

SWINE-ORIGIN INFLUENZA A (H1N1) VIRUS: AN OVERVIEW

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ABSTRACT- Influenza has been recognized as a respiratory disease in swine since its first appearance concurrent with the 1918 “Spanish flu” human pandemic. All influenza viruses of significance in swine are type A, subtype H1N1, H1N2, or H3N2 viruses. Swine Influenza is a respiratory disease of pig caused by Type A influenza viruses. Influenza A causes moderate to severe illness and affects all age groups. The virus infects humans and other animals. Influenza A viruses are perpetuated in nature by wild birds, predominantly waterfowl. The WHO declared the H1N1 pandemic on June 11, 2009, after more than 70 countries reported 30000 cases of H1N1 infection. In 2015 the instances of Swine Flu substantially increased to five year highs with over 10000 cases reported and 774 deaths in India. 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. The CDC recommends the use of Oseltamivir (Tamiflu) or Zanamivir (Relenza) for the treatment. In this review, a brief overview on swine flu is presented highlighting the characteristics of the causative virus, the disease and its advances made in its diagnosis, vaccine and control to be adapted in the wake of an outbreak.

Keywords: H1N1 influenza, Virology, diagnosis, vaccine, Centers for Disease Control and Prevention.

I. 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].

Swine-origin influenza A (H1N1) virus is currently responsible for an outbreak of infections in the human population, with laboratory confirmed cases reported in several countries and clear evidence for human-to-human transmission. The novel H1N1 strain which is responsible for the current outbreak of Swine origin influenza was first recognized at the border between Mexico and in almost span of 2 months became first pandemic of 21st century^[26].

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^[43].

II. 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)^[3]. Swine Influenza is a respiratory disease of pig caused by Type A influenza viruses that causes regular outbreak in pigs^[4,5]. Influenza virus belongs to the genus Orthomyxovirus in the family Orthomyxoviridae which consists of influenza A, B and C viruses^[2] and has an envelope, single-stranded, negatively sensed RNA, eight separate segments and pleomorphic appearance with an average diameter of 120nm^[6,7].

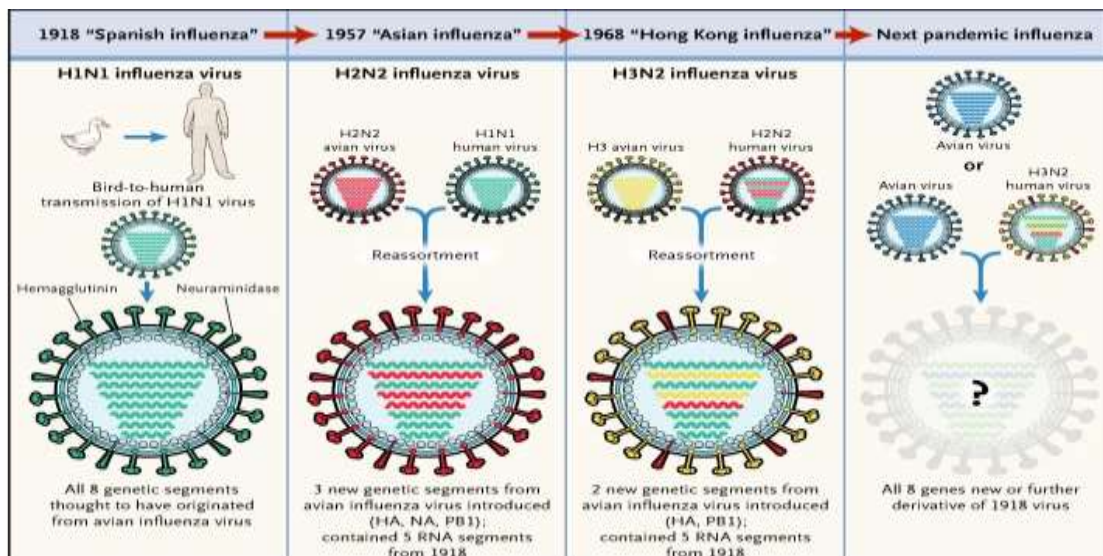


Figure: 1. New Findings on the H1N1 Virus^[41]

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 [13,14]

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 [16].

India reported its first case on 13th May, 2009. 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. [15].

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 [8,9]

III. 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 [10]. 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 [11].

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 [12].

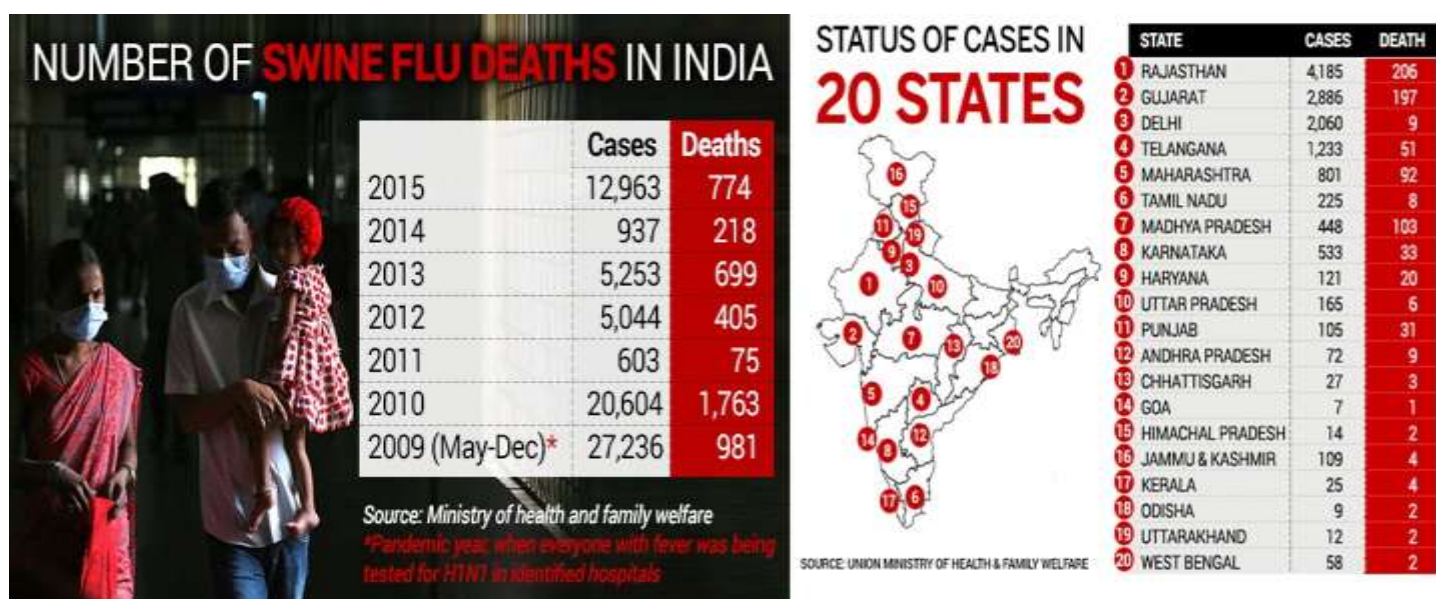


Figure: 2. Swine flu Cases report (2009-2015) in India & Status of Cases (2015) in 20 States [17]

A. Pandemic in Human:

The 1918 flu pandemic in humans was associated with H1N1 and influenza appearing in pigs [14]. 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 [18].

B. 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) [19]. Swine flu spread very rapidly worldwide due to its high human to human transmission rate and due to the frequency of air travel [20].

In 2015 the instances of Swine Flu substantially increased to five year highs with over 10000 cases reported and 774 deaths

in India [21]. The states reporting the highest number of cases and deaths are Rajasthan, Gujarat, Madhya Pradesh, Maharashtra, Delhi, and Telengana [22]. 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.

IV. 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 [23,24]. Vaccination of these workers against influenza and surveillance for new influenza strains among this population may therefore be an important public health measure [25].

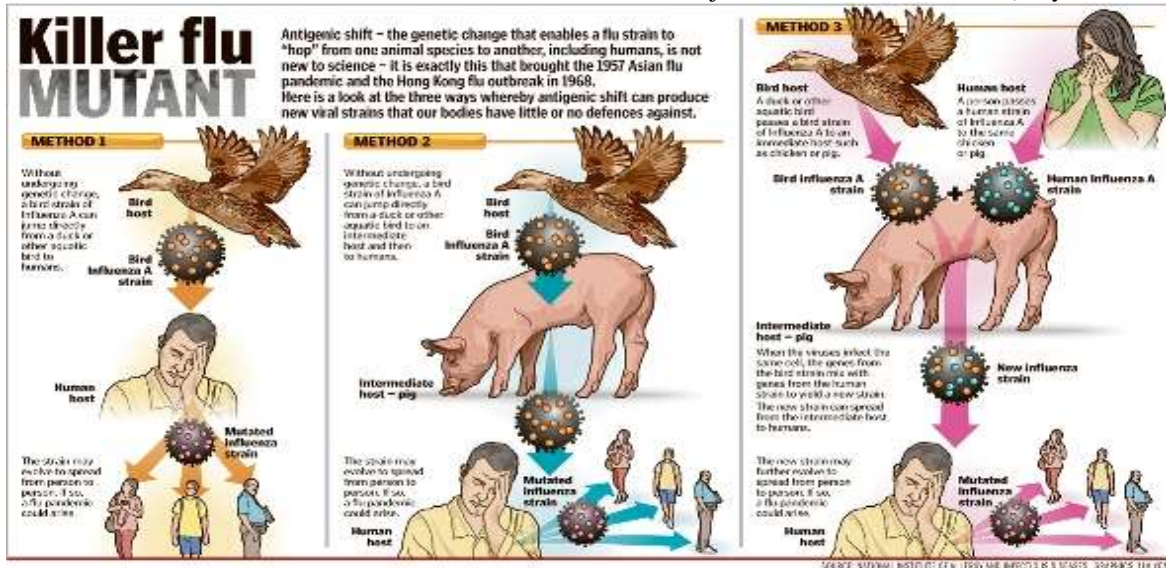


Figure: 3. Swine Flu Virus Transmission^[42].

A. Signs and symptoms:

Direct transmission of a swine flu virus from pigs to humans is occasionally possible (zoonotic swine flu)^[27]. 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^[28].

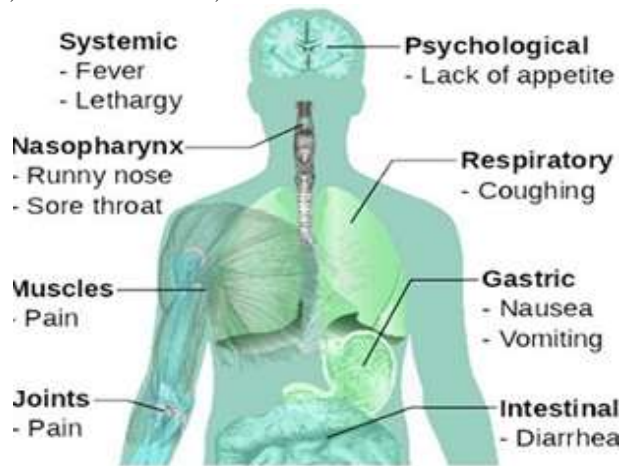


Figure: 4. Symptoms of Swine Flu^[43]

V. DIAGNOSIS

The CDC recommends real time PCR as the method of choice for diagnosing H1N1^[29]. 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 pandemic H1N1 detection, and compared their sensitivities with protocols developed by WHO reference centres^[30]. 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^[31].

VI. PREVENTION

Prevention of swine influenza has three components: prevention in swine, prevention of transmission to humans, and prevention of its spread among humans^[32].

A. 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^[2].

The transmission from swine to humans is believed to occur mainly in swine farms, where farmers are in close contact with live pigs^[33].

B. 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^[26,34]. "Avoid touching your eyes, nose or mouth. Germs spread this way^[35]

VII. 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^[36]. 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^[37].

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^[38].

VIII. 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).

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^[39]. The virus isolated in the 2009 outbreak has been found resistant to Amantadine and Rimantadine^[40]

IX. 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. Prevention and control measures for swine influenza are based on our understanding of seasonal human influenza and consideration of potential modes of transmission.

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REFERENCES

- [1] Ashishtha Vm, Kalra A, Choudhury P, Influenza Vaccination in India: Position Paper of Indian Academy of Pediatrics, IAP POSITION PAPER, 2013;50:867-874.
- [2] Van Reeth, K., Avian and swine influenza viruses: our current understanding of the zoonotic risk. *Vet Res.* 2007; 38(2), 243-260.
- [3] Smith, G.J. et.al, Origins and evolutionary genomics of the 2009 swine-origin H1N1 influenza A epidemic. *Nature.* 2009; 459(7250), 1122-1125.
- [4] Adeola OA, Adeniji JA, Olusaga BO. Isolation of influenza A viruses from pigs in Ibadan, Nigeria. *Vet. Ital.* 2009; 45(3): 383-90.
- [5] Ohwada, K., Kitame, F., Sugawara, K., Nishimura, H., Homma, M., and Nakamura, K. Distribution of the antibody to influenza C virus in dogs and pigs in Yamagata Prefecture, Japan. *Microbiol. Immunol.* 1987; 31(12):1173-1180.
- [6] Gurtler, L. Virology of human influenza. In: Kamps, B. S., Hoffmann, C., Preiser, W. (eds) *Influenza report 2006.* Flying Publisher, Wuppertel 2006;87-91
- [7] Fowotade A, Agbede O, Nwabuisi C, Fadeyi A. A review of swine influenza: an emerging pandemic. *NigHospPract.* 2009; 4: 3-4.
- [8] Shin JY, Song MS, Lee EH. Isolation and characterization of novel H3N1 swine influenza viruses from pigs with respiratory diseases in Korea. *J of ClinMicrobiol.* 2006; 44(11): 3923-7
- [9] Vincent AL, Lager KM, Ma W. Evaluation of haemagglutinin subtype 1 swine influenza viruses from the United States. *Vet Microbiol.* 2006; 12-22
- [10] Brown IH, The epidemiology and evolution of influenza viruses in pigs. *Vet Microbiol* 2000; 74:29-46
- [11] Knobler S, Mack A, Mahmoud A, Lemon S (ed.). "1: The Story of Influenza"
- [12] (<http://books.nap.edu/openbook.php?isbn=0309095042&page=75>) The Threat of Pandemic Influenza: Are We Ready? Workshop Summary (2005). Washington, D.C.: The National Academies Press. p. 75.
- [13] Olsen CW., "The emergence of novel swine influenza viruses in North America" *Virus Research*, 2000; 85 (2): 199-210.
- [14] Boffey, Philip M. "Soft evidence and hard sell" (<http://select.nytimes.com/gst/abstract.html?res=F10914FA3E5E14768FDAC0894D1405B868BF1D3&scp=9&sq=Swine+Flu+epidemic&st=p>) *New York Times*, (5 September 1976) [Accessed feb.26, 2015].
- [15] Taubenberger JK, Morens DM. "1918 Influenza: the mother of all pandemics" (http://wwwnc.cdc.gov/eid/article/12/1/05-0979_article) *Emerg Infect Dis*, 2006; 12 (1): 15-22.
- [16] Pandemic Influenza A H1N1: Directorate General of Health Services Ministry of Health and Family Welfare Government of India, (<http://karhfw.gov.in/H1N1/5.%20Clinical%20Management%20Protocol%20in%20influenza%20A%20H1N1.pdf>) [Accessed Feb. 26, 2015].
- [17] H1N1 (Swine Flu): WHO Says H1N1 Is Still a Pandemic (<http://emssolutionsinc.com/blog/h1n1-swine-flu-who-says-h1n1-is-still-a-pandemic/>) (updated July 25, 2010) [Accessed 26 Feb. 2015].
- [18] Swine flu outbreak: 774 deaths, 13,000 cases set alarm bells ringing (Source: Union Ministry of health & Family Welfare) (<http://www.hindustantimes.com/india-news/swine-flu-outbreak-743-deaths-12000-positive-cases-setalarm-bells-ringing-across-india/article1-1319158.aspx>) (Updated: Feb 22, 2015).
- [19] Vana G, Westover KM. "Origin of the 1918 Spanish influenza virus: a comparative genomic analysis". *Molecular Phylogenetics and Evolution*, 2008; 47 (3): 1100-10.
- [20] "Origins and evolutionary genomics of the 2009 swine origin H1N1 influenza A epidemic: Article" (<http://www.nature.com/nature/journal/v459/n7250/full/nature08182.html>). *Nature*. [Retrieved: Aug. 17, 201].

- [21] Chowell G, Bertozzi SM, Colchero MA, Lopez-Gatell H, Alpuche-Aranda C, Hernandez M et al. Severe respiratory disease concurrent with the circulation of H1N1 influenza. *N Engl J Med* 2009; 361:674-679
- [22] "Swine flu deaths soar past 660" (http://www.thehindu.com/scitech/health/policyandissues/swineflu_deaths_soarpast660/article6909436.ece) The Hindu. [Retrieved Feb.18, 2015].
- [23] Press Trust of India. Economic Times. New Delhi. 2015 February 13. 2015 swine flu toll at 485, more than two fold jump over 2014. (http://articles.economictimes.indiatimes.com/2015-02-13/news/591196371_swine-flu-h1n1temperature) (updated: Feb.13, 2015)[Accessed feb.26, 2015].
- [24] Gray GC, Kayali G "Facing pandemic influenza threats: the importance of including poultry and swine workers in preparedness plans". *Poultry Science*, 2009; 88 (4): 880-4.
- [25] Peiris M, Yen HL., Animal and human influenzas, *Rev Sci Tech*. 2014; 33(2):539-53.
- [26] Gray GC, Trampel DW, Roth JA. "Pandemic Influenza Planning: Shouldn't Swine and Poultry Workers Be Included?" *Vaccine*, 2007; 25 (22): 4376-81.
- [27] Centers for Disease Control and Prevention, Swine influenza A (H1N1) infection in two children-Southern California, March–April 2009. *Morb. Mortal. Wkly Rep.* 2009; 58, 400-402.
- [28] Anderson TK, et. al. Characterization of co-circulating swine influenza A viruses in North America and the identification of a novel H1 genetic clade with antigenic significance. *Virus Res.* 2015; S0168-1702(15)00079-9.
- [29] Myers KP, Olsen CW, Gray GC "Cases of Swine Influenza in Humans: A Review of the Literature" *Clinical Infectious Diseases*, 2007; 44 (8):1084-8.
- [30] "CDC H1N1 Flu, Interim Guidance on Specimen Collection, Processing, and Testing for Patients with Suspected Novel Influenza A (H1N1) (Swine Flu) Virus Infection" (http://www.cdc.gov/h1n1flu/specimen_collection.htm) (updated: May 13, 2009) [Accessed feb.26, 2015].
- [31] Lam WY et.al. Development and comparison of molecular assays for the rapid detection of the pandemic influenza A (H1N1) 2009 virus, *J Med Virol*, 2010; 82(4):675-83.
- [32] Çiçek C, et.al. Simultaneous detection of respiratory viruses and influenza A virus subtypes using multiplex PCR. *Mikrobiyol Bul.* 2014; 48(4):652-60.
- [33] Bridges CB, Kuehnert MJ, Hall CB. Transmission of influenza: Implications for control in health care settings. *Clin Infect Dis.* 2003;37:1094–101.
- [34] Ramirez A, Capuano AW, Wellman DA, Leshner KA, Setterquist SF, Gray GC. "Preventing Zoonotic Influenza Virus Infection" *Emerging Infect.* 2006; Dis. 12 (6): 996-1000.
- [35] "CDC H1N1 Flu | H1N1 Flu and You" (<http://www.cdc.gov/H1N1flu/qa.htm>) [last updated Feb.10, 2010].
- [36] Charoenvisal N., Experimental infection with a Thai reassortant swine influenza virus of pandemic H1N1 origin induced disease. *Virol J.* 2013; 16: 10:88.
- [37] Reynolds JJ, Torremorell M, Craft ME. Mathematical modeling of influenza A virus dynamics within swine farms and the effects of vaccination. *PLoS One* 2014; 9(8):e106177.
- [38] Allerson M, Deen J, Detmer SE, Gramer MR, Joo HS, et.al. The impact of maternally derived immunity on influenza A virus transmission in neonatal pig populations. *Vaccine*, 2013; 31: 500-505.
- [39] Uscher Pines, Lori, Jurgen Maurer, and Katherine M. Harris. "Racial and Ethnic Disparities in Uptake & Location of Vaccination for 2009 H1N1 & Seasonal Influenza." *Amer. J. of Pub. H.*, 2011; 101.7:1252-55.
- [40] Antiviral drugs for pandemic (H1N1) 2009: definitions and use (<http://www.who.int/csr/disease/swineflu/frequentlyaskedquestions/antivirals/definitionsuse/en/>) (updated: October6, 2009)[Accessed feb.27, 2015].
- [41] Vaccines and Immunizations: Antiviral Agents for Influenza (<http://www.cdc.gov/vaccines/pubs/pinkbook/flu.html>) [Page last updated: May 7, 2012]. [Accessed feb.27, 2015].
- [42] Passion animalia: A partner of the passion plantae network! Powered by, www.passionplantae.com (<http://passionanimalia.blogspot.in/2010/08/new-findings-on-h1n1-virus.html>) [Posted 6th August 2010].
- [43] Killer Flu Mutant from W3 | Triton World: (<http://bloggie-360.blogspot.in/2013/11/killer-flu-mutant-from-w3.html>) [Posted November 19, 2013]. [Accessed feb.27, 2015].
- [44] Safety Precautions to Deal with H1N1 Swine Flu: Symptoms of Swine Flu (<http://www.thefitindian.com/h1n1-virus-swine-flu/>) [Accessed: Feb.27, 2015].