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Comparison of Two Ebola Hemorrhagic Fever Outbreaks: Uganda 2000-01 and Republic of the Congo 2001-02

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Abstract

Many factors contribute to the severity of viral epidemics. Two outbreaks of Ebola, one in Uganda and one in the Republic of the Congo, were compared to assess their impact on social and political environment and the impact of viral strain on identification and containment of disease. The outbreaks were similar in many respects, allowing comparison of factors such as duration of outbreak, number affected and mortality. Both outbreaks were the first reported in the region and occurred during the same time of year. Both affected nations had the same access to international resources, such as the World Health Organization (WHO) and other aid groups willing to assist and provide financial support/resources. Data for this study was gathered from the United Nations Office for the Coordination of Humanitarian Affairs, the United States Centers for Disease Control (CDC) and the WHO's published data on the outbreaks in Uganda and Republic of Congo in 2000 and 2001, respectively.

The results demonstrate that the percent of the population infected, percent mortality, length of outbreak and virulence of the Ebola strain were all greater in the Republic of Congo outbreak, arguably due to differences in the social and political climate. The general response to the Ugandan outbreak was more rapid and more effective. Although different strains of the Ebola virus caused the outbreaks, mortality rates were high for both the Ebola-Zaire and Ebola-Sudan strains. Both outbreaks had decreased mortality rates compared to initial predictions. It is argued that the data from the Republic of the Congo outbreak was artificially low due to reporting bias and changes in outbreak parameters, resulting in a greater reported mortality. Indeed, prompt, organized and monitored infection control protocols are imperative to limit the morbidity and mortality of this disease, as seen in both the Uganda and the Republic of the Congo outbreaks. on the health and economy of this region and a potential target for medical intervention.

Introduction

Ebola is among the deadliest of any known virus, with up to 90% mortality in some cases.¹ Named after a river in Zaire (modern-day Democratic Republic of the Congo) where the first known cases were reported, the virus causes Ebola hemorrhagic fever. This disease has claimed many lives throughout central Africa. At present, there is no cure.

It is important to understand several points about Ebola in order to discuss its prevalence as well as strain variation. An RNA virus in the Filoviridae family, Ebola has five identified subtypes according to the CDC; however, only Ebola-Zaire, Ebola-Sudan, Ebola-Ivory Coast and Ebola-Bundibugyo are

known to affect humans. The last strain, Ebola-Reston, only affects non-human primates.¹ The outbreaks in Uganda and Republic of the Congo were caused by different strains. The outbreak in Uganda was caused by the Ebola-Sudan strain, which has a 60-65% mortality rate and is known to spread more easily than others.^{1,2} By contrast, the Republic of the Congo outbreak was caused by the Ebola-Zaire strain, which has a higher mortality rate of 85-95%.² The Zaire strain is more virulent but is easier to test for as some tests require only ten viral particles to obtain a positive result.³ The natural reservoir or animal host of Ebola virus remains unknown, but is generally thought to be a primate native to Africa.⁴ Initial Ebola spread is thought to

be initiated through blood contact with an infected primate; the virus then spreads from person to person through contact with contaminated body fluids.⁴ This is important to note, as epidemic containment would need to include both the education of local hunting populations and the ability to report sick or dead primates within a region. Furthermore, early studies of the virus in 1979 showed that most cases of Ebola resulted from secondary spread to family members and health care workers. In fact, 29 of the 34 cases first reported in Sudan were attributed to secondary spread, emphasizing the importance of proper infection control measures.⁵ Understanding how this virus spreads gives insight into the types of protective gear that health care staff need.

To better prevent viral spread and illness, learning more about how the virus works is crucial. The incubation period for this virus ranges from two to 21 days; thus, outbreaks are declared over when no new cases are found for 42 days—twice the longest incubation period.⁶ Symptoms of Ebola infection occur abruptly: fever, headache, muscle ache, sore throat and fatigue occur early, followed by diarrhea, vomiting and abdominal pain. Internal and external hemorrhages, the signature symptoms of Ebola, are only seen in the late stages of the infection.⁴ Because the early symptoms are nonspecific, Ebola must be diagnosed with specialized laboratory tests. First, antigen-capture enzyme-linked immunosorbent assays (ELISA) and immunoglobulin M (IgM) testing use antibodies to detect virus in the blood; then polymerase chain reactions (PCR) amplify viral DNA in blood samples; and finally, blood cultures isolate the virus. The presence of immunoglobulin G (IgG), an antibody produced by the body during recovery, can show prior infection in survivors. Although survivors do exist, it is not known why they are able to mount an adequate immune response while others cannot.⁴ Antigen-capture ELISA testing, PCR and virus isolation can also be used to confirm post-mortem identification of Ebola. Since there is no specific treatment for Ebola at this time, patients are only able to receive supportive care.

Further, discussions of political and social differences between the regions allow exploration of other sources of differences between the outbreaks. At the time of the outbreak in 2000, Uganda operated a free market economy, which had been growing since its establishment in 1987. The country had an established no-party democracy, and based on an survey in 2000, this was the favored mechanism of government for 90 percent of the voters (although admittedly, there were contentions about the legitimacy of this vote according to US human rights groups).⁷ In addition, Uganda held a presidential election in March of 2001, and reelected their previous leader, Yoweri Museveni. Reports suggest that he won with 69.3% of the votes compared to the 27.8% of the next closest competitor, although the election was rife with accusations of intimidation and fraud.⁷ Despite these flaws, the margin of victory was large enough that the government was fairly cohesive during his term. As in the case with Ebola, national and international recommendations were more easily instituted as a result of Uganda's stability. Thus, when there is little dissent among ruling parties and local populations support the national leadership, international aid workers can more effectively work to contain the epidemic with the assurance of personal safety.

In stark contrast, the Republic of the Congo's transition from a socialist to market economy was a more difficult one that began in the 1980s and left the country with a substantial budget deficit.⁷ Economic instability left some areas with limited resources, especially in healthcare facilities, where a lack of resources would be extremely detrimental in an Ebola outbreak. During this same period, the Republic of the Congo enacted democratic elections and in 1993 Pascal Lissouba became the country's first democratically elected leader. When elections loomed again in 1997, conflict broke out between supporters of Lissouba and supporters of his opponent, Denis Sassou-Nguesso, leading to a five-month civil

war. Sassou-Nguesso's forces won, and he declared himself president. However, more fighting ensued soon after and continued through the end of the millennium. By the start of the outbreak in 2001, no settlement had been reached and the civil war persisted.⁷ In the midst of civil war and unclear national leadership, possible warning signs and safety concerns about Ebola were more easily lost, under-reported or not reported at all. Compared to Uganda, the Republic of the Congo was less politically stable and thus unable to assure the safety of aid workers in its volatile climate.

Since the Ebola virus has a high mortality rate and is very infectious, it is a public health imperative to investigate and improve upon ways to manage outbreaks. The outbreaks in Uganda and Republic of the Congo, which spanned 2000-2001 and 2001-2002 respectively, were selected for this study because of several specific similarities and differences that make them appropriate for comparison. Both were the first known outbreak reported in each region, so there would be equally limited community knowledge about the disease and no previous containment policies in place. Furthermore, both occurred during roughly the same time of year in regions with similar weather conditions; thus, temporal and climatic effects are less disruptive to the main object of the paper. Known information and guidelines for care and prevention were the same in both regions, as was access to international resources. Because these variables are similar in the two groups, they may be removed from consideration as reasons for differences in outcome.

In contrast, the two outbreaks occurred in countries with vastly different political and social climates. The other major difference between the outbreaks was the strain of the virus: in the Republic of the Congo it was the Zaire strain, and in Uganda it was the Sudan strain. Controls used for expected mortality and spread for each strain were designated by WHO based on previous laboratory and human outbreaks that occurred without any official outbreak containment practices in place. This comparison was designed to elucidate the differences in the effects of the two viral strains, as well as the effects of social and political environment on identification and containment of the disease, length of outbreak, numbers affected and mortality.

Review

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the education of local hunting populations and the ability to report sick or dead primates within a region. Furthermore, early studies of the virus in 1979 showed that most cases of Ebola resulted from secondary spread to family members and health care workers. In fact, 29 of the 34 cases first reported in Sudan were attributed to secondary spread, emphasizing the importance of proper infection control measures.⁵ Understanding how this virus spreads gives insight into the types of protective gear that health care staff need.

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In contrast, the two outbreaks occurred in countries with vastly different political and social climates. The other major difference between the outbreaks was the strain of the virus: in the Republic of the Congo it was the Zaire strain, and in Uganda it was the Sudan strain. Controls used for expected mortality and spread for each strain



When faced with this outbreak of Ebola, the Ugandan government acted decisively, implementing national preventive measures and soliciting the assistance of international groups.

were designated by WHO based on previous laboratory and human outbreaks that occurred without any official outbreak containment practices in place. This comparison was designed to elucidate the differences in the effects of the two viral strains, as well as the effects of social and political environment on identification and containment of the disease, length of outbreak, numbers affected and mortality.

Discussion

The substantial disparity in the political environment at the time is inseparable from the differences in outcome between the two countries' Ebola outbreaks. Since the ruling party in Uganda was generally accepted, the economy was growing and there were few shifts in power, political views or policies at the time—as a result, the political climate was more stable than that of the Republic of the Congo. Political stability allowed for easier communication and coordination between local, national and international governing bodies, and therefore easier implementation of outbreak protocols. Ultimately, this led to better infection control.

The Republic of the Congo, on the other hand, had difficulty relaying information from local to national and international organizations and vice versa due to the ongoing civil war. Lack of cooperation between neighboring communities, national government and international aid organizations, secondary to the political climate in the Republic of the Congo, also hindered the rapid administration of adequate surveillance. This led to inconsistent and ineffective implementation of the WHO containment measures.¹² Thus, the Republic of the Congo fell short of using full containment measures.

There are other potential sources of variation between the two outbreaks. There is known variation in strain virulence, so the studied outbreak data was compared to the known data for that strain to establish an expected baseline. The Ugandan outbreak was caused by the Ebola-Sudan strain, whereas the more severe Republic of the Congo outbreak was caused by the more deadly Ebola-Zaire strain. Instead of comparing mortality rates from the different outbreaks to each other, the mortality rates were compared to the expected mortality rate based on strain

type. Discrepancies between expected and actual mortality rates would therefore decrease the influence of strain type when comparing outbreaks. According to data from previous cases of Ebola hemorrhagic fever caused by the Zaire and Sudan strains, human mortality resulting from Zaire strains was expected to be 85-90 percent, whereas expected mortality resulting from Sudan strains was expected to be 60-65 percent.¹⁴ The outbreaks from which this expected mortality is derived preceded, and thus did not employ, any official infection control measures. Therefore, there was no difference in strain-specific mortality due to different control measure effectiveness in the control data.

Previous studies of strain virulence performed on mice found that “fewer than ten infectious particles of a Zaire strain were lethal for suckling mice, whereas 10,000 infectious particles of a Sudan strain failed to kill any of these animals,” which further explains the higher mortality of the Zaire strain.² However, it was also found that the Zaire strain is easier to isolate in cell culture than the Sudanese agent.² Thus, it should be easier to identify the virus in a person infected with Ebola-Zaire, such as those in the Republic of the Congo; this suggests that, had control measures been put into place sooner, they would have been able to effectively identified infections. Unfortunately, the previously discussed political factors delayed implementation of this intervention.

Furthermore, in the original cases with the Sudanese strains, Ebola-Sudan was found to be more contagious.¹⁴ It is expected, therefore, that because it is more contagious, the Ebola-Sudan outbreak in Uganda would have a larger number of people infected. However, when the second wave of data from the Republic of the Congo was included, the number of infections was nearly the same when comparing the two countries.

It has been shown that initial cases are more virulent than later cases or subsequent waves of infection. Interestingly, the cause for this increased initial virulence is not known; the WHO states that “an unexplained phenomenon is that people who catch Ebola in the second or third wave of an outbreak have a better chance of survival.”¹² The mortality rate is sum of all deaths in all waves until the outbreak is declared over; however, cases that occur later within the outbreak have a better survival rate.

Although the Republic of the Congo's actual mortality was slightly lower than expected, this may be a function of inappropriate baseline analysis rather than effective containment. Much of the control data for the Zaire strain, from which the expected mortality was derived, came from an outbreak in the 1970's. In this outbreak, a high proportion of people contracted Ebola-Zaire directly from contaminated hypodermic needles, as opposed to contact with an infected person.^{3,5} As discussed previously, those closest to the original exposure source have a higher mortality rate, and many people in this 1970's outbreak were directly inoculated from a primary source.⁵ This creation of multiple primary waves may have caused this strain to appear more virulent in subsequent analyses than it actually was, and thus falsely elevated the 1970's mortality rate. Thus, if the mortality rate in the Republic of the Congo was more similar to the control or expected mortality, the effect of what little containment measures were applied are diminished.

Table 1: Outbreak Timelines

	Uganda	Republic of the Congo
First Identified Case	Oct 7, 2000	Oct 21, 2001
Local Authorities Alerted of Abnormal Primate Deaths	None	Nov 17
First Lab Tests Submitted	Oct 7	Nov 30
Local/National Authorities Alerted of Potential Outbreak	Oct 14	Nov 24
National Guidelines Announced	Oct 15	Dec 8
Lab Tests Confirmed Ebola	Oct 14-15	None
Broad Control Isolation Procedures Implemented	Oct 16	None
WHO Notified	Oct 15	Dec 8
WHO Task Force arrives	Oct 17	Dec 11
WHO Reports End of Outbreak	Feb 28, 2001	May 7, 2002
Next Known Outbreak in Region	Nov 30, 2007	June 21, 2002

Table 2: Infections and Mortality

	Uganda	Republic of the Congo (first wave only)	Republic of the Congo (both waves)
Total Number of Infections	425	124	267
Total Number of Deaths	224	97	225
Mortality	53%	78%	84%
Expected Mortality Based on Strain Type	60%-65%	85%-90%	85%-90%

When looking at the comparison between the two study populations in Uganda and in the Republic of the Congo, even without including the second wave data, the mortality rate was 53 percent compared to 78 percent, respectively, both falling seven to 12 percent from the expected values for each strain. However, with the inclusion of the second wave data in the Republic of the Congo data set, the mortality rate was 84 percent, which is roughly equivalent to the expected values of 85-90 percent for Ebola Zaire.¹ Further, when considering the argument that the expected value for mortality is artificially elevated, the outbreak in the Republic of the Congo shows even less improvement in mortality. When comparing the data in

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this way it is clear that political stability and a positive interaction with international aid groups decreases the percentage of people infected, and therefore decreases the mortality rate when comparing these two study groups.

Conclusion

There are clear differences in the manner in which the two Ebola outbreaks were handled, likely because of two countries' divergent political climates. The more stable political environment in Uganda was better able to put infection control measures in place promptly. The unstable political climate in the Republic of the Congo caused identification and implementation of infection control measures to be delayed by approximately 50 days. Furthermore, the safety of international infection control personnel was not assured and the WHO outbreak control staff were evacuated during the outbreak due to political unrest.

Thus, as might be expected, the duration of the outbreak in the Republic of the Congo was longer and more poorly contained, allowing further spread of disease than in Uganda, and percent mortality was greater when compared to strain specific controls.

The total number of cases was greater in Uganda; however, given the population of each region, a higher percentage of the population was infected in the Republic of the Congo. The Zaire strain found in the Republic of the Congo is known to be more virulent than Uganda's Sudan strain in both retrospective human studies and prospective mice studies.^{2,14} Although there are differences in strain virulence inherent to the viral genome, when compared to strain-specific outbreak mortality controls, in which no standardized infection control measures were used, it is clear that the difference in mortality was not a result of strain variation.³ Infection control measures were directly correlated with the regional political climate, which therefore played a role in mortality rate and proportion of population infected. These measures limited the number of infections and fatalities in both discussed outbreaks as compared to the expected outbreak mortality data; however, there was better survival and containment of spread when these infection control measures were put in place promptly, as seen in Uganda. It is evident from the mortality, length of the outbreak and the percentage of the population infected that infection control measures helped to contain the spread of disease. When the data with regards to the second wave was added to the original outbreak data in Republic of the Congo, this difference becomes even more evident.

In conclusion, because there is no known treatment for the viral infection, using prompt, organized and monitored infection control protocols is imperative to limit the morbidity and mortality of this disease. Ebola hemorrhagic fever is a deadly disease with extremely high mortality; however, when the WHO-recommended infection control measures were in use, there was a lower mortality rate than expected. Uganda promptly put into effect these control measures while the Republic of the Congo was unable to achieve control measures as quickly due to political instability. The improvement in percent mortality demonstrated that the WHO control measures were effective when compared to expected mortality, and they become more effective with prompt implementation.

Although strain virulence differed, it was controlled in this study with comparisons between each outbreak and the expected mortality rates based on strain. Differences in strain virulence may not be solely a function of viral genetics, as previously thought. As discussed, the expected percent mortality may be artificially elevated since initial calculations of Ebola-Zaire mortality rates came from patients who contracted the virus via direct inoculation. Accounting for all these factors, it becomes clear that political climate in the outbreak region plays a role in mortality and spread of disease, thus showing that sociopolitical differences are an important factor to account for when looking at the global health issue of Ebola.

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