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Swine Origin Influenza: A Brief Review

M. Satish Kumar [*1], Kalyani Jatoth[1], Ajmera Shanti Priya[2], T.Mangilal [3], Thirupathi [3], P. Veeresh Kumar[4]

[*1,3] *Geethanjali College of Pharmacy, Cheeryal, Rangareddy District,T.S, India.*
[1] *Department of Microbiology, Pingle College of science, Kakatiya University, Warangal, T.S, India.*
[2] *Department of Microbiology, Kakatiya University, Warangal, T.S, India.*
[4] *JPNES Group of Institutions, Faculty of Pharmacy, Mahabubnagar, T.S, India.*
*E-mail: smanthi@gmail.com

Subject: Pathology

Abstract
Swine origin influenza is a deadly infection caused by influenza H1N1 virus. It was first identified in the border of the United states and Mexico in April 2009, became the swine influenza pandemic within short span of two months causing several thousands of deaths. The novel influenza H1N1 virus emergingly produced by triple reassortment of genes from swine, avian and human viruses. These viruses transmitted by means of small fomities or droplets. Incubation period of influenza H1N1 virus is 2-9 days. Common symptoms like seasonal flu such as fever, sore throat, cough and myalgia. Children under five years, pregnant women, adolescents on aspirin and patients with chronic systemic illness are more susceptible to severe influenza complications. Acute respiratory failure and pneumonia are the most common complications caused by swine origin influenza. RT-PCR and viral culture are the detection techniques which show highest specificity (>90%) during the diagnosis of swine influenza virus. Antiviral drugs include: zamanavir and oseltamivir are highly effective against influenza H1N1 virus shows low fatality rate (<1%). Preventive measures should be followed to control or prevent the spread of influenza. Appropriate vaccines against influenza H1N1 are presently not available.

Keywords: *Pandemic, H1N1 influenza, Swine flu, oseltamivir, zamanavir.*

Introduction
Swine flu is a viral disease caused by influenza-A (H_1N_1) virus, primarily infected to the respiratory tract of pigs, and also infected to the human. It is commonly called as swine influenza, pig influenza, pig flu and hog flue. S-OIV (swine-origin influenza virus) or Swine influenza virus (SIV) has multiple strains include influenza A and C, strain A consisting the subtypes of H1N1, H1N2, H2N3, H3N1 and H3N2 (Swine influenza, 2008). Influenza-A (H_1N_1) virus is a pathogenic virus transmitted through air to the humans and causing promptly symptoms of barking-like cough, nasa secretions and decreased appetite.The rapidity of spreading and uncontrollable infection made swine flue as pandemic infection. (Wiwanitkit V, 2009). In severe cases, influenza can be fatal, causes pneumonia particularly for elders and young children. Inactivation of Influenza viruses can be performed by disinfectants, sunlight and detergents. In addition, soap and frequent hand washing can reduce the risk of infection.

History
Swine influenza has similarity with human influenza,was first proposed as a disease in 1918 flu pandemic, when pigs and humans were become sick at the same time (Nayak DP et al., 2004). The main cause for the 1918 flu pandemic was swine influenza H_1N_1 virus.The first isolated Swine influenza virus from pigs in the U.S. in 1930 (John W. Drake, 1993), after many years, in 2009, this virus was first detected in mexico and spreaded across the world. In the same year, WHO had raisen a global pandemic alert of phase 6 in regard to new influenza H_1N_1 virus. Few years before, between 1997 and 2002, three different subtypes and five different genotypes suddenly emerged as new strains, were the main cause of severe influenza in pigs in North America. The emergence of a new influenza H1N1 virus is due to triple reassortment of genes in pig host, the combined gene mutation of three different genotype viruses such as H1N1 swine virus, avian H_1N_1 and human H3N2 virus, caused the 2009 pandemic infection (John W. Drake, 1993).

Influenza
Nomenclature: The initial out break “H1N1 influenza”, this name was changed to pandemic H1N1/09 virus by WHO to distinguish it from other past and current seasonal H1N1 virus. The CDC started referring it as the novel H1N1 virus (J.Y et al., 2006).

Classification

Swine flu caused RNA viruses belongs to the family of orthomyxoviridae, and classified as three genera of influenza viruses that include influenza A, B and C. Pigs were most commonly infected with Influenza A and rarely infected with Influenza C. There were no reports that pigs were infected with Influenza B virus (Heinen PP et al., 2000).

Influenza-A: Swine influenza is not only caused by influenza H_1N_1 virus, but also caused with other Influenza-A strains that include H_1N_2 (4), H_2N_3 (5), H_3N_1 (6) and H_3N_2 (4),−9 in which three Influenza-A strains (H_1N_1, H_1N_2 and H_3N_2) are the most common subtypes in pigs (Kothalawala H et al., 2006).

Influenza-C: The transmission of Influenza-c viruses occurred between pigs and humans and also cause infection to both (Bouvier NM and Palese P., 2008; Kimura H, 1997). This genera of influenza is not involved in pandemic outbreak in humans (Lynch JP and Walsh EE, 2007) due to its less genetic diversity and limited host range ability.

Epidemiology

Influenza virus in the last century caused three pandemics- the Spanish flue in 1918, the 1957 Asian flu and the 1968 Hong Kong flu. The extent of severity, spreading and illness of these three outbreaks was different with each other (Kilbourne ED, 2006). The 1918 pandemic was the most severe and widespread across the world, caused infection to the one third of world's population. The strain responsible for the 1918 pandemic was H_1N_1. The virus regain its usual pattern after the control of this outbreak and caused smaller epidemics until the 1957 pandemic. The H_2N_2 strain is an antigenically distinct form emerged suddenly and caused influenza in less immunity population. After eleven years, this strain was found to be detected. The H_2N_2 strain finally transformed into as H_3N_2 strain which was the main responsible strain causing influenza in human until the 2009 outbreak (Kilbourne ED, 2006). The novel H1N1 strain was first identified in April 2009 at the border in between U.S. and Mexico, became the pandemic of swine origin influenza within two months of time (Chang LY et al., 2009). It has been a severe outbreak covers all the continents-170 countries with 1.7 lakh affected people across the world (WHO, 2009).

Incubation Period

Incubation period is time required to show the symptoms of disease after pathogen enters into the body, In general, the average incubation period of all influenza pathogens is two days. But, reports shown that the range of incubation period varies from one day to seven days based on the type of influenza pathogens effected. Furthermore, most of the U.S cases shown the incubation period ranges between 2-7days (Kay RM et al., 1994).

Role of pig: Susceptible pig cells has a vital role in transmission of influenza virus from one species to another species, consist receptors for both human (alpha 2 - 6 - linked sialic acids) and avian influenza strains (alpha 2 - 3 - linked sialic acids). These receptors allow more than one strain of different influenza species and facilitate the process of reassortment of genes from different influenza viruses (Ito T, 1998).

Infectious Period

The new influenza virus spreads quickly and vastly in the community than the seasonal flu due to less, or no immunity of people against influenza virus. An Influenza as pandemic can cause thousands of people sick within few weeks and make the situation worse, and also could impact day-to-day life of people.

Confirmation of Influenza-A (H_1N_1) Virus Infection

A person with acute respiratory illness within 7 days of close contact with other effected person, was a primary confirmation of influenza H_1N_1 viral infection, and other techniques – Influenza RT-PCR and IFA (Immunofluorescence Assay) were also significantly employed to confirm the infection caused by Influenza-A (H_1N_1) virus. These techniques confirm the infection by giving a positive report for influenza A and negative for influenza H_1 and H_3.

Transmission

Influenza virus can be easily transmitted to humans because the viral presence in respiratory secretions form small particle droplets and spreads quickly when the person is sneezing and coughing (Ito T, 1998). In addition, other body fluids also consider as potential transmitters of influenza virus (Lynch JP and Walsh EE, 2007). Thus, it is advisable to maintain 6 feet distance from infected person to prevent spreading of Influenza pathogen. Anintense exposed people work with swine have greater risk of zoonotic influenza virus endemic and reassorment of Influenza virus strains can also be occured in these animals.

Clinical Features

Common features

Patients liable to severe disease are – people with more than sixty five years of age, under five years young children, those who have systemic illness, pregnant women, adolescents using aspirin, immune suppressed patients and residents in nursing homes. The most commonly infected people are young adults (Novel swine team, 2009). Among them, two year young children have more complications with influenza virus such asfever and cough, apnea, tachypnea, dyspnea and dehydration (Dawood FS et

al., 2009). The most common complications occurred with swine origin influenza are pneumonia and acute febrile respiratory failure. Other manifestations of severe swine influenza disease include rhabdomyolysis, renal failure, multi organ dysfunction and myocarditis. 18 -1Few unusual symptoms are rarely appeared which include parotitis (Bastien N et al., 2009) and conjunctivitis (Shinde V et al., 2009). Diarrhea and vomiting are the most frequently occurred complications in children than adults (WHO, 2009). In addition, parotitis was also identified in children with swine influenza (Bastien N et al., 2009). Reye's syndrome and post influenza encephalitis also occurred with these viruses (Hayase Y et al., 2008).

The clinical symptoms of the 2009 influenza outbreak are a sudden fever above 100^0 F and sudden cough. Other symptoms include chills, tiredness, myalgias, cough and sneezing, headache, sore throat, runny nose, diarrhoea or stomach upset, etc. A patient infected with influenza should consult a doctor when that person has already been suffering from serious illness like cancer, pregnant woman, sick children under two years of age, and if the patient condition was suddenly worse.

Laboratory Diagnosis

RT-PCR

The viral load of an individual can be detected by the process of quantification of mRNA using RT-PCR detection technique. The development of PCR assay mainly depends on hemagglutinin sequences of swine influenza virus. In this assay, the amplification and detection of nasopharyngeal samples can be performed to extract the RNA from influenza viruses (Poon LLM et al., 2009). Other samples used are –bronchial aspirates and throat swabs (WHO, 2009). Respiratory specimen from infected person should be collected within 4-5 days after symptoms appered to diagnose the swine influenza-A infection. The high specificity of assay procedure was able to distinguish the swine origin H1N1 virus from other seasonal viral infections. These assays can produce results rapidly within few hours aften taking the sample (Poon LLM et al., 2009).

Viral Culture

The 100% specific diagnosis of swine influenza virus is possible with viral culture technique in which the virus was grown on culture medium. The high sensitivity and negative predictive values (Approximately 90%) are achievable by using this technique (Ginocchio CC et al., 2009). In this method, viral strains are developed on monkey kidney cell cultures as well as chick embryo cell within 2-3 days of its inoculation (Ginocchio CC et al., 2009).

Rapid Diagnostic Tests

The rapid diagnostic test shows 60-80 % sensitivity and used to detect viral antigens by comparing with the data of standard RT-PCR drawn from 65 patients (Anonymous, 2009) but it requires respiratory secretions containing a high virus concentration, if reports are negative, these reports are interpreted on the basis of clinical suspicion of illness (Anonymous, 2009).

Rise In Antibody Titer

This test mainly used to retrospect the past event cases but not for diagnostic purpose (Dolin R et al., 2005). In this technique, the comparison of antibody titer values during the time of acute illness with the titer values of 10-14 days after illness, this process will help to make diagnosis too.

Other Tests

Biological and haematological testing may suggest elevated lactate dehydrogenase, leucopenia and creatine kinase (Perez-Padilla R et al., 2009). Uncommon symptoms of thrombocytopenia may also appear. Chest X ray abnormalities may be noticed specifically in those hospitalized and severely affected people (Perez-Padilla R et al., 2009).

Treatment

Antiviral empiric treatment is highly recommended for any Swine influenza-A (H_1N_1) infected person. Antiviral treatment includes zanamivir alone, or combination of oseltamivir and amantadine or rimantadine are to be initiated immediately after the symptoms appeared. Five days duration is required or recommended for antiviral treatment. As per the guidelines of the CDC, the antiviral drugs should be administered to those who become severely infected, two drugs immediately recommended-zanamivir (Relenza) and oseltamivir (Tamiflu). To get higher effectivity, these drugs must be administered within 2 days of symptoms appeared. The main function of these drugs is to deactivating an enzyme which is responsible for the growth and spreading of the viruses. Oseltamivir is administered by oral route, where as zanamivir is given through inhalation device. This device should not be prescribedfor any person who suffers with respiratory complications, such as lung disease and asthma.

Alternative Treatment

Homeopathy: This alternative treatment mainly based on the symptoms of disease, homeopathy can offer an effective treatment for prevention and curing of swine flu with out any side effects.

Ayurveda: Ayurveda is a branch of medicine can promote an increased immunity to the people who suffering from swine flu by applying pure natural herbs or its decoctions. The panchgavya Medical Research Centre, Jodhpur, formulated Ayurvedic

alternative remedy for swine flu. This treatment is more safe and effective than the conventional allopathic system. “Flu-go” is an effective ayurvedic medicine used for the treatment of swine flu. The herb particularly Basil, Ocimum basilicum is a great Ayurvedic drug of choice for treating swine flu. Other Ayurvedic home drugs include ginger, garlic, gooseberry and aloe vera are also helpful for boosting the immune system of the body to respond aginst swine influenza virus.

Vaccines

Vaccines are developed and marketed as two different brands called Pandemrix and Celvapan. In general, pandemrix can be given in a single dose, where asCelvapan vaccine needs two doses should be taken until three weeks. Pregnant woman should be vaccinated at any stage of pregnancy and also children and people who suffering with severe swine flu infection can be vaccinated. The vaccine should not be prescribed to any person who suffers from severe allergic reaction of dose previously taken.

First Vaccination Priority Groups

CDC’s Advisory committee provided recommendations on a priority of receiving the novel H1N1 influenza vaccine as follow (Dharan NJ et al., 2009):

- Pregnant women are highly recommended to be vaccinated, because they have higher risk of complications and necessarily provide protection against influenza H1N1 virus to infants. Pregnant woman are four times more susceptible to serious complications like swine flu and five times more necessary to visit hospital than normal woman. In the later stages of pregnancy, highest risk of flu could make the condition worse may lead to abortion, or some times patient may die. Hence, pregnant woman should be vaccinated as early as possible.
- adults and children below 6 years of age should be vaccinated because children has a limited or no immunity at their early days. So they are susceptible to severe complications caused by influenza H1N1 virusthat include chronic diseases of lung, heart, kidney, liver and neurological diseases, and diabetes mellitus. Vaccination also to be given to those who are under immunosuppressant treatment, do not have spleen and have taken high dose systemic steroids.
- The Pandemrix vaccine shoud not be prescribed to any person who had egg allergy problem, because these vaccines are made with hen eggs, if a person exposed to these vaccines he might get severe anaphylactic reactions. Therefore, the Celvapan vaccine is highly recommended to people with egg allergies, no egg elements are necessarily to be employed while preparing Celvapan vaccines.

The side effects such as soreness, redness and swelling can be generally produced by vaccination. Adults and children must be aware of emergency warning signs occurred due to vaccination. These warning signs for adults include shortness of breath or difficulty breathing, pressure or pain in the abdomen or chest, confusion, sudden dizziness and persistent or severe vomiting. For children, these warning signs include bluish skin color, not interacting or not wake up, not drinking enough fluids, being so irritable, fever with rash, etc.

Antiviral Therapy

Adamantanes and neuraminidase inhibitors are under the class of antiviral drugs, used for the treatment and prevention of influenza by inhibiting the viral protein called M_2. Swine influenza-A (H_1N_1) virus was become a resistant strain for the drugs called adamantanes (Rimantadine and Amantadine). Neuraminidase inhibitors such as Zanamivir (Relenza) and Oseltamivir (Tamiflu) are the most commonly prescribed drugs by physicians (Ellis C et al., 2009). These drugs can reduce the infection caused by influenza by 70-90 %. Furthermore, these drugs have structural similarities and also approved by the US-FDA for the treatment and prophylaxis of influenza. The main advantage of these drugs is to work against several influenza strains such as current influenza A and B, The 1918 pandemic strain, and avian influenza strain (Tumpey TM et al., 2002).

Management

The spreading of disease is very fast and vigorous, increased cases of influenza are become a challenge for health care workers to treat an exponential cases with minimal facilities provided. All physicians must know the existing facilities and handling the cases of swine flu and also should be aware of principles of effective control and management of swine influenza virus.

The steps required to use optimal existing facilities that include:

1. Gathering of all patients in a designated place in hospital or clinic to reduce the spread of infection by screening the patients separately those who have suffering with Influenza like illness.
2. An assessing of severe swine flu symptoms, decision for admitting the patient, testing for swine influenza virus, and finally the treatment.
3. Prescribing supportive care for mildly swine flu suspected patient and referring appropriate hospital for testing of swine flu virus.

4. Admitting a critical suspected sick patients of swine flu in an ICU and arrangement to be made to start an antiviral treatment along with supportive care. Providing transport facility for reaching the designated centers where appropriate isolation facilities are available for swine flu patients.

Clinical Management Of Pregnant Woman Infected With Swine Influenza (H_1N_1) Virus

Pregnant women with respiratory complication must be admitted and managed by obstetric and midwifery teams and should be provided a continuous respiratory support facility in respiratory unit. The similar swine flu like symptoms caused by several other diseases such as urinary tract infections, chorioamnionitis, group A and B streptococcus infections and malaria can make the condition worse if the pregnant women neglect the clinical assesment of swine influenza. The most common disease caused by the 2009 H1N1 Influenza virus is pneumonia. Other complications of pregnant women include- intravascular coagulation, post viraemia/encephalitis impairment, pulmonary embolism and venous thromboembolism, and psychological effects. These complications should be recognized and appropriately treated. Co-amoxiclav (Augmentin) is an empiric antibiotic highly recommended for the pneumonia patients. In case of penicillin sensitive patients, a drug called clarithromycin is an alternative drug suggested by physicians to treat pneumonia.

Supportive Care

Patients with clinical deterioration symptoms such as chest pain, dyspnea, coughing up, altered sputum and confusion should be closely monitored. Serious ill patients need to be ventilated and provided an inotropic support as per the guidelines. Steroids can be administered if a critical ill patient suffering from suspected adrenal insufficiency.

Oxygen Therapy

The supplemented oxygen required for achieving oxygen saturation point can be monitored by pulse oximetry. The WHO recommended an optimum value of oxygen saturation to be maintained in hospitals at more than 90% for pneumonia patients.

Antibiotics

Antibiotics are alone to be recommended for pneumonia patients. It is advisable that these antibiotics should not be prescribed with chemoprophylaxis.

Dose Recommendations

For adults,the dose recommended of oseltamivir is 75mg, oral route, twice daily for 5 days. For children, the dosage regimen was prescribed as twice a day for 5 days and administered orally: < 15 kg - 30 mg; 15-23 kg - 45 mg; 24-40 kg - 60 mg; > 40kg - 75 mg. For infants, the drug administered orally twice a day for 5 days: <3 months - 12 mg; 3-5 months - 20mg; 6-11 months - 25 mg. Zanamivir is recommended for adults and children above 5 years of age, given by inhalation device, twice daily for 5 days (each dose contains 5mg of zanamivir)

Preventive Strategies

Chemoprophylaxis

Several studies reported that oseltamivir can be used in pre and post exposure prophylaxis, showed an efficiency of 68-89 % against seasonal influenza when it was given to house hold contacts. However, in pre exposure prophylaxis for 6 weeks, it showed an efficiency of 74% (Ellis C et al., 2009).Therefore, it concludes that post exposure chemoprophylaxis was suggested for all influenza affected patients. Health care professionals are also highly recommended to receive chemoprophylaxis due to their high chances of contact with probable, suspected and confirmed cases of swine influenza.

Vaccination

Currently there is no appropriate vaccine available for swine origin H1N1 virus. The seasonal flu vaccines can not boost up the immunity against novel H1N1 influenza. Since many years, researchers are working on the project of vaccine development for swine flu, few pharmaceutical companies have already reached the clinical trial-phase studies for human use. Influenza H1N1 virus is developed on egg cultures and related work currently under clinical trial.

General Measures

General cost effective measures include practicing respiratory etiquette, social distancing, good ventilation and hand hygiene. Several studies being evaluated the efficiency of masks to prevent or control the spread of viruses. Infected person should be aware the correct usage and disposing of masks appropriately. A person with mild symptoms must be isolated from his family members to control the spread of infection. The focus of health care professionals is essentially required on infected patients according to their risk of exposure and special disease controlling measures are need to be implemented that include separation of infected person, personal protective equipment (PPE) and usage of antiviral medicines.

Control Measures

These controlling measures can be used to minimize the pandemic impact, these include use of antiviral prophylaxis, vaccination, and use of antiviral drugs for treatement. Furthermore, simple measures are essential such as respiratory hygiene, standard precautions and cough etiquette. At initial stages, infected individuals are to be isolated in designated

hospitals can be helpful. During spreading stage, isolated individuals at home have more feasibility than isolation in healthcare centres. Hospitals and clinical centres plays a crucial role in controlling of transmission of virus, as a result, reducing the potential impact of flu pandemic (Nuno M et al., 2007).

Conclusion

Swine 2009 flu pandemic caused by nove swine influenza (H1N1) virus, spread quickly to several countries and caused infection to about 5 millions of people across the world. Swine H1N1 influenza is a potentially infectious affecting to humans as well as pigs. The viral mutation in host cell facilitates reassortation of strains to form new viral strains like influenza H1N1 cause more severe influenza related complications than normal mother strains. so we concluded that the scientists shoud find the solution to stop an emerging new viral strains and its complications to control the unprecedented deaths of innocent peopleen and also to enhance the quality of health conditions of social community.

"Cite this Article"

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References

- Anonymous. Evaluation of Rapid Influenza Diagnostic Tests for Detection of Novel Influenza A (H1N1) Virus — United States, 2009. *MMWR* 2009: 58; 826-829.
- Bastien N, Bowness D, Burton L *et al.* Parotitis in a child infected with triple-reassortant influenza A virus in Canada in 2007. *J Clin Microbiol* 2009 ; 47: 1896-1898.
- Bouvier NM and Palese P. The Biology of Influenza Viruses. Vaccine, 2008; 26(4): D49-53.
- Chang LY, Shih SR, Shao PL, Huang DT, Huang LM. Novel swine-origin influenza virus A (H1N1): the first pandemic of the 21st century. *J Formos Med Assoc* 2009; 108: 526-532.
- Clinical management of human infection with new influenza A (H1N1) virus: initial guidance. World Health Organisation:2009. http://www.who.int/csr/resources/publications/swineflu/clinical_management/en/index.html
- Dawood FS, Jain S and Finelli L. Emergence of a Novel Swine-origin Influenza A (H1N1) Virus in Humans. N Engl. J. Med., 2009; 360: 2605.
- Dharan NJ, Gubareva LV, Meyer JJ, *et al.* Oseltamivir-Resistance Working Group. Infections with oseltamivirresistant influenza A(H1N1) virus in the United States. *JAMA* 2009; 301:1034-1041.
- Dolin R. Influenza. In, Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson LJ (Eds). Harrisson's principles of internal medicine. *McGraw Hill* 2005. Pp 1066-1070.
- Ellis C, McEwen R. Who should receive Tamiflu for swine flu? *BMJ* 2009; 339: b2698.
- Ginocchio CC, Zhang F, Manji R, Arora S, Bornfreund M, Falk L et al. Evaluation of multiple test methods for the detection of the novel 2009 influenza A (H1N1) during the New York City outbreak. *J Clin Virol* 2009; 45: 191-195.
- Hayase Y, Tobita K. Influenza virus and neurological disease.*Psych Cin Neurosc* 2008; 51: 181-184.
- Heinen PP, Van Nieuwstadt AP, POL JMA, de Boer-Luijtze EA, van Oirschot JT, and ATJ. Systemic and Mucosal Isotype-Specific Antibody Responses in Pigs to Experimental Influenza Virus Infection. Bianchi. Viral Immunology.2000; 13(2): 237-247.
- Ito T. Molecular Basis for the Generation in Pigs of Influenza A Viruses With Pandemic Potential.J Virol., 1998; 72: 7367.
- John W. Drake. Rates of spontaneous mutation among RNA viruses Proc. Natl. Acad. Sci. USA, 1993; 90: 4171-4175.
- Kay RM, Done SH, Paton DJ. Effect of Sequential Porcine Reproductive and Respiratory Syndrome and Swine Influenza on the Growth and Performance of Finishing Pigs. Vet. Rec. 1994; 135 (9): 199–204.
- Kilbourne ED. Influenza pandemics of the 20th century.*Emerging Infect Dis.*, 2006; 12: 9-14.
- Kimura H, Abiko C and Peng G. Interspecies Transmission of Influenza C Virus between Humans and Pigs. Virus Res., 1997; 48(1): 71-79.
- Kothalawala H, M.J. Toussaint and E. Gruys. An Overview of Swine Influenza. Vet. Q., 2006; 28(2): 46-53.
- Laboratory-confirmed cases of pandemic (H1N1) 2009 as officially reported to WHO by States Parties to the IHR (2005) as on 6 August 2009. World Health organisation:Global alert and response. 12 Aug 2009. http://www.who.int/csr/don/2009_08_12/en/index.html.
- Lynch JP and Walsh EE. Influenza: Evolving Strategies in Treatment and Prevention. Semin.Respir. Crit. Care Med., 2007; 28(2): 144-158.

- Nayak DP, Hui EK, Barman S. Assembly and budding of influenza virus. Virus Res. 2004 Dec; 106(2): 147-65.
- Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. *NEJM* 2009; 360: 2605-2615.
- Nuno M, Chowell G, Gumel AB. Assessing the role of basic control masures, antivirals and vaccine in curtailing pandemic influenza: scenarios for the US, UK and the Netherlands. *J R Soc Interface* 2007; 4: 505–521.
- Perez-Padilla R, de la Rosa-Zamboni D,de Leon SP, *et al* for the INER Working Group on Influenza. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. *NEJM* 2009; 361
- Poon LLM, Chan KH, Smith GJ, Leung CSW, Guan Y, Yuen KY, Peiris JSM. Molecular detection of a novel human influenza (H1N1) of pandemic potential by conventional and Real-Time Quantitative RT-PCR assays. *Clin Chem* 2009; 55: 1555-1558.
- Shin, J.Y., M.S. Song, E.H. Lee, Y.M. Lee, S.Y. Kim and H.K. Kim. Isolation and Characterization of Novel H3N1 Swine Influenza Viruses from Pigs with Respiratory Diseases in Korea. J. Clin. Microbiol., 2006; 44(11): 3923-3927.
- Shinde V, Bridges CB, Uyeki TM *et al.* Triple reassortant swine influenza A (H1) in humans in the United States, 2005–2009.*NEJM* 2009; 360: 2616-2625.
- Swine influenza. The Merck Veterinary Manual. 2008. ISBN 1442167424. http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/121407.htm. Retrieved April 30, 2009.
- Tumpey TM, García-Sastre A, Mikulasova A. Existing Antivirals Are Effective Against Influenza Viruses With Genes from the 1918 Pandemic Virus. Proc Natl Acad Sci USA , 2002; 99:138-149.
- Wiwanitkit V. Swine Flu: The Present Pandemic Infectious Disease. Kulak Burun Bogaz Ihtis Derg., 2009; 19(2):57-61.