpreted according to the institutional reference ranges of the study center. SD: standard deviation; PT: prothrombin time; aPTT: activated partial thromboplastin time; INR: international normalized ratio; ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; CRP: C-reactive protein.

Figure 1. Patient screening, laboratory confirmation, referral decisions, and final study cohort.



CCHF: Crimean-Congo hemorrhagic fever.

Bleeding manifestations were observed in 27% (n = 5) of the patients. Four of these patients were referred to tertiary healthcare facilities, while 1 patient was managed at the secondary-level hospital with close clinical monitoring. Among the bleeding cases, 2 had vaginal bleeding, 1 had gastrointestinal bleeding, and 2 had hematuria.

On admission, the mean platelet count was 90,000/mm³, the mean leukocyte count was 3,100/mm³, and the mean alanine aminotransferase (ALT) level was 84 U/L. CCHF PCR was positive in 89% (n = 16) of the patients; in the remaining 2 PCR-negative patients, the diagnosis was confirmed by CCHF IgM positivity. The demographic and clinical characteristics of the 18 patients are summarized in Table 1.

Sixty-six percent (n = 12) of the patients were referred to tertiary care due to severe thrombocytopenia (< 50,000/mm³) or bleeding manifestations. All referred patients had a platelet count below 50,000/mm³, and 33% of them had bleeding manifestations documented in the medical records. Patients who were not referred were successfully managed with close monitoring and supportive care at the secondary healthcare facility and were discharged without complications.

Comparison of referred and non-referred patients

A comparison was performed between patients referred to a tertiary care facility and those managed entirely at the secondary-level hospital. Among the 18

patients, 12 (66%) were referred, and 6 (33%) were treated exclusively at the secondary center.

The mean age was slightly higher in the referred group (47.6 ± 20.5 years) than in the non-referred group (38.8 ± 10.7 years), although the difference was not statistically significant ($p = 0.57$). There was also no significant difference in gender distribution between the groups ($p = 1.00$).

However, the mode of admission differed significantly. All referred patients were admitted via the emergency department, while the non-referred patients were equally divided between the emergency room and outpatient clinic ($p = 0.02$).

A higher proportion of non-referred patients were engaged in animal husbandry (84% vs. 58%), though this was not statistically significant ($p = 0.60$). Comorbidities were more common in the non-referred group (33% vs. 16%, $p = 0.56$). Tick exposure history was reported in 66% of referred patients and 33% of non-referred patients, with no significant difference between groups. The median interval from tick contact to hospital admission was similar across groups (median: 6.5 days, $p = 0.79$).

Symptom duration before admission was slightly longer in the non-referred group (4.5 vs. 4 days), without statistical significance ($p = 0.41$). Bleeding manifestations were more frequently observed in the referred group (33% vs. 16%, $p = 0.61$).

Laboratory results revealed that the mean platelet count on admission was significantly higher in non-referred patients (116,000/mm³) compared to those referred (77,000/mm³, $p < 0.01$). Other laboratory parameters, including white blood cell (WBC) count, neutrophils, lymphocytes, coagulation indices (prothrombin time [PT], international normalized ratio [INR], and activated partial thromboplastin time [aPTT]), glucose, renal function parameters including glomerular filtration rate (GFR), liver enzymes (ALT, aspartate aminotransferase [AST]), creatine kinase, and C-reactive protein (CRP), showed no significant intergroup differences.

CCHF PCR positivity was more frequent among referred patients compared with non-referred patients (100% vs. 66%); however, this difference did not reach statistical significance when assessed using Fisher's exact test ($p = 0.10$).

When total hospitalization duration, including tertiary care stay, was considered, referred patients had a significantly longer overall length of stay (9 vs. 6 days, $p < 0.01$).

Exploratory logistic regression analysis was considered to assess predictors of referral; however, due to the small sample size and quasi-separation of key variables, multivariable modeling was not feasible. Therefore, comparisons were limited to univariate analyses.

Further clinical, laboratory, and management characteristics of both groups are detailed in Table 2. No deaths occurred during the study period, and all patients were discharged in good clinical condition.

Timing of referral and observation at the secondary-level hospital

Among the referred patients, referral was not immediate in all cases. Among the patients meeting the age-based referral criterion (≥ 65 years), 3 patients were followed for a total of 4 days at the secondary-level hospital before transfer due to ongoing clinical stability. In addition, 2 patients with transient aPTT prolongation were monitored for a total of 3 days without immediate referral. In these cases, referral was deferred based on preserved clinical stability and the absence of progressive bleeding or hemodynamic deterioration. Overall, a total of 52 patient-days of inpatient follow-up were safely conducted at the secondary-level hospital, without progression to severe bleeding, need for urgent transfusion, or in-hospital mortality.

Discussion

This study provides real-world evidence on the early clinical management and referral practices of laboratory-confirmed CCHF cases treated at a secondary-level hospital in a rural, resource-limited setting. Although CCHF is endemic in several regions

Table 2. Comparison of referred and non-referred patients.

Parameter	Referred (n = 12)	Non-referred (n = 6)	*p* value
Age (mean ± SD)	47.6 ± 20.5	38.8 ± 10.7	0.57
Male gender, n (%)	9 (75%)	4 (66%)	1.00
Animal husbandry, n (%)	7 (58%)	5 (84%)	0.60
History of tick exposure, n (%)	8 (66%)	2 (33%)	0.32
Bleeding findings, n (%)	4 (33%)	1 (16%)	0.61
Platelet count on admission, mean ± SD (cells/mm³)	77,000 ± 18,700	116,000 ± 16,800	< 0.01
CCHF PCR positivity, n (%)	12 (100%)	4 (66%)	0.10
Length of stay in secondary care (median, IQR)	2 (1–3)	6 (5–7)	< 0.01
Total length of stay (median, IQR)	9 (7.75–10)	6 (5.25–6)	< 0.01

SD: standard deviation; CCHF: Crimean-Congo hemorrhagic fever; PCR: polymerase chain reaction; IQR: interquartile range.

and has been extensively reported from tertiary referral centers, data reflecting routine care at secondary healthcare facilities—where many patients initially present—remain limited. The findings of this study help bridge the gap between guideline-based recommendations and real-world practice in endemic rural areas by focusing on triage decisions, referral timing, and short-term outcomes.

All patients in the cohort resided in rural areas and two-thirds were engaged in livestock farming, which aligns with previous studies from Türkiye and other endemic countries showing that individuals involved in agricultural and animal husbandry activities constitute the primary risk group for CCHF [4,8,9–13]. The presence of active tick exposure in 56% of the patients and self-removal of ticks in most cases further support the role of occupational and environmental exposure in CCHF transmission, consistent with the epidemiological profile reported in endemic regions [3,4,10]. In this context, the observed patterns of rural residence, occupational exposure, and tick contact provide a framework for understanding the frequent initial presentation of CCHF patients to secondary-level hospitals.

The seasonal distribution, clinical presentation, and laboratory findings observed in this cohort are consistent with previous reports from endemic regions [3,5,14,15]. All cases occurred during the summer months, coinciding with increased tick activity and agricultural exposure. The predominance of emergency department admissions and the non-specific early symptoms, such as fever, myalgia, and chills, mirror patterns described in tertiary care-based studies [14,15]. Similarly, laboratory abnormalities including thrombocytopenia, leukopenia, and elevated liver enzymes were comparable to those reported in the early phase of CCHF [3,5]. Molecular and serological diagnostic yields in this cohort were also in line with previously published data, supporting the applicability of standard diagnostic approaches at the secondary care level [4,15].

Most patients in the cohort reported self-removal of ticks following exposure, which is consistent with national recommendations encouraging early tick removal [8]. However, improper techniques may increase transmission risk, underscoring the need for targeted education in endemic rural communities [10]. In addition, the occurrence of a needlestick injury in a healthcare worker highlights the ongoing risk of nosocomial transmission and serves as a reminder of the importance of infection control practices among healthcare personnel in endemic settings.

In this study, 66% of patients required referral to tertiary care, although national guidelines recommend referral in the presence of one or more predefined risk factors, including severe thrombocytopenia, bleeding manifestations, advanced age, or comorbid conditions [8]. However, in real-world practice, referral decisions were largely driven by platelet count falling below 50,000/mm^3. This approach was primarily related to limited access to blood products in a secondary-level hospital and the anticipation that timely transfusion support might not be feasible in the event of sudden bleeding. In addition, the high patient burden at tertiary care centers and the reluctance or hesitation of some patients regarding transfer also contributed to decisions to closely monitor clinically stable patients at the secondary level. Accordingly, thrombocytopenia in this setting functioned not merely as a laboratory abnormality but as a practical threshold reflecting clinical manageability. The findings illustrate how guideline-defined risk factors are prioritized under secondary-care conditions and demonstrate that referral decisions are shaped not only by clinical severity but also by the prevailing system- and patient-related factors.

PCR positivity was more frequently observed among referred patients; however, this finding should be interpreted cautiously, as the difference did not reach statistical significance. In clinical practice, PCR positivity often reflects an earlier phase of infection, and patients presenting earlier in the disease course may exhibit a more dynamic clinical and laboratory profile that prompts closer monitoring or referral [15]. Therefore, the higher proportion of PCR-positive cases among referred patients in the cohort may be related to earlier presentation and rapid clinical evolution rather than PCR positivity itself directly influencing referral decisions.

Importantly, patients who were managed entirely at the secondary care level demonstrated stable clinical courses and were successfully treated with close monitoring and supportive care, without progression to severe disease or mortality. Notably, no deaths occurred in either the non-referred or referred groups, despite reported case-fatality rates ranging from 5% to 30% in endemic regions, particularly among patients with delayed presentation, severe bleeding, or advanced disease [4,5]. In contrast, referred patients had longer overall hospitalization durations, reflecting the need for prolonged observation and supportive management at higher-level care facilities. Taken together, these findings suggest that, with careful patient selection and close follow-up, selected mild to moderate CCHF cases

can be safely managed at secondary-level hospitals, potentially reducing unnecessary referrals and alleviating the burden on tertiary care centers.

From a broader perspective, the findings underscore the importance of functional secondary-level healthcare facilities in the early recognition and stabilization of CCHF cases in rural endemic areas. Given the high frequency of occupational exposure and self-removal of ticks, targeted community education on safe tick removal practices remains essential [10]. In addition, the identification of occupational exposure in a healthcare worker highlights the ongoing risk of nosocomial transmission and the need for continued infection control awareness among healthcare personnel working in endemic settings [16].

Limitations

This study has certain limitations that should be acknowledged. First, its retrospective design limits the ability to capture standardized clinical severity scores, such as bleeding severity classifications, and restricts causal inference. Second, the sample size was relatively small, which limits the statistical power and generalizability of the findings. Third, as this was a single-center study conducted in a secondary hospital located in a specific rural region, the referral patterns and management approaches observed here may not fully reflect practices in other endemic areas or healthcare systems with different resource capacities. Furthermore, long-term follow-up after discharge, particularly for referred patients, was not systematically documented, preventing a comprehensive assessment of delayed complications or relapse. Despite these limitations, the study provides valuable real-world evidence regarding early-phase CCHF management and referral dynamics within a secondary-level healthcare context in an endemic rural setting.

Conclusions

This study shows that secondary-level healthcare facilities can play an important role in the early recognition, stabilization, and triage of CCHF cases in endemic rural areas. In this cohort, carefully selected patients with mild to moderate disease were successfully managed with close monitoring and supportive care, without mortality, while patients requiring referral received timely transfer to higher-level centers. These findings suggest that secondary hospitals, when supported by appropriate clinical judgment and follow-up, may safely manage selected CCHF cases and help reduce unnecessary referrals and pressure on tertiary care services. Improving diagnostic access, refining context-specific referral criteria, and strengthening clinician preparedness may further enhance the quality of CCHF care in resource-limited settings. Future multicenter studies are needed to confirm these observations and guide the development of practical triage models applicable to secondary care environments.

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AI-assisted technologies

ChatGPT (OpenAI, San Francisco, CA, USA) was used to improve the clarity, grammar, and flow of the manuscript text. The tool was not used to generate data, analyses, or conclusions. All content was reviewed and approved by the author, who takes full responsibility for the integrity and accuracy of the work.

Ethical approval

The study was approved by the Scientific and Ethical Review Board for Medical Research of Ankara Bilkent City Hospital (Approval No: TABED 1-23-1449). Administrative permission was obtained from the Gümüşhane Provincial Health Directorate prior to data collection. Individual informed consent was not required because this was a retrospective study conducted using anonymized records. All procedures were performed in accordance with the principles of the Declaration of Helsinki.

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Conflict of interest

No conflict of interest is declared.

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