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Influenza A (H1N1) 2009 Strain: A Hidden Circulating Danger

KM Poornima[1], Prashasti Upreti[2], Narotam Sharma[3]

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Abstract

Starting from the encounter of the first case of H1N1 influenza virus in the year 2009 reported from the town of Mexico to its lay out across the globe; H1N1 virus has affected thousands of people in India. Since then this seasonal virus keeps on mutating (S181T and I312V) becoming more and more harmful and dangerous causing various serious complications. With its ability to regenerate and mutate at a faster rate this virus has RNA as its genetic material which is a combination of three different species; humans, avian and swine, targeting a larger spectrum of hosts turning out to be extra severe. Evidence have shown that the elderly and children are the most affected by the virus due to low immune response by the body. Common symptoms of H1N1 include fever, chills, sore throat, etc. The situation may turn fatal if left untreated.

Keywords: H1N1 Influenza; Pandemic; Mutation; Strains.

Introduction

H1N1 influenza is popularly known as swine flu, hog flu and pig flu.[1] H1N1 represents two important proteins present on the surface of the virus namely hemagglutin (HA) and neuraminidase (NA) responsible for binding to the receptors on the target tissues and for cleaving the sialic acid in order to release the progeny virus respectively.[2] As the name suggests it is a type of influenza which is caused by certain viral strains capable of infecting the swine population.[1] Mexican town of La Gloria in Veracruz witnessed the first case of H1N1 swine flu and was later declared a global pandemic by WHO from 11 June 2009.[3] The virion of influenza A virus is 80 to 120 nm in diameter and the viral RNA genomic size is of approximately 13.5 kb which is responsible for this communicable disease and belongs to the family of orthomyxoviridae.[4] Its genome has 8 segmented regions; one from human influenza A H3N2, two from avian influenza A H1N1 and five segments from swine H1N1, encoded by 11 different proteins.[4,5] Due to high susceptibility of the virus to get mutated, its severity has increased many folds thereby serious monitoring is essential to keep a track of the genetic variability altering the behavior of the virus.[6] The 2009 H1N1 is a human origin influenza virus detected in pigs however events shown reverse zoonosis cases since the pandemic.[7]

Epidemiology according to World Health Organization (WHO) more than 318,925 cases had been reported with a total of 3917 deaths in the year 2009. The severity of pandemic (H1N1) 2009 is still largely unknown, due to the fact that the situation is still evolving, and it may further increase because of more vulnerable populations being affected.[9] In India, this pandemic of 2009 affected thousands of people with 27236 cases and 981 deaths in the year 2009 with the first case reported from Hyderabad, Andhra Pradesh and eventually radiated across the

Author's Affiliation: [1,2]Research Trainee, Department of M Sc Microbiology, Graphic Era Deemed to be University, Dehradun, Uttarakhand 248002, India. [3]Head of DNA Labs, A Centre for Applied Sciences, Jhajra, Dehradun, Uttarakhand 248007, India.

Corresponding Author: Narotam Sharma, Senior Scientist and Head, DNA labs A Centre for Applied Sciences, Jhajra, Dehradun, Uttarakhand 248007, India.

E-mail: sharmanarotam5@gmail.com

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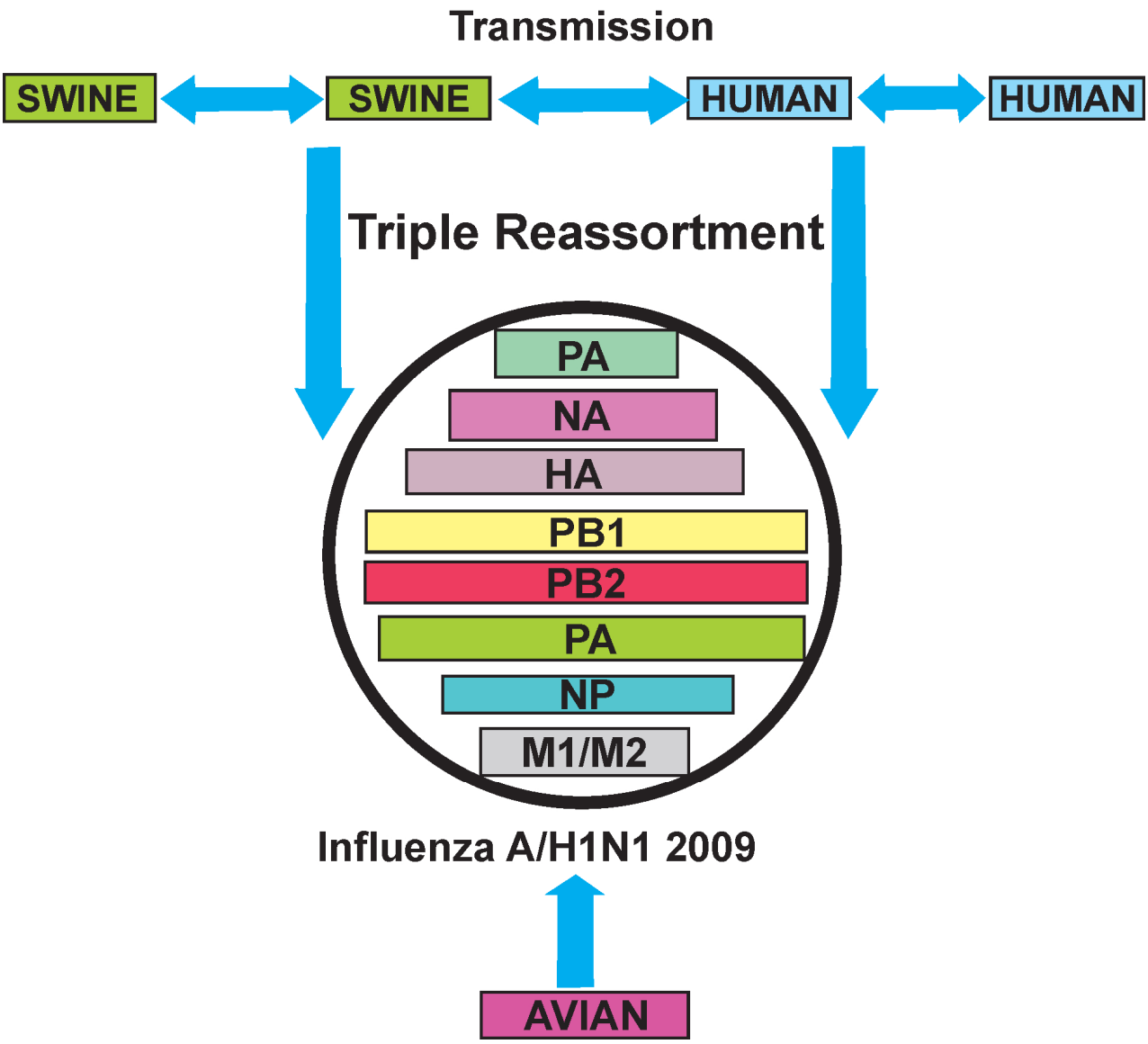

Fig. 1: Transmission of H1N1 in various hosts and evolution of influenza A/H1N1 2009.[8]

world accounting 20604 cases and 1763 deaths in the year 2010 and so far more than 100 thousand labs confirmed cases with over 7700 deaths.[10] Data implies that the number showed a spike in winter season. 2017 proved to be a crucial year when the virus started spreading rapidly across the country showing varying epidemiological features observing two peaks affecting largely the elderly and children.[11]

Molecular Characteristics of H1N1 2009 strain- The involvement of pigs had a prominent role in the emergence of pandemic 2009 (H1N1) and in the new outbreaks. The usual swine influenza viruses altered with a current human A (H3N2) influenza virus and American lineage avian influenza virus resulting in an appearance of a triple reassorted H3N2(rH3N2) swine virus persisting in the pigs found in North America. The successive rearrangement between the rH3N2 virus and original H1N1 swine virus is likely to be resulted in the emergence of further triple reassortant swine A (H1N1).[13]

The 8 segmented viral genome consisting of 8 negative sense single stranded RNA contain 12 proteins. The prominent ones include Hemagglutinin (HA), M proteins (M1 and M2), Neuraminidase (NA), Nucleocapsid Protein (NP), Non-Structural proteins (NS1 and NS2), and polymerase subunits (PA,PA-X,PB1-F1,PB1-F2,PB2) and two surface glycoproteins namely Hemagglutinin (H1 to H18) and Neuraminidase (N1 to N11).[14] α2-6SAL and α2-3SAL are the two receptors to which the H1N1 virus binds.[15] According to an evolutionary analysis both HA and NA genes are evolved into five different assembleges or clusters.[16]

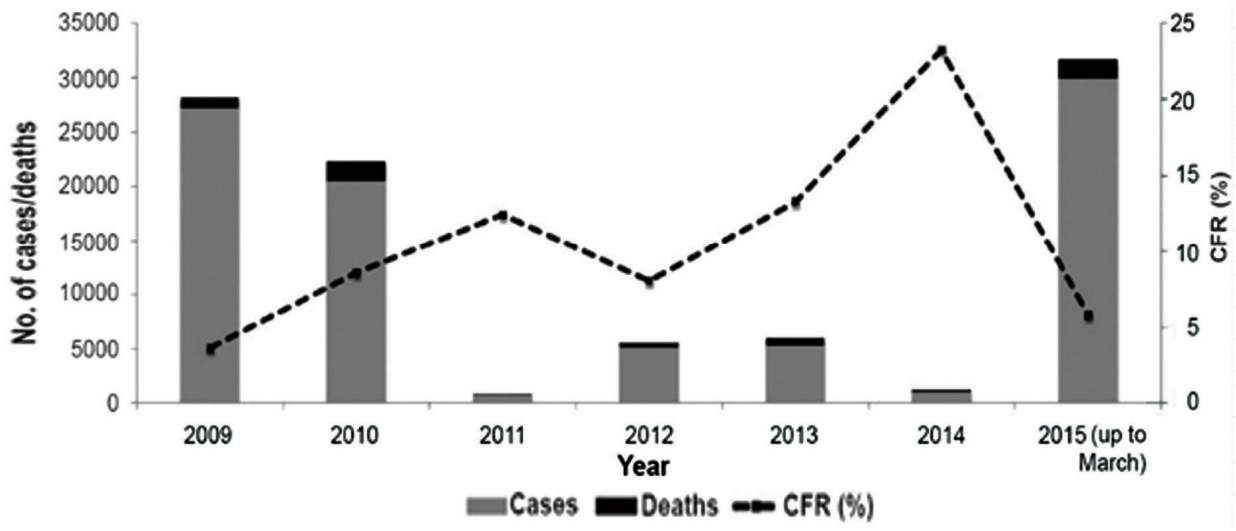

Fig. 2: Reported number of influenza A H1N1pdm09 cases and deaths, 2009-2015. CFR, case fatality ratio.[12]

Table 1: Different clusters present in H1N1 2009(16).

CLUSTER-1	strains from avian hosts
CLUSTER-2	strains from North American swine
CLUSTER-3	strains from Eurasian swine
CLUSTER-4	seasonal human H1N1 lineage
CLUSTER-5	pandemic 2009 strain

Antigenic sites: Viruses have the most varied antigenic sites that are only recognized by specific antibodies. In the case of H1N1, the H1 molecule of haemagglutinin has 5 antigenic sites that are Sa, Sb, Ca1, Ca2 and Cb with some of the sites present near to the Receptor Binding Site (RSB).[17] The antibodies are directed to each of the two strain specific (Sa and Sb) and antigenic sites (Ca and Cb) of the virus HA. However according to a study viruses showed alterations in the amino acids in the antigenic sites. Sa has the sites S157L, L161I and S164T; Ca1 has the sites R205K and Cb has S74R(50).[18]

Mutation: The H1N1 strain from India showed two mutations (S181T,1312V) accompanied by 17 mutations (V106I,N248D) found in the NA domain in the 2009 H1N1 lineage.[19] Whereas the Assam (H1N1) pandemic 2009 strains showed mutation in the HA genes (E391K, K180Q and S202T).[6]

Drug Resistance: The high susceptibility of H1N1 virus towards mutation attributed to its drug resistance property making the treatment procedures more complex and difficult to achieve. A single mutation in the neuraminidase (H275Y) made the virus Oseltamivir resistant without affecting the susceptibility to Zanamivir which was also detected in the NA gene of A/Assam H1N1. Evidence showed multidrug resistant strain of an influenza A 2009 H1N1 due to the occurrence of two mutations (H275Y,I223R).[20,6]

Circulating Dangers: Influenza A virus is susceptible to antigenic shift i.e (genome reassortment) and antigenic drift (accumulation of mutations). This makes the virus highly dangerous and difficult to treat. Instances have shown that the origin of new strains and subtypes of the virus are immune to previously formed antibodies in people who already got infected with the virus earlier. This is so because of the gradual changes in the genome imparting new antigenic properties to the virus that can't be recognized by the antibodies formed in response to the novel influenza virus. As a result people have very little or no protection against the on going or new upcoming viral strains paving way to more future outbreaks.[32] ln India, The 2009 pandemic of H1N1 influenza was a huge setback affecting not only the urban regions but also creating a panic situation in the rural areas of the country. The Western parts of the country were suffered drastically with Gujarat reported with more than 7600 cases along with approx. 430 deaths. This was followed by Maharashtra with around 6100 cases and 780 deaths. Rajasthan witnessed with approx. 3620 cases and over 140 deaths.[11]

Transmission: The symptoms of this viral infections and that of swine are similar to each other, most likely due to reassortment of the viral RNA structure allowing to human to human transfer.[4] The high transmission rate and spread of the virus is due to the ability of the virus to sustain in cold temperature that show coagulation during winter season which further expediate the spread of the

virus.[21] Similar to most of the viruses, it spreads like the other seasonal flu and can be transmitted to humans through mucous membranes (nose, eye or mouth) and direct touch. It can also transmit through respiratory droplets.[22]

Prognosis: The symptoms are indistinguishable to those of influenza including fever, chills, myalgia (muscle pain), sore throat, weakness, coughing, severe headache, abdominal pain, photophobia (sensation of pain on light exposure). Severe case of H1N1 may result in following medical conditions: Respiratory Distress Syndrome (RDS), Refractory Hypoxemiahypoxemia (RH), acute respiratory failure, Cardiac dysfunction, Secondary bacterial infection, Acute renal failure and Multiple organ failure.[27]

Diagnosis: There are various guidelines for the diagnosis of H1N1 virus issued by the WHO and Centers for Disease Control and Prevention (CDC) . Sample from nasopharyngeal swap followed by throat swab and tracheal aspirates are required for a confirmed and valid diagnostic test. Sample procurement is required within the first four days of symptoms.[23] The first case of H1N1 2009 was detectet by CDC using real time reverse transcriptase PCR that was originally designed for the detection of tr-SIV infection.[24] Various techniques are being used in the laboratories for the detection and diagnosis of the virus including Rapid Influenza Diagnostic Tests (RIDTs), Reverse Transcription Polymerase Chain Reaction (RT-PCR), fluorescent antibody tests, and antigen characterization of cultured virus strain.[25] DFA, R-mix culture and xTag RVP tests are the other methods that detected the novel H1N1 strain however their sensitivity showed variations.[26]

Prevention and Treatment: The spread of H1N1 Swine flu can be prevented by proper hygiene, avoiding person to person physical contact, proper hand washing with antibacterial soap, using alcohol based hand sanitizer, wearing face mask, increasing water intake.[28]

Some of the documented antiviral medications include: Zanamivir, Oseltamivir and Peramivir that should be taken within 2 days on the onset of symptoms.[4] However studies have shown that due to mutations in the viral genome; the virus has acquired resistance to some of the existing drugs. Rimantadine and Amantadine belong to the class of M2 ion channel protein inhibitors that block the transport of H+ ions through M2 protein channel obstructing the entry into the target cell. The other class is of NA inhibitor that trigger the inhibition of the release of new viral particles from the affected cells.[29]

Vaccine: Vaccination is another measure that can be taken to prevent the infection. According to the WHO Global Action Plan (GAP) for Influenza Vaccines, the vaccine production capability has been strengthen and regulated. There has been a switch from trivalent to quadrivalent seasonal vaccines with the use of high dose of antigen for the elderly. Also adjuvants are used to enhance the working of the vaccines. Now a days nanoparticles and chimeric have been increasingly used in phase-1 clinical trials.[30] In 2009 the two forms of vaccines designed for providing protection against the H1N1 swine flu were "live attenuated" and "dead virus.[28] The antiviral action of Iron Oxide Nanoparticles (IO-NPs) against the H1N1 influenza has been investigated aiming to synthesize glycine coated iron oxide for its proposed evaluation.[31]

Discussion

Amongst the other seasonal flu H1N1 influenza virus is the most efficient in the terms of replicating and evolving as it is evident due to the regular instances of variations seen in its genomic structure. Affecting thousands of people every year, it is transmitted through virus borne aerosols and physical contact, hence proper monitoring is required for Swine influenza viruses (SIVs) in pigs and their zoonotic potential has to be assessed. The common symptoms include fever and chills while severe cases have shown conditions like cardiac dysfunction, multiple organ failure etc. With some of the available drugs for the treatment, there are some vaccines[name the vccine?] being made and modified time to time as required due to the consistent mutations and variations seen in the virus.

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