


Immunization against dengue virus infection is coercive: A timely call

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Abstract

Background: In context, the dengue virus causes dengue fever, which is spread by mosquito bites. About 22,000 people every year lose their lives as a direct result of it. Dengue fever has been on the rise recently, and its spread has alarmed health officials throughout the world.

Discussion: Vaccination is essential for the prevention and management of dengue cases because there is currently no particular cure against dengue virus. The current dengue epidemic calls for urgent action in the form of immunization. However, there are serious drawbacks to using existing vaccines like Dengvaxia. Besides, the Qdenga vaccine has not yet been approved by the FDA in the United States. On the other hand, positive results from a phase II randomized and controlled clinical study of the TV005 tetravalent live-attenuated dengue vaccine were recently reported in Bangladesh. Only an effective vaccination can drastically lower dengue infection and mortality rates.

Conclusion: The development of safe and effective vaccination, as well as their correct dissemination, is an essential requirement for the people of Bangladesh and the rest of the globe, and we concentrated on this critical problem in this article.

KEYWORDS

aedes mosquito, dengue, dengue vaccine, immunization, viral infection

Dear Editor,

Dengue fever or breakbone fever is caused by the dengue virus (DENV). It has become a threat to public health in the recent years. It is mostly spread by *Aedes* mosquitoes. DENV, a flavivirus in the species DENV, genus *Flavivirus*, and family *Flaviviridae*.¹ It is a virus with positive (+) stranded RNA. DENV-1 to DENV-4 are four antigenically distinct serotypes with various genotypes having three structural proteins and seven nonstructural proteins in their structure.² In 2007, a newly identified fifth serotype (DENV-5) was

detected in a patient's blood in the Malaysian state of Sarawak.³ Dengue affects 400 million people worldwide annually, killing 22,000 people. More than 100 tropical and subtropical countries have reported dengue infection.⁴ With the upsurge of laboratory-confirmed cases and fatalities in 2023, the DENV outbreak in Bangladesh has taken an alarming turn. As of September 13, 2023, Bangladesh has reported 767 fatalities from this mosquito-borne disease. According to the public health authority of Bangladesh Directorate General of Health Services (DGHS), 2944 patients were

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admitted to the hospital with the dengue fever till September 13, 2023.⁵ Environmental factors like unusual rainfall, elevated temperatures, and humidity may have caused the increased population of *Aedes* mosquitoes. Hence, recent upsurges may be attributed to environmental factors as well new dengue serotype, DENV-4, has been observed in the current dengue breakout in addition to serotypes DENV-1 and DENV-3, and it appears to be more severe than other serotypes.² The prevention and management of DENV infection now depend heavily on effective vaccination. Vaccination will help in prevent new dengue infections, reduce severe cases and fatalities, reduce the burden on the healthcare system, and build herd immunity.⁶

Dengue is a zoonotic disease that has two transmission cycles: mosquitoes carrying the virus from nonhuman primate–nonhuman primate transmission and mosquitoes carrying the virus from human–human transmission.⁷ Depending on the viral load of the mosquito's blood meal, the virus may or may not spread from human to mosquito. Female *Aedes aegypti* and *Aedes albopictus* mosquito species are the main vectors of the virus. Although *A. aegypti* is linked to the majority of infections, cases of *A. albopictus* induced dengue infection is also growing. These mosquito species typically reside indoors and are active throughout the day.^{8,9} It has been reported that transmission can occur during pregnancy, during blood transfusions, through breast milk, and during organ transplantation.¹⁰ The effect of DENV infection ranges from asymptomatic or mild and self-limiting fever to a severe, potentially fatal illness. A febrile illness with one or more of the following symptoms is referred to as symptomatic dengue: high fever >40°C, headache, retro-orbital pain, nausea/vomiting, myalgia, arthralgia, and rashes.¹¹ Currently, there is no globally approved vaccine available for DENV infection. The supportive and symptomatic treatment is the ongoing treatment approach. Some antiviral drugs may lessen the severity of infection. However, the mutation of the DENV creates a problem with the proper efficacy of the drug.^{12,13}

Following the Second World War, dengue became a public health concern in Southeast Asia. Although the Second World War contributed to widening the geographic distribution of DENVs and their vector, it was postwar urbanization in Southeast Asia (SEA) that created the perfect environment for the transmission of the virus.¹⁴ 1.3 billion people out of 3.5 billion people living in the SEA Region are at risk of contracting dengue fever. Dengue cases in the SEA region increased by 46% from 2015 to 2019.⁸ In the year 2023, the DENV outbreak has already broken the previous records. Bangladesh's authority DGHS has recorded a total of 145,335 dengue cases and 134,421 recoveries so far this year with more than 700 deaths, which is only expected to grow.^{2,3} The high transmission of dengue in the rural and underdeveloped parts of Bangladesh is a matter of concern.

Given the gravity of the present circumstances, there is a pressing requirement for a robust vaccine to combat this lethal virus and halt the impending epidemic, as vaccines are the most efficient means of preventing viral infections.¹⁵ There are few existing vaccines like Dengvaxia available in the market but there are safety

concerns related to it.¹⁶ This vaccine is only recommended for those previously infected, leaving others vulnerable.¹⁷ Clinical trials have demonstrated that dengvaxia protects against dengue fever caused by any of the four DENV serotypes. Dengvaxia is approximately 80% effective against the outcomes of hospitalization for dengue, severe dengue, and symptomatic dengue with virological confirmation.¹⁸ Dengvaxia has the ability of the virus to raise the risk of severe dengue fever in people who have never had the illness before. Postapproval studies brought attention to this risk, which prompted regulatory actions in certain nations. The cost of Dengvaxia is also a matter of concern for the developing and under developing nations.¹⁹ Qdenga vaccine may be a potential vaccine that is active against all the serotypes of DENV.^{16,20} Indonesia has already approved C²¹; however, Qdenga has yet to receive the approval of the US FDA.²² A study consisting of 20,071 participants from Asia and Latin America showed that TAK-003 or Qdenga was effective against symptomatic dengue in dengue-endemic countries. Researchers observed the overall vaccine efficacy around 80.9% in the safety population.²³ It can be administered by both previously infected individuals and healthy individuals without prior dengue exposure.²⁴ Recently, phase II randomized and controlled clinical trial of TV005 tetravalent live-attenuated dengue vaccine have been conducted in Bangladesh. Researchers assessed 200 volunteers in four age cohorts from 1 to 49 years old. They received either vaccine or placebo over 3 years timespan. The study concluded that TV005 is well tolerated in terms of safety, immunogenicity, and 3-year durability.²⁵ Two randomized, controlled clinical trials with 319 participants showed that TV005 is the leading a contender for a tetravalent dengue vaccine that completely protects against infection with DENV2 and DENV3.²⁶ Research is still going on regarding the safety and efficacy of TV005 worldwide. Global vaccine deployment can curb disease spread and future outbreaks. The world has already witnessed the effectiveness of vaccines for infectious diseases like COVID-19.²⁷ Due to the alarming number of deaths and rising cases, Bangladesh as well as the low- and middle-income countries are in desperate need of an effective vaccine to fight against the DENV. Bangladesh has struggled to cope with the COVID-19 pandemic.^{28,29} Among these circumstances, the increased number of hospitalizations will definitely create an enormous burden on the public health sector. An effective and safe vaccine can be the solution to this fatal dengue outbreak.

To conclude, the public health sector of the entire world is still suffering from the devastating coronavirus outbreak. This new upsurge will put more strain on the public health sector. So, the development and dissemination of an effective and safe vaccine for DENV infection is an urgent need for the people of Bangladesh along with the entire population of the world.

AUTHOR CONTRIBUTIONS

Iftekhar Ahmed: Conceptualization; writing—original draft. **Rayhan Ahamed:** Conceptualization; writing—original draft. **Shamsun Nahar:**

Writing—original draft. **Lazima F. Bari**: Writing—original draft. **Syed M. R. Dewan**: Writing—review and editing; supervision. All authors have read and approved the final version of the manuscript.

ACKNOWLEDGMENTS

The authors express their appreciation to the worldwide community of medical researchers.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

TRANSPARENCY STATEMENT

The lead author Syed M. R. Dewan affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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How to cite this article: Ahmed I, Ahamed R, Nahar S, Bari LF, Dewan SMR. Immunization against dengue virus infection is coercive: a timely call. *Health Sci Rep.* 2024;7:e2170. doi:10.1002/hsr2.2170