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# Crimean-Congo Hemorrhagic Fever in Dubai, United Arab Emirates, 2010: Case Report

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## Abstract

**Introduction:** Crimean-Congo hemorrhagic fever (CCHF) is a severe infectious disease that is not endemic in the United Arab Emirates (UAE).
**Case Presentation:** We report two cases of confirmed CCHF diagnosed in Dubai, UAE, during Hajj season 2010. Both patients presented with an acute history of high-grade fever, skin rash, and hematemesis.
**Conclusions:** In spite of maximal supportive measures and intravenous ribavirin therapy, both patients died within a few days from start of illness. More than 250 health care workers came into variable degrees of contact with the index cases, and none of them developed signs or symptoms suggestive of acquiring the illness. Health care workers from nonendemic regions should be aware of zoonotic hemorrhagic fevers imported via infected cattle and ticks and be able to diagnose and properly manage suspected cases in a timely manner. In addition, proper infection-control measures should be undertaken to prevent nosocomial spread of infection.

*Keywords:* CCHF, UAE, Health Care Workers, Infection Control

## 1. Introduction

Crimean-Congo hemorrhagic fever (CCHF) is an arthropod-borne viral infection that infects domestic and wild animals and can be transmitted to humans via several routes. The causative agent of CCHF is an RNA virus of the genus Nairovirus belonging to the Bunyaviridae family of viruses (1). Over several decades, serious outbreaks with high case-fatality rates have been reported from different parts of the world, including the Middle East (2-6). CCHF is becoming a global problem, and more cases are expected to be diagnosed as the disease becomes endemic to more areas due to movement of livestock, changes in hunting activities and agricultural practices (7). A real threat exists to health care workers managing patients with CCHF and causing nosocomial outbreaks, which may have high fatality rates (8). Another concern is related to the potential use of the virus as a weapon of bioterrorism, given the limited availability of diagnostic laboratory services with Biosafety Level 4 facilities (9).

CCHF is not endemic to UAE; however, two documented limited outbreaks occurred in 1979 and 1994 and were associated with high mortality rates among infected health care workers (10, 11). Here, we report two recent cases of confirmed CCHF.

## 2. Case Presentation

### 2.1. Case 1

On October 28, 2010, a previously healthy 24-year-old male butcher working in Dubai Abattoir complained of fever, headache, and right lower quadrant abdominal pain, which was managed symptomatically in a private clinic, and he was discharged home. Two days later, he developed vomiting and non-bloody loose motions with generalized abdominal pain. He was admitted to another private hospital in Dubai for workup as a case of acute abdomen. Investigations on October 30, 2010, revealed the following: white blood cells (WBC) 11.8 $\times 10^3/\mu$L (87.9% neutrophils), hemoglobin (Hb) 15.1 g/dL, platelets (Plt) 145 $\times 10^3/\mu$L, creatinine 1.2 mg/dL, bilirubin 0.6 mg/dL, urine red blood cells (RBC) 10 - 15, AST 196 U/L, INR 1.7, GGT 55 U/L, alkaline phosphatase 79 U/L, PT 19 seconds. Chest X-ray was normal, and abdominal ultrasound showed a small right renal stone. The patient was given intravenous antibiotics and managed symptomatically for fever and abdominal complaints. On November 1, 2010, his condition deteriorated and he developed hematemesis and melena with worsening abdominal pain and continuous high spikes of temperature. Repeated labs were as follows: WBC 5.96 $\times 10^3/\mu$L (88.2% neutrophils), Hb 14.3 g/dL, Plt 35 $\times 10^3/\mu$L. He was referred to our hospital for further evaluation and manage-

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ment of his fever, severe thrombocytopenia, and acute gastrointestinal bleeding.

At the time of admission to our hospital, the patient was febrile (38.3°C), his pulse rate was 120/minutes, and BP was 90/60 mmHg. He looked acutely ill, though conscious and oriented. He had congested eyes and a petechial rash over the chest and lower limbs. There was generalized abdominal tenderness without organomegaly. A systemic examination revealed no other gross abnormality. Investigations revealed WBC 14.1 (neutrophilia with bandemia), Hb 14.2 g/dL, Plt 8 $\times$ $10^3/\mu$L, D-dimer 5.3, urea 55 mg/dL, ESR 120 mm in the first hour, LDH 3086 U/L, ALT 72 U/L, PT 32.4 seconds, PTT 159.8 seconds, INR 3.34, urine RBC 20 - 25. Repeated AST was 5400 U/L.

The initial differential diagnosis included tauleremia, leptospirosis, and severe community-acquired bacterial infection, and accordingly he was started on levofloxacin, ceftriaxone, and gentamicin. A presumptive diagnosis of viral hemorrhagic fever (most likely CCHF) was also entertained in view of his occupation, and a loading dose of intravenous ribavirin therapy was given a few hours later. The patient was transferred to a single room for isolation with barrier nursing, and strict infection-control measures were adopted to minimize the number of medical staff members in contact with the patient and eliminate exposure to the patient's body fluids. He underwent endoscopy, which showed severe hemorrhagic gastroduodenitis with active bleeding. The patient's condition continued to deteriorate, and he developed respiratory compromise requiring mechanical ventilation. Despite all supportive measures, maximum inotropic support, and IV ribavirin therapy, the patient died on November 4, 2010, due to severe DIC and circulatory failure.

A sample of the patient's blood and ticks collected from the abattoir were sent to a regional reference laboratory in Saudi Arabia, and polymerase chain reaction (PCR) testing for Crimean-Congo virus was positive for both samples.

Around 140 health care workers (physicians, nurses, and laboratory staff) came into variable degrees of contact with the patient or his body fluids during his admission to our hospital. They were classified into five groups according to their degree of contact:

Group 1 (high risk): percutaneous contact with blood (needle-sharp sticks or patient's blood contact with broken skin or mucosa): nil

Group 2: patient's blood contact to unbroken skin: 3

Group 3: patient's body fluid contact to unbroken skin: 2

Group 4: physical contact with the patient without exchange of fluids: 32

Group 5: close proximity to the patient (1 m) without physical contact: 103

Concerned staff members were requested to measure their temperature twice daily and to report to the emergency room if they developed any febrile illness (T> 38.3°C) or mucocutaneous bleeding. Staff members in groups 1 and 2 were also counseled regarding post-exposure prophylactic ribavirin therapy. All individuals preferred close follow-up with an infectious disease specialist, and nobody received ribavirin therapy. In addition to health care workers, the patient's roommates, work colleagues, and close family members were contacted and interviewed and were advised to report to our hospital immediately in case they developed fever, loose motions, or bleeding. All were followed for 21 days post-exposure to the index case, and none of the medical staff in our hospital or the referring hospital nor any of his close contacts developed symptoms suggestive of acquiring the infection. It should be noted that no serological testing was carried out to document subclinical infection.

### 2.2. Case 2

Another previously healthy young male (33 years old) presented to a private hospital in Dubai on November 23, 2010, with 5 days' history of high-grade temperature, vomiting, and loose motions. On the day of admission, he developed hematemesis and melena. Clinically, he was febrile, hypotensive, and tachycardic, with a generalized petechial rash. The patient was resuscitated and transferred to our hospital for further evaluation and management. Importantly, the patient was in Dubai Abattoir during the Hajj holidays, a few days prior to the start of his illness. Laboratory investigations revealed the following results: WBC 4.29 $\times$ $10^3/\mu$L, Hb 17 g/dL, Plt 40 $\times$ $10^3/\mu$L (dropped to 26 $\times$ $10^3/\mu$L within a few hours of admission), creatinine 2.1 mg/dL, NA 138 mmol/L, K 5.3 mmol/L, INR 1.947, D-dimer > 20. Chest X-ray was normal, and abdominal ultrasound revealed minimal ascites. CCHF was highly suspected in this case, and he was resuscitated and shifted to ICU and mechanically ventilated, with a loading dose of intravenous ribavirin started immediately. A few hours later, he passed a large amount of fresh blood per rectum, his general condition worsened with uncontrolled circulatory collapse, and he died on the day of admission, 7 days after the start of illness. The patient's blood sample was sent to the same regional hospital for CCHF viral PCR testing, and the results were confirmatory for CCHF by PCR. Similar infection-control measures were taken as in index Case 1, and no medical staff in our hospital or the referring hospital developed clinical infection. His wife and three children were also contacted, and they, too, did not develop the illness clinically.

**Table 1.** Patient Characteristics, Clinical Manifestations, and Laboratory Findings Upon Presentation

| | Case 1 | Case 2 |
|---|---|---|
| **Age, y** | 24 | 33 |
| **Gender** | Male | Male |
| **Symptom** | Fever, headache, abdominal pain, loose motions | Fever, vomiting, loose motions, melena, hematemesis |
| **Clinical finding** | | |
| | Febrile | Hypotensive febrile |
| | Maintained vital signs | Tachycardia |
| | | Petechial rash |
| **WBC** | $11.8 \times 10^3/\mu L$ | $4.29 \times 10^3/\mu L$ |
| **Hb** | 15.1 g/L | 17 g/L |
| **Platelet** | $145 \times 10^3/\mu L$ | $40 \times 10^3/\mu L$ |
| **Creatinine** | 1.2 mg/dL | 2.1 mg/dL |
| **CXR** | Normal | Normal |
| **Abdominal USS** | Renal stone | Minimal ascites |
| **PT,sec** | 19 | 21 |
| **INR** | 1.7 | 1.95 |

**Table 2.** Clinical Features

| Phase | Clinical Features |
|---|---|
| **Phase 1** | Incubation phase lasts 2 - 9 days and depends to some extent on how the infection was acquired. |
| **Phase 2** | Pre-hemorrhagic phase usually manifests as high-grade fever, body aches, abdominal pain, and loose motions. Clinically, the patient looks sick, with congested conjunctiva, and is often tachypnic. There is generalized skin flushing. This phase lasts 3 - 5 days. Ribavirin therapy might be most effective during this period (12); however, delays in suspecting CCHF often lead to delays in starting therapy, which affects the overall disease outcome. |
| **Phase 3** | Hemorrhagic phase ensues with persistent high-grade fever and gastrointestinal bleeding. In addition to massive hematemesis and melena, there might be epistaxis, gum bleeding, conjunctival hemorrhage, cerebral hemorrhage, vaginal bleeding, and hematuria. This is the most critical phase of the illness with the highest mortality rates. Patients develop circulatory collapse and severe coagulation disturbance, requiring massive and frequent blood transfusions. Reported case mortality is generally 10 - 40%, though figures as high as 80 - 100% (as in our patients) have been reported, particularly in instances of nosocomial infection. Of note is the difference in mortality between nosocomial cases and community-acquired cases, with significantly higher mortality rates in the former. One explanation could be a lower viral load from a direct tick bite in cases of community-acquired infection. |
| **Phase 4** | Convalescent phase usually begins 15 - 20 days after disease onset in patients who survive the hemorrhagic phase. Patients usually report generalized weakness, alopecia, memory loss, and poor appetite. |

## 3. Discussion

CCHF is not endemic in UAE, and only sporadic cases with limited nosocomial outbreaks have been reported, including one from this hospital. Regionally, the disease has been reported in Oman, KSA, Kuwait, Iran, Pakistan, India, and Iraq (13-24). In nonendemic Gulf countries, the risk of acquiring human infection is mostly related to imported livestock that carry infected ticks. The risk seems to be greatest during Hajj season, when hundreds of thousands of cattle are imported to the region for the ceremonial sacrifice.

Following initial infection by tick bite or contact with body fluids of an infected animal or human, four different phases of illness are recognized, as described first by Hoogstraal in 1979 and subsequently by others (25-28). Not all patients pass through the same phases, depending on the severity of their illness and their response to therapy.

Our patient in Case 1 initially presented to a private hospital in Phase 2 (pre-hemorrhagic), which progressed to Phase 3 (hemorrhagic), while the patient in Case 2 came in the hemorrhagic phase with persistent fever and circulatory collapse.

Laboratory and imaging findings in this disease depend on the stage in which the patient presents. In the hemorrhagic phase, the laboratory results usually indicate severe thrombocytopenia and disturbed coagulation profile. The hematological profile usually indicates leu-

copenia, anemia and thrombocytopenia. Hepatic transaminases are elevated, and figures in the thousands can be seen with severe hepatic necrosis. Ergonul et al. found that age, male gender, high platelet levels, and high ALT, AST, WBC, and PTT values and decrease in these values during follow-up are all indicative of a poor prognosis (12). Lactate dehydrogenase and creatinine kinases are nonspecifically elevated and have also been shown to be associated with poor outcome. Kidney function is usually preserved unless the patient develops acute renal failure. Ardalan et al. reported a case of CCHF presenting as thrombotic microangiopathy and acute renal failure (29). Case 2 in this study presented with renal impairment. Urinalysis reveals hematuria and proteinuria. Pulmonary manifestations of CCHF include pleural effusion with or without hemothorax, diffuse alveolar hemorrhage, and ARDS (30-32). Engin et al. conducted a prospective study on 44 confirmed cases of CCHF and found that patients with severe infection had lower left ventricular ejection fraction, higher systolic pulmonary artery pressure, and more frequent pericardial effusion compared with nonsevere cases and concluded that severe and fatal CCHF cases have impaired cardiac functions, which could be linked to increased fatality in severe infections (33).

Abdominal ultrasound can show ascites or organomegaly, as seen in our patient in Case 2. As highlighted above, the hallmark of CCHF is bleeding diathesis resulting from vascular endothelial injury, which in turns leads to prolonged bleeding time, PT, APTT, elevated fibrinogen degradation products, and decreased fibrinogen (34). In both cases discussed here, INR was raised at the beginning of presentation although higher in Case 2 and later progressed to DIC.

The confirmation of CCHF infection relies on antibody detection by ELISA, antigen detection, virus isolation and PCR tests. These tests should be performed in high biosafety-level laboratories. Both of our cases were confirmed by PCR in a reference laboratory.

Management of human cases with CCHF has two main objectives: managing index case(s) and preventing human-human transmission. Active management of infected patients mostly relies on optimal supportive measures and restoration of a normal coagulation profile, depending on the severity of the infection. Data on the efficacy of ribavirin therapy in treating CCHF is conflicting, and there is no consensus nor clear guidelines on its role in the management of confirmed or suspected cases of CCHF. To date, it is the only available option to treat viral hemorrhagic fevers, such as CCHF, hantavirus, and Lassa fever, although it is not yet approved by the FDA for the management of CCHF. Several studies have examined oral or IV ribavirin therapy during different stages of the illness and have shown variable results in terms of efficacy and mortality (35-38). Having that said, the authors of two recent meta-analyses of data on ribavirin therapy in managing CCHF concluded that there is no strong evidence supporting the use of the drug to reduce mortality among infected patients (39, 40). Accordingly, we can make no clear recommendations on the efficacy or optimal dose of oral or IV ribavirin therapy for the management of CCHF. In our studied cases, ribavirin was started within a few days of symptom initiation. Despite this, both patients died of severe hemorrhage.

Preventing human-human transmission is very important in this disease, especially among health care workers in nonendemic countries, who may not suspect the disease early in its course. The risk of transmission is highest during the hemorrhagic phase via incidental needlestick injuries or exposure to infected body fluids through broken skin. Microbiology laboratory personnel could be at risk when handling infected material without proper infection-control measures. To control nosocomial infections, it is important to take precautions; barrier nursing, hand washing, and use of surgical masks and gloves are mandatory and effective in controlling infection when managing a suspected case (41).

A debatable question is whether to give oral ribavirin prophylaxis to those who come into contact with confirmed CCHF patients or highly suspicious cases. This is not an easy question to answer, as we lack strong data on the efficacy of oral ribavirin in preventing secondary cases of CCHF, who should receive post-exposure prophylactic therapy, and the optimal dose and duration of prophylaxis.

Current recommendations suggest administration of oral ribavirin therapy to people with close contact to the index cases, particularly if exposed to body fluids or tissue. They should be followed closely and asked to report immediately if they develop any febrile illness. Basic laboratory workup includes CBC, liver enzymes, and coagulation profile. If the clinical suspicion of acquiring a secondary infection is high, then post-exposure prophylaxis is recommended with 200 mg ribavirin orally twice daily for 5 - 14 days (42, 43).

### 3.1. Conclusion

CCHF is not endemic to UAE and other Gulf countries, and both cases described above occurred as a result of importing cattle with infected ticks. In nonendemic countries, a high level of suspicion is required in patients with fever, low platelets, and hemorrhagic tendencies. CCHF should be strongly suspected if the patients' occupation involves exposure to animals. Health care providers and preventive medicine practitioners need to be aware of this serious and potentially lethal imported zoonotic illness

and should use proper infection-control measures to prevent the spread of such fatal cases in the future, especially during the Hajj season.

## Footnote

**Authors' Contribution:** Study concept and design, Laila Mohamed AL Dabal; analysis and interpretation of data, Ali Abro, Samar Badreedine, Ali Zaki; drafting of the manuscript, Laila Mohamed AL Dabal, Gulfaraz Khan. critical revision for important intellectual content, Mohammad Reza Rahimi, Ali Abro, Zulfa Deesi, Hassan Shuri; statistical analysis, Laila Mohamed AL Dabal, Essa Aleassa, Abid Abid.

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