

Swine Flu and Its Impact on Public Health

R P Diwakar¹, Pankaj Kumar², Vibha Yadav³, H C Verma⁴

Author Affiliation: ^{1&3}Assistant Professor, Veterinary Microbiology, ⁴Assistant Professor, Veterinary Extension CVSc & AH, Kumarganj, Ayodhya 224229, Uttar Pradesh, India, ²Disease Investigation Officer, Rohtak LUVAS, Hisar 124001, India.

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Abstract

Swine influenza has been recognized as a respiratory disease in swine. Swine influenza viruses belong to the family Orthomyxoviridae, including three genera, Influenza A, B and C. All influenza viruses of significance in swine are type A, subtype H1N1, H1N2, or H3N2 viruses. Influenza A causes moderate to severe illness and affects all age groups of swine and produces a symptom like fever, lethargy, sneezing, coughing and breathing difficulty. The virus infects humans and other animals in addition to pigs. It targets and damages the lining of the respiratory tract, leading to swelling and inflammation. It has also major public health importance by causing numerous respiratory symptoms in both adults and children. Diagnosis of the disease is based on clinical symptoms while confirmation is done via laboratory tests using PCR (polymerase chain reaction) based kits. Antiviral treatment associated with either *zanamivir* alone or in a combination with *rimantadine*, *Oseltamivir* or *amantadine* is considerably important. Control of the virus can be achieved through vaccination, biosecurity measures, decontamination and dietary management. Therefore, appropriate prevention methods should be chosen and employed according to the specific regional context.

Keywords: Control H1N1 Influenza Public Health and Swine.

Introduction

Swine influenza is an acute respiratory viral disease caused by influenza A virus (IAV) of the Orthomyxovirus family that decreases the health and welfare of pigs and results in a significant economic loss for the swine industry worldwide.¹ Etiology of Swine Influenza is complex according to the high genetic variation of the causative viruses, mainly on two glycoproteins: haemagglutinin (H) and neuraminidase (N). The known Swine Influenza

virus strains include influenza C and the subtypes of influenza A virus (IAV) known as H1N1, H1N2, H3N1, H3N2 and H2N3.² Clinical signs of influenza illness in pigs can display a range of severity but often occurs as mild respiratory disease with high morbidity and rapid recovery, with rare fatal cases in pigs. However, the disease has a substantial economic burden as a result of weight loss, reduced weight gain and, in some cases, reproductive failure in infected sows due to high fevers. Further, when associated with other respiratory pathogens,

Corresponding Author: R P Diwakar, Assistant Professor, Veterinary Microbiology, CVSc & AH, Kumarganj, Ayodhya 224229, Uttar Pradesh, India

Email: raj.diwakar74@gmail.com

as part of the porcine respiratory disease complex, it can lead to complicated pneumonia and severe clinical signs.³ In addition, swine influenza poses a threat to public health. Influenza viruses can transmit between pigs and humans, as observed during the 2009 pandemic, when a virus generated by reassortment between two established lineages of swine viruses became globally widespread and reached a pandemic level in humans. The virus then quickly transmitted from humans to swine. Since pigs are susceptible to both avian and human influenza viruses,^{4,5} they have been referred to as the “mixing vessel” of IAV with the potential to generate novel viruses.⁶ This can occur when infection with two or more strains leads to the development of swine, avian and human reassortant viruses that can then be transmitted between pigs and to other species.⁷ However, humans and other mammals can also be directly infected with avian and swine viruses, thus can potentially serve as mixing vessel hosts as well.^{5,8} Swine influenza was described for the first time in the Midwestern US in 1918; this description coincided with the human influenza pandemic.⁹ It was not until 1930 that the first SIV, belonging to the H1N1 lineage, was isolated from North American pigs, which also happened to be the first IAV ever to be isolated.¹⁰ The clinical signs of swine influenza resemble those also observed for humans and are characterized by an acute onset of the disease, fever, inactivity, inappetence, respiratory distress, coughing, sneezing, conjunctivitis and nasal discharge.¹¹

The morbidity rate is usually high and the case fatality rate is low, but more severe outbreaks may be seen and reduced growth rates in young pigs can cause economic losses. In people, clinical cases have tended to resemble human influenza. Most of these cases were not life-threatening, although serious and fatal illnesses do occur.^{9,10} Swine flu can be diagnosed by its clinical sign and in the laboratory through serological tests, detection of the virus by culture, necropsy finding etc. Even though there are various means to control the SI virus such as vaccination, biosecurity measures, decontamination and dietary management, there is no available specific treatment for SI in pgs. However, antibiotic treatment is given to minimized secondary bacterial complications.¹³

History of Swine Flu Virus: The Greeks were familiar with human influenza and the first epidemic was recorded by Hippocrates in 412 B.C. The viruses are now classified in the family of the Orthomyxoviridae, which has a Greek etymology: orthos meaning “standard, correct” and myxo “mucus”.¹⁵ The name influenza comes from the

Italian “influenza dellestelle” because in the middle ages people believed that there was an astrological influence on the disease. Several pandemics stroke the world with the “Spanish flu” of 1918 being the most famous.¹⁶ Although the disease in pigs was described during the following years.^{17,18}

It was first proposed to be a disease related to human flu pandemic, when pigs became sick at the same time as humans.²¹ The first identification of an influenza virus as a cause of disease in pigs occurred about ten years in 1930.²² Those who first noticed the disease in pigs, recognized similarities between the porcine and human disease and suggested they had a common etiology. Later, retrospective serological investigations confirmed that the disease in humans and pigs had been caused by closely related influenza A viruses in both cases. The causative agent was an H1N1 influenza A virus that had possibly derived from a common ancestor.²³⁻²⁵ Until 1997 swine influenza strains were almost exclusively H1N1. Then, between 1997 and 2002, new strains of three different subtypes and five different genotypes emerged as causes of influenza among pigs in North America. In 1997-1998, H3N2 strains emerged.

These strains, which include genes derived by reassortment from human, swine and avian viruses, have become a major cause of swine influenza in North America. In 1999 in Canada, a strain of H4N6 crossed the species barrier from birds to pigs, but was contained on a single farm.²⁶ The H1N1 form of swine flu is one of the descendants of the strain that caused the 1918 flu pandemic. As well as persisting in pigs, the descendants of the 1918 virus have also circulated in humans through the 20th century, contributing to the normal seasonal epidemics of influenza.²⁷ However, direct transmission from pigs to humans is rare, with only 12 cases in the U.S. since 2005.²⁸ In 2009 a new pandemic H1N1 virus (H1N1pdm09) occurred which differed from the earlier known H1N1 viruses.⁸ and since then, this IAV has gradually replaced the seasonal H1N1 virus and began co-circulating with H3N2 causing seasonal influenza epidemics in humans.²⁹

Etiology, Taxonomy and Characteristics: Etiology of Swine Influenza is complex according to the high genetic variation of the causative viruses, mainly on two glycoproteins: hemagglutinin and neuramidase. This swine influenza virus belongs to the family. Orthomyxoviridae, including three genera, Influenza A, B and C.³⁰ SIAVs have been isolated from a wide range of species, including humans, swine, birds, seals, cats, horses and dogs, but aquatic birds are considered the natural

reservoir of IAV.³¹ Swine influenza is caused by influenza A subtypes H1N1, H1N2, H2N3, H3N1 and H3N2. In pigs, four influenza A virus subtypes (H1N1, H1N2, H3N2 and H7N9) are the most common strains worldwide.³² Humans and seals and influenza C viruses have been isolated from humans and swine and usually only causes mild disease in the upper respiratory tract, but do not infect bird. Transmission between pigs and humans have occurred in the past. For example, influenza C caused small outbreaks of a mild form of influenza amongst children in Japan and California. Because of its limited host range and the lack of genetic diversity in influenza C, this form of influenza does not cause pandemics in humans.³³ Influenza B viruses can cause a wide variety of disease, but generally clinical symptoms are similar to those of IAV.³⁴

The swine influenza, genome consists of a total of 13588 nucleotides and virions are enveloped and spherical or pleomorphic with a size ranging from 50-120 nm in diameter.³⁵ The outer layer is a lipid membrane which is taken from the host cell in which the virus multiplies. Inserted into the lipid membrane are "spikes", which are proteins-actually glycoproteins, because they consist of protein linked to sugars known as HA and NA. These are the proteins that determine the subtype of influenza virus. The HA and NA are important in the immune response against the virus; antibodies against these spikes may protect against infection. The NA protein is the target of the antiviral drugs Relenza and Tamiflu.³⁶

Transmission: Influenza transmission depends on multiple factors, including swine age, immunity, vaccination status and the presence of maternal antibodies. The natural reservoir for SIAV is birds like water fall. From this wild life reservoir SIV are frequently transmitted to domestic and commercial poultry. Transmission between poultry and pigs can also occur. Humans and avian strain can both infect pigs when the reassortment exists. Pigs are proposed to act as a mixing vessel for influenza A virus, in addition, pigs and humans have a two ways transmission ecology.⁹

The main route of transmission is through direct contact between infected and uninfected animals. These close contacts are particularly common during animal transport. Intensive farming may also increase the risk of transmission, as the pigs are raised in very close proximity to each other. The direct transfer of the virus probably occurs either by pigs touching noses, or through dried mucus. Airborne transmission through the aerosols

produced by pigs coughing or sneezing is also an important means of infection.³² The virus usually spreads quickly through a herd, infecting all the pigs within just a few days.² Transmission may also occur through wild animals, such as wild boar, which can spread the disease between farms.⁴

People are usually infected with viruses from other species during close contact with the living host or its tissues, respiratory secretion and certain other body fluid. In addition to respiratory secretions, certain other body fluids should also be considered potentially infectious¹ indirect contact via fomites or other means is also thought to be possible.² During recent cases associated with fairs, many patients had been exposed to pigs for more than one day.⁴ Person to person transmission of swine influenza viruses has occasionally been reported to family members or other close contacts and a limited outbreak occurred on a military base; however, most viruses were not transmitted to other people.¹⁴

Pathogenesis and Pathology:

When swine influenza virus is introduced into the respiratory tract, by aerosol or by contact with saliva or other respiratory secretions from an infected individual, it attaches to and replicates in epithelial cells. The virus replicates in cells of both the upper and lower respiratory tract, notably the nasal mucosa, tonsils, trachea and lung, but almost never enters other tissues.³ There is a massive infection of epithelial cells of the bronchi, bronchioli accompany the typical respiratory disease.⁷ These inflammatory cells cause obstruction of the airways and substantial lung damage by release of their enzymes. Both the infection and disease are very transient and virus excretion in nasal swabs and virus replication in the lungs last for 6-7 days. Virus has occasionally been isolated from the serum of experimentally infected pigs, in barely detectable amounts, but virus isolation from extra-respiratory tissues is very rare. Viral replication combined with the immune response to infection lead to destruction and loss of cells lining the respiratory tract. As infection subsides, the epithelium is regenerated, a process that can take up to amonth.⁸

In uncomplicated infections, the gross lesions are mainly those of a viral pneumonia and are usually confined to the respiratory tract. Affected parts of the lungs are clearly demarcated and are atelectic or consolidated and dark red to purple-red. The lesions may be found distributed throughout the lungs but tend to be more extensive and

confluent ventrally.³² Other areas of the lung may be pale and emphysematous. The airways are often dilated and filled with copious mucopurulent exudate. The bronchial and mediastinal lymph nodes are typically oedematous but not congested. Pulmonary oedema may also be seen. Some strains of swine influenza viruses produce more marked lesions than others. Generalized lymphadenopathy, hepatic congestion and pulmonary consolidation were reported in one outbreak of severe disease in swine. Histologically, the fully developed lesions are primarily those of an exudative bronchiolitis with necrosis, metaplasia, or attenuation of the bronchiolar epithelial cells and varying degrees of some interstitial pneumonia. Exudative tracheitis and rhinitis may also be present.²¹

Clinical Sign:

The influenza virus affects all ages of pigs. In an influenza outbreak on farm, clinical signs can be explosive, affecting all or part of a herd in a very short period of time. In pigs H1N1 virus infection produces fever, lethargy, sneezing, coughing, difficulty breathing and decreased appetite.²⁹ In some cases the infection can cause abortion sows and sub infertility in affected boar. Although mortality is usually low, the virus can produce weight loss, reduce milk production due to fever and poor growth, causing economic loss to farmers when infected pigs can lose up to 12-pound body weight over a 3 to 4 weeks.³² Swine flu produces most of the same symptoms in pigs as human flu produces in people. Swine flu can last about one to two weeks in pigs that survive. In a number of instances, people have developed in human the most common cause of death is respiratory failure; other causes of death are pneumonia, high fever which leading to neurological problems, dehydration due to excessive vomiting, diarrhea and electrolyte imbalance.³² Fatalities are more likely in young children and the elder. The typical symptoms appear after an incubation period of 1 to 7 days.³ The common symptoms include: temperature (fever), sore throat, headaches, chills, fatigue, body aches, cough, diarrhea (less common), tiredness (fatigue), vomiting, difficulty breathing, chest pain, purple or blue discoloration of the lips, signs of dehydration, dizziness when standing, reduced urine volume, in infants lack of tears when crying, dry diapers and seizure.⁴ Public Health Significance: Swine influenza is one of the most common respiratory diseases in humans and one of the most significant, due to the generally high morbidity and the increased mortality of infants, elderly and chronically ill persons.⁵ There are three

types of influenza viruses: A, B and C. The type A viruses are the most virulent human pathogens among the three influenza types and cause the most severe disease.² Influenza B almost exclusively infects humans and is less common than influenza A. The only other animals known to be susceptible to influenza B infection are the seal and the ferret. This type of influenza mutates slower than type A and consequently is less genetically diverse, with only one influenza B serotype.⁵ As a result of this lack of antigenic diversity, a degree of immunity to influenza B is usually acquired at an early age. This reduced rate of antigenic change, combined with its limited host range, ensures that pandemics of influenza B do not occur. Influenza C virus can infect humans, dogs and pigs, sometimes causing both severe illness and local epidemics. However, influenza C is less common than the other types and usually only cause mild disease in children.⁷ Actual total is somewhat larger, because not all victims are tested for H1N1 influenza.⁶ The flu usually involves: Abrupt onset of severe symptoms, which include headache, muscle aches, fatigue, high fever, cough and sometimes a runny nose with sore throat.²⁴ Children may experience vomiting, diarrhea and ear infections, as well as other flu symptoms. The symptoms usually resolve in 4 to 5 days, although some people can experience coughing and feelings of illness for more than 2 weeks. In some cases, flu can become more severe or make other conditions worse.²⁰ The swine flu virus has potential to cause severe economic consequences because of the mortality and production loss in pigs, trade sanctions on exporting animal products from an infected country or region, public health concerns leading to pig culling operations and reduced pork consumption and public health burden of the diseases.¹⁴ It also mainly striking younger individuals, as most individuals under.¹⁸

Diagnosis and Treatment: The explosive appearance of an upper respiratory syndrome, including conjunctivitis, sneezing and coughing with low mortality rate, can be serves for presumptive diagnosis of SI in pig, but these signs are not enough to differentiate from other common respiratory diseases of swine.²²

Viral Culture:

A virus culture is a diagnostic which is important for isolation of the virus. The best source for detection swine influenza viruses are bronchial swabs from post mortem tissues. But, culture is usually too slow to help guide clinical management. A negative viral culture does not exclude pandemic S-OIV (swine origin influenza

virus) infection. The virus was first cultured in embryonated chicken eggs.¹³ This can be done with 10-11 day old embryonated chicken eggs inoculate 0.1-0.3 ml of inoculum into the allantoic cavity and amniotic sac, generally, 3-4 eggs are inoculated per sample, then incubate eggs at 35-37°C for 3-4 days and candle daily. Eggs with embryos that have died within 24 hours of inoculation are discarded and refrigerate eggs with embryos that have died later than 24 hours after inoculation. Harvest amniotic and allantoic fluids from eggs with dead embryos and from eggs with viable embryos at the end of the incubation period. All egg materials should be considered to be potentially infectious and should be treated accordingly to prevent SIV exposure to the laboratory worker. Centrifuge fluids at 1500-1900 g for 10-20 minutes at 4°C. Transfer the supernatant to another tube for testing, fluids are evaluated for the presence of SIV with the haemagglutination.¹⁶

Serology:

The primary serological test for detection of swine influenza virus antibodies is the hemagglutination inhibition test conducted on paired serum that most widely used for detection of antibodies to swine influenza virus. However, it is tedious and has only moderate sensitivity and high specificity. It has been adapted, modified and subtype specific [26]. Collection of paired serum is generally recommended 10-21 days apart. A four-fold or greater increase in titer between the first and second sample is suggestive of a recent swine influenza virus infection.³⁶

Necropsy Findings: Molecular Diagnosis (PCR):

The PCR can be performed on a wide range of samples including nasal swabs, lung tissue or cell culture isolates. Currently, the PCR test is rather expensive and therefore it is used more for research than for diagnostic purposes.²⁶ RT-PCR tests have been developed for the diagnosis of swine influenza and for hemagglutinin and neuraminidase typing.¹⁸ With the identification of the pandemic H1N1 in 2009, molecular assays based on an avian influenza matrix real-time PCR were adapted for use in swine. Modifications to the assay vary by country and a swine influenza reference laboratory should be consulted for the most suitable matrix PCR assay. Additional real-time PCR assays that can differentiate the novel H1N1 from seasonal flu H1N1 based on differentiable matrix realtime or N1 real-time assays have also been developed for use in North America. In many instances it is necessary to conduct partial or complete gene sequencing

of one or more of the SIV genes (i.e. matrix, neuraminidase, haemagglutinin) to ascertain the subtype of detected virus.³⁶

The outstanding lesions are present in the upper respiratory tract. Swelling and marked edema of the cervical and mediastinal lymph node is evident. There is congestion of the mucosa of the pharynx, trachea and bronchi and more tenacious, colorless, frothy exudates is present in the air passages.³⁷ Copious exudates in the bronchi are accompanied by collapse of the ventral part of the lung. This atelectasis is extensive and often irregularly distributed, although apical and cardiac lobes are more affected and the right lung more so than the left. The lesions are clearly demarcated, dark red to purple in color and leathery in consistency [36]. Surrounding the atelectatic area the lung is often emphysematous and may show many petechial hemorrhages. There is often moderate to severe engorgement of spleen and severe hyperemia of the gastric mucosa especially along the greater curvature. Patchy congestion and mild catarrhal exudation occur in the large intestine, but there are no erosions of the mucosa.²⁷

Differential Diagnosis:

Swine influenza virus is one of the several agents involved in acute respiratory disease in pigs and can frequently be accompanied by other respiratory diseases such as Hog cholera, PRRS (Porcine Reproductive and Respiratory Syndrome) virus, Aujeszky's disease virus, porcine circovirus type 2, Bordetella bronchiseptica, Pasteurella multocida and Mycoplasma hyopneumoniae.³⁵

Treatment:

As swine influenza is rarely fatal to pigs, little treatment beyond rest and supportive care is required.

Instead veterinary efforts are focused on preventing the spread of the virus throughout the farm, or to other farms. Vaccination and animal management techniques are most important in these efforts. Antibiotics are also used to treat this disease, which although they have no effect against the influenza virus, do help prevent bacterial pneumonia and other secondary infections in influenza-weakened herds.³⁰

Prevention and Control:

Biosecurity: A biosecurity plan for swine influenza must identify potential pathways for the introduction and spread of disease. Because swine influenza virus is spread predominantly through

the respiratory route and is highly transmissible between pigs, effective biosecurity can be difficult to achieve. Once swine influenza is established on a farm, it can be very difficult to completely eradicate without complete depopulation.³⁰ Partial depopulation, segregation of early weaned piglets, all-in all-out systems, combined with good hygiene practices, are steps that can be taken to control the incidence and minimise the economic impact on an affected farm.³⁶ Because cross species transmission of influenza viruses can occur between humans and pigs, biosecurity measures must also take into account human-pig interactions, particularly the exposure of pigs to persons with influenza-like illness. Additional sources of infection to consider in biosecurity plans include contact with wild and feral pigs, wild birds (especially waterfowl and other birds from aquatic habitats), poultry, unsafe water sources that may contain viruses and possibly even other species such as horses.³⁷

Vaccination: Vaccination is commonly used as a control measure for influenza in swine farms. Vaccine candidates should be shown to be pure, safe, potent and efficacious. Inactivated vaccines may not protect against a new strain that appears to be antigenically different than the vaccine strain.

Conclusions and Recommendations

Swine influenza is a highly contagious viral infection in pigs and it is widely distributing in various continent. Swine flu is one of the most significant respiratory diseases of human due to its high morbidity and mortality of infants, elderly and chronically ill persons. It also has an immense economic consequence due to production loss, swine mortality, herd culling and trade sanctions on affected.

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