Risk Evaluation and Mitigation Strategies for Potential Outbreaks of Adenovirus Infection: Evidence From the Recent Incidences in West Bengal, India

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ABSTRACT: Recent outbreaks of highly virulent and pathogenic viruses such as COVID-19, monkeypox, and Nipah virus have prompted global concerns. Another threat has emerged in West Bengal, India, in the form of Human Adenovirus (HAdV), particularly affecting children and immunocompromised individuals. The DNA virus HAdV can cause respiratory, liver, renal, and neurological issues. Politically unstable areas with military and medical camps and refugee communities are at risk because they spread in densely populated areas. Due to its rapid mutation and dissemination, the virus represents a global threat. Although scientists have developed vaccines for specific serotypes of HAdV, their primary application is limited to military contexts. Antiviral and immunotherapy research is continuing, but treatment choices are limited. Public awareness programs and hygiene measures are essential to preventing a global pandemic. Governments should invest in healthcare infrastructure and diagnostics, and researchers should focus on developing vaccines and therapies. The West Bengal outbreak is a clear reminder that governments, healthcare professionals, and researchers must work together to control and prevent HAdV. To effectively comprehend and address this rising viral threat, it is imperative to engage in further research and documentation.

KEYWORDS: Adenoviridae, Adenovirus, Adenoviridae infections, disease outbreaks, epidemiology

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In recent years, viruses with increased virulence and pathogenicity have emerged; COVID-19, monkeypox, and the Nipah virus are the most noteworthy.[1-3] Now, another virus called Human Adenovirus (HAdV) has shown up in West Bengal, India. It's causing more deaths among children there.[4] HAdVs are DNA viruses that can infect the respiratory system and be fatal in immunocompromised individuals and those undergoing allogeneic transplants.[5] Symptoms include liver and kidney problems, neurological issues, and respiratory, digestive, and eye complications. However, it usually goes away on its own for generally healthy people. This virus spreads more easily in crowded places like military camps.[6] It can be transmitted through the air, touching contaminated surfaces, or contaminated food and water. It can survive outside the body long and is not easily killed by disinfectants.[5] The current political unrest has led to more military camps, hospitals, and refugee camps, making it easier for HAdV to spread.[7] The global healthcare system is struggling due to the COVID-19 pandemic, with supplies, equipment, and healthcare worker shortages.[8-11] This makes it even more dangerous if the adenoviral infection spreads widely. The outbreak in West Bengal, India, is a warning to the world, and local and international governments must take action. Scientists, epidemiologists, and policymakers should work together to control this epidemic immediately.

Adenoviruses were first identified in 1953 in adenoidal tissue.[12] Since then, this virus is found to infect people globally throughout the any time of a year. Adenovirus causes severe respiratory infections with a mortality rate between 27% and 45%. When dealing with pediatric patients, this proportion might be raised. The infection incidence among immunocompromised individuals ranges from 3% to 21%, with a 7.7% to 38% mortality rate.[13] Depending on a person's age, immunological condition, and demographic factors, the signs and symptoms of an adenovirus infection will vary.[14] Pneumonia and diarrhea are the leading causes of newborn mortality, although upper respiratory tract infections, pharyngooconjunctivitis, and hemorrhagic cystitis are more prevalent in older children.[14] Significant symptoms vary from serotype to serotype. The most prevalent infections are pharyngoconjunctival fever for serotype 3, conjunctivitis for serotypes 8, 19, and 37, adenoviral pneumonia for serotypes 3, 7, 14, 21, acute gastroenteritis for serotypes 40 and 41, hemorrhagic cystitis for serotypes 11 and 21, and tubulointerstitial nephritis and hemorrhagic cystitis for ser Serotypes 7 and 14 are primarily responsible for one-fifth of all infections.[5] Currently, 88 types of HAdV have been isolated which are classified in 7 group from A to G. 57 of them are classified into HAdV-D (group D).[15] According to Centers for Disease Control and Prevention (CDC) 2,138 cases were identified as adenoviral infection during 2003 to 2016. But in 2014, Formal infected case surveillance was started by United States After that the numbers risen 269 in 2014 and 362 in 2016.[16] But in recent years, infection

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cases found in hundreds in several Asian population and most of them were infected by serotype 7. Among 21,000 US military trainees' samples between 2004 and 2009, who were suffering from febrile respiratory illness 63.6% were confirmed adenovirus infection.[5,17] Last year at least 300 children of 34 countries were shown positive result in HAdV test. In recent weeks, there has been a rise in the number of children in West Bengal (Kolkata), India exhibiting symptoms similar to seasonal flu. It has been found adenovirus is associated with this illness. When it comes to the symptoms, the first sign is a slight fever, followed by a rise in body temperature to between 102°F and 103°F.[18] Children may also experience diarrhea in addition to throat infections and stomach-aches when they have gastroenteritis.[18] Also, several of the children are showing signs of respiratory distress. In the state's major hospitals, between 500 and 800 new acute respiratory illness (ARI) cases with the same symptoms are documented daily.[19] There have reportedly been 10 999 cases of children being diagnosed with ARI, as stated in a statement released by the administration of the state.[20] Since January, around 32% of samples have tested positive for adenovirus, when at this time of year, this ratio is generally below 10%.[21] Transmission rate is higher this year. Several media sites have reported that the unofficial death toll is around fifty.[18] From January 1, 2023, to March 15, 2023, the authority recorded more than 12,000 adenovirus infection cases and 19 related deaths in West Bengal with or without other co-morbidities. Also, they reported more than 3,000 hospital admission of children with severe flu-like symptoms in West Bengal during the first quarter of 2023.[4]

People of all age and different class of demography has reported infected by this virus and create a severe illness to young children, immunocompromised people and people who spent their time in crowded places.[22] This increased transmissibility and the fatality rate of adenovirus infection is frightening for the world's population. While COVID-19 is underway, another viral epidemic will pose a massive danger to the healthcare system, as the health burden and distress among the general community will escalate. Due to past COVID-19 infections, immunocompromised individuals are more vulnerable to HAdV; 750 million people are included in this risk group.[23] HIV causes immunodeficiency, and the number of infected individuals has climbed to 38.4 million, including 1.7 million under-15 children.[24] This virus is readily transmissible within the dense population of South Asia. This region also comprises several refugee camps and overcrowded slums, which are distinguished zones for transmitting this virus. The armed forces of these nations are dispatched to various parts of the globe for various development projects in the least developed countries and peacekeeping operations in conflict zones. In both instances, the likelihood of HAdV transmission increases by a factor of many since the least developed nations have a poor diet and, thus, low immunity. The war-torn area has refugee camps, military bases, and medical facilities. These elements will substantially enhance infectivity and virulence. HAdVs have several serotypes, and their rapid spread and global dissemination can result in the emergence of more lethal serotypes.

For serotypes 4 and 7, the U.S. Food and Drug Administration approved vaccination is available, although it is only intended for the military. This vaccination is effective and safe for avoiding illness in military training camps. Other than immunization, there is no particular therapy for this virus. Antiviral medicines are often prescribed to immunocompromised individuals. Cidofovir, a nucleotide analog of cytosine, looks to be an effective antiviral medication against this virus.[5] Using 2 or more doses of cidofovir decreased the death rate from 75% to below 20%.[25] Low bioavailability and nephrotoxicity are nevertheless 2 of its shortcomings. Several antiviral medications, including ganciclovir, ribavirin, vidarabine, and foscarnet, include no active compounds that are effective against adenovirus.[5] Despite being an adjuvant treatment, intravenous immune globulin has demonstrated promising efficacy against adenovirus. In addition, research is being conducted on T-cell-mediated immunotherapy, an antiviral therapeutic option.[26,27]

Adenovirus, commonly known as a self-limiting viral illness, is on the threshold of a global outbreak if no action is taken. It is time to take decisive measures to control and prevent this epidemic; if not, it has the potential to be as devastating as the COVID-19 pandemic, which brought the globe to its knees. As a result of prior experience with COVID-19, the public is now familiar with cleanliness procedures.[28,29] NGOs, government institutions, and international organizations should immediately relaunch awareness-raising campaigns. People must follow practices such as frequent handwashing with soap for 30 seconds, avoiding contacting eyes, mouth, and nose with unclean hands, and maintaining a safe distance from individuals exhibiting HAdV infection symptoms.[30] Infected persons must remain home, whereas HAdV-infected hospitalized patients must be isolated from immunocompromised patients. Healthcare professionals must take measures when treating these people to avoid spreading the disease to non-infected persons. Most HAdV infections in healthy adults and children are self-limiting. Hence, it is possible to prevent the virus from causing lethal epidemics by maintaining social and individual cleanliness. Nonetheless, immunocompromised individuals, neonates, and infants are susceptible to death from this virus. Hence, these more vulnerable populations must be addressed with additional precautions when a local epidemic emerges. Due to their elevated risk, allogeneic transplant patients must keep on monitoring. In schools, childcare centers, and hospitals, frequent handwashing is crucial.

Government Should expand the infrastructure and technical facilities of the healthcare system. Hospitals should have many intensive care unit (ICU) ventilators to assist patients with respiratory system problems, the most common symptoms of a severe HAdV infection. The diagnostic system must

be supported by qualified personnel and appropriate tools. The correct diagnosis of influenza-like illness should inform the organization of the public education campaign. As this infection is a self-limiting viral infection with lethal effects on immunocompromised individuals, various programs designed to increase immunity will help reduce mortality. In this regard, physical activity and a nutritious diet will be beneficial.[31] Due to the rapid spread of this virus in close quarters, densely populated neighborhoods, and medical centers, military camps should undergo frequent HAdV examinations and screenings. A dedicated institution must meticulously document incidences, case data, and mortality to comprehend the virus and its tendencies fully. The production of vaccines with the potential for efficacy and safety should be prioritized. However, it is essential to establish a safe and effective treatment strategy and medication for symptomatic relief. For a thorough understanding and to determine the future direction of treatment for this viral infection, the researcher should focus on its characteristics, signs and symptoms, and mutation trend.

The recent epidemic of Human adenovirus infection in West Bengal, India, with a high transmission rate and infant mortality, has caused widespread alarm and a substantial health burden in the context of the continuing COVID-19 pandemic. With concurrent viral infection, a deficient healthcare system, and a wide vulnerable population, this virus can become more lethal. Thus, the government should take the required actions to prevent this new viral epidemic. Researchers should perform further investigations to produce vaccines and treatments against this virus. To elucidate the treatment and prevention of adenovirus infection in humans, further study and careful documentation are required.

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RS and ASMR, conceived the study and wrote the first draft. N and MRI revised and gave intellectual inputs in the manuscript. MRI conceived and supervised the work. All the authors approved the final version for submission.

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Ethics Statement
It was an analysis of online available aggregate data. No Ethical approval was needed.

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