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Prognostic and Predictive Factors of Ebola Virus Disease Outcome in Elderly People during the 2014 Outbreak in Guinea

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Abstract. Elderly people occupy a prominent position in African societies; however, their potential linkage to high case fatality rate (CFR) in Ebola virus disease (EVD) was often overlooked. We describe the predictive factors for EVD lethality in the elderly. A total of 2,004 adults and 309 elderly patients with confirmed EVD were included in the analysis. The median age (interquartile range) was 35 years (23–44) in adults and 65 years (60–70) in the elderly. The proportion of funeral participation was significantly higher in the elderly group than in the adult group. Duration (in days) between the onset of symptoms and admission was significantly longer in elderly. CFR in the elderly people was also significantly higher (80.6%) than in the adult group (66.2%). Funeral participation constituted a risk factor for the transmission of EVD in elderly people.

INTRODUCTION

The recent Ebola outbreak has been proved to be devastating to vulnerable populations in West Africa. Because the primary focus had been on adults and children, apparently the casualties among the elderly were left unnoticed and rarely reported.[1] Previous report showed that participation in traditional funeral rites during the outbreak increased the risk of acquiring Ebola virus disease (EVD).[2] Traditional funerals are a kind of social happenings which interconnected to many other aspects of social life, including the logic of parenthood, the concept of authority, and care of sickness.[3]

In Africa, especially in Guinea, elderly people are the key members in any funeral activities and their roles include, but not limited to, leading mourning ceremonies, providing important information to attendees, and performing rituals and burial.[4] At the time of outbreak, traditional funeral was made one of the main topics by media coverage related to Ebola transmission.[3] Attending a funeral ceremony was perceived to facilitate and expose adults and the elderly to the risk of contracting EVD.[5] It has been suggested that this situation contributed to the spread of the disease and hindered outbreak control efforts. Unfortunately, there is no comprehensive analysis of EVD in this key population (the elderly) to understand their potential role(s) in transmission and high fatality. Therefore, we sought to identify the predictors of EVD mortality during the 2014 outbreak in Guinea.

MATERIALS AND METHODS

Ethics statement. This study was approved by the National Ethics Committee for Healthcare Research Board (No: 071/CNERS/15) with a waiver of informed consent for the collection and analysis of anonymized data.

Patients and study design. It was a retrospective and analytical study, which included patients of 20 years or older admitted during January 2014 to December 2015 (2 years) in the Guinean Ebola Treatment Centers (ETCs) and confirmed positive for EVD by real-time polymerase chain reaction using blood or swab samples. All patients were managed using the World Health Organization (WHO) standardized EVD care path, improving consistency in clinical, laboratory, treatment, and outcome data.[6] The patient's care path included documentation of symptoms, examination findings, and laboratory parameters.

Case definitions. We used the case definition developed by WHO for EVD surveillance, which classified EVD cases into suspected, probable, or laboratory-confirmed cases.[6,7] Elderly is a descriptive term referring to people past midlife and in old age. At the moment, there is no universal standardized numerical criterion; therefore, we classified elderly patients based on the United Nations recommended cut-off for older population.[8] In this study, patients aged 60 years and older according to the previously mentioned definition were considered as "elderly," whereas patients between 20 and 59 years old were defined as "adults."

Data collection. The data originally designed for an Ebola outbreak containment purpose were retrieved from the database of National EVD Committee of Ministry of Health and Public Hygiene, which is the public body responsible for retaining EVD outbreak-related data in Guinea. The data were collected from 29,742 EVD suspected or probable cases

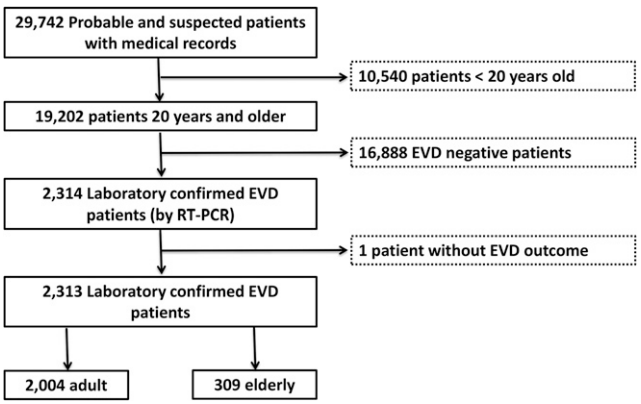

FIGURE 1. Flow diagram of this retrospective study.

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TABLE 1
Comparison of demographic and clinical features of EVD in adult and elderly patients in Guinea

Variables	Number of patients	Adults (*N* = 2,004)	Elderly (*N* = 309)	*P* value
Sociodemographics				
Median age, years (IQR)	–	35 (23–44)	65 (60–70)	*< 0.001**
Gender (male), *n* (%)	1,128	986 (49.2)	142 (45.8)	*0.14*
Residence, *n* (%)				
Macenta	**490**	418 (20.9)	72 (23.2)	–
Conakry	390	360 (18.0)	30 (9.7)	–
Forecariah	**270**	231 (11.5)	39 (12.6)	–
Gueckedou	**179**	156 (7.8)	23 (7.4)	–
Coyah	150	128 (6.4)	22 (7.1)	–
N'Zerekore	145	121 (6.0)	24 (7.7)	–
Kerouane	113	100 (5.0)	13 (4.2)	–
Kissidougou	**53**	40 (2.0)	13 (4.2)	–
Kindia	52	45 (2.2)	7 (2.3)	–
Profession, *n* (%)				
Housewife	309	253 (19.1)	56 (22.4)	*0.13*
Farmer	141	119 (9.0)	22 (8.8)	*0.51*
Health-care worker	98	88 (6.6)	10 (4.0)	*0.69*
Business person	45	43 (3.2)	2 (0.8)	*0.01*
Religious leader	2	2 (0.2)	0 (0)	*0.70*
Transporter	20	19 (1.4)	1 (0.4)	*0.14*
Traditional healer	2	2 (0.6)	0 (0)	*0.25*
Risk factor for exposure to EVD, *n* (%)				
History of contact with suspected or confirmed cases	513	457 (79.5)	56 (86.2)	*0.13*
History of traveling to hot spot areas	104	96 (19.7)	8 (14.5)	*0.23*
History of attending funeral	213	184 (37.8)	29 (50.9)	*0.039*
Symptoms, *n* (%)				
Fever	1,302	1,152 (92.2)	150 (91.5)	*0.41*
Fatigue	1,233	1,077 (91.1)	156 (94.5)	*0.08*
Anorexia	1,099	804 (81.7)	93 (80.9)	*0.45*
Vomiting	835	751 (78.4)	84 (73.7)	*0.15*
Diarrhea	793	701 (77.0)	92 (76.0)	*0.44*
Muscle pain	897	503 (61.5)	71 (68.9)	*0.86*
Joint pain	800	403 (56.0)	45 (56.3)	*0.53*
Headache	448	658 (74.8)	76 (74.5)	*0.51*
Hiccups	140	129 (23.6)	11 (18.6)	*0.24*
Abdominal pain	507	452 (59.9)	55 (59.1)	0.48
Difficulty in swallowing	49	43 (16.3)	6 (13.3)	0.09
Chest pain	138	124 (36.9)	14 (29.8)	0.21
Cough	124	107 (32.6)	17 (34.0)	0.48
Difficulty in breathing	86	78 (25.2)	8 (16.7)	0.13
Sore throat	81	74 (24.9)	7 (14.9)	0.40
Unexplained bleeding	190	167 (25.9)	23 (29.5)	0.28
Gum bleeding	6	6 (1.5)	0 (0.0)	0.54
Hematemesis	11	11 (2.7)	0 (0.0)	0.30
Jaundice	17	16 (9.6)	1 (4.2)	0.33
Conjunctivitis	88	85 (28.9)	3 (7.9)	*0.03*
Comorbodity: malaria, *n* (%)	116	98 (25.2)	18 (30)	*0.36*
Case fatality rate, *n* (%)	1,574	1,324 (66.1)	250 (80.6)	*< 0.001*
Other parameters, median in days (IQR)				
Time between onset and admission		4 (3–6)	5 (3–7)	*< 0.001**
Length of hospitalization		8 (4–13)	6 (3–11)	*< 0.001**
Survival time		11 (7–16)	9 (6–15)	*0.007**

EVD = Ebola virus disease; IQR = interquartile range; N = the number of patients in each comparison group; *n* = the number of patients having a specific demographic or clinical feature.
* Continuous variables.

previously recorded on WHO standardized forms during admission at the ETCs. Among them, information of 2,313 confirmed EVD patients was extracted by a medically trained research assistant and analyzed after appropriate data cleaning. The detailed flow diagram of the study is shown in Figure 1.

Data analysis. Baseline characteristics and outcomes were compared between adult (20–59 years old) and elderly (60 years and older) patients. Descriptive analyses were presented as frequency with percentage and median with interquartile range (IQR). Chi-square test or Fisher's exact test was used to compare dichotomous variables, and Mann–Whitney *U* test was used for continuous variables, as appropriate. The association between different variables and EVD mortality was assessed using univariate logistic regression to obtain unadjusted odds ratios (ORs) and their 95% confidence intervals (CIs). Variables with a P value < 0.05 in the univariate analysis were combined and included in a stepwise fashion in a multivariate logistic regression model. The Kaplan–Meier method was used to measure the fraction of EVD patients living for a certain amount of time after admission to ETCs. The effect of age as a predictor was investigated by Cox regression. Statistical significance for all tests was set at a probability value < 0.05. All statistical analyses were performed using SPSS version 22 (IBM, SPSS Inc., Chicago, IL).

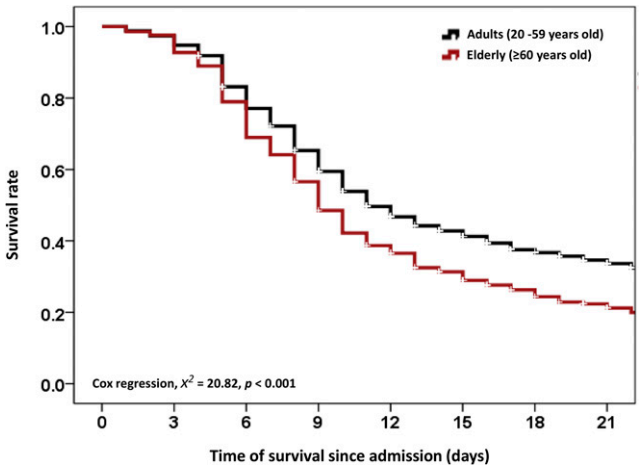

FIGURE 2. The Kaplan–Meier curves of laboratory-confirmed Ebola virus disease in adult and elderly patients in Guinea. The Cox regression test yielded a χ^2 value of 20.82 at 3 degree of freedom (P < 0.001). This figure appears in color at www.ajtmh.org.

RESULTS

In the cohort of 2,313 laboratory-confirmed EVD patients, 2,004 were adults and 309 were elderly (Figure 1). The median age (IQR) was 35 years (23–44) and 65 years (60–70) for adults and elderly people, respectively. The proportion of males was 49.2% and 45.8% in the adult and elderly groups, respectively. Most of the patients were from Macenta Prefecture (20.9% adults and 23.2% elderly); however, there was no significant difference between the proportion of adult and elderly in any location including Macenta. The most frequent profession in both groups was housewife (19.1% adult and 22.4% elderly) followed by farmers (9.0% and 8.8%).

The proportion of elderly people participating in the funeral was significantly higher than in the adult group (P = 0.039). However, we did not observe any difference between adult and elderly groups in the history of contact with confirmed or suspected EVD patients. In addition, the two groups were not different in terms of history of traveling to the hot spot of transmission during the outbreak (Table 1).

Among the elderly group, fever (91.5%), fatigue (94.5%), vomiting (80.9%), and diarrhea (84%) were the most common clinical features; however, bleeding signs were present in only 29% patients. There was no difference in symptom manifestation between adult and elderly groups (Table 1). The median time (in days) between the onset of symptoms and admission was significantly longer in the elderly (P < 0.001), which indicates delayed hospital presentation. In contrast, both the median length of hospitalization and median survival time (in days) were significantly shorter in the elderly group (P < 0.001). The survival analysis using Kaplan–Meier curves showed that the median survival period was significantly different between adults and elderly groups (Cox regression χ^2 = 20.82; P < 0.001) (Figure 2).

Case fatality rate (CFR) of EVD was also significantly higher in the elderly group (80.6%) (P < 0.001). In multivariable analysis, there was a significant association between increasing age and risk of death with EVD in the elderly group (OR [95% CI] = 1.05 [1.003–1.098]; P = 0.036) (Table 2). However, no clinical symptom was found to be predictive of the poor outcome in EVD among elderly people. Cox regression analysis showed that age was the only factor that could influence the EVD outcome. Therefore, age was considered as an independent factor that predicts EVD death in the elderly group.

DISCUSSION

To the best of our knowledge, this is one of the few studies to systematically compare the risk factors of exposure, clinical characteristics, and outcomes of EVD between adult (20–59 years old) and elderly (60 years and older) cases with

TABLE 2
Logistic regression analysis of factors associated with death in the elderly patients (N = 309) with EVD in Guinea

	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (years)*	1.05 (1.003–1.098)	0.036	1.05 (1.003–1.098)	0.036
Gender	1.12 (0.64–1.98)	0.691	–	–
History of contact with suspected or confirmed cases	2.009 (0.0–3.38)	0.99	–	–
History of traveling to hot spot areas	1.03 (0.18–5.79)	0.975	–	–
History of attending funeral	1.4 (0.97–1.96)	0.077	–	–
Fever	0.70 (0.19–2.64)	0.600	–	–
Unexplained bleeding	1.47 (0.42–5.11)	0.544	–	–
Vomiting	0.94 (0.38–2.47)	0.940	–	–
Diarrhea	1.00 (0.36–2.81)	0.997	–	–
Fatigue	0.75 (0.15–3.76)	0.727	–	–
Anorexia	0.68 (0.21–2.20)	0.516	–	–
Abdominal pain	1.05 (0.41–2.69)	0.926	–	–
Joint pain	0.92 (0.32–2.59)	0.869	–	–
Muscle pain	0.55 (0.20–1.53)	0.252	–	–
Headache	1.54 (0.57–4.16)	0.392	–	–
Cough	1.04 (0.23–4.78)	0.963	–	–
Hiccups	1.04 (0.19–5.66)	0.965	–	–
Difficulty in swallowing	0.44 (0.06–2.87)	0.390	–	–
Comorbidity: malaria	0.85 (0.38–1.88)	0.687	–	–
Time between onset and admission	0.95 (0.89–1.02)	0.199	–	–

CI = confidence interval; EVD = Ebola virus disease; OR = odds ratio.
* Age includes patients from the elderly group only.

confirmed EVD in Guinea. In this study, the CFR was significantly higher in the elderly group than in the adult group. Although there is no report on CFR in the elderly group, previous reports showed higher CFR among the patients aged 45 years and older.[9,10] Higher mortality rate in elderly patients might be attributable not only to the age-related fragility of the immune system, causing a high viral load at the time of admission that subsequently contributes to multiorgan failure in the EVD,[11,12] but also to the longer duration between onset and presentation to ETCs and other preexisting morbidities.[13,14] Apart from that, the lack of trained caregivers and equipment in the treatment facilities possibly contributed to high fatality[15] in general (among both groups). Moreover, the limited access to healthcare facilities probably due to a strong social resistance to outbreak control interventions[16,17] would have delayed hospital admission in both groups. In this regard, the WHO also reported the challenges in community engagement in some affected prefectures of Guinea, with several reported incidents of violence against the Ebola fighters team.[15]

We found that the proportion of EVD patients participating in the funeral was significantly higher in the elderly group than in its adult counterpart. Although the elderly in our study were not asked directly about participation in preparation of funeral rituals, cultural practices suggest this is highly likely.[18] Our finding also concords with a previous report which pointed out participation in traditional funeral rites as a major risk factor.[18] Among these risk factors, caring practices before the moment of death (in the role of traditional health caregivers) and dead body preparation such as washing and cleaning (in the role funeral ceremony leader) were reported as a source of contamination in countries affected by EVD.[17,18] These practices put the elderly at differing patterns of risk of contracting EVD compared with younger adults.[5]

In Guinea, although most of the elderly and adults had a history of contact with suspected or confirmed cases, no significant difference was observed. This observation demonstrates that the conditions required for EVD to spread from person to person were not specific to one age.

We found that delay in seeking treatment was significantly longer in the elderly group. In addition, the length of hospital stay and survival time were significantly shorter in the elderly group. This observation is similar to previous reports.[19,20] Providing instruction to seek medical attention as soon as any symptom appears in the population could reduce this delayed admission and educating them could improve the awareness of this disease.

In this study, clinical features of EVD in elderly, characterized by nonspecific signs and symptoms such as fever, diarrhea, anorexia, abdominal pain, joint pain, and headache, were similar to those reported elsewhere.[21] Bleeding, previously considered as a hallmark of EVD,[19] was seen relatively in low numbers compared with other reports.[19,21] This finding suggests that bleeding was not a major characteristic of this West African EVD outbreak.

The logistic regression analysis showed that age was significantly associated with death. In other words, elderly patients had a higher probability to die when infected with the Ebola virus than the adult group. This observation was also concordant with the earlier report.[9]

The retrospective design of the present analysis is the primary limitation, and as with other retrospective studies, caution must be exercised when interpreting the results because selection, information, and recall bias in the elderly cannot be totally excluded.

In summary, the present cohort study demonstrated that the CFR was significantly higher in the elderly group than in the adult group, and that participation in funeral was a risk factor for EVD. The duration between the onset of symptom and presentation to ETCs was significantly longer in the elderly group. In elderly people, age was found to be associated with death due to EVD. Based on our observations, the EVD control program should focus on educating the elderly and/or providing new strategies for behaviors and practices among those involved in handling the deceased. This information could be important for the management of future EVD outbreaks.

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REFERENCES

1. Elston JW, Moosa AJ, Moses F, Walker G, Dotta N, Waldman RJ, Wright J, 2016. Impact of the Ebola outbreak on health systems and population health in Sierra Leone. *J Public Health (Oxf) 38:* 673–678.
2. Brainard J, Hooper L, Pond K, Edmunds K, Hunter PR, 2016. Risk factors for transmission of Ebola or Marburg virus disease: a systematic review and meta-analysis. *Int J Epidemiol 45:* 102–116.
3. Pellecchia U, 2015. *Do Traditions Spread Ebola?* Available at: http://www.ebola-anthropology.net/case_studies/do-traditions-spread-ebola/. Accessed January 4, 2017.
4. Thomas LV, 1986. *La vieillesse en Afrique noire: transmission orale et rarete individuelle.* Quebec: Universite du Quebec a Chicoutimi, Departement des sciences humaines.
5. Fairhead JRP, 2014. *Ebola and Older People in Sierra Leone, Liberia and Guinea.* Available at: http://www.ebola-anthropology.net/key_messages/ebola-and-older-people-in-sierra-leone-liberia-and-guinea/. Accessed June 30, 2017.
6. WHO, 2014. *Case Definition Recommendations for Ebola or Marburg Virus Diseases.* Geneva, Switzerland: World Health Organization.
7. Rico A et al., 2016. Epidemiology of epidemic Ebola virus disease in Conakry and surrounding prefectures, Guinea, 2014–2015. *Emerg Infect Dis 22:* 178–183.
8. WHO, 2002. *Definition of an Older or Elderly Person: Proposed Working Definition of an Older Person in Africa for the MDS Project.* WHO Health statistics and information systems. Geneva, Switzerland: World Health Organization.

9. Bower H, Johnson S, Bangura MS, Kamara AJ, Kamara O, Mansaray SH, Sesay D, Turay C, Checchi F, Glynn JR, 2016. Exposure-specific and age-specific attack rates for Ebola virus disease in Ebola-affected households, Sierra Leone. *Emerg Infect Dis 22:* 1403–1411.
10. Hartley MA, Young A, Tran AM, Okoni-Williams HH, Suma M, Mancuso B, Al-Dikhari A, Faouzi M, 2017. Predicting Ebola severity: a clinical prioritization score for Ebola virus disease. *PLoS Negl Trop Dis 11:* e0005265.
11. Pisani MA, 2009. Considerations in caring for the critically ill older patient. *J Intensive Care Med 24:* 83–95.
12. Marik PE, 2006. Management of the critically ill geriatric patient. *Crit Care Med 34:* S176–S182.
13. Leligdowicz A et al., 2016. Ebola virus disease and critical illness. *Crit Care 20:* 217.
14. Fitzpatrick G, Vogt F, Moi Gbabai OB, Decroo T, Keane M, De Clerck H, Grolla A, Brechard R, Stinson K, Van Herp M, 2015. The contribution of Ebola viral load at admission and other patient characteristics to mortality in a Medecins Sans Frontieres Ebola Case Management Centre, Kailahun, Sierra Leone, June–October 2014. *J Infect Dis 212:* 1752–1758.
15. WHO, 2015. *Guinea: The Ebola Virus Shows Its Tenacity: One Year into the Ebola Epidemic.* Emergencies preparedness, response. Geneva, Switzerland: World Health Organization.
16. Wilkinson A, Fairhead J, 2017. Comparison of social resistance to Ebola response in Sierra Leone and Guinea suggests explanations lie in political configurations not culture. *Crit Public Health 27:* 14–27.
17. Carrion Martin AI, Derrough T, Honomou P, Kolie N, Diallo B, Kone M, Rodier G, Kpoghomou C, Jansa JM, 2016. Social and cultural factors behind community resistance during an Ebola outbreak in a village of the Guinean Forest region, February 2015: a field experience. *Int Health 8:* 227–229.
18. Manguvo A, Mafuvadze B, 2015. The impact of traditional and religious practices on the spread of Ebola in West Africa: time for a strategic shift. *Pan Afr Med J 22 (Suppl 1):* 9.
19. Ji YJ et al., 2016. Clinical presentations and outcomes of patients with Ebola virus disease in Freetown, Sierra Leone. *Infect Dis Poverty 5:* 101.
20. Yan T et al., 2015. Clinical characteristics of 154 patients suspected of having Ebola virus disease in the Ebola holding center of Jui Government Hospital in Sierra Leone during the 2014 Ebola outbreak. *Eur J Clin Microbiol Infect Dis 34:* 2089–2095.
21. Cherif MS, Koonrungsesomboon N, Diallo MP, Le Gall E, Kasse D, Cherif F, Kone A, Diakite M, Camara F, Magassouba N, 2017. The predictor of mortality outcome in adult patients with Ebola virus disease during the 2014–2015 outbreak in Guinea. *Eur J Clin Microbiol Infect Dis 36:* 689–695.