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THE EVOLUTION OF EBOLA VIRUS DISEASE OUTBREAKS

Abstract: The paper presents general information regarding descriptive epidemiology of Ebola virus disease (EVD) outbreaks. Some observations have shown the decrease in case fatality ratio after several generations of patient-to-patient passage. An increase in the frequency of EVD outbreaks across decades was also noticed. The knowledge about the past outbreaks may provide crucial information about the evolution of EVD epidemic, which may be useful for future preventions..

Key words: Ebola virus disease, outbreak, epidemic, past, Ebola cases, case-fatality ratio.

INTRODUCTION

The current outbreak of the Ebola virus disease (EVD) is the largest among observed Ebola epidemics [1]. The rapid increase in number of cases counted in thousands in west Africa, and some cases recognized in North America and Europe caused justified concern to public health authorities in almost every country. The purpose of the current paper is to describe shortly the evolution of EVD outbreaks over time starting from the first known EVD epidemic.

THE FIRST *FILOVIRIDAE* INFECTION IN HUMANS AND PAST EBOLA OUTBREAKS

Ebola virus is a representative of the *Filoviridae* family — the viruses causing severe viral haemorrhagic fever with a high case fatality ratio (CFR). To trace back haemorrhagic fever outbreaks observed in humans one should back to the year 1967, when the first known infections caused by so called the Marburg virus had been diagnosed in laboratory workers in Germany and in former Yugoslavia. This first heamorrhagic fever disease outbreak was observed mainly among laboratory workers and some of their families. The virus was transmitted through a direct contact with blood and tissues of monkeys (of the species *Cercopithecus aethiops*) and cell culture material — and these were responsible for the infection

in the first and in the second generation of patients. The third group contracted the pathogen from other patients' blood. The household exposure leading to the development of the disease was rare and attributable to sexual contact only [2].

The first EVD outbreak among men was observed in a natural environment in 1976 in Sudan. The outbreak started in June 1976, and the retrospective investigation showed that the index case was a storekeeper working in the cotton factory in the city of Nzara. This individual developed symptoms of severe febrile illness, headache, and chest pain on June 27. On June 30, he was admitted to hospital in Nzara, developed haemorrhagic manifestations on the fifth day of illness (the second hospitalization day) and died on July 6. Next cases were 2 co-workers of the primary case working in the same factory, and several people who nursed or contacted ill at home or at hospital. The disease spread at the Nzara was caused by a direct close contact, usually involving nursing and care of infected individual. There were also some other cases recognized in the cotton factory, which were unrelated to direct contact with a sick person, but these infection pockets were self-limiting due to a relatively remote homestead these individuals and their family lived in. During this epidemic the disease was also introduced to Maridi hospital (approximately 128 km away from Nzara) and in the second place spread around the Maridi Township mainly by hospital contacts including visitors to the hospital who often helped to care for patients. The number of cases declined in October 1976, probably as a result of the use of protective clothing. The last known case of infection was reported on October 27, 1976 in Nzara, and on November 25, 1976 in Maridi. Finally, the outbreak accounted for 284 cases leading to 151 deaths [3].

The second known 'non-laboratory' epidemic of EVD appeared with the beginning of September 1976 in Zaire (now known as the Democratic Republic of the Congo). During this outbreak majority of cases were reported in the surrounding area of Yambuku, north-west Republic of Zaire. The first identified case for that outbreak was a 44-year-old male instructor at the Mission School presented on August 26, 1976 at Yambuku Mission Hospital with a febrile illness thought to be malaria. The patient was treated by chloroquine administered by parenteral injection. There were no sterilization strategies implemented at the hospital, and the hospital staff used regularly "five syringes and needles which were issued for the nursing staff each morning for use at the inpatient department, the prenatal clinic, and the inpatient wards. These syringes and needles were apparently not sterilized between their use on different patients but rinsed in a pan of warm water." As a result the hospital was the main source of dissemination of EVD. This EVD epidemic resulted in 318 cases recognized till October 24, 1976 with 280 death (giving the CFR of 88%) [4].

The next remarkable EVD outbreak was recognized in 1979 in southern Sudan. The outbreak appeared on July 31 and ended on October 6, 1979, and there were two modes of transmission observed during this event. The first involved hospital

transmission and the second transmissions among family members. Overall, the outbreak involved 34 cases, out of which 22 led to death, and finished after 7 generations of virus transmission. One of the interesting finding from the outbreak investigation was the change in CFR between the first four generations, which was of 89% and the remaining three later generations, being of 38%. This change suggested that the virus was less virulent after several generations of person-to-person passage [5].

For the next 15 years there were not noticed outbreaks of EVD in humans. In the year 1994 Ebola virus appeared again as a cause for an epidemic in Gabon. This epidemic was primarily recognized as an increase in the incidence of yellow fewer as the Yellow fever virus (YFV) was recognized by polymerase chain reaction in serum of the patients. However, the course of a disease was atypical, and retrospective investigation showed the presence of Ebola virus concomitantly with the YFV in this outbreak. Due to several cultural and political difficulties, the information regarding the spread of an epidemic was very limited. In general, the outbreak started early December 1994 and ended on February 17, 1995. In total, 49 patients were identified, and 29 of them died (CFR: 59%) [6].

In the year 1995 another epidemic of EVD was observed in Kikwit, Democratic Republic of the Congo. The spread of this epidemic was determined by contacts between family members in the first phase and was changed into a nosocomial infection in the second. The total number of infected individuals was 315 (including 80 health care workers), 254 of whom died. The analysis of the CFR over the course of the epidemic revealed the decrease from 100% at the beginning to 62% at the end of the outbreak [7].

There were also two more EVD outbreaks till the end of 20th century. Both appeared in Gabon: at the beginning and at the end of 1996. The spring (first) 1996 epidemic resulted mainly as a consequence of the primary transmission of the virus from ill chimpanzee, resulted finally in 31 cases and 21 deaths. The same (chimpanzee) source of infection was probably for the fall (second) 1996 epidemic leaded to 60 cases and 45 deaths [6].

Starting with the year 2000 there were 13 more EVD outbreaks (understood as epidemics involving more than 10 cases), and, additionally, some small episodes or even single infected cases. The EVD outbreak in Uganda (2000–2001) was responsible for 425 cases and 224 deaths [8], the outbreaks 2001–2002 in Gabon and in Congo involved 65 and 59 recognized cases and led to 53 and 44 deaths, respectively [9]. The next two epidemics recognized in 2003 took place also in Congo. These episodes accounted for 178 infected individuals (143 in the first and 35 in the second) and were responsible for 157 deaths (128 and 29, respectively) giving the case fatality ratio of 88% in average [9, 10]. In 2004 one small outbreak (17 cases, 7 deaths) was recognized in Sudan [11], and in 2005 another one (12 cases, 10 deaths) in Congo [12]. A larger outbreak appeared in 2007 in Democratic Republic of the Congo. Starting with the exposure to fruit

bats (freshly killed to eat) developed to the size of more than 260 infections with the case fatality ratio of 71% [13]. In the same year the epidemic involving 149 individuals (37 out of them died) was observed in Uganda [13, 14]. After that time, relatively smaller EVD outbreaks were observed before the current (2014) one. In 2008 Ebola virus appeared again in Democratic Republic of the Congo leading to 32 cases and 15 deaths [15] and after the period of 4 years three outbreaks were observed in 2012: two in Uganda (24 infected, 17 deaths, and 11 infected, 4 deaths) [16, 17], and one in Democratic Republic of the Congo (57 cases, 29 deaths) [18].

There were also some episodic EVD infections diagnosed in different circumstances and among different individuals. In 1976 an investigator at the Microbiological Research Establishment, Porton Down, was exposed to a new virus called Ebola, which was investigated at laboratory in infected guinea-pigs. The laboratory worker pricked his thumb accidentally, and although the standard safety protocol was implemented immediately after exposure and there was no bleeding and no signs of a puncture wound, he developed the signs of the EVD 6 days after the accident. Fortunately, implemented treatment helped the patient to recover [19]. Other incidental single EVD cases were diagnosed in 1994 in Cote d'Ivoire [20], in 1996 in the South Africa [21], and in 2011 in Uganda [22].

The current problem associated with the development of the EVD outbreak in Africa was recognized on March 10, 2014 in Guéckédou, Guinea and became to life after a one-year only, epidemic-free time in 2013.

SUMMARY

In summary, EVD has threatened mankind for about 40 years. Primarily considered as a local self-limiting problem with a very high case-fatality ratio. Until the end of the eighties there were only three remarkable EVD outbreaks, during the next 10 years — four of them. This number was increased 2.5-times in the next 10-year period (from 2000 to 2009). Finally, there were 3 EVD outbreaks in the 2012 only (Fig. 1). This changing frequency clearly showed an increase in the risk of a development of the EVD outbreak in the next years. Some variability in CRF was observed across different outbreaks (Fig. 2) and a decrease associated with the increase in generations of person-to-person passage.

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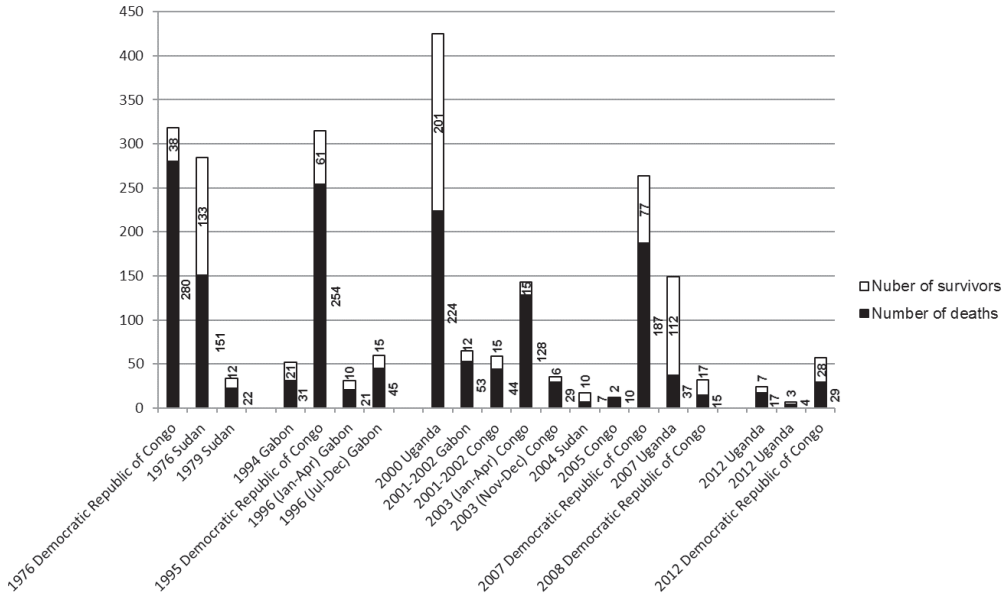

Fig. 1. The chronology of the past Ebola virus disease larger (meaning >10 cases) outbreaks with number of deaths and survivors.

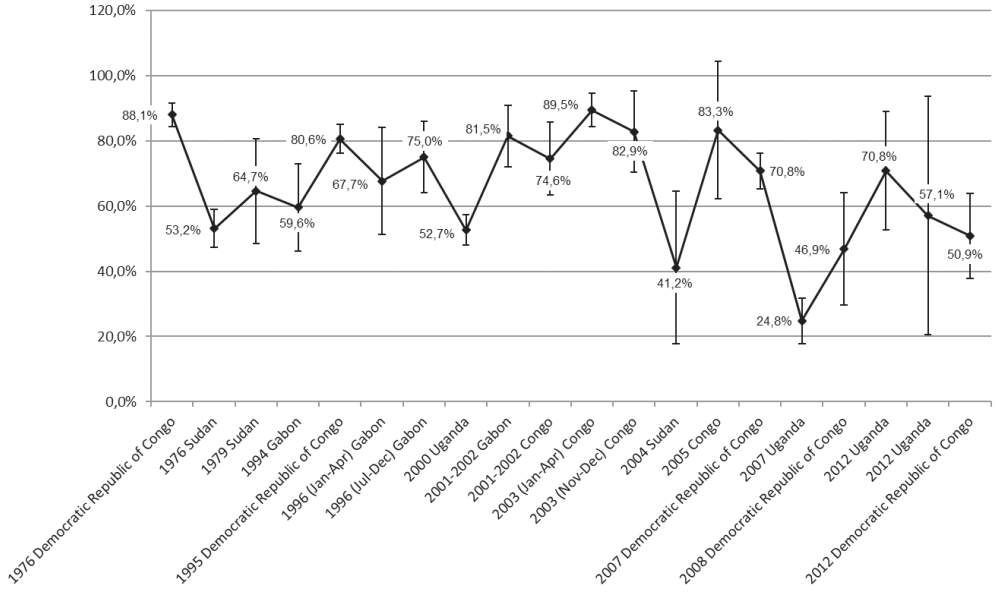

Fig. 2. Case-fatality ratio for the past Ebola virus disease larger (meaning >10 cases) outbreaks (with 95% CI).

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