Review Article **ISSN: 2349 – 7114**

Asian Journal of Research in Pharmaceutical Sciences and Biotechnology

Journal home page: www.ajrpsb.com

INFLUENZA SURVEILLANCE: SWINE-ORIGIN INFLUENZA A (H1N1) VIRUS

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ABSTRACT

Swine Influenza is a respiratory disease of pig caused by Type A influenza viruses that causes regular outbreak in pigs. Flu is caused by influenza viruses, and is spread mainly by coughing, sneezing, and close contact. The Wild aquatic bird populations have long been considered the natural reservoir for influenza A viruses with virus transmission from these birds seeding other avian and mammalian hosts. While most evidence still supports this dogma, recent studies in bats have suggested other reservoir species may also exist. Extensive surveillance studies coupled with an enhanced awareness in response to H5N1 and pandemic 2009 H1N1 outbreaks is also revealing a growing list of animals susceptible to infection with influenza A viruses. Although in a relatively stable host-pathogen interaction in aquatic birds, antigenic, and genetic evolution of influenza A viruses often accompanies interspecies transmission as the virus adapts to a new host. The evolutionary changes in the new hosts result from a number of processes including mutation, reassortment, and recombination. The CDC recommends real time PCR as the method of choice for diagnosing H1N1. Prevention of swine influenza has three components: prevention in swine, prevention of transmission to humans, and prevention of its spread among humans. If a person becomes sick with swine flu, antiviral drugs can make the illness milder and make the patient feel better faster. They may also prevent serious flu complications. For treatment, antiviral drugs work best if started soon after getting sick.

KEYWORDS

H1N1 influenza, Virology, Swine influenza in humans, India, Diagnosis and Vaccine.

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INTRODUCTION

Influenza ("flu") is a contagious disease that spreads around the World or India every winter, usually between October and May. There are three types of Influenza viruses A, B and C. The subtypes of type A Influenza virus is determined by haemagglutinin and neuraminidase. Both A and B viruses are responsible for seasonal influenza epidemics, and out-of season sporadic cases and outbreaks[1]. The Influenza type A causes moderate to severe illness in all age groups in

humans and other animals whereas type B primarily affects children and causes usually a milder illness. The illness by type C Influenza virus is rarely reported in humans (Figure No.1)[2,3].

Flu is caused by influenza viruses, and is spread mainly by coughing, sneezing, and close contact. Anyone can get flu, but the risk of getting flu is highest among children. Symptoms come on suddenly and may last several days. They can include: fever/chills, sore throat, muscle aches, fatigue, cough and headache. Flu can make some people much sicker than others. These people include young children, people 65 and older, pregnant women, and people with certain health conditions - such as heart, lung or kidney disease, nervous system disorders, or a weakened immune system. Flu vaccination is especially important for these people and anyone in close contact with them. Flu can also lead to pneumonia, and make existing medical conditions worse. It can cause diarrhea and seizures in children[4-7].

VIROLOGY

The types of influenza virus found in pigs are known as swine influenza generally called swine flu or swine-origin influenza virus (S-OIV)[6]. Swine Influenza is a respiratory disease of pig caused by Type A influenza viruses that causes regular outbreak in pigs[8-10]. Influenza virus belongs to the genus Orthomyxovirus in the family Orthomyxoviridae which consists of influenza A, B and C viruses[4] and has an envelope, single-stranded, negatively sensed RNA, eight separate segments and pleomorphic appearance with an average diameter of 120nm[3,11,12].

Swine influenza (Figure No.2), also called pig influenza, swine flu, hog flu and pig flu, is an infection caused by any one of several types of swine influenza viruses. Swine influenza virus (SIV) or swine origin influenza virus (SOIV) is any strain of the influenza family of viruses that is endemic in pigs[13-16]. As of 2009, the known SIV strains include influenza C and the subtypes of influenza A known as H1N1, H1N2, H2N1, H3N1, H3N2, and H2N3[17,18]. Various international agencies (US CDC and WHO) have determined that this swine influenza A (H1N1) virus is contagious and is spreading from human to human. WHO has escalated the world pandemic phase from Phase 3 to Phase 4, indicating that a worldwide pandemic due to swine flu H1N1 is possible (Figure No.3)[5,19,20].

EPIDEMIOLOGY

Swine flu is an infection caused by a virus. It's named for a virus that pigs can get. People do not normally get swine flu, but human infections can and do happen[21]. Swine influenza was first proposed to be a disease related to human flu during the 1918 flu pandemic, when pigs became ill at the same time as humans[22]. The first identification of an influenza virus as a cause of disease in pigs occurred about ten years later, in 1930. For the following 60 years, 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[23].

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[24,25].

In 2009 a strain of swine flu called H1N1 infected many people around the world. In August 2012, the Center for Disease Control and Prevention confirmed 145 human cases (113 in Indiana, 30 in Ohio, one in Hawaii and one in Illinois) of H3N2v since July 2012[26].

According to the WHO's most recent weekly statistics released on July 16, H1N1 has killed more than 18,000 people globally. The WHO declared the H1N1 pandemic on June 11, 2009, after more than 70 countries reported cases of H1N1 infection[28].

As on 13th August 2009 World Health Organization has reported 1, 82,166 laboratories confirmed cases of influenza A/H1N1 and 1799 deaths from 178 countries.

India reported its first case on 13th May, 2008. Most of the cases reported subsequently were travel related cases among those traveling to India from affected countries. As on 20th August, 12,604 persons have

been tested so far out of which 2401 are positive for Swine Influenza A H1N1 (Figure No.4-6)[27].

Pandemic in Human

The 1918 flu pandemic in humans was associated with H1N1 and influenza appearing in pigs[25]. This may reflect a zoonosis either from swine to humans or from humans to swine. Although it is not certain in which direction the virus was transferred, some evidence suggests, in this case, pigs caught the disease from humans. For instance, swine influenza was only noted as a new disease of pigs in 1918, after the first large outbreaks of influenza amongst people[22]. Although a recent phylogenetic analysis of more recent strains of influenza in humans, birds, and swine suggests the 1918 outbreak in humans followed a reassortment event within a mammal, the exact origin of the 1918 strain remains elusive. It is estimated that anywhere from 50 to 100 million people were killed worldwide[30].

H1N1 virus pandemic history

A study conducted in 2008, and published in the journal Nature, has managed to establish the evolutionary origin of the flu strain of swine origin (SOIV)[31].

The mid1970s were important for the evolution of flu strains. First, the reemergence of the human H1N1 strain became a seasonal strain. Then, a small outbreak of swine H1N1 occurred in humans, and finally, the human H2N2 strain apparently became extinct. Around 1979, the avian H1N1 strain infected pigs and gave rise to Euroasiatic swine flu and H1N1 Euroasiatic swine virus, which is still being transmitted in swine populations. Swine flu spread very rapidly worldwide due to its high human to human transmission rate and due to the frequency of air travel[32,33].

In 2015 the instances of Swine Flu substantially increased to five year highs with over 10000 cases reported and 774 deaths in India [34].The states reporting the highest number of cases and deaths are Rajasthan, Gujarat, Madhya Pradesh, Maharashtra, Delhi, and Telengana[35]. The circulating strain of influenza being the same, unmutant strain that caused global pandemic in 2009 (A H1N1 pdm 09), the sudden spurt of the cases in the beginning of 2015 left the Indian government unexplained but concerned. Government instructed the affected states to investigate into the epidemiological reasons of such spurt in the states, and had detailed the advisory guidelines to all states. The guidelines are mainly for (a) description of A H1N1 for prompt identification, detection, and distinction from the symptoms of other similar infection such as common flu (cold) (b) categorization of screening of influenza A H1N1 cases, (c) clinical management protocol of Pandemic influenza A H1N1, (d) providing home care, (e) collection of human sample[36].

Besides, through the National Centre for Diseases Control (NCDC), Directorate General of Health Services (DGHS), Government of India (GoI) had placed a tender to procure 8 kits of Assay sets, 37 kits of one step RT-PCR kit, and 36 kits of viral RNA extraction kits[37].

TRANSMISSION

People who work with poultry and swine, especially those with intense exposures, are at increased risk of zoonotic infection with influenza virus endemic in these animals, and constitute a population of human hosts in which zoonosis and reassortment can co-occur [38,39]. Vaccination of these workers against influenza and surveillance for new influenza strains among this population may therefore be an important public health measure (Figure No.7)[40].

Signs and symptoms

Direct transmission of a swine flu virus from pigs to humans is occasionally possible (zoonotic swine flu)[42]. In all, 50 cases are known to have occurred since the first report in medical literature in 1958, which have resulted in a total of six deaths. Of these six people, one was pregnant, one had leukemia, one had Hodgkin's lymphoma and two were known to be previously healthy. Despite these apparently low numbers of infections, the true rate of infection may be higher, since most cases only cause a very mild disease, and will probably never be reported or diagnosed (Figure No.8)[43].

According to the Centers for Disease Control and Prevention (CDC), in humans the symptoms of the 2009 "swine flu" H1N1 virus are similar to those of

influenza and of influenza like illness in general. Symptoms include fever, cough, sore throat, body aches, headache, chills and fatigue[7].

DIAGNOSIS

The CDC recommends real time PCR as the method of choice for diagnosing H1N1[45]. The oral or nasal fluid collection and RNA virus preserving filter paper card is commercially available. This method allows a specific diagnosis of novel influenza (H1N1) as opposed to seasonal influenza. Near patient point of care tests are in development. Rapid case identification is essential for prompt patient management and public health actions. This study developed real-time and conventional reverse transcription-polymerase chain reaction (rRT-PCR and cRT-PCR) assays for pandemicH1N1 detection, and compared their sensitivities with protocols developed by WHO reference centres[46].

The most accurate laboratory tests, such as real-time reverse transcriptase polymerase chain reaction (rRT-PCR) are only available in certain laboratories, and these tests can take several days to obtain results [47].

The CDC Realtime RTPCR (rRTPCR) Protocol for Detection and Characterization of Swine Influenza includes a panel of oligonucleotide primers and duallabeled hydrolysis (Taqman ®) probes to be used in real-time RT-PCR assays for the in vitro qualitative detection and characterization of swine influenza viruses in respiratory specimens and viral cultures. The Influenza A primer and probe set is designed for universal detection of type A influenza viruses. The Swine Influenza A primer and probe set is designed to specifically detect all swine influenza A viruses. The Swine H1 primer and probe set is designed to specifically detect swine H1 influenza. This assay is utilized for testing influenza A positive respiratory specimens (unsubtypable) taken from suspect swine influenza A infected patients[48,49, 50].

PREVENTION

Prevention of swine influenza has three components: prevention in swine, prevention of transmission to humans, and prevention of its spread among humans[51].

Prevention of pig to human transmission: Swine can be infected by both avian and human flu strains of influenza, and therefore are hosts where the antigenic shifts can occur that create new influenza strains[4].

The transmission from swine to humans is believed to occur mainly in swine farms, where farmers are in close contact with live pigs. Although strains of swine influenza are usually not able to infect humans, this may occasionally happen, so farmers and veterinarians are encouraged to use face masks when dealing with infected animals[52,54]. The use of vaccines on swine to prevent their infection is a major method of limiting swine to human transmission. Risk factors that may contribute to swine to human transmission include smoking and, especially, not wearing gloves when working with sick animals, thereby increasing the likelihood of subsequent hand to eye, hand to nose or hand to mouth transmission[53].

Prevention of human to human transmission: Influenza spreads between humans when infected people cough or sneeze, then other people breathe in the virus or touch something with the virus on it and then touch their own face[41,55]. "Avoid touching your eyes, nose or mouth. Germs spread this way[57]. "Swine flu cannot be spread by pork products, since the virus is not transmitted through food [56]. The swine flu in humans is most contagious during the first five days of the illness, although some people, most commonly children, can remain contagious for up to ten days. Diagnosis can be made by sending a specimen, collected during the first five days, for analysis[58].

Recommendations to prevent spread of the virus among humans include using standard infection control, which includes frequent washing of hands with soap and water or with alcohol based hand sanitizers, especially after being out in public. On the whole, Oshitani says, "this pandemic came too early. If we had had two more years, we would have been better prepared[59]. Chance of transmission is also reduced by disinfecting household surfaces, which can be done effectively with a diluted chlorine bleach solution[60].

Experts agree hand washing can help prevent viral infections, including ordinary and the swine flu infections. Also, avoiding touching one's eyes, nose or

mouth with one's hands helps to prevent the flu[57]. Influenza can spread in coughs or sneezes, but an increasing body of evidence shows small droplets containing the virus can linger on tabletops, telephones and other surfaces and be transferred via the fingers to the eyes, nose or mouth. Alcohol based gel or foam hand sanitizers work well to destroy viruses and bacteria. Anyone with flulike symptoms, such as a sudden fever, cough or muscle aches, should stay away from work or public transportation, and should contact a doctor for advice[61].

VACCINATION

Influenza transmission depends on multiple factors, including swine age, immunity, vaccination status and the presence of maternal antibodies. Vaccination is commonly used as a control measure for influenza in swine farms[62]. Vaccination has been shown to reduce influenza A virus transmission in pigs in experimental settings but the effects of vaccination at the farm level remain unclear[64,70].

Vaccines are available for different kinds of swine flu. The U.S. Food and Drug Administration (FDA) approved the new swine flu vaccine for use in the United States on September 15, 2009[63].

The seasonal flu jab is available for free on the NHS for those at risk and is given as an annual injection to [65]:

- Adults over the age of 18 at risk of flu (including everyone over 65).
- Children aged from six months to two years who are at risk of flu.

The flu vaccine is also given as an annual nasal spray to:

- Children aged 2 to 18 years at risk of flu.
- Healthy children aged two, three and four.

In the aftermath of the 2009 pandemic, several studies were conducted to see who received influenza vaccines. These studies show that whites are much more likely to be vaccinated for seasonal influenza and for the H1N1 strain than African Americans[66].

Treatment

If a person becomes sick with swine flu, antiviral drugs can make the illness milder and make the patient feel better faster. They may also prevent serious flu complications. For treatment, antiviral drugs work best if started soon after getting sick (within two days of symptoms). Beside antivirals, supportive care at home or in a hospital focuses on controlling fevers, relieving pain and maintaining fluid balance, as well as identifying and treating any secondary infections or other medical problems. The U.S. Centers for Disease Control and Prevention recommends the use of oseltamivir (Tamiflu) or zanamivir (Relenza) for the treatment and/or prevention of infection with swine influenza viruses; However, the majority of people infected with the virus make a full recovery without requiring medical attention or antiviral drugs[67]. The virus isolated in the 2009 outbreak has been found resistant to Amantadine and Rimantadine[68].

In the U.S., on April 27, 2009, the FDA issued Emergency Use Authorizations to make available Relenza and Tamiflu antiviral drugs to treat the swine influenza virus in cases for which they are currently unapproved. The agency issued these EUAs to allow treatment of patients younger than the current approval allows and to allow the widespread distribution of the drugs, including by volunteers[69].

DISCUSSION

Influenza A viruses causes recurrent outbreaks at the local or global scale, with potentially severe consequences for human health and the global economy. Swine influenza virus infections in humans have been reported in the United States, Canada, Europe and Asia. There are no unique clinical features that distinguish swine influenza in humans from typical influenza. Although a number of the case patients have predisposing immune compromising conditions, healthy persons are also clearly at risk for illness and death from swine influenza. Sporadic cases of swine influenza in humans, combined with seroepidemiological studies demonstrating increased risk of swine influenza in occupationally exposed workers, highlight the crucial role that this group may play in the development of new strains of influenza virus. Persons who work with swine should be considered for sentinel influenza surveillance, and may be an important group to include in pandemic planning.

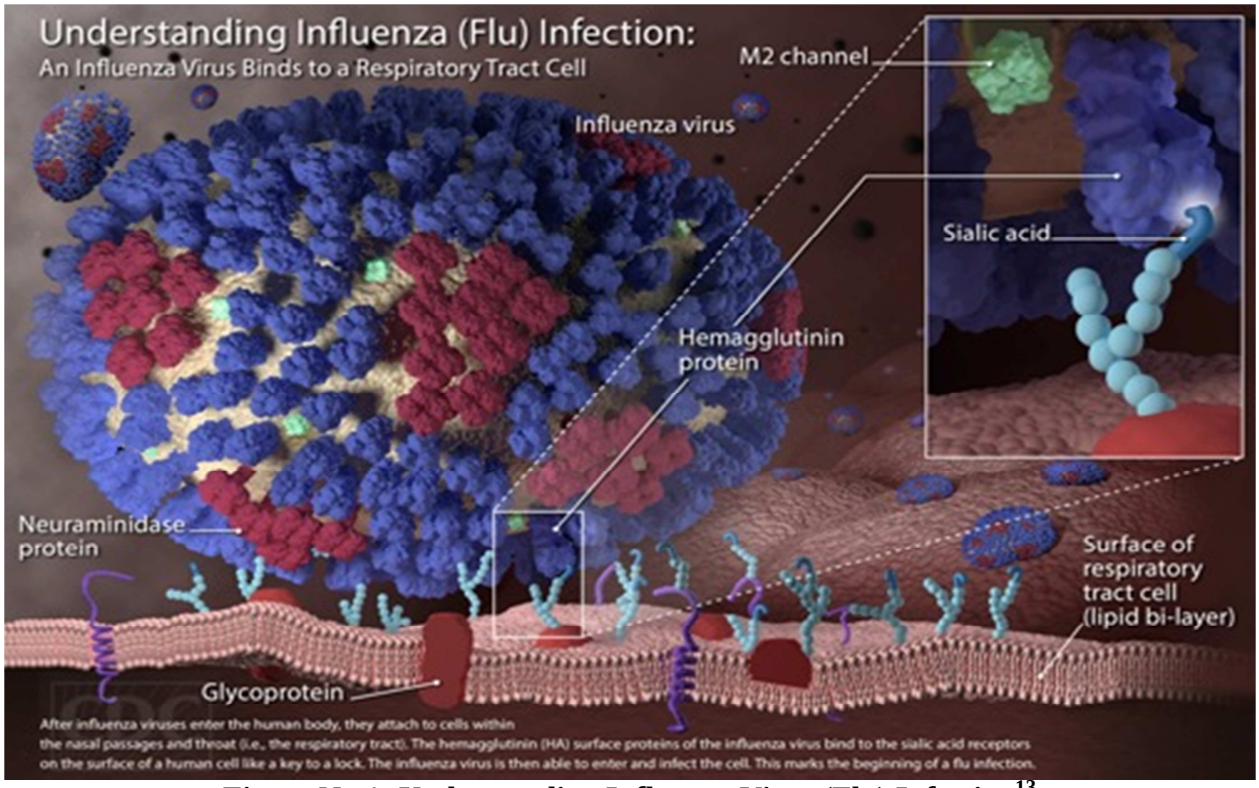


Figure No.1: Understanding Influenza Virus (Flu) Infection[13]

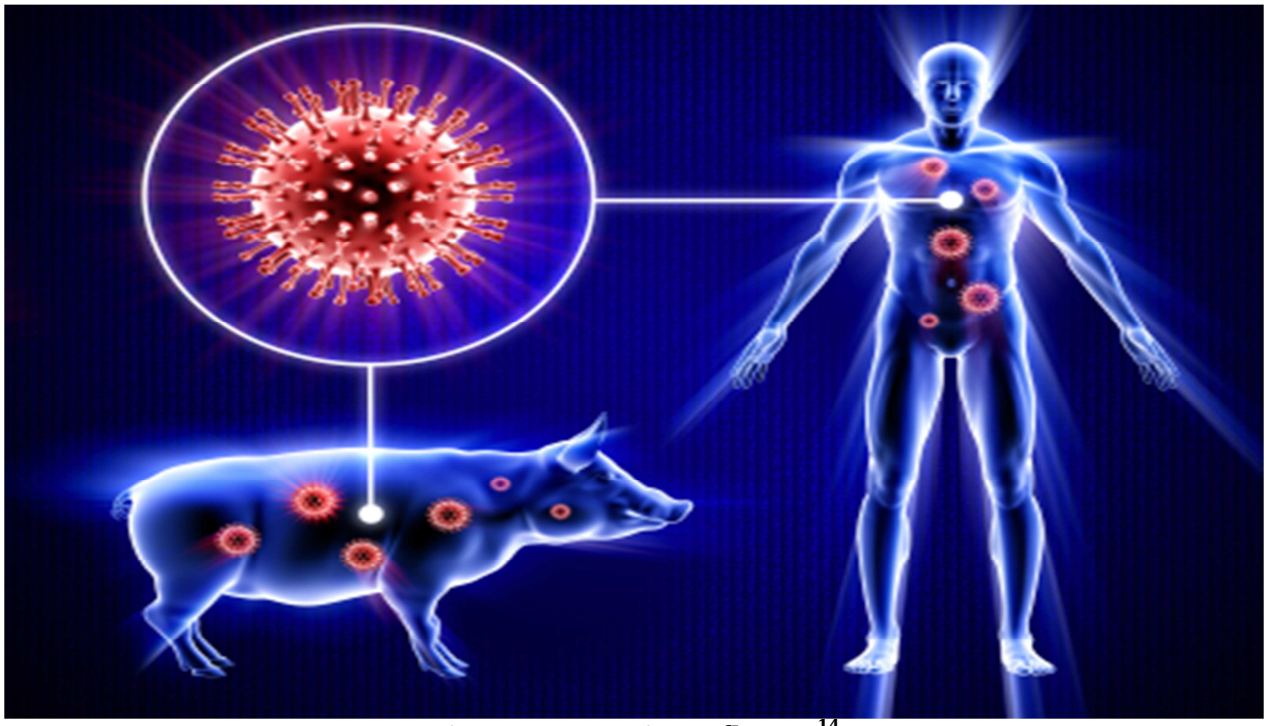


Figure No.2: Swine Influenza[14]

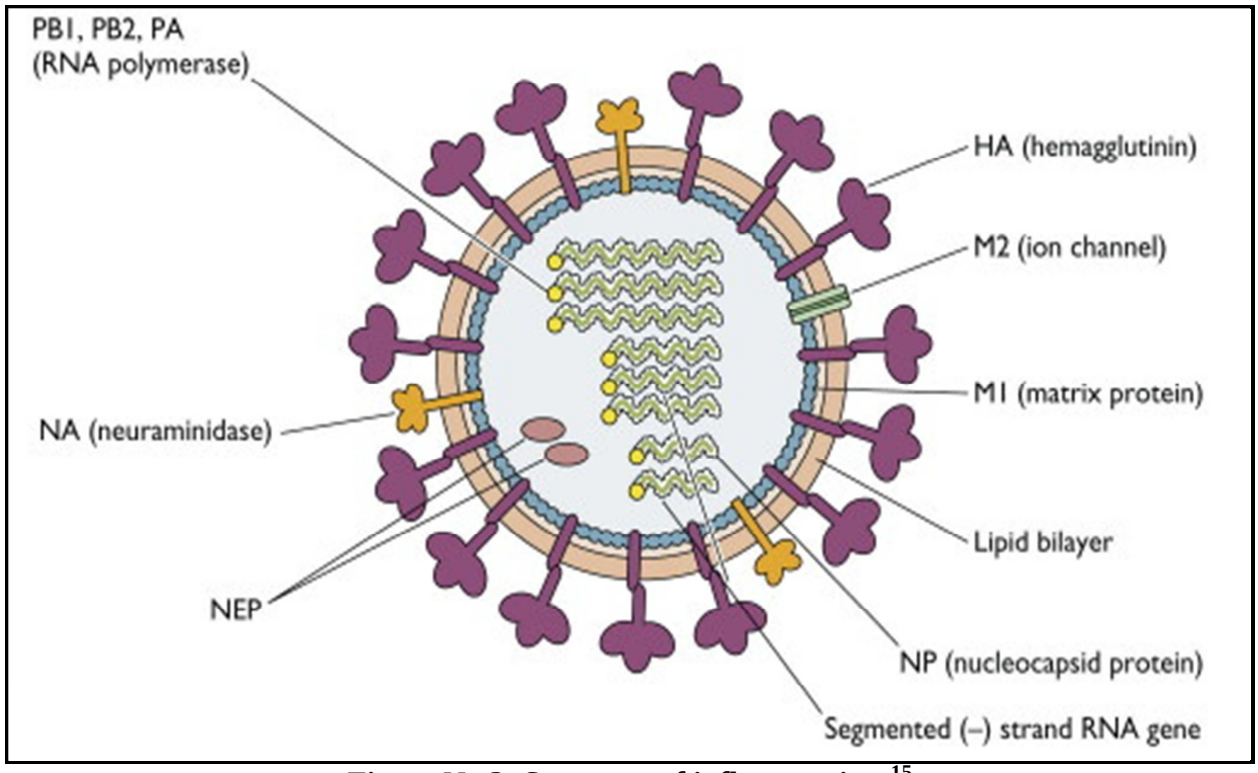


Figure No.3: Structure of influenza virus[15]

Figure No.4: Worldwide pandemic influenza activity[28]

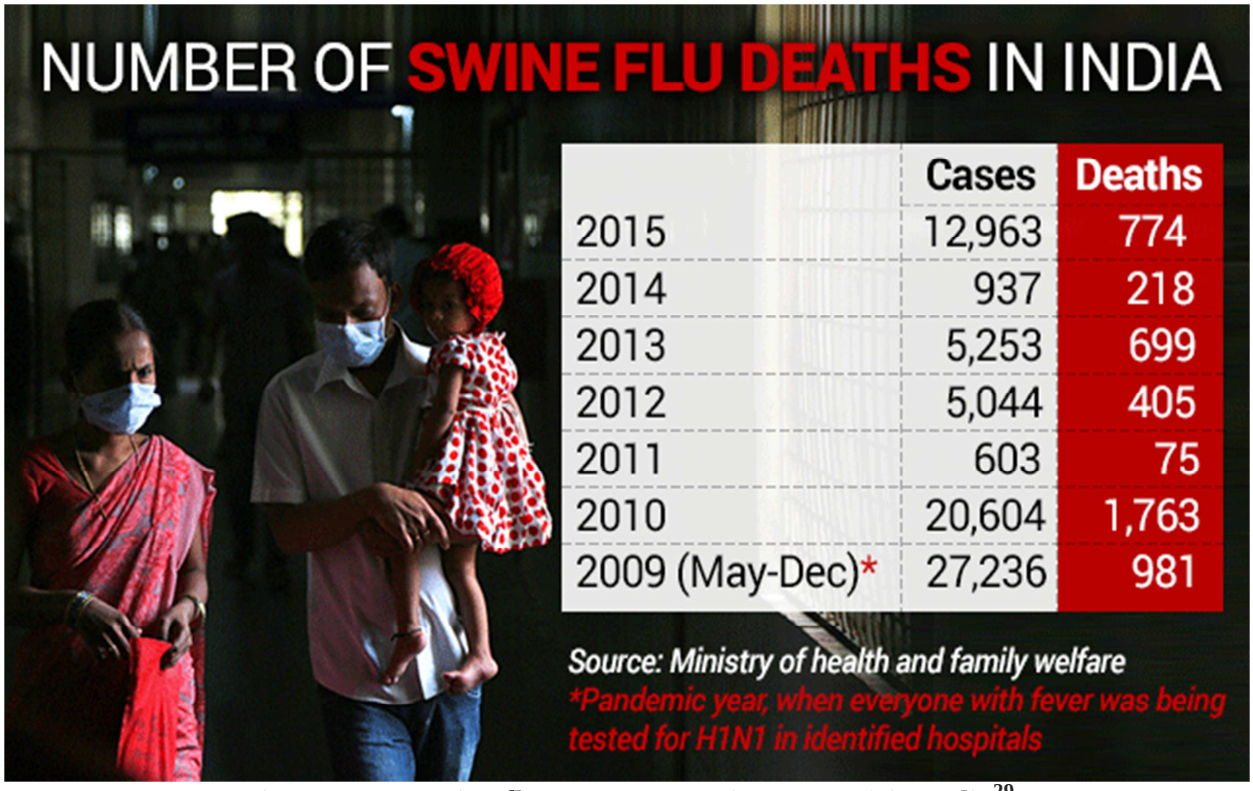
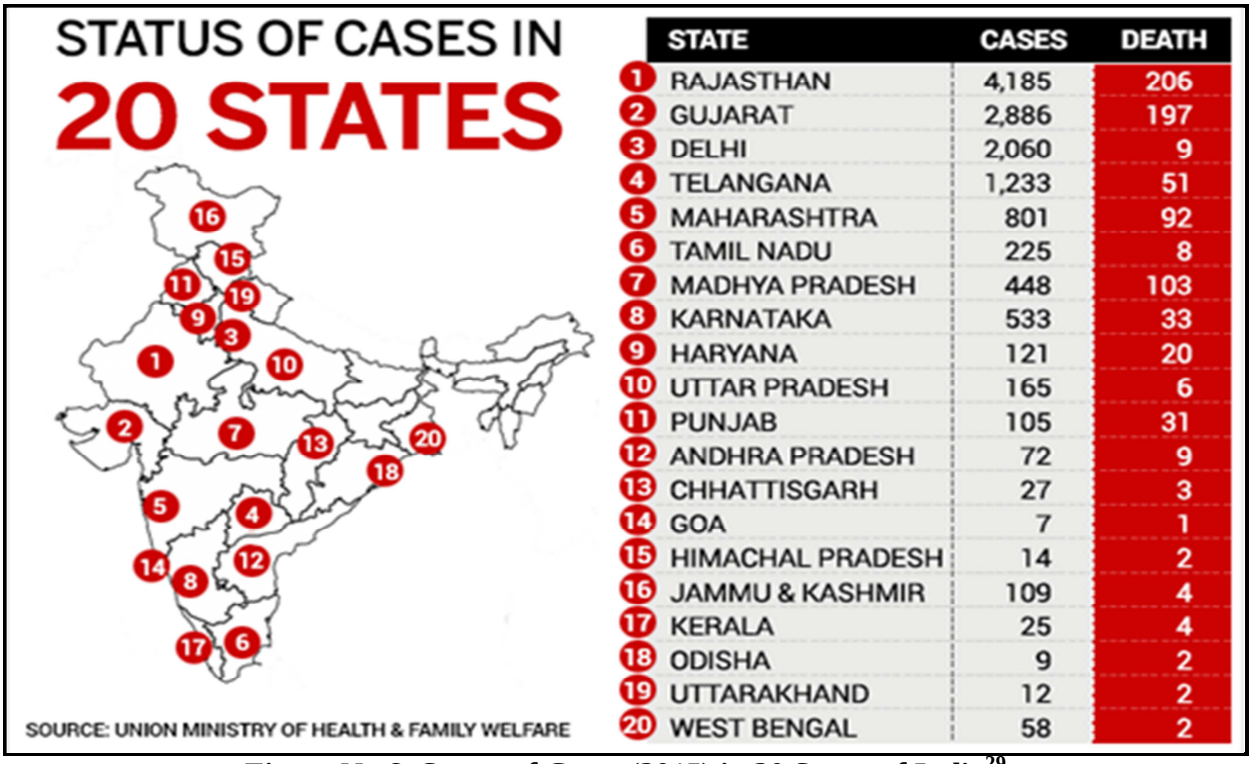


Figure No.5: Swine flu Cases report (2009-2015) in India[29]



	STATE	CASES	DEATH
1	RAJASTHAN	4,185	206
2	GUJARAT	2,886	197
3	DELHI	2,060	9
4	TELANGANA	1,233	51
5	MAHARASHTRA	801	92
6	TAMIL NADU	225	8
7	MADHYA PRADESH	448	103
8	KARNATAKA	533	33
9	HARYANA	121	20
10	UTTAR PRADESH	165	6
11	PUNJAB	105	31
12	ANDHRA PRADESH	72	9
13	CHHATTISGARH	27	3
14	GOA	7	1
15	HIMACHAL PRADESH	14	2
16	JAMMU & KASHMIR	109	4
17	KERALA	25	4
18	ODISHA	9	2
19	UTTARAKHAND	12	2
20	WEST BENGAL	58	2

Figure No.6: Status of Cases (2015) in 20 States of India[29]

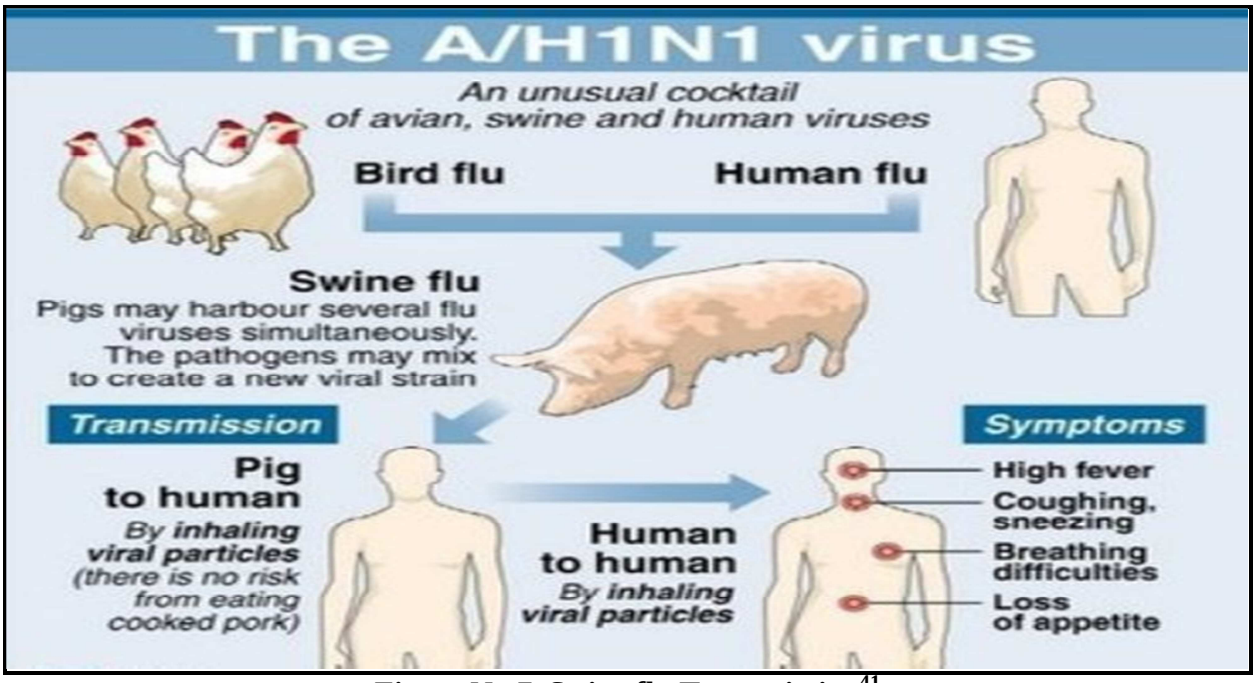


Figure No.7. Swine flu Transmission[41]

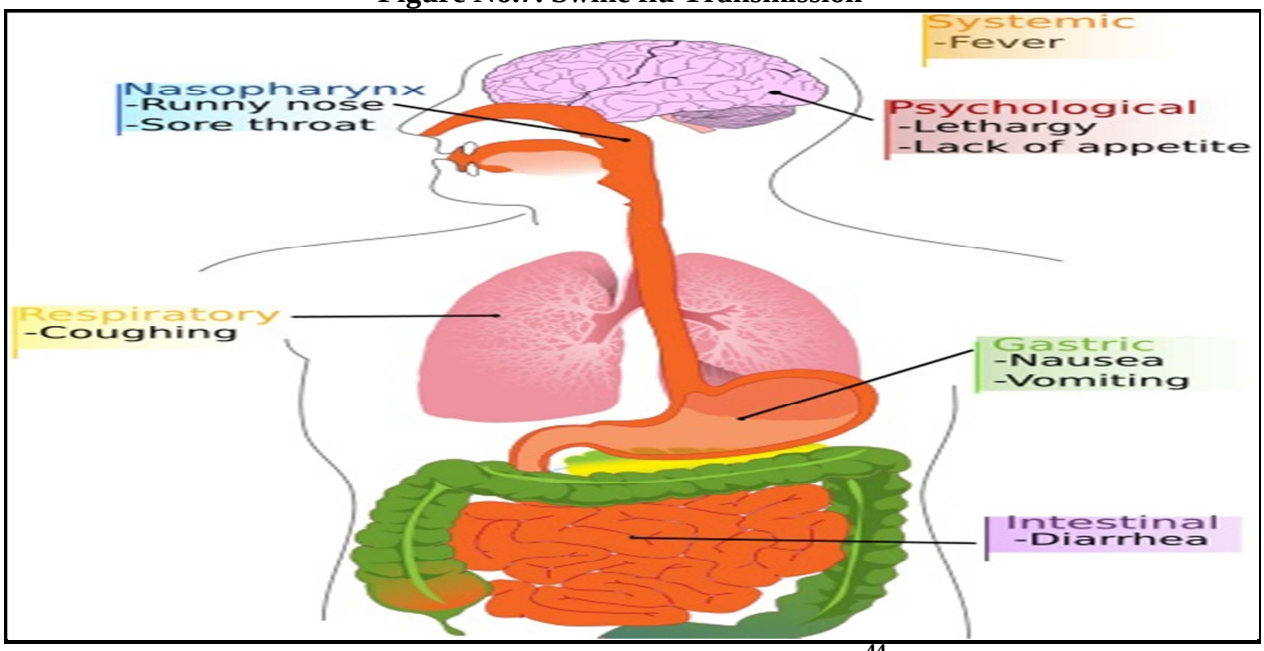


Figure No.8: Symptoms of Swine Flu[44]

CONCLUSION

Swine flu refers to swine influenza or the viral infection caused by any of the several types of swine influenza virus. Only people who used to have direct contact with pigs were observed to get swine flu in the past. But, H1N1 virus is a new swine flu virus and it contains the genetic material of swine, bird and human influenza virus. H1N1 is an Influenza A virus. Swine Flu is caused by influenza viruses, and is spread mainly by coughing, sneezing, and close contact. Flu can make some people much sicker than others. These people include young children, older, pregnant women and immunocompromised patients. Prevention and control measures for swine influenza are based on our

understanding of seasonal human influenza and consideration of potential modes of transmission.

At present, it is difficult to predict which viruses might cause a human pandemic. Therefore, both human and veterinary research needs to give more attention to the potential cross-species transmission capacity of influenza A viruses. Advances in vaccinology and structural analysis have revealed common antigenic epitopes on hemagglutinins across all influenza viruses and suggest that a universal influenza vaccine is possible.

ACKNOWLEDGEMENT

The authors reported no conflict of interest. The authors alone are responsible for the content and writing of the paper and no funding has been received on this work. Ethical Approval was not required.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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Please cite this article in press as: Suresh Rewar. Influenza Surveillance: Swine-Origin Influenza A (H1N1) Virus, *Asian Journal of Research in Pharmaceutical Sciences and Biotechnology*, 2(3), 2014, 70 - 82.