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Factors Prognosis of Ebola Virus Disease at the Wonkifong Ebola Treatment Center, Coyah, Guinea

Mamadou Saliou Sow[1]*, Alioune Camara[2], Boushab Mohamed Boushab[3], Mamadou Oury Safiatou Diallo[1], Kadio Jean-Jacques Olivier Kadio[2], Ismael Camara[1], Alseny Modet Camara[1], Mandy Kader Kondé[2], Moussa Seydi[4]

[1]Infectious and Tropical Diseases Department, University Hospital Center of Conakry, Conakry, Guinea
[2]Department of Public Health, Faculty of Medicine, University of Conakry, Conakry, Guinea
[3]Internal Medecine and Infectious Diseases Department, Centre Hospitalier of Kiffa, Kiffa, Mauritania
[4]Infectious and Tropical Diseases Department, Fann Teaching University Hospital, Dakar, Senegal
Email: *smsaliou@gmail.com

Abstract

Background: The Ebola Virus Epidemic epidemic in Guinea was marked by its rapid spread in the capital, forcing the authorities to build several Ebola treatment centers including Wonkifong (Coyah), Conakry. **Objective:** To evaluate the case fatality rate of Ebola Virus Disease in this center and to identify associated factors. **Patients and Method:** There is a prospective study at wonkifong Ebola treatment center from January 1st, 2014 to April 30th, 2015. All patients diagnosed with an Ebola Virus Disease from January 1st, 2014 to April 30th, 2015 were enrolled in this study. Kaplan-Meier curves and multivariate regression model were used to analyze factors associated with death. **Results:** 216 patients were included, the mean age was 30.52 ± 17 years and 53.2% were female. The average time between admission to the Ebola treatment center and the onset of signs was 5.13 ± 3.8 days. The average period of stay in the Ebola Treatment Center was 12.64 ± 11.31 days and duration median of death after admission in Wonkifong ETC was 11 days. According to the source, more than half of the patients were from Forécariah, *i.e.* 60.2% (n = 134). The case fatality rate was 64.4%. This rate was 72.0% in Dubréka, 65.1% in Coyah and 64.6% in Forécariah. The factors independently associated with Ebola Virus Disease death were signs of diarrhea [OR = 2.22 (1.17 - 4.20)], anorexia [OR= 0.40 (0.19 - 0.81)] and period of patients stay in ETC [OR = 0.96 (0.93 - 0.99)]. **Conclusion:** These results show that the fatality rate linked to the Ebola virus disease remains high. The factors independently associated with death were Diarrhea, anorexia and period between beginning of illness and date of latest news. Biological monitoring and resuscitation seem interesting for the reduction of this mortality.

1. Introduction

Ebola virus disease is a serious and often fatal disease caused by viruses of the genus Ebola virus of the family Filoviridae. The genus Ebola virus has five subtypes of which the most virulent is Ebola-Zaire. During the disease, the clinical signs are not specific and are characterized by the appearance, fever, headache, myalgia, asthenia and gastrointestinal disorders. The first known epidemic occurred in the Democratic Republic of Congo (Ex Zaire) in 1976, is caused by the strain of Zaire virus. It is a rare disease whose epidemics are limited but each time creating panic because the outcome is fatal in 25% to 90% of cases.

The last cases described in the region date back to 1994 in Côte d'Ivoire and in Africa more widely in the Democratic Republic of Congo (RCD) and Uganda in 2012.

Between December 2013 and 10 April 2016, a total of 28,616 confirmed, probable and suspect cases were reported mainly in Guinea, Liberia and Sierra Leone, including 11,310 deaths according to WHO data [1]. In Guinea, the epidemic began in December 2013 [2], and was officially declared by the World Health Organization (WHO) on March 23, 2014. In mid-September 2014, the number of cases and death has continued to grow despite the efforts of the national and international committee to control it. With rapid spread in the capital, it has surpassed all previous epidemics in terms of extent, number of infected or affected individuals [3]. In November 2014, it reached the highest peak in Guinea with 2693 cases and 1659 deaths, a lethality of 62%. In the Ebola treatment center (ETC) in Conakry, the crude mortality rate was 43.8% [4]. Given its scale and rapid expansion in Conakry and surrounding prefectures, it has been proposed to set up several other Ebola treatment centers (ETCs), including Wonkifong (Coyah), 61 km away. Conakry. The goal was to strengthen the surveillance and care of patients but also to stop the spread of the epidemic in the capital Conakry. The objective of this study was to evaluate the fatality rate of Ebola Virus Disease (EVD) at Wonkifong ETC (Coyah) and to identify associated factors from December 2014 to May 2015.

2. Materials and Methods

2.1. Type, Period and Frame

This prospective and analytic observational study was conducted in the Ebola ETC treatment center in Wonkifong, Coyah, administrative region of Kindia, and located 61 km from Conakry. The center received all the patients coming from the different surrounding prefectures of Conakry including Forécariah, Coyah and Dubréka. Other patients of Conakry as well as those of other cities

more distant from Guinea are also received there. The confirmation of suspected cases of Ebola virus disease in the laboratory was based on the results of the molecular biology of the quantitative RT-PCR (*Reverse Transcriptase Polymerase Chain Reaction*) performed in a laboratory of the European Union installed within the ETC. All the suspected patients had a PCR that confirmed or confirmed the Ebola virus disease.

2.2. Study Population

Criteria for inclusion: All patients diagnosed with an Ebola Virus Disease from January 1st, 2014 to April 30th, 2015wereenrolled in this study.

Criteria for non-inclusion: Patients under therapeutic trials (Favipiravir-based, Interferon) were not included.

For using a standardized definition of suspected cases of Ebola virus disease from the World Health Organization (WHO) and the Guinean Ministry of Health [5]. Patient care was provided by multidisciplinary teams from different national and international partners.

Patients were treated according to protocols established for viral hemorrhagic fevers by Medecin Sans Frontieres Doctors (MSF) and the WHO according to the Provisional Emergency Guide for Case Management, approved by the Ministry of Guinean health [6] [7]. All patients received symptomatic treatment during their hospitalization in ETC, based on rehydration solution (oral rehydration solution, Ringer's lactate, saline serum), vitamin therapy, antibiotic prophylaxis (ceftriaxone, cefixime, metronidazole). At the exit, two PCR samples in the interval of 48 hours are made to confirm the clinical and biological cure.

2.3. Data Collection

Sociodemographic variables (sex, age in past year, occupation, number of contacts) and clinical reports reported by the patient or his entourage or observed by health personnel at the time of admission to the ETC were collected. These symptoms were grouped into general signs (fever, asthenia anorexia), digestive (vomiting, nausea, abdominal pain, diarrhea) neurological (headache, disorder of consciousness, insomnia), hematologic (bleeding internal or external type of hematemesis, melena, epistaxis, conjunctival injection), respiratory (cough, dyspnea), cardiac (dyspnoea, edema of the lower limbs). The information related to the treatment (antibiotic, analgesic, anti-inflammatory), the time and duration of hospitalization, the evolution (cure or death) were notified. Data was entered with Epi Info software version 3.5 and analyzed by SPSS 20 software. It was verified to identify duplicate or outlier and corrected data. Continuous variables were presented as mean and standard deviation and as median with interquartile intervals. The categorical variables as describe by proportion. Student test was used to compare the average of groups. The calculation of the case fatality rate consisted in determining the proportion of EVD-related deaths in relation to the total number of cases recorded in the Wonkinfong ETC. The Kaplan-Meier

curve was used to estimate the median duration of death as a function of the duration of symptoms before admission to the ETC. An initial analysis consisted of conducting a univariate logistic regression analysis to determine the factors that were associated with EVD death. Variables that were significant ($p \leq 0.0$) in univariate analysis were introduced into a multivariate model in a second analysis. A stepwise multivariate regression analysis was conducted to evaluate the combined effect of several factors associated with EVD death. The interaction terms between significant independent variables in the full model were evaluated. Odds ratios and their 95% confidence interval were calculated and a value of $p < 0.05$ was considered statistically significant. Ethical Consideration: To ensure confidentiality, all individuals' personal information was anonymous

3. Results

During a period of 5 months, 216 patients with the definition of a suspected case of Ebola virus disease and confirmed by the laboratory were included in our study. The mean age of confirmed cases was 30.52 ± 17 years and 53.2% were female. 79.2% were over 16 years old versus 20.8% 16 years old and under. The average length of stay was 6.43 ± 5.8 days. The average time between admission to the ETC and the onset of signs was 5.13 ± 3.8 days. According to the origin, more than half of the patients were come of Forecariah and Coyah respectively 60.2% (n = 134) and 19.9% (n = 43). The proportion of females was higher in Dubréka and Coyah with 85.7% and 81.8% respectively. Parental contamination was also more reported in other prefectures (77.8%) and Dubreka (68%). In 5.1% the transmission was related to care. All these characteristics are described in Table 1. Clinical symptomatology at admission was nonspecific and included mainly, asthenia 80.1%, anorexia 70.4%, fever in 65.3%, headache 64.8%, nausea and vomiting in 54.6% (Table 2).

We recorded 139 deaths, a fatality rate of 64.4%. Deaths occurred on average 5 ± 13 days after onset of symptoms and the median duration of death (Figure 1) was 11 days depending on the onset of illness and the date of the latest news. This rate was 72.0% in Dubréka, 65.1% in Coyah and 64.6% in Forécariah. Of the 260 patients, 30 of them had performed biochemistry. It has been noted that Alanines Aminotransferases (ALATs) are higher than Aspartates Aminotransferases (ASATs). This Table 3 shows a significant metabolic disorder.

In the univariate analysis (Table 4) there was no significant association between EVD-relateddeath and the patient's geographic origin, sex, source of infection, marital status, or occupation. However, the factors that remained significantly associated with death in EVD were signs of bleeding [OR = 2.8 (1.29 - 6.26)], dysphagia [OR = 2.22 (1.03 - 4.78)], diarrhea [OR = 2.13 (1.17 - 3.87)], Duration between the onset of symtoms and the last contact at the ETC [OR = 1.12 (1.02 - 1.23)].

In multivariate analysis (Table 5), were independently associated with death the signs of diarrhea [OR = 2.7 (1.22 - 6.26)], anorexia [OR= 0.40 (0.19 - 0.81)]

Table 1. Demographics cases of Ebola Virus Diseases at the Wonkinfong Ebola Treatment Center (Coyah), Guinea 2015.
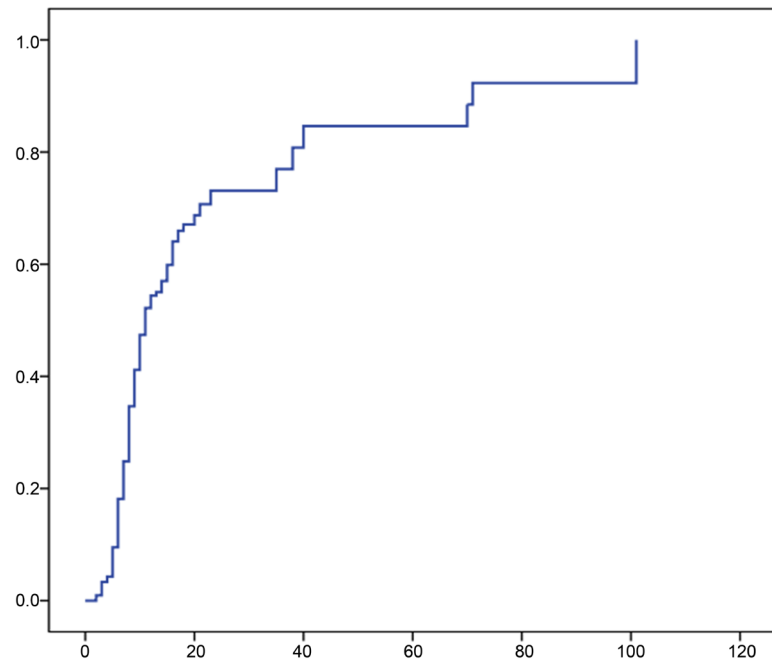
Characteristics		Origin									
		Elsewhere		Forécariah		Coyah		Dubreka		Total	
		N*	%*	N	%	N	%	N	%	N	%
Mode of contamination	Unknown	3	16.7	42	32.3	9	20.9	5	20	59	27.3
	Other* person	1	5.6	4	3.1	3	7.0	3	12.0	11	5.1
	Parent	14	77.8	84	64.6	31	72.1	17	68	146	67.6
Age range	≤16 years	2	11.1	31	23.8	9	20.9	3	12	45	20.8
	>16 years	16	88.9	99	76.2	34	79.1	22	88	171	79.2
Sex	Female	8	44.4	68	52.3	24	55.8	15	60	115	53.2
	Male	10	55.6	62	47.7	19	44.2	10	40	101	46.8
Profession	Household	5	27.8	41	31.5	11	25.6	11	44	68	31.5
	Student	1	5.6	26	20	8	18.6	2	8	37	17.1
	Cultivators	3	16.7	23	17.7	4	9.3	2	8	32	14.8
	Liberal	5	27.8	19	14.6	13	30.2	4	16	41	19
	Medical	3	16.7	1	0.8	2	4.7	4	16	10	4.6
	Other	1	5.6	20	15.4	5	11.6	2	8	28	13.0
Marital status	Single	2	11.1	49	37.7	15	34.9	3	12	69	31.9
	Married	16	88.9	81	62.3	28	65.1	22	88	147	68.1

N*: Number; %: percent; Other*: person.

Table 2. Clinical characteristics of cases of Ebola Virus Diseases at the Wonkinfong Ebola Treatment Center (Coyah), Guinea 2015.

Clinical signs	Effect	Percent
Hemorrhage	47	21.8%
Myalgia	93	43.1
Arthralgia	103	47.7
Dysphagia	45	20.8%
Abdominal pain	105	48.6%
Nausea/vomiting	118	54.6%
Headache	140	64.8%
Hiccough	49	22.7%
Fever	141	65.3%
Dizziness	19	8.8%
Cough	47	21.8%
Diarrhea	86	39.8%
Asthénia	173	80.1%
Anorexia	152	70.4%
Others*	3	1.4%

and Duration between the onset of symtoms and the last contact at the ETC [OR = 0.96 (0.93 to 0.99)].

Figure 1. Probability of death from Ebola Virus Disease cases according to period of stay at the Wonkinfong Ebola Treatment Center (Coyah), Guinea 2015.

Table 3. Biological characteristics of 30 cases of Ebola Virus Disease Clinics at the Wonkinfong Ebola Treatment Center (Coyah), Guinea 2015.

Biological parameters	Effect	Percent
Glucose (mmol/l)		
0.60 - 3.2	6	20
3.3 - 6.1	19	63.3
≥6.2	5	16.7
Mediane(IIQ)	4.5 (3.5 - 5.8)	
Creatinine (μmol/l)		
<50	4	14.8
50 - 110	10	37.0
>110	13	48.1
Median (IIQ)	107 (59 - 400)	
Total bilirubin (μmol/l)		
2 - 18	20	80
>18	5	20
Median (IIQ)	11 (7.5 - 16.5)	
Albuminemia (g/l)		
>4.0	30	100
Median (IIQ)	27 (20.7 - 33.0)	
alanine aminotransferases (UI/L)		
0 - 35	4	14.8
>35	23	85.2

Continued

Median (IIQ)	110 (55 - 306)	
Aspartate aminotransferases (UI/L)		
0 - 35	1	4.0
>35	24	96.0
Median (IIQ)	399 (69 - 1150)	
Creatinine Kinase (UI/L)		
0 - 130	1	4.5
>130	21	95.5
Median (IIQ)	521.5 (191 - 2653.5)	
Amylase (UI/L)		
0 - 130	20	69.0
>130	9	31.0
Mediane (IIQ)	115 (76.5 - 212)	
Sodium (mmol/l)		
<135	19	73.1
135 - 147	5	19.2
>147	2	7.7
Mediane (IIQ)		
Potassium (mmol/l)		
<3.5	7	29.2
3.5 - 5.0	13	54.2
>5.0	4	16.7
Median (IIQ)	131 (128 - 136.5)	
Calcium (mmol/l)		
>1.15	29	100
Median (IIQ)	2.0 (1.67 - 2.20)	
C-Reactive Protein (mg/l)		
<5	1	5
≥5	19	95
Median (IIQ)	29.7 (9.5 - 71.6)	
Urea (mmol/l)		
>2.5	6	20
2.5 - 7.9	7	23.3
≥8.0	17	56.7
Median (IIQ)	12.2 (2.8 - 31.4)	

4. Discussion

Using data from hospital records, epidemiological records from the Coyah ETC, Republic of Guinea, we analyzed the relationship between different sociodemographic and clinical characteristics collected at admission and death from Ebola.

Table 4. Univariate analysis of factors associated with death cases of Ebola Virus Disease at the Wonkinfong Ebola Treatment Center (Coyah), Guinea 2015.

(a)

Characteristics		Death				OR	95% IC	p
		No		Yes				
		Effect	%	Effect	%			
Origin	Elsewhere*	9	50	9	50	1	Reference	-
	Forécariah	46	35.4	84	64.6	0.38	0.10 - 1.38	0.14
	Coyah	15	34.9	28	65.1	0.71	0.26 - 1.82	0.47
	Dubreka	7	28	18	72	0.72	0.24 - 2.12	0.55
Source of contamination	Unknown	19	32.2	40	67.8	1	reference	
	Other person	6	54.5	5	45.5	1.16	0.61 - 2.21	0.64
	Parents	52	35.6	94	64.4	0.46	0.13 - 1.58	0.21
Average Age (in years)		27.97 ± 15.63		31.78 ± 18.32		1,01	0.99 - 1.03	0.13
Sex	Female	41	35.7	74	64.3		reference	
	Male	36	35.6	65	64.4	1.00	0.57 - 1.74	0.99
Profession	Other	10	35.7	18	64.3	1	reference	-
	Household	20	29.4	48	70.6	1.6	0.52 - 3.38	1.33
	Student	17	45.9	20	54.1	0.81	0.23 - 1.79	0.65
	Cultivators	8	25	24	75	1.6	0.54 - 5.07	1.66
	Liberal	18	43.9	23	56.1	1.1	0.264 - 1.90	0.71
	Medical	4	40	6	60	0.81	0.18 - 3.67	0.83
Marital status	Single	26	37.7	43	62.3	1	reference	
	Married	51	34.7	96	65.3	0.87	0.48 - 1.59	0.66

(b)

Characteristics		Death				OR	95% IC	p
		No		Yes				
		Effect	(%)	Effect	(%)			
Hemorraghe*	No	68	40.2	101	59.8	1	-	-
	Yes	9	19.1	38	80.9	2.8	1.29 - 6.26	0.009
Myalgia	No	40	32.5	83	40	1	-	-
	Yes	37	39.8	56	37	0.72	0.41 - 1.27	0.27
Arthralgia	No	40	35.4	73	64.6	1		
	Yes	77	35.6	66	64.1	0.97	0.56 - 1.71	0.93
Dysphagia	No	66	38.8	104	61.2	1		
	Yes	10	22.2	35	77.8	2.22	1.03 - 4.78	0.04
Abdominal pain	No	42	37.8	69	62.2	1	-	
	Yes	35	33.3	70	66.7	1.21	0.69 - 2.12	0.49
Nausea/vomiting	No	35	35.7	63	64.3	1	-	-
	Yes	42	35.6	76	64.4	1.00	0.57 - 1.75	0.9
Headache	No	21	27.6	55	72.4	1	-	-

Continued

	Yes	56	40.0	84	60.0	0.57	0.31 - 1.05	0.07
Hiccough	No	59	35.3	108	64.7	1	-	-
	Yes	18	36.7	31	63.3	0.94	0.48 - 1.82	0.86
Fever	No	26	34.7	49	65.3	1	-	-
	Yes	51	36.2	90	63.8	0.93	0.52 - 1.68	0.82
Dizziness	No	66	34.5	126	65.5	1	-	-
	Yes	9	47.4	10	52.6	0,58	0.22-1.50	0.26
Cough	No	58	34.3	111	65.7	1	-	-
	Yes	19	40.4	28	59.6	0.77	0.39 - 1.49	0.44
Diarrhea	No	55	42.3	75	57.7	1	-	-
	Yes	22	25.6	64	74.4	2.13	1.17 - 3.87	0.01
Asthenia	No	12	27.9	31	72.1	1	-	-
	Yes	65	37.6	108	62.4	0.64	0.30 - 1.34	0.24
Anorexia	No	18	28.1	46	71.9	1		
	Yes	59	38.8	93	61.2	0.61	0.32 - 1.16	0.14
Duration between the onset of symtoms and the last contact at the ETC		15.43 ± 8.9		11.10 ± 12.18		0.96	0.93 - 0.99	0.02

*Haemorrhage: Epistaxis 10 cases, Rectal bleeding and melena 2 cases, gingivorrhage 4 cases, hematemesis, etc...

Table 5. Multivariate analysis of factors associated with death cases of Ebola Virus Disease at the Wonkinfong Ebola Treatment Center (Coyah), Guinea 2015.

Characteristics	OR$_{ajusted}$	95% IC	p
Hemorraghe	2.12	0.97 - 5.11	0.05
Headache	0.55	0.28 - 1.06	0.07
Diarrhea	2.64	1.35 - 5.13	0.04
Anorexia	0.40	0.19 - 0.81	0.01
Duration between the onset of symtoms and the last contact at the ETC (continuous)	0.96	0.93 - 0.99	0.02
Age (continuous) (years)	1.01	0.99 - 1.03	0.06

This work allows us to compare the epidemiological, clinical and lethal characteristics according to the prefectures. More than half (82%) of the patients came from Forécariah and Coyah. This is the reason for the establishment of this center at the entrance to Conakry, to ensure the care of people infected with Ebola from different surrounding prefectures. Community resistance and the flight of the people contacted could be higher in Forécariah than the other areas observed. There are many reasons, the most important being the geographical location of Forecariah (border zone of Sierra Leone) and the high mobility of local populations that results. In addition there are areas of uncontrolled interconnection. Moreover Dubréka is closer to Conakry. The patients who are from this

city do not want to go to Conakry for fear of being in the ETC of Donka National Hospital. Conversely, sick people in Conakry or Forécariah can easily find themselves in Dubréka, to find refusal to loans from their parents. It is therefore a vicious circle that makes it difficult to research and refer cases to acute care facilities. In the communities, the health teams encountered problems of lack of knowledge and the denial of the disease, respect for the customs refusing hospitalization as described by Boumandoyki *et al.* [8]. However, in an isolation center, patients willingly accept therapeutic and psychosocial support. This study shows that the overall lethality rate of Wonkifong ETC (Coyah) CVE was 64.4% (n = 139/216). This rate is comparable to the EVD case fatality rate reported in the literature [3]. It remains lower than that reported at the beginning of the EVD epidemic in Guinea, Sierra Leone and Liberia. It is, however, superior to that found in Nigeria and Barry *et al.* [3] [9] in ETC Donka. The clinical manifestations of Ebola [10], the duration of the disease and the case-fatality rate are similar to those of previous epidemics. This lethality could be reduced if biological monitoring such as CRP, blood ionogram, renal or hepatic assessment were systematic as shown by other authors [11]. The Coyah ETC is open on December 19, 2014, 10 months after the declaration of the outbreak in Guinea Conakry. Its medical staff is composed initially of Guineans who have already worked in other Ebola treatment centers (Conakry, Guéckedou) but also other personnel of the ECOWAS, African Union, Cubanese) and all medical specialties combined (internal medicine, infectious diseases, resuscitation, general practitioners). Others, too, have already managed cases of hemorrhagic diseases in their countries. Fever, one of the main signs of EVD, was found in 65.3% of patients in this study. This frequency is identical to that found by Barry *et al.* [9], but inferior to that of the others [3] [11]. This can be explained by the fact that the temperature collected is that of admission to the ETC. It would be biased by self-medication based analgesics and antipyretics before arrival. Moreover, patients would come to different stages of the evolution of their disease. Some come at the beginning, the others at the later stage or convalescence. According to the results of this study, univariate (Table 4) analysis had shown that signs of hemorrhage, diarrhea, dysphagia, Duration between the onset of symtoms and the last contact at the ETC, were significantly associated with death by EVD. According to recent data from the literature [3], diarrhea, bleeding gums were found in 66% and 3% of patients respectively, they were factors associated with death.

In the multivariate analysis, diarrhea, anorexia and duration Duration between the onset of symtoms and the last contact at the ETCwere independently associated with death. In the Barry *et al.* [12] study hemorrhages and myalgias were independently associated with death. However, our study has limitations; the registration of clinical data is limited by the prohibition to take any object, including paper outside the treatment center. The priority being care, some data were not mentioned in the records. The epidemiological survey is not easy in a zone with strong reluctance. The analysis focused only on cases that received

symptomatic treatment. Therapeutic trials were not included. Biochemical parameters were not introduced into the univariate and multivariate analysis by the limited number of people who did. However the study is original, it is the first made in the ETC of Wonkifong (Coyah), which had a team of very heterogeneous care. This center received patients from several prefectures near the capital, Conakry, and whose population is reluctant.

5. Conclusion

These results show that the fatality rate linked to the Ebola virus disease remains high. The factors independently associated with death were Diarrhea, anorexia and period between beginning of illness and date of latest news. Biological monitoring and resuscitation seem interesting for the reduction of this mortality.

Conflicts of Interest

There is no conflict of interest with the co-authors or institutions involved in this study.

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