

Clinical Features of Patients With Ebola Virus Disease in Sierra Leone

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Background. Clinical and laboratory data available on patients with Ebola virus disease (EVD) remain extremely limited. We summarized the clinical characteristics of patients with EVD and analyzed the factors related to their death.

Methods. Patients admitted for care at the Freetown China–Sierra Leone Friendship Hospital during 1 October–14 November 2014 were enrolled in this study. The clinical data of these patients were retrospectively analyzed.

Results. Sixty-one patients were confirmed to have EVD; 28 of them (45.9%) were male and 33 (54.1%) were female. Their median age was 28 years (range, 1.17–67 years). The median duration from symptom onset to clinic visit time was 5 days (range, 1–16 days). Among these patients, 42 of them (68.9%) died. Of the confirmed cases, 18.0% did not present with fever. Patients aged >30 years had a higher fatality rate than those <30 years (87.0% vs 57.9%; $P = .0175$). The mean duration from symptom onset to clinic presentation of the survivors (4.57 ± 2.79 days) was shorter than that of the nonsurvivors (6.34 ± 3.33 days). Clinical factors associated with a fatal outcome included weakness, extreme fatigue, vomiting, diarrhea, mental symptoms, bleeding, and loss of appetite. No statistical difference in the case fatality rate between males and females was found ($P = .2061$).

Conclusions. The mortality of patients with EVD was closely associated with age and duration from symptom onset to presentation for care. Patients with EVD identified in the current outbreak did not necessarily have fever. Early diagnosis of the disease and timely symptomatic treatment may greatly contribute to the reduction of fatality rate of patients with EVD.

Keywords. clinical features; Ebola virus disease; Sierra Leone.

Ebola virus disease (EVD), formerly known as Ebola hemorrhagic fever, is a severe infectious disease caused by *Ebolavirus* species [1–3], with an average case fatality rate of approximately 50%. Case fatality rates in previous outbreaks range from 25% to 90% [2]. With the first case being reported in March 2014, the 2014 outbreak in West Africa was the largest and most complex Ebola outbreak since *Ebolavirus* was first discovered in 1976 [4]. As of 23 November 2014, the World Health Organization (WHO) had reported a cumulative total of

15 935 clinical cases of EVD worldwide (with a death toll of 5689) [5]. This outbreak was mainly focused in Guinea, Liberia, and Sierra Leone. Currently, the situation in Guinea and Liberia is relatively stable; in Sierra Leone, the outbreak was still serious by the time of the data collection in this study [6, 7]. Therefore, we summarized the clinical characteristics of patients with EVD admitted for treatment at the Freetown China–Sierra Leone friendship hospital from 1 October to 14 November 2014, aiming at assisting the research of EVD treatment by providing more current data on patients with EVD.

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METHODS

Study Design

We conducted a retrospective observational study on all patients with confirmed EVD who were admitted for care at the Freetown China–Sierra Leone friendship hospital from 1 October to 14 November 2014. The

standard case definition established by the WHO [8] was used for this study.

Eighty-three patients were enrolled in this study. Laboratory confirmation of EVD was made on the basis of the results of real-time polymerase chain reaction. Treatment was conducted in line with the protocols for viral hemorrhagic fever under the urgent interim guidance for case management established by the WHO [9]. The protocol for this study was approved by the Ethics Committee of Beijing 302 hospital and the Department of Health in Freetown. Written informed consent was given to every patient enrolled prior to the start of this study.

Data Collection

Epidemiologic and demographic data such as exposure history, sex, age, onset date, virus infection situation, medical history and complications, treatments, death, cure, dropout status, and laboratory test results of all the patients were collected for analysis.

Statistical Analysis

The cure rate, death rate, and incidence of various symptoms of patients of different sexes and ages were listed in detail. The χ^2 test was used to analyze statistical differences in sex, age, and symptoms. To explore the effect of an in-time presentation on patients' final results, the Wilcoxon rank-sum test was performed to compare the duration from symptom onset to clinic presentation between cured patients and patients who died. All statistical tests were 2-tailed and conducted with SAS software (version 9.1.3), with a significance level of $P < .05$.

RESULTS

Demographic Data

We enrolled 83 patients with suspected EVD, which was later confirmed. Twenty-two of them dropped out due to their transfer to other hospitals; therefore, their data were excluded from the study. Among the remaining 61 patients, 42 died and 19 recovered from the Ebola infection. The mean age (\pm standard deviation [SD]) was 26.4 ± 5.81 years and the median age was 28 years (range, 1.17–67 years).

Patient Features by Sex

Of the 61 remaining patients confirmed with EVD, 28 of them (45.9%) were male and 33 (54.1%) were female. Seventeen male patients (60.7%) and 25 female patients (75.8%) died as a result of the Ebola infection; the rest of them recovered from the disease. Statistical analyses indicated no statistical difference in case fatality rates between male and female patients ($P = .2061$; Table 1). However, a higher trend of mortality was indicated among female patients, which requires further evidence from the observation of more EVD cases.

Table 1. Demographic Data of Patients With Confirmed Ebola Virus Disease

| Factor | Survival Status | No. | Proportions, % | Mean \pm SD, Median (Min–Max) | P Value |
|--|-----------------|-----|----------------|---------------------------------|--------------------|
| Total | | 61 | | | |
| | Died | 42 | 68.9 | | |
| | Cured | 19 | 31.1 | | |
| Sex | | | | | |
| Male | Total | 28 | | | .2061 |
| | Died | 17 | 60.7 | | |
| | Cured | 11 | 39.3 | | |
| Female | Total | 33 | | | |
| | Died | 25 | 75.8 | | |
| | Cured | 8 | 24.2 | | |
| Age | | | | | |
| <10 y | Total | 9 | | | .0175 ^a |
| | Died | 6 | 66.7 | | |
| | Cured | 3 | 33.3 | | |
| 10–20 y | Total | 7 | | | |
| | Died | 4 | 57.1 | | |
| | Cured | 3 | 42.9 | | |
| 21–30 y | Total | 22 | | | |
| | Died | 12 | 54.5 | | |
| | Cured | 10 | 45.5 | | |
| ≤ 30 y ^a | Total | 38 | | | |
| | Died | 22 | 57.9 | | |
| | Cured | 16 | 42.1 | | |
| 31–40 y | Total | 18 | | | |
| | Died | 16 | 88.9 | | |
| | Cured | 2 | 11.1 | | |
| 41–50 y | Total | 4 | | | |
| | Died | 3 | 75.0 | | |
| | Cured | 1 | 25.0 | | |
| >50 y | Total | 1 | | | |
| | Died | 1 | 100.0 | | |
| | Cured | 0 | 0.0 | | |
| >30 y ^a | Total | 23 | | | |
| | Died | 20 | 87.0 | | |
| | Cured | 3 | 23.0 | | |
| Time from symptom onset to clinic visit, d | Total | 61 | | 5.79 \pm 3.30 5 (1–16) | |
| | Died | 42 | | 6.34 \pm 3.33 6 (2–16) | .0365 |
| | Cured | 19 | | 4.57 \pm 2.79 4.5 (1–10) | |

Abbreviation: SD, standard deviation.

^a Comparison between patients aged ≤ 30 years and those aged > 30 years.

Patient Features by Age

Nine patients were aged < 10 years, and 6 of them (66.7%) died from the infection (Table 1). Seven patients were aged 10–20 years, and only 3 of them (42.9%) recovered from the disease;

the other 4 patients (57.1%) died. Of the 22 patients aged 21–30 years, 12 of them (54.5%) died. Among the 18 patients aged 31–40 years, only 2 of them (11.1%) survived the infection, and 16 died (88.9%). Three of the 4 (75.0%) patients aged 41–50 years died. Only 2 patients enrolled in the study were aged >50 years; 1 of them dropped out from the study and the other died from the infection, making the death rate in this age group 100%.

Among the patients aged <10 years, 10–20 years, and 21–30 years, similar proportions of deaths were found (66.7%, 57.1%, and 54.5%, respectively); among the patients aged 31–40, 41–50, and >50 years, the death rates (88.9%, 75.0%, and 100.0%, respectively) were similar and much higher than in the other 3 groups (Table 1). An age of 30 years was taken as the separation for the comparison of the clinical characteristics among patients in this study. Patients aged <30 years had a much lower case fatality rate (22/38 [57.9%]) than those aged >30 years (20/23 [87.0%]) ($P = .0175$).

Interval From Symptom Onset to Clinic Visit

Of 61 patients with confirmed EVD, the mean \pm SD duration and the median duration from onset symptom to clinic visit were 6.34 ± 3.33 days and 6 days (range, 2–16 days), respectively, in the nonsurvivor group, and 4.57 ± 2.79 days and 4.5 days (range, 1–10 days), respectively, in the survivor group. A statistically significant difference was shown in the interval from symptom onset to clinic presentation between survivors and nonsurvivors ($P = .0365$; Table 1).

Clinical Features of the Survivors and Nonsurvivors

The mean \pm SD duration from symptom onset to clinic visit among the patients with confirmed EVD was 5.79 ± 3.30 days and the median duration was 5 days (range, 1–16) (Table 1). During their hospitalization period, 11 patients (18.0%) did not present with fever; of these patients, 6 died from the infection (54.5%), and 5 were cured. Fourteen of the 50 patients with fever were cured (28.0%), and 36 died (72.0%). Weakness was observed in 52 patients in this study: 10 patients with this symptom recovered from the infection, and 42 died (80.7%); however, all 9 patients without this symptom were cured. Thirty-four patients suffered from extreme fatigue; among those, 30 died (88.2%) and 4 recovered. In comparison, among the 27 patients without the symptom of extreme fatigue, 15 of them recovered from the infection and the remaining 12 died (44.4%). Headache was observed in 46 patients, among whom 14 were cured and 32 died (69.6%); among the 15 patients without headache, 5 were cured and 10 died. Death rates between the patients with headache and those without headache were similar (69.6% vs 66.7%, respectively). Forty-five patients in the study suffered from muscle and joint pain; 34 (75.6%) of those patients died. However, among the 16 patients without muscle and joint pain, half of them managed to recover from the

infection, with a death rate in this group of 50%. Fifteen of the 18 patients with abdominal pain died (83.3%); among the 43 patients without abdominal pain, 27 died (62.8%). Twenty patients presented with sore throat; 4 of them recovered and 16 (80.0%) died. Among the 41 patients without sore throat, 15 of them were cured, and 26 (63.4%) died. The symptoms of vomiting, diarrhea, bleeding, loss of appetite, dyspnea, and mental symptoms (ie, irritability, nervousness, restlessness, screaming, and insomnia) were only observed in nonsurvivors. Statistical analyses showed that there were significant differences in symptoms between the survivors and the nonsurvivors. Those symptoms included weakness ($P < .0001$), extreme fatigue ($P = .0002$), vomiting ($P < .0001$), diarrhea ($P < .0001$), mental symptoms ($P < .0001$), bleeding ($P = .0488$), and loss of appetite ($P = .0017$) (Table 2).

DISCUSSION

In this study, we found that patients aged >30 years old had a higher fatality rate than those aged <30 years. The possible reasons for this were as follows: First, the duration from symptom onset to clinic presentation was relatively longer for patients aged >30 years than for patients aged <30 years. Second, patients aged >30 years were more likely to suffer from malnutrition and common diseases. Some of the patients (18.0%) who did not develop a fever (temperature $>38^{\circ}\text{C}$) in this study also faced fatal outcomes, which might be due to immune evasion in those patients [10–13]. However, a relatively small number of patients in this study did not suffer from a fever; therefore, we cannot suggest that the absence of fever might be a more dangerous signal. Data collected from studies with larger samples are needed to verify the importance of the absence of fever. Bleeding has also been noted in previous outbreaks among patients; however, in this study, only 8 of 61 patients (13.1%) suffered from overt bleeding—a much lower occurrence rate of bleeding than in previous reports [14, 15]. This result suggests that bleeding might not be a main feature of patients with EVD in the current outbreak.

The most common EVD symptoms that manifested among the patients in this study during their hospitalization were gastrointestinal symptoms and fatigue, similar to the results in the reports of previous outbreaks [16]. The overall case fatality rate (68.9%) among the 61 patients with EVD was similar to the 74% reported previously [17]. Among the 42 patients who died, the median time from symptom onset to death is also consistent with the existing literature [18, 19].

The incubation period, which is the duration from viral infection to symptom onset, recorded in this study was within the ranges reported from previous EVD epidemics [20–23]. In this study, nonsurvivors were more likely to have symptoms of weakness, extreme fatigue, vomiting, diarrhea, mental symptoms, bleeding, and loss of appetite. This finding is inconsistent

Table 2. Comparison of Clinical Features Between Ebola Virus Disease Survivors and Nonsurvivors

| Variable | With Symptom, No. | Without Symptom, No. | P Value ^a |
|--------------------------|-------------------|----------------------|----------------------|
| Fever | | | |
| Total | 50 | 11 | .2577 |
| Survivor | 14 | 5 | |
| Nonsurvivor | 36 | 6 | |
| Weakness | | | |
| Total | 52 | 9 | <.0001 |
| Survivor | 10 | 9 | |
| Nonsurvivor | 42 | 0 | |
| Extreme fatigue | | | |
| Total | 34 | 27 | .0002 |
| Survivor | 4 | 15 | |
| Nonsurvivor | 30 | 12 | |
| Headache | | | |
| Total | 46 | 15 | .8333 |
| Survivor | 14 | 5 | |
| Nonsurvivor | 32 | 10 | |
| Muscle/joint pain | | | |
| Total | 45 | 16 | .0580 |
| Survivor | 11 | 8 | |
| Nonsurvivor | 34 | 8 | |
| Vomiting | | | |
| Total | 24 | 37 | <.0001 |
| Survivor | 0 | 19 | |
| Nonsurvivor | 24 | 18 | |
| Diarrhea | | | |
| Total | 28 | 33 | <.0001 |
| Survivor | 0 | 19 | |
| Nonsurvivor | 28 | 14 | |
| Abdominal pain | | | |
| Total | 18 | 43 | .1141 |
| Survivor | 3 | 16 | |
| Nonsurvivor | 15 | 27 | |
| Sore throat | | | |
| Total | 20 | 41 | .1892 |
| Survivor | 4 | 15 | |
| Nonsurvivor | 16 | 26 | |
| Mental symptom | | | |
| Total | 26 | 35 | <.0001 |
| Survivor | 0 | 19 | |
| Nonsurvivor | 26 | 16 | |
| Bleeding | | | |
| Total | 8 | 53 | .0488 |
| Survivor | 0 | 19 | |
| Nonsurvivor | 8 | 34 | |
| Loss of appetite | | | |
| Total | 16 | 45 | .0017 |
| Survivor | 0 | 19 | |
| Nonsurvivor | 16 | 26 | |

Table 2 continued.

| Variable | With Symptom, No. | Without Symptom, No. | P Value ^a |
|----------------|-------------------|----------------------|----------------------|
| Dyspnea | | | |
| Total | 6 | 55 | .1639 |
| Survivor | 0 | 19 | |
| Nonsurvivor | 6 | 36 | |

^a Comparison between the survivor group and nonsurvivor group.

with the results of a previous report that indicated the only symptoms significantly associated with a fatal outcome were weakness, dizziness, and diarrhea [9].

Our data showed that in the 2014 outbreak in Sierra Leone, there was no specific clinical manifestation among patients, and some patients did not suffer from fever, leading to difficulties in early diagnosis. Patients' lack of knowledge regarding EVD resulted in delays in clinic visit time after viral infection and symptom onset, which further resulted in delays in receiving proper treatment. Many patients died on their way to the hospital. Even among the patients who managed to arrive at the hospital for treatment, most died within 2 days after admission, as it was too late for those patients to receive proper treatment for such a severe disease. Normally, if a patient has a body temperature of <38.6°C (101.5°F) and no other obvious symptoms of Ebola infection, healthcare workers will not diagnose the patient as a suspected case of EVD.

Possible reasons for the high case fatality rate are as follows: A severe reaction appeared in patients' digestive tract; during the late period of disease; and some patients presented with mental deterioration, hemorrhage, dyspnea, loss of appetite, and inability to walk, indicating that they were suffering from severe pathological and physiological disorders such as electrolyte balance disorder, acid-base imbalance, coagulation disorders, and damage in such organs as liver, kidney, and lung.

An early positive intervention could significantly improve the prognosis of disease. However, laboratories mainly depend on virus detection to diagnose EVD; routine tests such as blood, urine, stool, biochemistry, blood gas, and blood coagulation are not routinely performed to diagnose suspected cases of EVD. Due to the lack of detailed information about patients' conditions, doctors can only conduct a comprehensive treatment such as antimalarial treatment, antibacterial therapy, and injection of physiological saline and Ringer's solution based on possible predicted outcomes; however, comprehensive treatment of patients with EVD does not result in much actual treatment effect. Therefore, doctors should carry out conventional tests in time among patients with suspected EVD with

appropriate self-protection, and then follow up with positive symptomatic treatment on the basis of EVD characteristics so as to improve the prognosis.

In conclusion, mortality of patients with EVD was closely associated with age and the interval from symptom onset to clinic visit, and it is noteworthy that patients with Ebola virus infection do not necessarily present with fever. Early diagnosis and timely symptomatic treatment may greatly contribute to the reduction of the case fatality rate, and therefore are essential to the recovery of patients with EVD.

Note

Potential conflicts of interest. All authors: No potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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