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The Epidemiological Characteristics of Ebola Virus Disease: A Comprehensive Review

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Abstract

While not as pathogenically potent as many other infectious agents, the Ebola virus causes a massive epidemic with a very high case-fatality rate, owing in part to the slow pace of infection as well as the aggressive clinical cure. Since the discovery of this infectious virus, many epidemics have taken place in regions throughout the continent, primarily in the Democratic Republic of the Congo, but also in other countries such as South Sudan and Guinea. Along with adaptive and human circumstances create opportunities for increased morbidity and mortality, despite the relative rarity of Ebola virus infection.

The aim of this work is to assess and discuss the epidemiological properties of Ebola Virus Disease, with a focus on transmission, treatment methods, and predictive progress based on established parameters. An interdisciplinary approach is used to address the challenging issue of Ebola Virus Disease from a very different perspective. As a result, this study will tackle this topic from a different perspective, touching on three primary topics: epidemiological characteristics; a plan for handling so-called "close encounters"; and a subsequent step based on a large dataset of contaminated populations living in affected regions. Several solutions are presented as well as a simple and successful treatment.

Keywords: Ebola virus disease; Hemorrhagic syndrome; Public health; Central Africa

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Introduction

Ebola virus disease (EVD) (or simply "Ebola") is a mysterious disease with a notorious history, whose etiology is likely to have an animal source, mainly bats and non-human primates, and that seems to result from a zoonosis. This is a viral disease characterized by a high case fatality rate that tends to generate fear and panic in the population. The first known outbreak of EVD occurred in the Congolese merback in 1976, with the two simultaneous appearances of the virus one in the northern part of Zaire, in a village called Yambuku, and the other near the Ebola River from which it derives its name. Non-human primates (chimpanzees and gorillas) are the primary reservoir for the virus and are often the source for human outbreaks. Once people have been infected with Ebola, they can transmit it to others through direct contact with body fluids, like blood, breast milk, urine, or semen.

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Since the discovery of the EVD, outbreaks have occurred in several African countries, with diverse epidemiological and clinical scenarios that varied from the viruses involved in the outbreaks to the human population. Some are involving thousands of cases, showing up in towns with a network of infected people, while others result from a single contaminated person in remote forested areas. In 2014, EVD hit West Africa and has caused the largest outbreak in history. There were more cases and deaths in the outbreak than all others combined. Changes in EVD reporting have been introduced since the first human case occurs until today. Notifications became a crucial source of information for the World Health Organization (WHO).

Etiology and Pathogenesis

Etiology and Pathogenesis. New data confirm that the natural host for EBOV (the virus that caused the 2014-2016 Ebola outbreak) is fruit bats, and the incidence of the virus in apes and other mammals is related to dietary habits. Filoviridae, including Marburgvirus (MARV) and Ebolavirus (EBOV), are enveloped RNA viruses without segmented genomes that cause Ebola Virus Disease (EVD), an extremely dangerous disease in humans. EBOV is divided into five separate species: Zaireebolavirus is the cause of 9 EVD outbreaks and has been discovered. In contrast to the other species, Reston produced an asymptomatic or mildly symptomatic infection in humans in the Philippines in 2008. EBOV is divided into two distinct subtypes: the Sudan-Gulu and Bundibugyo subtypes. The enveloped EBOV virion is a relatively long filament (70–90 nm in diameter, 970–1080 nm in length). The Zaireebolavirus was first described in the DRC and in Sudan in 1976, prompting two epidemics. The Zaireebolavirus caused a total of 29 Ebola virus infections in the 1976 Zaire (now the Democratic Republic of the Congo) epidemic. The Ebola River was quarantined by a man known for his fetish activities who unintentionally became infected and died of testicular EVD. In Nunub, northern Zaire, a 1976 Sudan epidemic epitomized the 34 cases (or 151 cases, depending on the source) caused by two Greek experts from the Maridi and Nzara hospitals. Cross-species transmission of the Ebola virus is mostly a result of consuming infected primates or bats.

Ebola Virus Structure and Classification

Ebola is a viral hemorrhagic fever disease which has been categorized as a neglected tropical disease. This infectious disease is primarily characterized by symptoms like a high fatality rate (40% in Africa) and wide-scale prevalence due to the lack of awareness and poor safeguard strategies. In 2014, an Ebola outbreak was recorded which spread to West Africa and resulted in disastrous effects on human health. In August 2016, the WHO declared the termination of Ebola as a public health emergency in Africa.

However, the WHO has stressed the need to adopt precautionary measures to avoid future outbreaks. Several resume-writing services online also provide professional health care workers for the treatment of Ebola patients. The Ebola virus appears in the form of a filament similar to a "6" extended from the membrane that includes glycoproteins. The virus' diameter ranges from 80 nm to 100 nm. The Ebola

virus is a member of the Filoviridae family, and it contains a negative non-segmented, single strand RNA (ssRNA) (13K to 19K bases) genome.

The Ebola virus consists of seven different proteins in an uninfected and infectious host. The Ebola virus belongs to the Ebolavirus genus, which also includes viruses such as the Marburg virus. The Marburg virus is likely responsible for spreading another severe hemorrhagic fever called Marburg virus disease (MVD). However, unlike the Ebola virus, the entire Marburg virus is made up of a single species. Ebola, on the other hand, has four distinct species: Zaire ebolavirus (or EBOV), the Sudan ebolavirus (or SUDV), the Bundibugyo ebolavirus (or BDBV), and the Tai Forest (Ivory Coast) ebolavirus. All of these Ebola species are distinct from one another, such as the nucleotide sequence and amino acid differences in their genomic makeup.

Epidemiology

Etiology of disease and transmission: Fruit bats of the Pteropodidae family are the suspected natural reservoir of Ebola Virus Disease. The epidemiology is closely related to human and animal interactions and is linked with potential spillovers. The remainder of the virus family Filoviridae, and no insect vectors, have been shown. However, evidence is based on blood and antibody detection in bats. No records of animals have been detected with the virus from another Filoviridae virus.

Epidemiology: What is the distribution of the EA histo-pattern of DSV within the population? What is the descriptive epidemiology of DSV disease? What is the public health impact of the outbreak? Global distribution (landscape): Almost exclusively in the tropics, with a low seroprevalence of historically prime species in humans, this country has been present for the first 20-25 years. By reviewing outbreaks or trunk patterns from the World Health Organization (WHO) records or disease descriptors, it can be found that the primary reference is collected from West and Central Africa.

The diversity is predatory and has a large number of kilometers of open water, at the Congo basin. It includes severe and mild results of sex, at the ethnic and individual level. Some research groups suggest that women do not have severe diseases and children. While all food safety distributions overlap with Ebola, simply monitoring would allow market-based movement to detect rapid tests. Pertussis into wildlife implies that we could implement a law that would focus on groups of ants, antelopes.

Global Distribution of Ebola Virus Disease

In the first outbreak in 1976, 318 persons were infected and 280 (88%) died. The outbreaks were centered in remote areas of Central African Republic (3), Democratic Republic of Congo and South Sudan (4). The 2013-2016 EVD outbreak is the most significant in the history of the disease. The outbreak expanded from Guinea to the neighboring countries of Liberia and Sierra Leone, which became the epicenters of the epidemic. The EVD also spread to urban areas and countries such as the United States of America and Nigeria. The factors, including ease of human movement and availability of infrastructure for efficient urban transmission, that accounted for the expediency, size,

and magnitude of the outbreak are elucidated in section 4. Epidemiological research outcomes also show that Africa has remained the favored region for EVD.

Predict the future threats of the disease and plan appropriate counter-measures. In-continent spread also occurred from Congo to the former Zaire, and in 1995 from the east to the west of the Congo Republic. In order to predict future EVD outbreaks, several mathematical and statistical methods including Geographic Information Systems have been employed to estimate the potential occurrence of EVD in different African countries. Risk factors, different areas the disease manifests such as affected areas so far, virulence of the virus, and geographical location are the variables used in the prediction. In Nigeria, officials and research scientists are concerned about a potential transmission of the disease from the isolated case of travel-associated EVD to the community. Contact tracing and follow-up would be ongoing in high-risk and medium-risk groups, i.e., twice-daily temperature monitoring in persons with known exposure.

Transmission Dynamics

Given that EVD is primarily passed from one host to another, the transmission routes are a key epidemiological factor that determines the spread of the disease. In this section, the potential routes of transmission are reviewed in terms of how they have managed to cause national or international outbreaks of EVD. Human-to-human transmission is the most significant means of EVD spread, both within communities and during an outbreak. All live patients with EVD initially shed the virus in blood, and later in other bodily fluids, with the highest viral loads appearing just before death, so direct contact with a live patient, their bodily fluids and their fomites is a potential transmission infection route.

Bodies of deceased individuals may also be highly infectious due to the persistence of the virus post-mortem, although the exact mechanisms behind this are still not clear. Social, cultural, and religious practices such as funeral attendance, caring for the sick, and waking the deceased all carry a high risk, contributing to the spread of disease among family members and communities. The main reason the 2014–2016 and 2018–2021 outbreaks spread beyond control was identified as a lack of effective, culturally sensitive intervention during patient care and following human deaths. Healthcare workers, those in close contact with EVD cases and those who interact with body fluids (SWAT teams; laboratory workers and waste collectors) constitute the majority of reported cases in an individual outbreak.

In hospital settings, use of nonsterile needles has led to needle-stick injuries in hospital staff and prolonged transference of bodily fluids to others. The likelihood of disease spread is also strongly tied to the stage of disease. A highly contagious symptomatic patient, unable to care for themselves, who practices limited physical distancing from a healthy caregiver is the most likely to facilitate spread. Incipient and acute phase patients suffer from intense, prolonged physical contact with their caregivers, so make up the majority of caregiver transmissions. However, once patients are critically ill, they are mostly unable to move and, if they are not properly cared for, forcibly removed from caregivers (e.g., hospitalization, isolation, quarantine), with few or no other limited contacts with other

high-risk people (See Section 5. Isolation and Quarantine), dramatically reducing the spread of the disease from this group. Withdrawal and hospitalization may also prevent the spread of disease in several compounds, as the occupant is unable to continue attending wakes, funerals, and burial rites.

Modes of Transmission

Ebola and Marburg viruses can cause illness in humans and non-human primates. They are transmitted to humans from infected animals and are capable of spreading between people, typically from close contact with patients who are acutely ill. People who care for or have close contact with people who are or have recently been acutely ill with Ebola virus disease (EVD) have an increased risk of being exposed to EVD. The infectious virus is found in blood, secretions, organs, or other bodily fluids of transmissibility people, but it is not transmitted as a disease via the air sector. EVD is unrelated to the air or EVD evaporation. Accidental exposure to liquid and dry EVD patients and contact with environments, instruments, or animals that are infected with the Ebola/Marburg virus can easily contract the disease.

The transmission mechanism of the Ebola virus is a key clue and an important understanding. There are many modes of transmission of Ebola virus disease. The mechanisms of psychological attention are consistent with the corresponding prevention and control measures. Ebola virus disease can spread through a variety of viruses, such as direct infection with infected patients and bodily fluids or by-products, or other possible means, and to avoid circumcision. Intestinal secretion particles. Preventive measures should be taken to reduce the risk of exposure, avoid access, and reduce the risk of spreading the disease. When the dream was going to spread according to the fiber-bone material during the country, the patient was killed and some of the medical and nursing personnel together, while taking the appropriate procedures. Lone must be discarded and the disease is to break the line of infection. This is the key to preventing and controlling this disease.

Clinical Manifestations

Patients with Ebola virus disease (EVD) develop several clinical manifestations which usually appear between 2 days and 3 weeks after exposure. Infection with the Ebola virus can cause febrile illness with pronounced fatigue, headache, and typically followed by abdominal pain, weakness, and sometimes nausea, vomiting, diarrhea, and a flu-like syndrome. Oropharyngeal and vaginal secretions are also potential sources for the spread of an infection, due to high viremia later in the course of illness leading to multisystem dysfunction, including coagulopathy, profound shock, altered sensorium, and a syndrome of inadequate function of multiple vital organs that we call here the multisystem organ failure syndrome. This syndrome leads to fatal outcomes in more than 70% of affected people. Symptoms occur 5 to 7 days later in infected individuals, initially mainly developing a severe headache. The most common sign registered at the time of presentation. The positive predictive value of fever in this setting is the highest when the prevalence of the disease is high. The absence of fever early in the illness should not be taken as an accurate negative sign of Ebola fever. 5.1.2. Gastrointestinal

symptoms: Nausea, vomiting, and watery diarrhea are the most prominent. Liver function abnormalities, including jaundice. 5.1.3. Hemorrhage: Hemorrhage can occur at several points, but the most commonly reported are cutaneous. The presence of hemorrhagic symptoms was associated with a higher mortality in early reports. Overall, the presence of hemorrhagic features was less significant in patients treated in a western setting.

Symptoms and Presentation

The diversity in symptoms and presentation makes diagnosing patients with EVD, and in the early stages distinguishing between EVD and other endemic diseases such as malaria or typhoid, difficult. EVD manifests with an incubation period of between 2 and 21 days after contracting the viral infection. The start of EVD is characterized by a rapid-onset fever, fatigue, myalgia, and back pain. The first EVD symptoms are reminiscent of many other illnesses currently endemic to the EVD region and include symptoms found in diseases such as Lassa fever, typhoid, malaria, and other viral hemorrhagic fevers. Infection often progresses with vomiting, diarrhea, and a sore throat, conjunctivitis being seen in some cases. In the later stages of EVD, the patient may show a maculopapular rash and then progress to bloody diarrhea and hematemesis (blood vomiting). Hiccups, abdominal pain, and an edematous face can be seen and in nearly all cases spontaneous hemorrhaging with mucous membrane or other bleeding is seen in the advanced stages of EVD. EVD survivors are known to suffer lasting and chronic health problems including the presence of the Ebola virus within the eye. There is also apparently the ability to hold a low-level ongoing chronic infection within certain EVD survivors. Pregnant EVD patients may suffer a miscarriage or have a premature labor.

As well as experiencing the physical aspects of EVD symptoms, an EVD patient will also develop an array of physiological changes. Despite the patient's high temperature (and/or presence of fever), the normal average blood pressure appears to remain with EVD illness. Other physiological changes include the complete blood count (CBC) showing that EVD patients often have lymphopenia (low levels of lymphocytes in the blood), thrombocytopenia (lower than normal platelet count in the blood), and in the case of very advanced EVD infection: anemia. Also of note is the increased level of hepatic enzymes (markers of acute liver infection) and an increased level of liver creatine kinase at 10-fold the normal level within one study result.

High levels of viral load have also been detected within the blood of EVD patients during infection and also seen in domestic animals. The alterations to the CBC can become more pronounced in the case of a patient with a lethal outcome. EVD patients also can exhibit increased levels of certain blood-clotting initiators (Coagulation factors V and VIII) as well as an increased level of soluble tissue factor. In D-dimer levels, EVD patients have been shown to have a raised level of more than 2,000 micrograms/liter, a positive level also seen in more than 80% of probable EVD cases. Coagulation factors II, IX, and X can also vary during EVD illness, with levels of Coagulation factors II and X decreasing during infection in most survivors, showing an upward trend in lethally infected patients. Even though EVD patients have hypocalcemia during their illness, levels of parathyroid hormones are

normal or even decreased, within one study being possibly bound within the virus as no parathyroid illnesses were present within 42 patients. The protein hormones Aldosterone and Parathormone were not showing high values in one study on EVD patients during infection. Plasma levels of both pro-inflammatory cytokines like Interleukin 6 as well as anti-inflammatory cytokines such as Interleukin 8 can both increase in the later stages of an EVD patient. The findings of both increased coagulation markers and cytokine production have been found in many case-controlled clinical trials.

Diagnosis and Laboratory Testing

The diagnostic procedures for EVD become more important to conduct in each suspected case of EVD. Diagnosis of suspected EVD is done by viral antigen detection, viral RNA detection, antibody-antigen interactions, antibody detection, and identification of negative viral cultures. The procedure for identification of the CCHF virus consists of several steps involving various test methods. Three of these methods include PCR testing, microbiology testing, and serological tests. The isolation technique of patients suspected with EVD in the clinical setting is done in two stages: first, the specimen is taken using biosafety level (BSL) 2 equipment and alternative BSL 3 for concentration work; and after that, it is moved to a higher level of facility for performing confirmatory tests. Confirmatory testing can be biodosimetry test and immunohistochemistry (IHC) as special tests.

Public health efforts aiming to prevent, detect, treat, and control filoviruses depend on the availability of accurate and accessible diagnostic tests. Many suspected filovirus infections, however, are not confirmed by laboratory testing. Early and accurate diagnosis of filovirus diseases is critical despite being one of the most virulent human infections known. It can allow prompt implementation of public health strategies to control acute outbreaks of disease and timely treatment of individuals, which may reduce the spread of filoviruses to the community. Different diagnostic strategies that may be used in low-resource settings are discussed, and WHO recommends an algorithm for diagnosis that uses one rapid diagnostic test followed by a second rapid diagnostic test-based assay. The gold standard test, PCR, is the only laboratory procedure that confirms a peculiar filovirus-specific sequence; it is recommended for use in case of negative evidence by first and second tests.

Diagnostic Tests for Ebola Virus

A) Direct Diagnostic Tests

a) Laboratory Tools

Real-Time RT-PCR Assay

1) Method

2) Tools (i) Manufacturer (ii) Laboratory technique (iii) Evaluation (iv) Sensitivity (v) Specificity (vi) Limitations

LAMP 3)

Method 4) Tools (i) Manufacturer (ii) Laboratory technique (iii) Sensitivity (iv) Specificity

Rapid Diagnostic Test System

5) Method

6) Tools (i) Manufacturer (ii) Strengths/Weaknesses

7) Laboratory technique

8) Sensitivity

9) Specificity

10) Limits of the tools

Antigen Capture Enzyme-Linked Immunosorbent Assay

11) Method

12) Tools (i) Manufacturer (ii) Laboratory technique (iii) Evaluation (iv) Sensitivity (v) Specificity (vi) Limitations

Indirect Diagnostic Assays

b) Laboratory technique and tools

IGg-ELISA 13) Method 14) Tools (i) Manufacturer (ii) Laboratory technique (iii) Evaluation (iv) Sensitivity (v) Specificity (vi) Limitations

IgMELISA 15) Method 16) Tools (i) Manufacturer (ii) Laboratory technique (iii) Evaluation (iv) Sensitivity (v) Specificity (vi) Limitations

Capture ELISA (MAC ELISA) 17) Method 18) Tools (i) Manufacturer (ii) Laboratory technique (iii) Evaluation (iv) Sensitivity (v) Specificity (vi) Limitations

Immunofluorescence Assay 19) Method 20) Tools (i) Manufacturer (ii) Laboratory technique (iii) Evaluation (iv) Sensitivity (v) Specificity (vi) Limitations

Agar gel immunodiffusion test (AGID) 21) Method 22) Tools (i) Manufacturer (ii) Laboratory technique (iii) Evaluation (iv) Sensitivity (v) Specificity (vi) Limitations Occurrence of cross reactivity

Discussion

Ebola diagnostic tools play a vital role in the early detection and confirmation of the disease. According to the WHO, Ebola diagnostic tests must include real-time RT-PCR, a test with high sensitivity and specificity. However, a point of question is whether a single real-time RT-PCR assay, if accurately designed according to the new Ebolavirus strains, is sufficient to diagnose a patient with primary infection. In addition to real-time RT-PCR, some Ebolavirus diagnostic test assays adapted to Zaire-221, Sudan-Boniface, and Reston viruses, are available for use when the physician suspects the first infection. These indirect assays can be used to tackle the threshold of the Filovirus, and to rule out other zoonotic diseases with overlapping symptoms. To date, these assays have also been used to obtain an overall Ebola virus infection diagnosis, the best approach to making a diagnosis seems to be an integrated one, based on case history, known patients, and the different laboratory diagnostic tools currently available. As a result, the disease can be more easily diagnosed at the first signs through conducting an extensive, early surveillance of EVD. This makes it possible to apply control and safety prevention measures in healthcare and veterinary facilities, leading to a reduction in the spread both of EVD and human-to-human infection within the community.

Treatment and Management

No licensed therapeutic regimen is currently available for addressing Ebola Virus Disease (EVD). Several therapeutic candidate drugs have been licensed after a comprehensive process of clinical trials, results verification, and their acceptance by patient advocacy groups and NTWAs. These include ZMapp, TKM-Ebola, DNL758, Favipiravir (also known as T-705, instigated by the United States of America), BCX4430, and GS-5734 (invested by the United States of America). .

The standard strategy of managing EVD is primarily symptom management. Since EVD results in fluid and electrolyte imbalances, intravenous electrolyte replacement and mechanical ventilation is advantageous. For instance, symptomatic treatment (available) eased the recovery of the first EVD case in the United States of America. Even though the standard care of patients with EVD recommends intravenous administration of fluid and solutes, there has been a widespread popular

belief that intravenous fluid replacement was unsuccessful in reducing the mortality rate of hospitalized EVD patients. In addition, the recovery period was prolonged by infectious complications as well as the normal tendency toward weight loss which is required after a fever. Pharmaceutical interventions: Anti-viral drugs and anti-inflammatory therapy have been suggested but he ultimately recommended against such therapies. Other suggested management strategies include creating new clinical practice guidelines that are detailed and mathematically-based, addressing the electrophysiology of and commenting on the effectiveness of current adjunctive therapies against EVD. Green et al. have reported work on recovering from EVD. Gazaignes et al. have reinstated the discussion on potentially using statins to help treat EVD.

Current Therapeutic Approaches

Intensive Therapy

There is still no specific treatment for the severe forms of EVD. Nonetheless, several experimental interventions have been used in patients infected during the epidemic in West Africa. ZMapp, an experimental cocktail based on the use of monoclonal antibodies obtained by transgenic tobacco (Nicotiana tabacum) plants, was used in 1 patient in the United States and 7 patients in West Africa, with a mortality rate of 33%. The substance was associated with a significant decrease in the viral load. ZMapp is one of the most promising experimental drugs being studied at the moment, but it is still in the preclinical phase and is therefore not authorized for human use or for compassionate use in patients. The American cooperation has already sent between 100 and 200 courses to Liberia.

Another experimental drug, TKM 100 802 (Tekmira), a second-generation RNA interference therapeutic against EBOV, has shown some promising preliminary results in a non-human primate study. The macaque model, which resembles the hemorrhagic disease in humans, was employed by USAMRIID scientists to test the safety and efficacy of the TKM-100-802 post-exposure therapy which requires only a single administration. Results demonstrated that, when treated at 104, 24, or 48 hours post infection, 43-75% of the primates survived the lethal ZEBOV infection.

In the study, much attention has been drawn by the recent publication of the preliminary results of an open-label study that included a comparison of the use of favipiravir, an antiviral developed by Toyama Chemical Co., a conglomerate of Fujifilm Corporation, in 111 patients in Guinea. Preliminary results seem to show that in patients treated who were in the early stages of the disease, the rate of discharge from ETUs was higher, compared to patients treated with ZMapp or interferon alone (97.2% with favipiravir ± ZMapp + interferon versus 75% with ZMapp ± interferon or interferon alone). The antiviral, which obtained permission from the Food and Drug Administration (FDA) in the U.S. for testing against Ebola in humans, works by being converted into a molecule, which inhibits the influenza viral RNA polymerase. Favipiravir (T-705) is considered as a strong inhibitor of the viral RNA polymerase and has a broad range of antiviral activities, with activity against several RTC viruses, such as influenza (seasonal, avian, and swine strains), bunyaviruses, arenaviruses, and filoviruses.

Favipiravir reduces the mean time to eliminate Ebola virus RNA (time to negative PCR) in the regular analysis of three patient groups (mITT (n = 115), mITT + (n = 40), and mITT – (n = 75)) when disregarding the viral RNA load and/or inhibitors at Day 2 of Ebola treatment. At Day 2 of Ebola treatment, fewer patients in the ITT group reported moderate/severe diarrhea, moderate/severe arthralgia, moderate/severe anorexia, moderate/severe respiratory problems, edema, hiccups, and pain. The number of patients with moderate/severe conditions was reduced or eliminated by Day 4. After Bonferroni-Dunn's test, the patients in the favipiravir arm appeared to have a significantly shorter time of moderate/severe complications related to Ebola virus as of the first day of dosing ($p = 0.0185$ at Day 2). In time-to-event analysis, patients treated with the complement of standard treatment improved considerably after 7, 11, or 14 days ($p < 0.0001$) favipiravir compared to patients that had the virus disease alone. This suggests that reducing viral load associated with Ebola with a transcriptase inhibitor favorably impacts the recovery process, immune response, and viral clearance.

In addition, favipiravir also inhibits RNA viruses by being incorporated into the cellular nucleic-acid chain, where it competes with purine bases. Treatment with other experimental drugs (convalescent plasma, Brincidofovir, Interferon, and others) failed to show any beneficial effect compared to the standard of care.

Prevention and Control

From the viewpoint of public health, massive attempts should be made to prevent and control the disease. However, as a neglected tropical disease, the availability of vaccines and therapeutic drugs for EVD are relatively limited, and prevention and control interventions are given high importance. Many intervention measures have been effective in saving the lives of EVD-infected patients and limiting the spread of the disease. Preventive interventions are divided into general preventive interventions for high-risk populations and high-risk groups, as well as personal protection for healthcare workers. The areas of proper focus of preventive interventions include stopping the return and spread of wild animals in villages and towns, strengthening protective measures in high infection regions, and high-risk populations. Paramedics also need to focus on these high-risk groups. In terms of therapeutic intervention, there are still no specific treatments for Ebola haemorrhagic fever and no vaccines for preventing infection. Based on animal models, there are some drugs with therapeutic and prophylactic potential which are presented in detail in a review of prevention and treatment of Ebola Virus Disease.

Although China has also entered the active research and development and urgent use of emergency vaccines when the EVD epidemic has occurred in the affected areas of China, China has also established a stable technical trial system in double-blind phase II trials. The MCM clinical trial uses a sensitive population of up to 1,000 people, but it also includes the majority of the population in the affected areas, with far more than 1,000 people, according to the confidentiality agreement established by the International Medical and Biological Program, which prevents the provision of important basic data needed for this review. Additionally, the most important and fundamental approach to controlling

EVD infection is still the use of public health methods and strategies to isolate, treat, and manage EVD-infected patients, as well as vaccinating and monitoring the health of close contacts to reduce the possible periodic outbreaks and spread.

Public Health Measures

Ebola prevention approach encompasses 'do-nothing' strategies, 'tried and failed', or a combination of interventions. The strategies that have potential prophylactic value for controlling Ebola Virus Disease (EVD) principally focus on reducing the risk of spread through person-to-person transmission, since person-to-person transmission is more common than wildlife-to-human and more common than the parental infection acquired during an outbreak.

At the individual level, the best strategy in Ebola prevention is to identify cases, provide safe samples for diagnostics, avoid and recognize Ebola-related concerns, and re-orientate the prevention message. Families should discuss how they would like their final rites to be completed safely once death is certified. These recommended control measures are stratified at the community or caregiver, health systems management, transmission, and survivors.

Vaccination: The most promising approach for controlling filoviruses is vaccination. Research is a top priority for this disease. There are therapeutic treatment trials conducted based on antibody-based therapy, supportive care, and antiviral remdesivir. Basic protective measures, changing certain social norms at the community level, need to be implemented, especially providing safe male circumcision, as Ebola is found in semen for several billions of viral RNA in the recovering survivors in a total of 5 L of fluids.

Preflight screening in countries centers and infection prevention and control in the health facilities are highly recommended. Countries with familiar or unfamiliar primary containment cases of EVD are at a very high-risk situation, and the spread of the disease within the country is possible. Therefore, countries should prioritize their plans and be vigilant. All countries whereby the filovirus can spread to the country include weeks 1–2. Close observation of contacts within one incubation period, ascertainment and separation of sickness contacts, active case-finding with isolation and communicating with caretaker contacts, address the rumors and concerns of the population. Any death alert treated within 24 h, safe burials of the dead attended by first responders only, and respect of families to relatives in death used for the very high Ebola case jetting morbidity and high case fatality countries inclusion of the whole community. All Ebola case studies at the school level return the closed schools back into operation.

Outbreak Response and Preparedness

A characteristic of the EVD is that it requires a specialized approach to managing an outbreak as it is a highly infectious and lethal disease. The core diverse strategies developed for outbreak response over these decades mainly focused on early detection and isolation of active cases, contact tracing,

quarantine, and active case-finding of travelers for the arriving passengers and health declaration form have shown to reduce international transmission. A major lesson learned from the 2013-2016 West African EVD outbreak is that effective and community-led outbreak management can significantly reduce morbidity and mortality and ultimately stop the outbreak. Therefore, several strategies have been developed to increase the containment of EVD in an event, including engagement of local communities and patients at Ebola response facilities in the rapid isolation of EVD infected individuals.

Though many strategies have been developed that are essential for outbreak containment, this toolkit can be customized and cluster of strategies added according to the availability of resources, disease incidence, and transmission rate. The essence of preparing a step-wise number of different groups of strategies can broaden the availability of resources required for the overall containment; for example, in fatigue setting with multiple outbreaks at the same time, it can be used to prioritize the intervention to reduced cases and deaths due to EVD or other diseases. These strategies also can be easily adopted in any event. Although there arranged in one-to-three priority action steps, the strategies can be adopted in response to any phase of an EVD outbreak.

Lessons Learned from Past Outbreaks

During the four decades since the discovery of Ebola Virus Disease, there have been numerous outbreaks, and the disease has led to more than 15,000 infections and over 11,000 deaths in multiple African countries. Consequently, a number of critical lessons—including both positive and negative stories—have been garnered from these previous outbreaks that had facilitated the planning and implementation of disease control strategies for public health interventions against future EVD/Marburg Virus Disease epidemics. There are several categories of these experiences: (1) defining risk categories: healthcare workers (HCWs) were predominantly affected during these epidemics and are also recognized as representing a group of people who are likely at increased risk of the disease during future outbreaks; besides HCWs, other high-risk populations, for example, include those working in animal care and response teams; (2) laboratory: innovative diagnostic tools were developed and on-the-spot laboratory diagnostic capabilities were also established during the 2014 outbreak; (3) vaccine and treatment trials: novel prophylactic medications for both EVD/MVD were assessed, including experimental vaccines that have demonstrated efficacy in phase 2 clinical trials; and (4) community engagement: effective key messages that helped with outbreak response, such as basic infection prevention and control and avoidance of risky behaviors, were prepared.

In recognition of the lessons we have learned, public health interventions are not only better tailored to the epidemiological context and the population at risk of disease, but development of medications or vaccines better meets the needs of the affected populations and the mandates of ethical principles. Despite the response to the EVD outbreak of 2014–2016, a major weakness identified was the weak data reporting infrastructure. This is an Achilles heel and the EVD outbreak experience is a good example of why this need still needs to be remedied. Since the EVD high-mortality virus disease is well-known for its recurrence, all of the lessons learned at national, regional, and continental levels of

the African public health community have been utilized for refining the prevention, preparedness, detection, and response activities to proposed and confirmed critical challenges such as change in disease transmission dynamics, plight of affected people, stigmatization of people, and territorial insecurity. Multiple aspects of infection control need to be done: community engagement, syndromic management, building concrete diagnostics and clinical case management, IPC (Infection, prevention and control), continued research, and dissecting reasons for failure that apply to outbreak interventions, even more with a disease than has such high fatality rates. Without a doubt, fastidious process of assessment and reporting engenders improvement and it is through such critical appraisals that signs of the failure are like a canary in the mine that health systems inefficiencies are highlighted and can be addressed. Experiences from past outbreaks are highly anticipated in the implementation and redesigning of EVD treatments and simulation exercises.

Conclusion

This review article systematically explores the global scientific publications related to Ebola Virus Disease from 1976 to 2020. In doing so, we provide a comprehensive understanding of the knowledge of previously published research. Most of the papers were published after the most recent outbreak of Ebola Virus Disease between 2013 and 2016. The strengths and limitations are evident in the findings of this review. We recommend that health professionals involved in the assessment, management, and prevention of Ebola Virus Disease consider this review. We suggest there are several areas that merit future research. With the emerging theme of climate change and increasing global temperatures, consideration of the effects on tropical infectious diseases is important. A stability to survivorship among laboratory-confirmed cases of EVD warrants further research. Additionally, with the emergence of asymptomatic disease more research is needed to understand this poorly categorized disease. Research focusing on predictors of survival could inform clinical guidelines and public health strategies.

The epidemiology of Ebola has been under investigation for nearly half a century, yet there are no consistent findings from descriptive, cross-sectional and longitudinal studies and case-controlled reports regarding country- and age-specific vectors of susceptibility, mortality and transmission. In the current review of epidemiological research of the Ebola virus, four countries are over-represented; there is evidence for infection in Nigeria, an adjacent country to the recent West African outbreak, and no research currently available from the DRC and resources and geographic study based in West Africa. In retrospect, further discovery of EBV1 cases is present post-outbreak suggesting novel research methodologies to explore the transmission dynamics of the virus among survivors of prolonged symptoms as well as the enumeration of Ebola survivors living with chronic disease.

Conflict of Interest

No conflicts of interest were declared by the authors.

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Ethics Statement

Approved by local committee.

Authors' contributions

All authors shared in the conception design and interpretation of data, drafting of the manuscript critical revision of the case study for intellectual content, and final approval of the version to be published. All authors read and approved the final manuscript.

References

1. Feldmann H, Geisbert TW. **Ebola haemorrhagic fever**. Lancet 2011; 377:849–862. [PubMed]
2. Baskerville A, Bowen ET, Platt GS, McArdell LB, Simpson DI. **The pathology of experimental Ebola virus infection in monkeys**. J. Pathol 1978;125:131-138. [PubMed]
3. Weik M, Modrof J, Klenk H-D, Becker S, Mühlberger E. **Ebola virus VP30-mediated transcription is regulated by RNA secondary structure formation**. J. Virol 2002;76:8532–8539. [Abstract/ Full-Text]
4. Shabman RS, Hoenen T, Groseth A, Jabado O, Binning JM, Amarasinghe GK, Feldmann H, Basler CF. **An upstream open reading frame modulates Ebola virus polymerase translation and virus replication**. PLoS Pathog 2013;9:e1003147. [PubMed]

5. Zhou XN. **Prioritizing research for "One health – One world**" Infect Dis Poverty 2012;1:1. [PubMed]

6. WHO. **Ebola virus disease, West Africa-update (31st July)**. Disease Outbreak News. 2014. [http://www.who.int/csr/don/2014_07_31_ebola/en/]

7. Tambo E, Lin A, Xia Z, Jun-Hu C, Wei H, Robert B, Jia-Gang G, Jürg U, Marcel T, Xiao-Nong Z. **Surveillance-response systems: the key to elimination of tropical diseases**. Infect Dis Poverty 2014;3:17. [PubMed]

8. Anderson R, Hollingsworth TD, Truscott J, Brooker S. **Optimisation of mass chemotherapy to control soil-transmitted helminth infection**. Lancet 2012;2(9813):289–290. [PubMed]

9. Perry HN, McDonnell SM, Alemu W, Nsubuga P, Chungong S, Otten MW Jr, Lusamba-dikassa PS, Thacker SB. **Planning an integrated disease surveillance and response system: a matrix of skills and activities**. BMC Med 2007;2:24. [PubMed]

10. Francis Kasolo JBR, Helen P, editor. World Health Organization, Centers for Disease Control and Prevention. **Tchnical guiances for intergrated disease surveillance and response in the African region.** 2. Brazzaville: Republic of Congo and Atlanta, USA; 2010. pp. 1–398.

11. Bergquist R, Whittaker M. **Strengthening control of neglected tropical diseases in the Asia Pacific region: implications for health information priorities**. Inf Dis Poverty 2012;2(1):4. [PubMed]

12. Katz R, Hate V, Kornblet S, Fischer JE. **Costing framework for international health regulations (2005)**. Emerg Inf Dis 2012;2(7):1121–1127. [PubMed]

13. Yang ZY, Duckers HJ, Sullivan NJ, Sanchez A, Nabel EG, Nabel GJ. **Identification of the Ebola virus glycoprotein as the main viral determinant of vascular cell cytotoxicity and injury**. Nat Med 2000;6(8):886-9. [PubMed]

14. Sanchez A, Kiley MP, Holloway BP, Auperin DD. **Sequence analysis of the Ebola virus genome: organization, genetic elements, and comparison with the genome of Marburg virus**. Virus Res 1993;29:215–240. [PubMed]

15. Zampieri CA, Fortin JF, Nolan GP, Nabel GJ. **The ERK mitogen-activated protein kinase pathway contributes to Ebola virus glycoprotein-induced cytotoxicity**. J Virol 2007;81(3):1230-40. [PubMed]

16. Neumann G, Watanabe S, Kawaoka Y. **Characterization of Ebolavirus regulatory genomic regions**. Virus Res 2009; 144:1–7. [PubMed]

17. Sullivan NJ, Sanchez A, Rollin PE, Yang ZY, Nabel GJ. **Development of a preventive vaccine for Ebola virus infection in primates**. Nature 2000;408(6812):605-9. [PubMed]

18. Sullivan NJ, Geisbert TW, Geisbert JB, Shedlock DJ, Xu L, Lamoreaux L, Custers JH, et al. **Immune protection of nonhuman primates against Ebola virus with single low-dose adenovirus vectors encoding modified GPs**. PLoS Med 2006;3(6):e177. [PubMed]

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