Review article:

Ebola Hemorrhagic Fever - Should India Fear?

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Abstract:

Ebola virus disease (EVD), a disease with high mortality, has shaken the world with a deadly epidemic. A disease with no cure, Ebola virus disease has progressed as an unconquered killer for over a year. Prevention remains the only option available for the communities worldwide. The management of Ebola virus disease requires a high level of technical equipment, manpower and above all, the will to take the challenge. With high fatality, EVD threatens not only the developing nations but also the developed nations. If Ebola virus disease occurs, in a highly populous nation like India, could result in dismal consequences. The consequences of introduction of this dreaded disease in Indian subcontinent may be disastrous due to limited resource settings, presence of virgin population and predominantly rural set up with minimal access to preventive and curative care. Currently the disease has not yet spread to India, but given its highly infectious nature and migration of individuals across nations, India may soon fall prey to this disease. This article throws light on Ebola virus disease epidemiology, barriers to containment of epidemic and the implications and preparedness in India.

Keywords: Ebola epidemiology, containment, prevention

Ebola Virus Disease (EVD) or Ebola Hemorrhagic fever is the recent scare to the world. A disease with high fatality, this virus has hit the Western regions of the African continent with the worst kind of epidemic. It was named after the river Ebola, in the region of which it was first identified. Historically, EVD has not been a mass killer. In fact, other conventional medical conditions like malaria, measles, dengue, tuberculosis etc. kill many more people each year. However, during the current spread in West Africa, the severity, territorial extent, number of persons infected and agonizing deaths has been unprecedented. The failure to contain the spread of Ebola during the current outbreak has alarmed and stunned the world.

The total number of probable, confirmed and suspected cases in the current outbreak of Ebola virus disease (EVD) in West Africa was 28 005 reported up to 23 August 2015, with 11 287 reported deaths. Three new confirmed cases were reported in Guinea in the week to 23rd August 2015[1].The countries currently affected by this deadly disease, localized to the West African region include, Sierra Leone. Liberia, Guinea, in order of numbers infected. Following the roadmap structure [2] country reports fall into three categories: those with widespread and intense transmission (Guinea, Liberia, and Sierra Leone); those with an initial case or cases, or with localized transmission (Nigeria, Senegal, Mali, Spain, USA, UK); and those countries that neighbor areas of active transmission (Benin, Burkina Faso, Corte d'Ivoire, Guinea-Bissau, Mauritania etc) [2]

The most important epidemiological quantity to estimate for an infectious disease is typically the

basic reproductive ratio, R0, defined as the expected number of secondary cases produced per primary case early in the epidemic[3] When R0 is greater than 1, the expectation is that a new epidemic will eventually infect a significant percentage of the population if it is not stopped by interventions or chance extinction; conversely, when R0 is less than 1, chance events may lead to a large number of cases, but these are always expected to be much less as compared to the total population size. Previous attempts to estimate R0 for Ebola have found values between 1.34 and 3.65 in the Democratic Republic of Congo in 1995 and Uganda in 2000[4-6]with similar results obtained for the ongoing outbreak[7].The latest epidemic 2013-2014 is the largest till date[8]. Although past outbreaks have been associated with almost 90% mortality [9] the case fatality proportion in this outbreak has been approximately 55–75% [10].Not many countries are equipped adequately to meet the multiple and stiff challenges that further spread of this virus would pose. Thus, it is imperative to be prepared for any such occurrence.

In view of the gravity of the situation, in August 2014, the Director General of the World Health Organization (WHO) declared the current Ebola outbreak a Public Health Emergency of International Concern[11,12].WHO formed an Ebola response roadmap in Aug 2014 with the aim of stopping Ebola transmission in affected countries within 6-9 months and to prevent international spread[2].First time in the history of UN, a new mission, the United Nations mission for Ebola emergency response or UNMEER, was formed. The aim was to diagnose and treat 100% of the cases and perform 100% burials safely and with dignity burials. The first known case in human beings was reported in 1976 in 2 simultaneous outbreaks at Nzara, Sudan and in Yambuku in the Democratic Republic of Congo.Ebolavirus is one of the three members of the *Filoviridae* family (filovirus), along with genus Marburg virus and genus Cuevavirus. Genus Ebola virus comprises 5 distinct strains. The current outbreak has been caused by the Zaire Ebola virus. The other species have caused outbreaks in the past [13].

Ebola is an elongated filamentous virus, with length of 800 - 1000 nm and uniform diameter of 80 nm [14-17]. Each virion contains a single-strand of non-segmented, negative-sense viral genomic RNA[17,18].Ebola is an RNA virus highly sensitive to 3% acetic acid, 1% glutaraldehyde, alcohol-based products, and dilutions of 5.25% household bleach (sodium hypochlorite) and bleach powder[19-23], heating for 30- 60 minutes at 60°C, boiling for 5 minutes, or bye gamma irradiation combined with 1% glutaraldehyde[19,21,24]. Filo viruses are capable of surviving for weeks in blood and on contaminated surfaces, particularly at low temperatures (4°C) [25, 26]. This virus can infect humans, various monkey species, chimpanzees, gorillas, baboons, and duikers which are ideal hosts for Ebola virus [27-35].Bats are considered to be a plausible reservoir for the virus [36-39].

EVD being a Zoonosis, the first patient becomes infected as a result of contact with an infected animal [28]. Spread of the disease occurs via person-to-person transmission following close personal contact with an infected individual or their body fluids during the symptomatic stages of infection or after death [14, 27, 28, and 40]. Blood, serum, urine, respiratory and throat secretions, semen, and organs from human or animal hosts are the major causes of infection [14, 27]. Nosocomial infections can occur through contact with infected body fluids [14]. Humans may be

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infected while handling sick or dead non-human primates and also when handling the bodies of deceased humans in preparation for funerals [14, 24, and 41].This poses high risk of infection among health professionals and workers.

EVD has an incubation period of 2 to 21 days [27, 42, and 43] and is communicable as long as blood, body fluids or organs, contain the virus. Transmission through semen has been noticed even 7 weeks after clinical recovery [14, 27, 44, and 45]. Patients become contagious only after the onset of symptoms. As symptoms worsen, the ability to transmit the virus increases. Highly infected patients generally die within 6-16 days of catching the illness. The infection commences with sudden fever, chills, malaise, and myalgia. The subsequent signs and symptoms include prostration, gastrointestinal (anorexia, nausea, vomiting, abdominal pain, diarrhea), respiratory (chest pain, shortness of breath, cough, nasal discharge), vascular (conjunctival injection, postural hypotension, oedema), and neurological (headache, confusion, coma) manifestations [46]. Hemorrhagic manifestations arise during the peak of the illness and include petechiae, ecchymoses, uncontrolled oozing from venipuncture sites, mucosal hemorrhages, and post-mortem evidence of visceral hemorrhagic effusions. In later stages, shock, convulsions, severe metabolic disturbances occur. Death occurs due to multiorganfailure[46].EVD is highly infectious and has no tested and proven treatment available[47].

Ebola virus infections can be diagnosed definitively in a laboratory through several types of tests [13] viz serology, virus isolation and polymerase chain reaction (PCR). Laboratory surveillance of Ebola is extremely hazardous [14, 27, 48, 49] and testing should be conducted under maximum biological containment conditions. Supportive care remains the only resort for the infected patient since no specific curative treatment is available [47].Patients have a better chance of survival if they receive early treatment. New drug therapies are being evaluated. Existing supplies of all, even experimental medicines, are either extremely limited or have already been exhausted[47,50].Safety of experimental medicines is also unknown, raising the possibility of adverse side effects when administered to humans.The experimental drug ZMapp has recently been used to treat several patients with encouraging success rate.The treatment is a mixture of three monoclonal antibodies that attack proteins on the surface of the virus[51].Another experimental drug TKM-Ebola has been tested on monkeys and on a handful of healthy human volunteers. It is designed to target strands of genetic material of the virus (RNA) [51].The vaccines are currently in the clinical trial phase. Results from Phase I clinical trials for two vaccine candidates – ChAd3-ZEBOV, developed by GlaxoSmithKline (GSK) in collaboration with the US National Institute of Allergy and Infectious Diseases (NIAID), and VSV-EBOV, developed by NewLink Genetics and Merck Vaccines USA in collaboration with the Public Health Agency of Canada – were obtained in January 2015. Both vaccine candidates have been shown to be safe and well tolerated in humans. Currently, Phase II and Phase III clinical trials for VSV-EBOV are underway in Guinea (Ebola çasuffit!) and Sierra Leone (STRIVE). The data from the Guinea Phase II Front Line Worker and the Phase III ring vaccination trials will be reviewed in the coming weeks by the trial Data Safety and Monitoring Board (DSMB) [52].

Existing barriers to containment of outbreak

- This outbreak has occurred in countries which are virgin to this virus. Previous

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outbreaks have occurred in central parts of the African continent. Countries like Democratic republic of Congo, Uganda,Sudan have experience of rapid containment of the disease as evident in the recent and unrelated outbreak that occurred in Democratic republic of Congo in August 2014. In those places the education message about avoiding contact took years to enter the collective consciousness. West Africa, however, is experiencing the menace for the first time, hence, falling prey to the worst possible outcomes of this viral infection.

- Civil wars in Guinea and Sierra Leone in the recent past have ruined the political, economical and health infrastructures in these regions. Doctors were not available for basic curative services when this disease hit these nations with full force.
- Ebola virus disease has a history of being confined to remote and rural areas in the past, hence the transmission chain was somewhere weak since the spread was lesser .Current outbreak has occurred in the most densely populated regions of these 3 countries including the capitals.
- Lack of resources in these countries have further added to their misery:
    1. Early detection and isolation of cases, contact tracing and monitoring, and rigorous procedures for infection control, are difficult because of a lack of skilled manpower and material resources.
    2. Supplies of personal protective equipment and disinfectants are inadequate.
    3. The outbreak continues to outstrip diagnostic capacity, delaying the confirmation or exclusion of cases and impeding contact tracing. Diagnostic capacity is especially important as the early symptoms of Ebola virus disease mimic those of many other diseases commonly seen in this region, including malaria, typhoid fever, Lassa fever, shigellosis, cholera, leptospirosis, plague, rickettsiosis, relapsing fever, meningitis, hepatitis and other viral hemorrhagic fevers.
    4. Paucity of treatment facilities has led to overburdening the existing ones. Many existing facilities lack reliable supplies of electricity and running water.
- Fear causes contacts of cases to escape from the surveillance system, families to hide symptomatic loved ones or take them to traditional healers, and patients to flee treatment centers. The prospect of seeing a beloved one getting away from one without a proper good bye, embrace, kiss or even a hand shake, knowing that he / she may not ever return alive, is too sentimental and emotional a prospect for most to bear. This has led to threatening the security of national and international response teams. A common feature of Ebola epidemics is the stigma attached to it. Sufferers and survivors are often stigmatized by the community.

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- In the West African countries currently affected by the outbreak, some cultural and social practices involve close physical contact. Hugging is a normal part of religious worship in Liberia and Sierra Leone and across the region the ritual preparation of bodies for burial involves washing, touching and kissing. Those who handle the body and come in contact with the blood or other body fluids, with such high viral load, are at greatest risk of catching the disease. It is a very difficult message to get across.
- The highly contagious nature and high case fatality of Ebola virus have made it a menace to containment.

India with its large population of over 1.4 billion and high density is at high risk. Potentially, each infected individual has the capacity to spread the virus exponentially. An epidemic, if and when it occurs, may not take too long to spread, killing millions. Considering the high virulence of the organism, the country may face extremely high rate of fatalities. Since most of the cities in India are not home to fruit bats, cases of filo viral diseases have not been known to occur till date. Hence, introduction of a new disease in this virgin population, with no natural immunity can lead to disastrous consequences. It is reported that the affected countries have over 45,000 Indians living there on different engagements. This is a high risk proposition, given the fact that escalation of infection could generate large scale return to India. As of now no case of EVD has been reported in India. A cured case had arrived from Liberia in November 2014, was quarantined and as such did not pose a threat to the nation. The WHO has instructed countries to adopt the WHO Ebola preparedness checklist for preparing themselves lest the need arises in case of an Ebola outbreak. The ten components of the checklist are: capacity building for points of entry, rapid response, public awareness & community engagement, infection prevention and control, case management, safe burials, epidemiological surveillance, contact tracing, laboratory capacity and overall coordination.

The international sea ports and airports in India have been equipped with entry and exit screening for the disease by thermal scanners and a self reporting bola form. These facilities are currently available and appropriately being used in a few states only. In flight announcements and aircraft disinfection procedures are carried out on board. The airlines have been advised to keep first aid kits, universal precaution kits as per the International Civil Aviation Organization (ICAO) guidelines. Apart from this a stock of triple layer masks (25 Nos.), disposable hand gloves (around 25), hand sanitizers and disposal bags are to be present on board for use by a symptomatic passenger or their co passengers. Public health passenger locator cards are provided to passengers under high index of suspicion so that they can be traced by ground personnel. Individuals suspected of having the disease or showing signs and symptoms of the disease are tracked up to four weeks. Tracking system has been put in place under the Integrated disease surveillance program(IDSP).State governments are responsible for contact tracing ,follow-up activities, management of cases, regular reporting to Director (NCDC) and Director (EMR).They are supported by State Surveillance Officers, State Rapid response teams, District surveillance officers and local administration.

Given the dismal state of coverage of health care in India, there are hardly any hospitals with

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acceptable standards for management of a disease as deadly and infectious as Ebola virus disease. With a doctor population ratio of 1:1800[53] the healthcare delivery system of India is not even ready for the routine services, let alone epidemic preparedness. Majority of the Indian population falls under rural setup making it even more difficult for people to access preventive / curative health care services, if need arises. Limited resource settings are a big drawback for the Indian sub continent. The management of Ebola virus disease requires a high level of technical equipment, manpower and above all, the will to take the challenge. The Ram Manohar Lohia hospital in New Delhi is the only designated hospital approved by the government for isolation and treatment of cases of Ebola virus disease. Most hospitals had been rejected in the review process. Ministry of health and family welfare has also issued a set of guidelines for the isolation, treatment and contact tracing of cases and suspects of Ebola virus disease.

A Bio safety lab (BSL) III or IV are considered safe for handling Ebola virus. Ebola virus requires high India does not have any BSL-4 lab. The designated laboratories for detection of the virus in India are National institute of virology (NIV), Pune (BSL-4) and National center for disease control (NCDC), New Delhi (BSL-3). Laboratories across the country, be it government or private are incapable of managing this virus. Apart from these, Bhubaneswar, Dibrugarh, Port Blair, Lucknow, Guwahati, Bangalore, Chandigarh, Thiruvananthapuram and Jaipur are also being proposed to have Ebola testing labs.

Public awareness is being generated via mass communication including television, radio etc. A 24 hour helpline has been set up by ministry of health and family welfare for information regarding Ebola virus disease. Apart from this health care workers at different levels are being trained and prepared for this deadly disease. Training is being conducted by Ministry of health and family welfare and incorporates demonstrations and mock drills. The overall co-ordination and supervision falls under the Ministry of Health and family welfare with inputs from multiple agencies. To conclude, a wide and highly populated nation like India needs to fear from Ebola virus disease due to low coverage of health care services and inadequate epidemic preparedness.

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