

## **CRIMEAN CONGO HEMORRHAGIC FEVER MANAGEMENT IN ERBIL DURING 2010-2011**

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### **Abstract**

Crimean- Congo Hemorrhagic Fever (CCHF) is a viral zoonotic tick-born disease with a mortality rate of up to 50% in human. CCHF is caused by genus *Nairovirus*, in the family of *Bunyaviridae*, and can be transmitted to humans through the bite of ticks *Hyalomma* species or its contact with blood or tissues of CCHF patients or infected livestock. CCHF is a public health problem in many regions of the world e.g. Eastern Europe, Asia, Middle East, and Africa. The history of CCHF in Iraq shows that the disease has been detected in Iraq since 1979. During 2010-2011, five cases were referred to the infectious unit of Erbil teaching hospital on assumption of acute febrile illness, including some of them with hemorrhagic manifestations. Patients' serum samples were obtained at the time of admission and sent to the Central Public Health laboratory (CCHF.REF.LAB), Baghdad. Diagnosis was confirmed by ELISA for anti-CCHFV IgM. However, all of them that handled livestock had accounts of slaughtering animals within two weeks before symptom onset ,and the most commonly encountered symptom and signs were fever , malaise(100%) ,headache(80%) ,abdominal pain , myalgia, petechiae , ecchymosis(60%),

nausea, vomiting, bleeding from gastrointestinal system, gingival, nose and vagina .Others include thrombocytopenia(100%), elevated liver enzymes(S.ASTandS.ALT) 80%,prolonged prothrombin time, anemia ,and Albuminuria (60%). Patients were treated following strict infection prevention measures and supporting circulation using intravenous fluid, blood with blood product support (platelet and fresh frozen plasma), with specific treatment with ribavirin .Thus, all of them positively responded to the treatment, and was cured, and discharged home.

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**Keywords:** CCHF, Thrombocytopenia, Erbil.

### **Introduction**

Crimean-Congo hemorrhagic fever (CCHF) disease is one of the most virulent viral hemorrhagic fevers which are a life threatening disease reported in many countries in Europe, Asia and Africa (Williams RJ *et al.*, 2000; **Chinikar S** *et al.*, 2009). CCHFV is a member of the *Nairovirus* genus of the family, *Bunyaviridae* (Whitehouse CA, 2003). CCHF was first recognized in the Crimean peninsula in the mid-1940s (**Chinikar S** *et al.*, 2009; Whitehouse CA, 2003). Crimean-Congo Hemorrhagic Fever (CCHF) virus causes a hemorrhagic and toxic syndrome disease in humans and high mortality rates of up to 50% (Lyudmila *et al.*, 2003) An outbreak in China in 1965 had a case fatality rate of 80%. A large number of cases have also been reported from Middle Eastern countries such as Iraq, United Arab Emirates, Saudi Arabia and Oman (Ergonul O, 2006). Since 2000, outbreaks of CCHF have been reported in Albania, Kosovo, Turkey, Pakistan, Iran, Mauritania, Kenya and Greece (S. Chinikara *et al.*, 2010; Krauss, H. *et al.*, 2003).

The occurrence of CCHF closely approximates the known distribution of *Hyalomma* spp. ticks. Humans become infected through the bites of ticks, or possibly by crushing engorged infected ticks, or by contact with blood or tissues from viremic livestock or by direct contact with a patient with CCHF during the acute phase of the infection which occurs primarily at the hospital (nosocomial infection) and is generally characterized by more severe clinical symptoms and high mortality rate (Dorsten C *et al.* 2003; Ergonul O and Whitehouse CA, 2007; Flick R and Whitehouse CA, 2005). In Iraq, the Crimean-Congo Hemorrhagic Fever was unknown till September 1979, when a 24 years old lady was admitted to AL-yarmok hospital in Baghdad with bleeding tendency on the 7th of Sep.1979, and after 2 days, she died. After 4 days, the physician and one of the health workers who were in close contact with the patient developed fever, headache, and bleeding from gastrointestinal tract. Unfortunately, they died too. During that same year, 10 cases were reported (8 were female and 2 were male) also; and seven out of ten died. All the cases were in contact with

animal except the physician and the health worker (Tantawi HH, 1980; Emad S. *et al.*, 2012). Therefore, the objective of this paper is to show the epidemiologic, clinical, and laboratory outcome of patients with proven Crimean Congo Hemorrhagic Fever admitted to the infectious unit of Erbil teaching hospital during 2010 -2011.

## **Patients and Methods**

One case (September 2010) and four cases (June 2011) were referred to the infectious unit of Erbil Teaching Hospital on the assumption of acute febrile illness. All were treated as typhoid fever but in some cases, bleeding was present, and did not improve in any way. Patients with infection prevention protocol were admitted to our center, and detailed history was taken regarding residency, occupation and the animals they had contact with. The case definition for suspected cases included individuals who had fever, myalgia, malaise, diarrhea, history of tick bites, slaughtering of animal, contact with patients in acute cases and travel to endemic area.

The probable cases included patients who had leucopenia, thrombocytopenia, elevated liver enzymes (ALT, AST), Proteinuria and hematuria. Probable cases with the isolation of virus, Detection of antigen, or Detection of antibody were considered as CCHF confirmed cases (Emad S. *et al.*, 2012).

Patients were admitted to the unit and complete investigation was done which includes complete blood count, blood film, renal function test, Liver function test, infectious panel including viral hepatitis (HAV, HBV, and HCV), HIV, typhoid fever, brucellosis, malaria, ANA and general urine examination, stool examination, Chest X-ray and blood culture.

Patients' serum samples were obtained at the time of admission and sent to Central Public Health laboratory (CCHF.REF.LAB), Baghdad. Diagnosis was confirmed by ELISA for anti-CCHFV IgM as described [CCHF IgM ELISA Kit National Institute for Comm. Dis. Special Pathogens Unit]. Patients were treated by supporting circulation via intravenous fluid, broad spectrum antibiotics and blood with blood product support (platelet and fresh frozen plasma), with specific treatment with Ribavirin for 10 days (30 mg/kg as an initial loading dose, then 15 mg/kg every six hours for four days, and then 7.5 mg/kg every 8 hours for six days). Patients were closely observed during admission (15-20 days).

## **Results**

There were five cases (four males and one female) with age ranging from 19 to 50 years, and median age of 22 years. Three were from Erbil – Soran, Majidawa and they were from one family, while one was from Khalifan –Gomazard and another was from Duhok –Bardarash and were all

referred to our center for management. Figure (1) shows geographic distribution of patients affected by CCHF (areas are marked yellow)(Wikipedia, the free encyclopedia. Erbil province. [http://en.wikipedia.org/wiki/Arbil\\_Province](http://en.wikipedia.org/wiki/Arbil_Province)) (6<sup>th</sup> March, 2013).



Figure (1) Geographic distribution of patients affected by CCHF.

Table (1): Shows epidemiologic characteristics of confirmed cases of CCHF.

Epidemiologic characteristics		No. (%)
		Total No.=5
Sex	Male	4 (80)
	Female	1 (20)
Occupation	House wife	1 (20)
	Student & worker	2 (40)
	Shepherd	1 (20)
Residency	Cattleman	1 (20)
	Erbil, Soran, Majidawa	3 (60)
	Erbil ,Khalifan, Gomazard	1 (20)
Contact to animals*	Duhok, Khabate, Daratu	1 (20)
History of Slaughtering animal*	Yes	5 (100)
Type of animal at home(goat &cow)	Yes	5 (100)
Ticks on animal	Yes	3(60)
	No	2 (40)

\* Within two weeks of symptom onset.

Regarding the occupation of patients, one of them was a shepherd and one was an auctioneer of goats and cows, two other male patients were students but were helping the shepherd sometimes, where as a female patient was a house wife but was dealing with animals at home.

As a matter of fact, all of them handled livestock and had the history of slaughtering animals within two weeks before symptom onset. Though, there were ticks on animals in Majidawa as shown in figure (2), none of them described tick bite, none of the family members of all the patients were affected, and there was no history of travel outside the area where they are residing or other histories as reported in the previous case.



Figure (2): Ticks on infected cows from Majidawa.

Symptoms and signs observed in patients are shown in the table (2).The most commonly encountered signs and symptoms were fever, malaise, headache, abdominal pain, myalgia, nausea, vomiting, petechiae , ecchymosis (figure -3) and bleeding from gastrointestinal system, gingiva , nose and vagina.

Table (2): Symptoms and signs of confirmed cases of CCHF.

Symptom and Signs	No. (%)
	<b>Total No. = 5</b>
Fever	5 (100)
Malaise	5 (100)
Headache	4 (80)
Hematuria	4 (80)
Melena	4 (80)
Hypotension	3 (60)
Abdominal pain	3 (60)
Petechiae-ecchymosis	3 (60)
Myalgia	3 (60)
Bleeding from puncture sites	2 (40)
Nausea and vomiting	2 (40)
Epistaxis	2 (40)
Splenomegally	2 (40)
Hematamesis	1 (20)
Vaginal bleeding	1 (20)
Gum bleeding	1 (20)
Arthralgia	1 (20)
Hepatomegaly	1 (20)



Figure (3): shows patient with ecchymosis.

Serologic test results for hepatitis A, B, C viruses (HAV, HBV, and HCV), HIV, Brucella and Typhoid fever were negative .Anti nuclear antibody, malaria peripheral blood smear examinations and bacterial blood cultures were negative too.

Abnormal laboratory test results are shown in table (3). However, diagnosis of CCHF was confirmed by ELISA for anti-CCHFV IgM. Complete blood counts showed thrombocytopenia in all patients (median 18

x 10<sup>3</sup>/ML, range: 2–31 x 10<sup>3</sup>/ML), leucopenia in 2/5 (median 4000/ML, range 2000–8000/ML), and anemia in 3out of 5 patients (median 9.8g/dL, range 6.1–14 g/dL). Serum aspartate aminotransferase (AST) (median 120 U/L, range 80–250U/L), alanine aminotransferase (ALT) (median 140 U/L, range 66–260 U/L, Alkaline phosphates, renal function test and blood glucose were within normal ranges for all patients . Coagulation tests showed prolonged prothrombin time (PT) (median 14.5 second, range 14.1–22.5 second) and activated partial thromboplastin time (aPTT) (median 36.9 second, range 33.2–59.1 second) in 2out of 5patients. Also, urine examination showed RBC in 4 patients and Albuminuria in 3 patients.

Table (3): Laboratory parameters of confirmed cases of CCHF.

Laboratory parameters	No. (%)
	Total No. = 5
CCHF virus IgM (Positive)	5 (100)
Thrombocytopenia	5 (100)
RBC in urine	4 (80)
RBC in stool	4 (80)
S AST(elevated )	4 (80)
SALT(elevated )	4 (80)
PT(prolonged )	3 (60)
Anemia	3 (60)
Albuminuria	3 (60)
APTT(prolonged )	2 (40)
Leucopenia	2 (40)

Patients were treated in isolated room following strict infection prevention measures and supporting circulation by intravenous fluid, broad spectrum antibiotics and blood with blood product support (platelet and fresh frozen plasma), with specific treatment with ribavirin for 10 days (30 mg/kg as an initial loading dose, then 15 mg/kg every six hours for four days, and then 7.5 mg/kg every 8 hours for six days).Thus, all of them positively responded to the treatment, and was cured after being admitted (within 15-20 days),and then were discharged home. When they were followed up by telephone, they were still doing very well. The veterinary team from the directorate of health visited the sector and village of the affected patients, and they checked animals and gave those appropriate instructions and proper management.

**Discussion**

This study shows the epidemiologic, clinical, and laboratory outcome of patients diagnosed with CCHF.Cases were found in rural area where animals were kept at home and had direct contact with infected goats and cows which act as livestock for CCHF virus. Table (1) demonstrated that the main route of transmission of CCHF was through handling blood and tissues

of slaughtered viremic livestock at home. Though, they slaughtered sheep in their house, none of them had tick bite. It is clear that when livestock and other hosts are in the viremic period, they are dangerous for transmission of CCHFV to human and this is the main route of transmission of Crimean Congo Hemorrhagic Fever Virus in Iraq, Iran and Turkey (**Chinikar S et al., 2009**; S. Chinikara *et al.*, 2010; Emad S. *et al.*, 2012; S. Sami Kartiet *al.*, 2004). In addition, it could also affect neighboring countries where such animals have been transported to. The most common clinical signs and symptoms reported in CCHF are fever, myalgia, malaise, headache, nausea, vomiting, diarrhea, abdominal pain, petechiae, ecchymosis, and visceral bleeding. Most of these signs and symptoms were also observed in our patients (S. Sami Karti *et al.*, 2004).

Prolongation of PT and PTT was thought to be caused by liver damage. Of the viral hemorrhagic fevers, CCHF infection has the most florid hemorrhage and highest frequency of large ecchymosis. Besides elevated PT, A-PTT, and thrombocytopenia, damage to vascular endothelium directly by the virus and cytokine storm can lead to bleeding tendencies(S. Sami Karti *et al.*, 2004; Peters CJ. *et al.*, 2002 ;Burt FJ. *et al.*, 1997;Swanepoel R *et al.*, 1989).

Overall laboratory findings in our patients were consistent with the findings of other CCHF case series. Liver transaminases levels were high in our patients, beside the hepatic vascular involvement and resulting infarctions in liver parenchyma. Also, direct Hepatocellular involvement may also be responsible for elevated serum aminotransferase (Peters CJ. *et al.*, 2002; Swanepoel R *et al.*, 1989).Mortality rates for various CCHF outbreaks have varied greatly. The average fatality rate is often 30–50 % ( S. Sami Karti *et al.*, 2004; Burt FJ. *et al.*, 1997)but mortality rates from 10% to 80% have been reported in various outbreaks, e.g. 72.7% and 80% from the United Arab Emirates and China, respectively(**Chinikar S et al.,2009** ; Schwarz TF *et al.*,1995; Schwarz *et al.*,1997). Although very high death rates are reported in some series(S. Sami Karti *et al.*, 2004), no death rates in our patients were reported and this can be explained with better supportive care of the patients, and regional strain differences in CCHFV also play a role in the differential death rates. Nosocomial transmission of CCHFV through infected blood or body secretions from patients has been reported many times in the literature(Tantawi HH,1980; Papa A *et al.*, 2002; Colebunders R *et al.*, 2002; Fisher-Hoch SP *et al.*,1995; Weber DJ *et al.* 2001;Mardani M1999-2000).In addition, there are reported cases of nosocomial infection in Iraq in 1979and in other parts of the world like Iran and Turkey(**Chinikar S et al.,2009**;Emad S. *et al.*, 2012; S. Sami Karti *et al.*, 2004),but in our center, none of the cases of nosocomial infection were



reported and it could be due to strict and cautious dealing with cases of applying infection prevention program .

There are about 192 confirmed cases of CCHF which have been reported from different provinces in Iraq (between 1992 and Dec. 2010); however, five cases of nosocomial infections were recorded in 1979, 1992 and 1996(Emad S. *et al.*, 2012). It is of great importance to diagnose suspected cases of CCHF in the early stages as early as possible. Blood samples from suspected CCHF virus cases should be handled carefully, to prevent the transmission of CCHF among medical and laboratory staff, as it is applied in our center.

One of the factors that contributed to the control of this outbreak was the well-coordinated and efficient surveillance system for CCHF that is in place in Erbil and Duhok. This system is not only responsible for continuous monitoring of this disease, but it also deals with outbreaks. Thus, rapid and precise laboratory diagnosis of CCHF facilitates the control of this outbreak. Nevertheless, a higher level of training and precautionary measures for healthcare workers such as the use of isolation chambers in hospital wards, mask and other medical shields when contacting CCHF patients and other high risk professions could help in decreasing the outbreak rate in the endemic areas(Emad S. *et al.* ,2012).Patients remaining in hospital for about 15-20 days corresponds to Convalescence period which begins about 15–20 days after the onset of the illness(Whitehouse CA,2004; Assimina Zavitsanou *et al.* ,2009; Pierre Nabeth *et al.* ,2004).They were discharged home in good health and through a periodic telephone follow up, they remained healthy.

In conclusion, Iraq is an endemic country for CCHF and contact with livestock is the main source of human infection. However, through early referral, intensive supportive circulation using intravenous fluid, blood with blood product support (platelet and fresh frozen plasma), with specific treatment, mortality and morbidity from CCHF infection would be decreased.

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