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Multi-center prospective evaluation of discharge criteria for hospitalized patients with Crimean-Congo Hemorrhagic Fever

Hakan Leblebicioglu [a, *], Mustafa Sunbul [a], Sener Barut [b], Seyit Ali Buyuktuna [c], Zulal Ozkurt [d], Derya Yapar [e], Gurdal Yilmaz [f], Rahmet Guner [g], Ayse But [h], Gonul Cicek Senturk [i], Naci Murat [j], Resat Ozaras [k], Crimean Congo Hemorrhagic Fever Research Network of Turkey, Mehmet Bakir, Nurcan Baykam, Hurrem Bodur, Ilkay Bozkurt, Iftihar Koksal, Irfan Sencan

[a] Department of Infectious Diseases and Clinical Microbiology, Ondokuz Mayis University Medical School, Samsun, Turkey
[b] Department of Infectious Diseases and Clinical Microbiology, Gaziosmanpasa University Medical School, Tokat, Turkey
[c] Department of Infectious Diseases and Clinical Microbiology, Cumhuriyet University Medical School, Sivas, Turkey
[d] Department of Infectious Diseases and Clinical Microbiology, Ataturk University Medical School, Erzurum, Turkey
[e] Department of Infectious Diseases and Clinical Microbiology, Hitit University Medical School, Corum, Turkey
[f] Department of Infectious Diseases and Clinical Microbiology, Karadeniz Technical University Medical School, Samsun, Turkey
[g] Department of Infectious Diseases and Clinical Microbiology, Yildirim Beyazit University Medical School, Ankara, Turkey
[h] Department of Infectious Diseases and Clinical Microbiology, Ankara Numune Education and Research Hospital, Ankara, Turkey
[i] Department of Infectious Diseases and Clinical Microbiology, Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey
[j] Department of Industrial Engineering, Ondokuz Mayis University, Faculty of Engineering, Samsun, Turkey
[k] Department of Infectious Diseases and Clinical Microbiology, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey

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ABSTRACT

Introduction: The information of discharge criteria in patients with Crimean-Congo Hemorrhagic Fever (CCHF) is limited. In this study, we aimed to determine the clinical and laboratory parameters used in discharging the patients by the experienced centers.

Materials and methods: The study was done in 9 reference centers of CCHF from May 1, 2015 to December 1, 2015 and included laboratory-confirmed patients with CCHF. The study was prospective, observational and non-interventional.

Results: The study included 260 patients. Mean age was 51.3 ± 16.3 years; 158 (60.8%) were male. Mean hospital stay was 7 ± 2.6 days. The decision of discharging was taken considering clinical and laboratory findings. On discharge, no patients had fever or hemorrhage. The patients were followed-up clinically and a repeat CCHF PCR was not studied. All centers considered the following criteria for discharge: no fever and hemorrhage, improvement in clinical findings and laboratory studies. For all patients except one, platelet count was >50,000/mm^3 and had a tendency to increase.

Prothrombin time and international normalized ratio (INR) were normal in 258 (99.6%) and 254 (98.1%) patients respectively. Alanine aminotransferase (ALT) was either normal or not higher than 10-fold and had a tendency to decrease in 259 (99.6%) patients. ALT and aspartate aminotransferase (AST) levels were not taken as discharge criteria with priority. During 30 days following the discharge, complication, relapse, or secondary transmission were not reported.

Conclusions: The discharging practice of the centers based on clinical and laboratory parameters seems safe considering no complications, relapses, or secondary infection thereafter. Current discharge practice of the centers composed of no fever and hemorrhage, improvement in clinical findings, platelet count of either >100,000/mm^3 or >50,000/mm^3 with a tendency to increase, and normal bleeding tests can be used as the criteria of discharge.

1. Introduction

Crimean-Congo Hemorrhagic Fever (CCHF) is characterized by fever and hemorrhages; complications of multiple organ failure

* Corresponding author.
E-mail address: hakanomu@yahoo.com (H. Leblebicioglu).

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and disseminated intravascular coagulation can cause mortality with a range of from 4 to 20% (Bente et al., 2013; Leblebicioglu et al., 2016a,b). CCHF is commonly seen in Eurasian countries such as Turkey, Iran, Pakistan, Russia and Kazakhistan (Leblebicioglu, 2010) and Balkan countries (Albania, Bulgaria, Kosova)(Dreshaj et al., 2016) It is more common in Turkey with approximately 900 cases a year for the past 10 years and that this provides opportunities to study many aspects of the disease (Leblebicioglu et al., 2016a).

The disease shows seasonality with a peak incidence in the summer (Leblebicioglu, 2015). High number of patients in summer season needed cohorting of the patients in some centers. Lack of enough beds in the units has caused patients to wait in emergency units. Increasing number of patients also leads to an increase in laboratory workload and cost (Bozkurt et al., 2016; Leblebicioglu et al., 2016a). The discharge criteria in infectious diseases are generally taken as the absence of fever in patients by 48–72 h, hemodynamic stability, and the disappearance of the complaints related with the disease, and absence of transmission after the discharge.

For another viral hemorrhagic fever, dengue, World Health Organization (WHO) recommended the discharge criteria as normal body temperature for more than 48 h, clinical improvement, hemodynamic stability, and platelet count tending to increase (WHO, 2009). For other viral hemorrhagic diseases that have potentials of human-to-human transmission such as Ebola, Lassa, and CCHF, WHO recommended the criteria of discharge as being asymptomatic for 3 days and a negative PCR (WHO, 2016). Especially Ebola can persist for long periods in bodily fluids such as semen, aqueous humor, urine and breast milk (Chughtai et al., 2016). and there is a risk of sexual transmission during the convalescence period and Center for Disease Prevention and Control (CDC) recommend to use condom for male survivors when have sex (Christie et al., 2015) For CCHF, it has been reported that patients with a good clinical situation and without hemorrhage can be discharged (Swanepoel, 2012). However the recommendations are not evidence-based (O'Dempsey et al., 2015).

CCHF shares many features with Ebola virus disease, including the occasional transmission of disease from person to person through direct contact with body fluids. In the recent West African epidemic, the WHO recommended that doctors obtain a negative RT-PCR on a serum sample before discharging a patient. CCHF appears to be much less transmissible from person to person than Ebola (Leblebicioglu et al., 2016d). In Turkey, RT-PCR is often used for diagnosis of CCHF, but it has not been the practice to perform the test again before discharge. Therefore, we aimed to determine the clinical and laboratory parameters used in the decision of discharging CCHF patients using real life setting data and to determine if not performing RT-PCR before discharge has had negative consequences for patients or their family members.

2. Material and methods

2.1. Study design

The study was done in high-volume 9 reference centers of CCHF from May 1, 2015 to December 1, 2015 and included laboratory-confirmed patients with CCHF. The study was prospective, longitudinal, observational and non-interventional. The centers in the study were also members of a network; Crimean-Congo Hemorrhagic Fever Research Network of Turkey (CCHF-RNT) (Sunbul et al., 2015).

The centers are reference hospitals in the endemic region of the disease (Leblebicioglu et al., 2016a). The centers are found in the cities of Ankara (3 centers), Corum, Erzurum, Samsun, Sivas, Trabzon, and Tokat.

2.2. Study population

The study included patients with CCHFV infection confirmed by PCR and/or detection of CCHFV IgM antibodies Patients who died, those having an underlying disease that may have an impact on the hematological parameters and chronic liver or renal disease, and the patients transferred to another centers were excluded.

2.3. Study oversight

The physicians recorded the socio-demographic features, duration of hospitalization, and clinical and hematological features of the patients to the forms. The laboratory data prospectively collected over a period of up to discharge. The primary outcome measure was readmission or death within 30 days after discharge from the hospital.

2.4. Statistical analysis

In the analysis of data, descriptive statistics were used. The normality of data was checked using Shapiro-Wilk test. Mean + SD was used for normally distributed data. For the data not normally distributed, minimum and maximum values, median (range) and/or frequency were given. This analysis was performed using SPSS program tool (IBM SPSS Statistics 23, Armonk, New York, USA).

2.5. Ethics approval

This study was approved by Ondokuz Mayis University Ethical Committee (OMU KAEK, 2015/120). There was no funding sources for this research.

3. Results

In the 9 centers involved in the study, 304 patients were followed-up in 2015 and 18 (5.9%) died. The study form was filled for the survived 276 out of 286 (96.5%) patients. Two patients were excluded since they have underlying disorders that may influence the laboratory studies (one chronic renal failure and one warfarin use). Other two patients were excluded since they were transferred to other centers and 12 were not included because their data were not complete; 260 patients (94.2%) were included into the study.

3.1. Demographics

Among 260 patients included 158 (60.8%) were male; mean age was 51.3 ± 16.3 years, mean duration of hospitalization was 7 ± 2.6 (range 2–17 days) days.

3.2. Clinical features

The rates of the patients with fever (>37.2 °C) and hemorrhage on admission were 61.5% and 24.4% respectively. No patients had fever or hemorrhage on discharge.

3.3. Laboratory features

The laboratory results (complete blood count, coagulation tests, biochemical studies, and CRP) are given in Table 1.