SWINE INFLUENZA AND THE EMERGING PANDEMIC INFLUENZA A (H1N1)

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Swine Influenza, (also called swine flu, hog flu and pig flu), is caused by an enveloped and segmented RNA virus belonging to Family Orthomyxoviridae. This family has 3 genera of influenza viruses – Influenza A, B and C. All the 3 genera can cause human influenza and 2 genera, viz., Influenza A and C can cause influenza in pigs, with Influenza A virus commonly producing disease in swine and Influenza C rarely. Influenza B virus has not been reported in pigs. The subtypes of influenza are defined based on the glycoprotein peplomers, Haemagglutinin (H) and Neuraminidase (N), present on the envelope of the virus. Five Influenza A virus subtypes have been identified in pigs- H1N1, H1N2, H3N1, H3N2, and H2N3. Of these, the subtypes H1N1, H3N2 and H1N2 are the most common strains worldwide. Swine Influenza (SI) is common in pigs in the midwestern United States, Mexico, Canada, South America, Europe (including the United Kingdom, Sweden and Italy), Kenya, Mainland China, Taiwan, Japan and other parts of eastern Asia.

The H1N1 form of swine flu is one of the descendants of the strain that caused the 1918 Spanish flu pandemic in which approximately 1 billion people were affected and 50 million people died. During this pandemic, Swine Influenza was first proposed to be a disease related to human influenza when pigs became sick at the same time as humans, contracting the infection from humans. The first identification of an influenza virus as a cause of disease in pigs occurred about 10 years later, in 1930. Phylogenetic analysis of the strains of influenza in humans, birds and swine suggests that the 1918 outbreak in humans followed a reassortment event within a mammal, but the exact origin of the 1918 strain remains elusive. Besides persisting in pigs, the descendants of the 1918 virus have also circulated in humans through the 20th century, contributing to normal seasonal epidemics of influenza. However, direct transmission from pigs to humans was rare. Nevertheless, the retention of influenza strains in pigs after these strains have disappeared from the human population might make pigs a reservoir wherein influenza viruses could persist, later emerging to reinfect humans once human immunity to these strains has waned.

The Influenza A (H1N1) outbreak in humans is due to a new strain of Influenza A virus subtype H1N1 that contains genes closely related to Swine Influenza. The origin of this new strain is unknown. However, the World Organization for Animal Health (OIE) reports that this strain has not been isolated in pigs. This strain can be transmitted from humans to humans, causing symptoms of influenza. Even though many of the genes of this H1N1 strain of virus were very similar to influenza viruses normally occurring in pigs in North America, studies have shown that this new virus was very different. This new strain of virus, involved in the present outbreak of influenza in humans, is a reassortment of several strains of Influenza virus subtype H1N1 that are found separately, in humans, birds and pigs. Pigs can become co-infected with various strains of influenza viruses and act as 'mixing vessels', resulting in the emergence of potentially dangerous influenza virus strains, capable of producing a pandemic, as a result of the reassortment of genes from different strains. Hence the virus involved in the pandemic is now identified as Influenza A(H1N1). The current outbreak of H1N1 virus infection can be transmitted from person to person and is spreading fast via travelers to all corners of the globe. This situation has prompted the World Health Organization (WHO) to set its pandemic alert to the maximum level of 6, indicating that a global pandemic is underway. The outbreak has affected almost 30,000 people in 74 countries and claimed 145 lives. In India, 23

confirmed cases of SI in humans have been reported so far.

Transmission of the virus

Transmission in swine: The main route of transmission of the virus in swine is through direct contact between infected and uninfected animals, particularly during animal transport and in intensive farming, wherein pigs are raised in close proximity to each other. The direct transfer of the virus can occur through pig-to-pig nasal contact, since the virus is shed in nasal secretions. Airborne transmission through the aerosols produced by coughing or sneezing of pigs is also an important means of infection. The virus usually spreads quickly through a herd, infecting all the pigs within just a few days.

Transmission to humans: People who work with poultry and swine, especially people with intense exposures, are at increased risk of zoonotic infection with influenza virus endemic in these animals. Others at risk are veterinarians and meat processing workers. The 2009 H1N1 influenza virus is not zoonotic swine flu, as it is not transmitted from pigs to humans, but from humans to humans. The virus spreads between humans through coughing or sneezing and through hands after touching objects with the virus on it and then touching their own nose or mouth. Studies have shown that influenza virus can survive on environmental surfaces and can infect a person for up to 2-8 hours after being deposited on the surface. As per the joint Food and Agriculture Organisation (FAO)/ WHO/ OIE statement on Influenza A H1N1, these viruses are not known to be transmissible to people through eating processed pork or other food products derived from pigs. Heating pork to 75-100^0 C readily destroys the virus. The flu in humans is most contagious during the first 5 days of the illness, although some people, most commonly children, can remain contagious for up to 10 days.

Signs and Symptoms

In swine: The incubation period is 24-72 hours. Onset of the disease is abrupt, often appearing in many animals in a herd at the same time. The affected animals show fever (>42^{0}C), apathy, inappetance, huddling with reluctance to move, respiratory distress, paroxysmal coughing, sneezing, rhinitis with nasal discharge, laboured breathing and bronchial rales at auscultation. After 3 days, the swine usually recover. Some animals develop severe bronchopneumonia which may result in death. In some cases, the infection can cause abortion. Although the mortality is usually low, (around 1-4%), the virus can produce weight loss and poor growth, causing economic loss to farmers.

In humans: The symptoms include fever, cough, sore throat, body aches, headache, chills and fatigue. In addition, an increased percentage of the present H1N1 infected patients have shown diarrhea and vomiting. In severe cases there may be pneumonia, which may lead to respiratory failure and death.

Diagnosis

In swine: Diagnosis of swine flu can be made by several techniques including fluorescent antibody technique, immunohistochemical test, virus isolation, haemagglutination inhibition coupled to neuraminidase inhibition test, ELISA and reverse transcriptase- polymerase chain reaction (RT-PCR). Sometimes several techniques must be combined to identify subtypes. Preferred samples are nasal or pharyngeal swabs from live animals. Samples must be suspended in glycerol saline and kept at 4^{0}C if they are tested within 48 hours and at -70^{0}C or shipped in dry ice if they are tested after a longer delay. Alternatively, lungs from recently dead or sacrificed animals can be sent under similar conditions. The disease has to be differentiated from Aujeszky's disease, Atrophic rhinitis and pneumonia due to Mycoplasma, Pasteurella or Haemophilus spp.

Blood samples (about 20ml each), taken at the time of onset of disease from affected animals and repeated 2-3 weeks later show 4-fold rise in H1N1 virus specific neutralizing antibodies, in positive cases. Samples of animal origin will be diagnosed at High Security Animal Disease Laboratory, Bhopal.

In Human: The following investigations are done to confirm a suspected case of Influenza due to H1N1 subtype.

a. RT-PCR: confirms the presence and detects the viral load in an individual.

b. Viral culture: throat swab is generally taken to culture the virus from suspected cases. But non-detection of the virus does not rule out the disease.

c. Detection of antibodies: This is a sensitive test and in positive cases there is a 4-fold increase in SI A (H1N1) virus specific neutralizing antibodies.

A timely detection and confirmation of the case can not only save the life of the patient, but also can be helpful in restricting the spread of the disease, as the outbreak has now become a pandemic. India has got facilities for confirmatory diagnosis of suspected human samples at National Institute of Communicable Diseases (NICD- Delhi), National Institute of Virology (NIV- Pune), National Institute of Cholera and Enteric Diseases (NICED- Kolkata) and Regional Medical Research Centre (RMRC- Dibrugarh).

Treatment

In swine: As Swine Influenza is rarely fatal to pigs, little treatment beyond rest and supportive care is required. Infected pigs require a dry, clean, dust free environment. Antibiotics are also essential to treat and control any secondary bacterial infections in influenza-weakened herds.

In Human: Antiviral drugs such as Tamiflu (Oseltamivir) or Relenza (Zanamivir) can be used for the treatment and / or prevention of infection with Influenza A (H1N1) viruses. For treatment, antiviral drugs work best if started soon after getting sick (within 2 days of symptoms). India has a stockpile of 10 million doses of Tamiflu.

Prevention and Control

Prevention of Influenza A (H1N1) has 3 components- prevention in swine, prevention of transmission to humans and prevention of its spread among humans.

Prevention in swine: Methods of prevention include facility management, herd management and vaccination.

Facility management includes using disinfectants and ambient temperature to control virus in the environment. The virus is unlikely to survive outside living cells for more than 2 weeks, except in cold (above freezing) conditions and it is readily inactivated by disinfectants. It is destroyed by heat (75-100°C), chemical germicides such as chlorine, hydrogen peroxide, detergents (soap), iodophors and alcohols, if used in proper concentration for sufficient length of time.

Herd management includes not adding pigs carrying influenza to herds that have not been exposed to the virus. The virus survives in healthy carrier pigs for up to 3 months and can be recovered from them between outbreaks. Carrier pigs are usually responsible for the introduction of Swine Influenza virus into previously uninfected herds and countries and hence new animals should be quarantined. After an outbreak, as the immunity in exposed pigs wanes, new outbreaks of the same strain can occur.

Since in most cases the illness and death associated with swine flu involves secondary infection by other pathogens, control strategies relying on vaccination alone may be insufficient. Moreover, control of Swine Influenza by vaccination has become difficult as the evolution of the virus has resulted in inconsistent responses to traditional vaccines. Vaccination in pigs against Swine Influenza is practiced in Europe and North America, but not in India.

Prevention in humans: Prevention of pig to human transmission: The transmission from pigs to human occurs mainly in pig farms where farmers are in close contact with pigs. Although strains of Swine Influenza are usually not able to infect humans, this may occasionally happen and so farmers and veterinarians have to use a face mask when dealing with infected animals. The use of vaccines on swine to prevent their infection is a major method of limiting swine to human transmission.

Prevention of human to human transmission: Recommendations to prevent the spread of the virus among humans include frequent washing of hands with soap and water or with alcohol based hand sanitizers, especially after being in public. Alcohol based gel or foam sanitizers work well to destroy viruses and bacteria. Anyone with

flu-like symptoms such as sudden fever, cough or muscle aches should stay away from work or public transportation and should contact a doctor immediately to be tested. Social distancing i.e., staying away from other people who might be infected is another method of prevention.

At present there is no vaccine for humans against this recombinant H1N1 strain of Influenza, but several countries have started earnest efforts to produce an effective vaccine. In India, the Indian Council of Medical Research (ICMR) in collaboration with Indian Virology Institute has started work on the development of a vaccine against this new H1N1 strain and the vaccine will be available within 6 months. Meanwhile the Government of India is keeping a close vigil against the spread of the infection in India. All the entry points of visitors from other countries are carefully monitored and all suspected cases are hospitalized for further investigation and treatment.

Conclusion

Swine Influenza is a rarely fatal disease of swine, caused by various strains of Influenza viruses. Swine can act as a 'mixing vessel', when co-infected with strains of influenza viruses affecting other species, resulting in the emergence of potentially dangerous influenza virus strains, capable of starting a pandemic. This new strain of H1N1, involved in the present outbreak of influenza in humans, is a reassortment of several strains of Influenza virus subtype H1N1 that are found separately, in humans, birds and pigs. The World Organization for Animal Health (OIE) reports that this strain has not been isolated in pigs. The 2009 H1N1 virus is not zoonotic swine flu, as it is not transmitted from pigs to humans, but from humans to humans. Hence the virus involved in the pandemic is now identified as Influenza A(H1N1). Due to its rapid spread globally, affecting quite a large number of people, the WHO has given the highest pandemic alert of 6. Efforts are going on in various countries including India, to develop an effective vaccine against this virus. Let us hope this pandemic threat will pass off without assuming catastrophic proportions.

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