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Recent advances on Ebola virus

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ABSTRACT

The 2014–2015 Ebola epidemic in West Africa was the largest of its kind, with more than 11 000 deaths and 28 637 cases. The epidemic mobilized a coalition of countries from US to China, European Union, and African countries. The international community was not prepared to face this unprecedented epidemic. Numbers of research groups are working to find a potent vaccine against Ebola. Ebola virus has the ability to dodge the immune system either by blocking interferon production or by glycoprotein-based immune diversion. Individuals who survived from the Ebola virus are facing different health issues after the infection. The rate of miscarriage is also high in Ebola survivors while there are variable reports of the presence of Ebola virus in semen of Ebola survivors. There are many asymptomatic Ebola patients under consideration. West African countries lack the basic healthcare system, for which the actual number of deaths by the Ebola outbreak are much more than the deaths caused by the direct viral infection. The hospitals were empty due to fear and death of nurses and doctors. Millions of children missed the vaccine against measles. Hundreds of thousands of people could not get food. The Ebola epidemic also affected the mental health of people living in endemic countries. The families affected by Ebola are facing discrimination in the society. There is a dire need to adopt United Nations Sustainable Development Goal 3, which stresses to prepare ourselves to face any national or global health risk.

1. Introduction

The 2014–2015 Ebola epidemic in West Africa was largest of its kind, with more than 11 000 deaths and 28 637 cases. The epidemic mobilized a coalition of countries from US to China, European Union, and African countries. International community was not prepared to face this unprecedented epidemic. World Health Organization (WHO) declared it as the most deadly outbreak till date. The last Ebola-affected country, Liberia is declared free of Ebola virus transmission in January 2016, by WHO. Researchers and scientists are striving hard to make a potent vaccine for it. Currently, there is no vaccine for Ebola virus approved by US Food and Drug Administration.

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2. Ebola virus vaccine

There is a strong need to design a potent and efficient candidate for Ebola vaccine[1]. Remarkable progress has been done by using different platforms to design an efficacious vaccine for Ebola. Scientist has targeted DNA, subunit, viral vectors approaches, replicating and non-replicating techniques, surface epitopes receptors of Ebola in nonhuman primate models, *etc*. Several vaccine studies employing virus like particles or replication defective virus particles are under consideration. One of the studies employs Ebola glycoprotein (GP) by using virus like particles of vaccinia virus. Another vaccine candidate is using nearly full virus particle as it had nucleic acid and other viral proteins that could lead to a much broader and stronger immune response than virus displaying GPs. It is actually replication defective viral particle as viral protein 30 (VP30), a necessary transcription factor required for replication is deleted[2]. Numbers of studies are also in progress to predict a vaccine candidate for Ebola virus by using bioinformatics

tool[3]. To date, there is no vaccine for Ebola virus approved by U S Food and Drug Administration.

3. Survivor's blood – An alternative approach

An Ebola survivor from Congo 1995 outbreak produced highly effective proteins and antibodies against Ebola. One of these antibodies named dubbed mAb114 produced immunity against Ebola when monkeys were challenged with virus. These retentive antibodies in Ebola survivors can be used as effective therapeutic against Ebola. The successful outcome of the animal model that derived monoclonal antibodies in nonhuman primates reflects the importance of monoclonal antibodies against Ebola[4].

4. Dodging the immune system

Ebola virus has the ability to dodge the immune system. Ebola virus interferes with the immune system in two ways: either by blocking the interferon (IFN) production or by GP/soluble GPs-based immune diversion.

4.1. Blocking the IFN production

Ebola manages to escape the immune response to prevent antiviral state in the host. It expresses a powerful transcription factor, namely, VP35, part of Ebola polymerase, which plays an important role in preventing the activation of hosts' innate immune response in combination with VP30, nucleoprotein and the L-protein. It also prevents the activation of retinoic acid-inducible gene I and protein kinase-R by hiding its nucleic acid from host's sensor proteins[5]. Other protein of Ebola virus that interferes with IFN production is VP24. Ebola virus evades the host's immune system by interrupting the signalling pathways involved in activation of host's immune response.

4.2. Role of GPs

The role of GPs in Ebola life cycle is not well characterized. But different research papers have shown that Ebola GPs interfere adsorbing the antibodies against GP1 of full length GP. GPs also reduced the tumour necrosis factor-alpha (TNF-α)-induced permeability. This may suggest that virus has evolved this trait to prevent white blood cells from infiltrating at the site of infection so that immune cells cannot counter the virus. Ebola GPs also showed some anti-tetherin activity that allows mature virion particles to release out of the cell. Ebola, like other infectious viruses, is evolving its immune evasion strategies[6].

5. Can Ebola survivor conceive?

Individuals who survived from Ebola virus disease (EVD) face some health issues after the infection. Post-Ebola effects include uveitis, headache, musculoskeletal pain and insomnia[7]. These issues may have effects on pregnancy. The risk of stillbirths is more in pregnancy after 1 or 2 months of post-Ebola. If one conceives after 5 or 6 months of post-Ebola infection, normal birth is observed. EVD survivors who suspected problems with their pregnancy may have been more likely to seek medical attention than those who did not. It has been hypothesized that persistence of Ebola virus in immune-privileged sites such as brain and retina may affect the developing fetus[8]. Male survivors had shown to shed Ebola virus with ribonucleic acid in semen for at least 18 months after onset of EVD[9]. In August 2015, an apparently healthy mother passed on the Ebola virus to her nine-month old daughter by breast-feeding milk and the child died from Ebola[10].

Seventy EVD pregnant survivors from Margibi and Montserrado countries were studied, of which 15 women miscarried, four neonates were stillborn and two women terminate their pregnancies. The rate of miscarriage in Ebola survivors (15/68; 22.1%) was higher than the expected rate of miscarriage from healthy women in developed countries (10%–15%). The overall rate of adverse pregnancy outcomes in the study was very high (19/68; 27.9%), suggesting that the Ebola virus affects reproductive health even after the disease is resolved[10].

6. Ebola lingering in survivors

Ebola survivors are providing scientists with some new findings. A study revealed that Ebola lingers longer in survivors than scientists thought. This remaining virus can relapse the EVD depending upon the environmental conditions of the survivor. In a study including 466 men, Ebola virus was detected in semen up to 18 months after the recovery from infection[11]. That was alarming. It was also observed that a man transferred the Ebola virus to his sexual partner even after the 17 months after recovering from Ebola[12]. Another study including 26 male subjects demonstrated the elimination of virus from semen in 4 months after recovery.

Keeping these finding in mind, more researches on Ebola lingering in survivor should be done to conclude the after-effects.

7. Asymptomatic or sub-symptomatic Ebola patients

During the recent Ebola epidemic, there were certain people who were infected with Ebola but escaped from detection. There were 80 people were traced who had contact with Ebola patients but did not become ill. It was surprised to see that 15%–20% of these contacts developed antibodies against Ebola, suggestting that they had mild infections that went undetected. There are many asymptomatic or sub-symptomatic people with Ebola infection. Studies are in progress on these patients[13].

8. Future prospect in Ebola diagnosis

RT-PCR is the best technique used for the detection of Ebola virus. But it has some limitations in Ebola case, like safety fears of venepuncture blood, field laboratories, expensive and high throughput machinery, *etc*. There is a dire need for the establishment of RT-PCR facilities in Ebola epidemic areas. The laboratory

technicians in the Ebola affected countries also need training of molecular diagnostic techniques, quality control and biosafety practices. As diagnosing algorithms and strategies evolve, they remain a critical responsibility of health care agencies to safeguard means for safe and efficient sample management, tracing and reportage[14].

9. Fragile healthcare system in West Africa

West African countries lack the basic healthcare system, for which the actual number of deaths by the Ebola outbreak are much more than the deaths caused by the direct viral infection. The hospitals were empty due to fear and death of nurses and doctors. Millions of children missed the vaccine against measles. Hundreds of thousands of people could not get food[15].

Prior to Ebola outbreak, the expenditure on healthcare was underfunded in the West African countries. Liberia, Sierra Leone and Guinea were spending $20, $16 and $9 per person per year on health care, respectively. These figures are much lower than the WHO's recommendation of $86 per person per year . The total expenditure on the Ebola outbreak was more than 4 billion United States dollars[16].

The Ebola epidemic also affected the mental health of people living in endemic countries. Families affected by Ebola are also facing discrimination in the society. There is also shortage of mental health workers in West Africa[17].

The first Ebola case appeared in December 2013 in a village of Guinea while the first laboratory confirmation was done in March 2014. It took four months from first case to laboratory confirmation while the local health authorities were suspecting Cholera or Lassa virus infection. In August 2014, WHO declared it as public health emergency[18].

The public health authorities remained unsuccessful to tackle a familiar disease agent. There were different parameters which make this outbreak the most serious public health issue of recent times. These parameters include weak health systems, absence of disease preparedness, lack of equipped laboratories and trained medical staff, poor disease awareness, lack of community engagement, fear and misinformation about the disease, absence of antiviral drug or vaccine and lack of research[19].

After the Ebola outbreak, there is a dire need to prepare ourselves to face any national or global health risk. United Nations Sustainable Development Goal 3 stresses the strengthening of early warning, risk reduction and management of national and global health risks[20].

Conflict of interest statement

We declare that we have no conflict of interest.

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