A Review On Swine Flu

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Abstract: Swine flu is a highly infectious emerging viral zoonosis of global significance caused by Influenza-A virus subtypes which belong to the family *Orthomyxoviridae* and it ischaracterized by high morbidity rate and low mortality rate. It poses a significant health risk to humans ever since the first human and porcine outbreaks in the USA in 1918 which is believed to killed 50 million persons in the world. The geographical distribution of swine flu is worldwide and the disease is reported from North America, Asia, Europe, South America, Australia, and Africa. Out of the 198 countries affected by swine flu in the world (2009 - 2011) a total of 1,643,281 cases of H1N1 were reported with total deaths of 19,660 people. Swine have receptors for both avian and mammalian influenza viruses, and is uniquely important as a "mixing vessel" for genetic reassortment and evolution of influenza viruses. It is transmitted through direct contact, coughing, sneezing and contaminated fomite. Signs in humans include fever, coughing, sneezing runny nose, sore throat, headache, fatigue and sometimes diarrhea and vomiting. People who work with poultry and swine, especially those with intense exposures, like veterinarians, swine farmers and meat processing workers, are at increased risk of zoonotic infection with swine flu. Therefore, public health awareness creation by giving primary attention on mode of transmission of the disease and implementation of good bio-security system including quarantine to avoid contact among infected wild and domestic birds, pigs and humans should be applied to prevent the diseases efficiently.

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1. Introduction

Global swine population is estimated to be 923 million whereas in Africa, the swine population is estimated to be 18 million heads. Though Ethiopia has 29,000 heads which is representing only 0.1% of the African swine population, zoonotic diseases like swine influenza can jeopardize swine health or production and endanger public health significantly (Birhan *et al*, 2015; Clement, 2013).

Swine flu (also called hog flu, pig flu, swine influenza) is a highly infectious emerging viral zoonosis of global significance and the disease is caused by influenza-A virus subtypes that belongs to the family *Orthomyxoviridae*. H1N1 form of swine flu virus was responsible for the human outbreak in 1918-1919, which is believed to infect 500 million people and killed 50 million persons in the world (Pal and Mahendra, 2015). Swine flu is common throughout swine population worldwide and is characterized by low mortality (usually around 1–4 %) and high morbidity rate (approaching 100%) (Tekle *et al.*, 2015). Commonly, swine flu is a disease of pigs, but some swine influenza viruses can also cause disease in humans, birds, cats, dogs, ferrets and mink. In pigs, influenza infection produces fever, lethargy, sneezing, coughing, difficulty breathing, depression, discharge from the nose or eyes, eye redness or inflammation and decreased appetite (Heinen, 2003).

There are five genera of Influenza viruses that include Influenza-A virus, Influenza B virus, Influenza C virus, Thogoto virus, and Isa virus (Vincent *et al.*, 2008). Influenza A causes the most serious infections, followed by type B. Type C does not cause epidemics. The subtypes of type A Influenza virus is determined by haemagglutinin and neuraminidase (Sar *et al.*, 2010). Swine flu is caused by influenza viruses, and is transmitted to humans via contact with infected pigs or environments contaminated with Swine influenza viruses. It is also spread by coughing and sneezing. Anyone can get flu, but the risk of getting flu is highest among children. Symptoms come on suddenly and may last several days (Rewar, 2015). Apart from zoonotic importance, the economic importance of Swine flu includes loss of weight, poor growth, delayed weight gain, and sometimes abortion (Quinn *et al.*, 2011). Costs of control and prevention cause great economic loss to the farmers, country, and world (Tekle *et al.*, 2015).

Swine-origin influenza A (H1N1) virus is currently responsible for an outbreak of infections in the humans 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 in United States and has became first pandemic of 21st century (CDC, 2009).

Diagnosis of swine flu include history, viral isolation, cell culture, identification of the viral genotype by hemaglutinin and neuraminidase specific Real-time Polymerase Chain Reaction (RT-PCR) test with confirmation by sequence analysis of the amplified products. Virus can be detected in tissue sample by immunofluorescence and immunohistochemistry. Serological test, such as Haemagglutinin Inhibition (HI) and Enzyme Linked Immunosorbent Assay (ELISA) can be used to detect infection of unvaccinated swine (Machlachelan and Dubovi, 2011).

Swine flu affects both upper and lower respiratory (breathing) system of pigs and has become the world's fastest spreading influenza pandemic and epidemic, sweeping across many countries in a short period of time. Swine flu has been reported from tropical zone, temperate zone, northern hemisphere, and southern hemisphere. According to the World Health Organization (WHO) worldwide more than 209 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H1N1 (Mahore *et al*., 2011).

Therefore the objective of this paper is:

- ✓ To overview zoonotic and economic importance of swine flu
- ✓ To highlight epidemiological patterns of swine flu
- ✓ To overview transmission, control and prevention of swine flu

2. Historical Background Of Swine Flu

The presence of influenza in pigs was first recognized clinically during the summer of 1918 in the United States (US), at about the time of the Spanish influenza pandemic. Influenza virus was first isolated from pigs from North America 1930 (Thacker and Janke, 2008). During the 20th century, new strains of Influenza A viruses resulted in three influenza pandemics in US. These were the Spanish Flu (1918-1919), the Asian flu (1957-58) and the Hong Kong Flu (1968-1969) (Edwin, 2006).

Spanish flu(1918- 1919) : also called influenza A H1N1 epidemic, the first influenza pandemic of the 20th century, wrought havoc on the world population between 1918 and 1919. It killed at least 50 million people, five times as many as those who died fighting in the First World War (Kilbourne, 2006). More than 600,000 people died in the US directly or indirectly because of the epidemic. The 1918 flu pandemic in humans was associated with H1N1 and influenza appearing in pigs. This may reflect a zoonosis either from swine to humans or from humans to swine (Taubenberger and Morens, 2006).

Asian flu (1957–1958): also called influenza A H2N2 pandemic, was started in 1957 in the southern Chinese province of Guizhou. It spread in to Hunan Province and in to Singapore and Hong Kong. Although H2N2 viruses were first isolated in the United Kingdom (UK) and the US in 1957, peak incidence of influenza caused by the new pandemic strain did not occur until October 1957. This first wave of disease in both countries was followed by a second wave in 1958; both waves were accompanied by excess mortality. The highest attack rates during this pandemic reached 50% and occurred in children aged 5–19. Total influenza-associated excess mortality during this pandemic was estimated at 69,800 (Cox and Subbarao, 2000).

The Hong Kong Flu (1968-1969): also called Influenza H3N2 pandemic, was started in Hong Kong in early 1968. Later in the year, it spread to the US and caused 34,000 deaths. The Hong Kong Flu was the mildest pandemic of the 20th century (Kilbourne, 2006). The attack rates reached 40% and were highest in the 10-14 year old age group (Knipe and Howley, 2007).

Table 1: Salient point in the history of swine influenza.

History of swine influenza	
1918	Swine influenza H1N1 described in north central USA, Hungary, and China.
1930	Shope isolated influenza virus from pigs. The prototype classic swine influenza H1N1 strain transmitted experimentally to pigs.
1941	Recognized in Europe and disappeared.
1970	Transmission of human H3N2 virus to pigs. Avian like H3N2 in pigs in Asia
1976	Classical H1N1 reappears in European pigs.

1979	Introduction of whole H1N1 virus from birds to pigs. Antigenically distinguishable from classical strains. Still circulating
1984	Reassortment between human H3N2 and avian H1N1 in swine resulting in reassortant H3N2 virus with avian internal gene segments. Still circulating today
1986	Classical H1N1 reappears in UK, similar to classical H1N1 in continental Europe.
1987	Reassortant H3N2 associated with respiratory epizootics in UK.
1989	Avian like swine H1N1 is dominant and widespread in Europe.
1992-1993	Avian like H1N1 strains widespread in UK.
1993	Infection of children with reassortant H3N2 virus from pigs and isolation of avian like swine H1N1 virus from a pneumonia patient in the Netherlands.
1994	H1N2 first isolated in pigs in UK. Human avian reassortant virus.
1992-1998	H3N1 (H3 human, N1 swine) and H1N7 (H1 human, N7 equine) also occurred in swine in the UK but failed to spread.
1998	H9N2 in pigs and humans in Asia. Apparently an avian virus that has adapted to pigs.
1998	For the first time, H3N2 viruses cause severe disease in North America.
1999	Single case of isolation of avian H4N6 from pigs with pneumonia in Canada.
2002	Current situation in Europe: avian like H1N1, and reassortant human like H3N2 and H1N2. In North America: classical swine H1N1, triple reassortant H3N2.

Source: (FAO, 2009)

3. Etiology, Structure And Classification Of The Virus

Swine flu is an infection caused by any one of several subtypes of swine influenza A viruses which are an enveloped RNA viruses in the family Orthomyxoviridae (from Greek orthos, meaning correct or right and myxa meaning mucus) (Machlachelan and Dubovi, 2011). Influenza A subtypes that cause swine flu are H1N1, H1N2, H2N3, H3N1 and H3N2. In swine, H1N1, H1N2, H3N2 and H7N9 are the most common strains worldwide. The swine flu virus is susceptible to alcohol, formalin, sodium hypochlorite, and chlorine, and may be inactivated by heat, and low pH (Pal and Mahendra, 2015).

The influenza virion is an envelope, single strand and negatively sensed RNA virus which has eight separate segments and pleomorphic appearance with an average diameter of 120nm (Reeth, 2007).There are two types of glycoproteins.These are haemaglutinin (HA) and neuraminidase (NA). 16 haemaglutinin antigen (H1-H16) and 9 neuraminidase antigen (N1-N9) are recognized. In addation to glycoproteins, matrix proteins, nucleoprotein, polymerase protein, and RNA are involved in the viral structures as shown in (Fig. 1) (Lefevre *et al*., 2010).

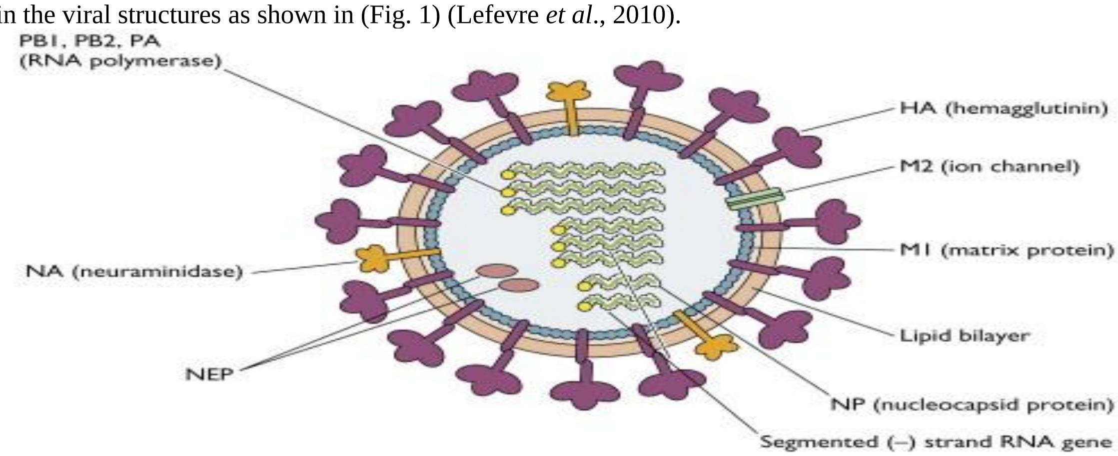


Figure 1: Structure of the influenza virion. (Source: Vincent, 2009).

Influenza viruses comprising five genera: Influenza A, B and C viruses, Thogoto virus, and Isa virus (Vincent *et al*., 2008). Influenza A causes the most serious infections, followed by type B. 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 with influenza A being common in pigs and influenza C being rare. Influenza B has not been reported in pigs (Heinen, 2003).

4. Zoonotic Importance Of Swine Flu

Isolation of swine influenza virus from humans 1974 confirmed that swine influenza viruses are zoonotic in nature (Thacker and Janke, 2008). People can be infected with zoonotic or variant influenza-A viruses that are commonly circulating in pigs. These include swine influenza virus subtypes A (H1N1) and (H3N2). Influenza virus infection in swine is a potential source of viruses for the next pandemic among humans. Swine flu was responsible for the 1918-20 outbreaks (Spanish flu pandemic) in human that caused an estimated 20-50 million deaths worldwide and accounted for 675,000 deaths in the US (Taubenberger and Morens, 2006). Until 16th April, 2010, pandemic influenza H1N1 2009 causes at least 17,798 deaths in humans in the worldwide (Syeda *et al*., 2010).

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. Vaccination of these workers against influenza and surveillance for new influenza strains among this population may therefore be an important public health measure (Gray *et al*., 2007). Even though human swine influenza virus infections without direct swine contact are possible, most patients (61%) with zoonotic swine influenza infections reported have been a recent exposure to pigs. Farmers, meat processing workers, abattoir workers and veterinarians were found to have significantly elevated serologic titers against H1N1 and H1N2 swine influenza viruses compared to control subjects. From zoonotic swine influenza subtypes, the most common one is H1N1 (Myers *et al*., 2006).

4.1. Disease in pigs

The incubation period usually appears within 1 to 3 days. Swine influenza virus causes epidemics of acute upper and lower respiratory disease in pigs. The affected swine exhibits the signs of fever (40.5 to 41.7^{o}C), coughing, sneezing, dyspnea, anorexia, conjunctivitis, ocular discharge, nasal discharge and sometimes vomiting and diarrhea. There is also lethargy, and hyperthermia (Pal and Mahendra, 2015). Loss of weight, poor growth, and sometimes abortion are also described and used as an economic importance in pig industry (Quinn *et al*., 2011). If pigs are forced to move, respiratory distress becomes more evident. Open mouth abdominal breathing may be seen and movements are characterized by paroxysms of coughing. SIV can also contribute to more chronic, multifactorial respiratory disease problems in combination with other viruses or bacteria (Dubey, 2009). In pigs, morbidity rapidly reaches 100% but mortality is low and usually ranges from 1% to 4% (OIE, 2009).

4.2. Disease in humans

The incubation period for influenza can vary from 1 to 4 days. The severity of swine flu disease depends on the prior immunologic experience with antigenically related virus variants. In general, only about 50% of infected persons will develop the classic clinical symptoms of influenza (Rewar, 2015). The symptoms of swine flu are a sudden fever of at least 38 ^{0}C, coughing, chills, lethargy, dehydration, headache, sore throat, Runny nose, diarrhea, vomiting, abdominal pain, myalgia or arthralgia as shown below (Fig. 2)(Lim and Mahmood, 2011). Signs of a more serious swine flu infection might include pneumonia and respiratory failure (Lokwani *et al*., 2011).

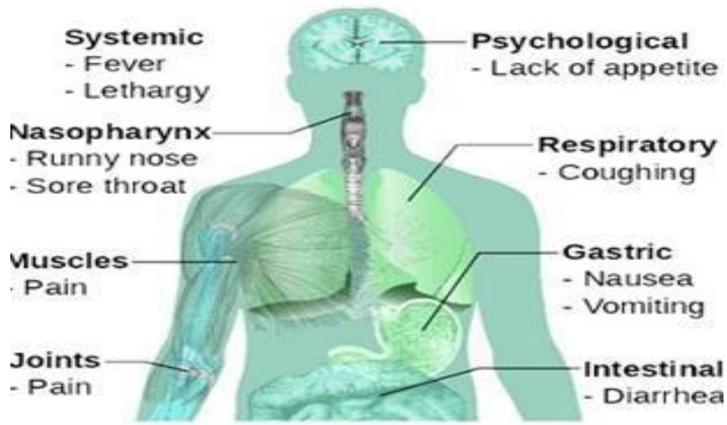


Figure 2: Symptoms of Swine Flu. (Source: Rewar *et al*., 2015).

Risk factors for severe disease from pandemic (H1N1) 2009 virus infection include the following groups: Infants and young children, in particular less than 2 years, Pregnant women, Persons with chronic pulmonary disease, chronic cardiac disease, metabolic disorders, chronic renal disease, chronic hepatic disease, certain neurological disorder, immunosuppression and Persons aged 65 years and older (WHO, 2009).

5. Epidemiological Patterns Of Swine Flu

5.1. Geographical distribution

The outbreak of swine flu has been reported from North America, South America, Europe, Africa, Australia and Asia. The serotypes of influenza A that circulate in swine population include H1N1, H1N2, H3N1, and H3N2. Until 16th April, 2010, worldwide more than 209 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including at least 17,798 deaths (Syeda *et al*., 2010). Even though many countries were affected, Out of 198 countries affected by swine flu in the world, from April 2009 to June 2011, a total of 1,643,281 cases of H1N1 were reported with total deaths of 19,660. The different names given for swine flu are as follows: H1N1 influenza or swine flu or pandemic H1N1/09 virus or novel influenza A (H1N1) or 2009 H1N1 or pig flu (Adetunde *et al*., 2012).

H1N1 and H3N2 are the influenza-A sub types which have been reported widely in pigs, associated frequently with clinical disease. These include classical swine H1N1, `avianlike' H1N1 and `human'- and `avian-like' H3N2 viruses. These viruses have remained largely enzootic in pig populations world-wide and have been responsible for one of the most common respiratory diseases in pigs (Brown, 2000). Global influenza surveillance indicates that influenza viruses are isolated every month from humans somewhere in the world. Influenza activity peaks during the winter months in temperate regions. In tropical regions, influenza can occur throughout the year. In the Northern Hemisphere, influenza outbreaks typically occur between November and March, whereas in the Southern Hemisphere, influenza activity occurs between April and September (Cox and Subbarao, 2000).

5.1.1. North America

The first influenza virus to be recognized in pigs was an H1N1 virus known as the ‘classical’ swine influenza virus in the US in 1918, at the same time as the severe ‘Spanish flu’ pandemic in humans. H1N1 viruses seem to have been transmitted between people and pigs during this pandemic. H1N1 viruses circulated in both species after this time, but diverged genetically in the two host populations (CFSPH, 2016). Before 1998, only classical-swine H1N1 viruses (cH1N1) were isolated from the US pig population. For nearly 70 years, swine influenza virus in North America was relatively stable with the cH1N1 as the only predominant subtype. In 1998, influenza-A viruses of the H3N2 subtype outbreak was observed in pigs on a farm in North Carolina with additional outbreaks in swine herds in Minnesota, Iowa and Texas (Ma *et al*., 2008).

Swine influenza is endemic throughout the US and causes a high morbidity rate among swine herds. The influenza-A subtypes (H1N1, H3N2, and H1N2) are the most common infection circulating in swine in the US (Vincent *et al*., 2008). In April 2009, the outbreak of

H1N1 influenza-A (swine flu) was detected in USA. Estimates in the US for the first 6 months of the pandemic report approximately 22 million people in the US became ill from the H1N1 influenza (swine flu), and about 3900 have died. Deaths include an estimated 540 children younger than 18 years, 2900 adults aged 18-64 years, and about 440 elderly individuals (Mahore *et al*., 2011).

In 2016, influenza activity in the US remains low, but is increasing and is expected to increase substantially over the weeks to come. As with any season, influenza activity is variable across the country. Most influenza seasons peak nationally in the US during January to March. The US CDC has received reports of critical illness and deaths in the US associated with influenza this season. Influenza A (H3N2), A (H1N1) pdm09, and influenza B viruses have all been detected in the US this season, and influenza-A 2009 pandemic H1N1swine flu (A(H1N1)pdm09 viruses have predominated in recent weeks (Rubinson, 2016).

5.1.2. Europe

Swine influenza viruses circulate in Europe includes H1N1, H1N2 and H3N2. While some viruses are widespread, there is regional variability, and some variants only occur in limited areas (Watson *et al* 2015). Based on various studies conducted in Europe, the seroprevalence of the three subtypes (H1N1, H1N2 and H3N2) is very high in those countries with a large pig production. For example, in Belgium, Denmark and Spain, the seroprevalence of the three subtypes is higher than 30%. In Spain, 94% of farms are positive to at least one subtype. In France and the UK high prevalence of H1N1 or H1N2 can be detected; however, the H3N2 subtype has not been recently isolated. In other countries such as the Ireland and Poland, the prevalence of SIV seems to be lower (Martin Valls, 2015).
After first, man A (H1N1)pdm09 by European countries reported the number of cases have been reduced, but in some countries like England, and Greece many cases were reported during the second pandemic swine flu of 2010/11 (Mytton and Rutter, 2012). Between February 2015 and September 2015 many Europian countries reported regional or widespread outbreaks of influenza A (H3N2) in February and March with co-circulation of A (H1N1) pdm09 and influenza B (WHO, 2016).

5.1.3. South America

In South America reports about Swine flu are generally scarce. H3N2 and H1N1 viruses are known to circulate in South America (CFSPH, 2016). Isolates found in Argentina include a human H3N2 virus, A (H1N1) pdm09 virus in many farms, and recombination of the A (H1N1) pdm09 with the HA and NA from human like swine influenza virus. In Colombia there was evidence of classic H1N1 and pandemic 2009 swine influenza (H1N1) circulating in swine populations. Peru has serological Agarose gel immune diffusion positives. Bolivia, Ecuador, Colombia and Peru have been trained on influenza diagnostic testing but no results are forthcoming yet because other swine diseases that are prevalent get more focus (OIE, 2012).

5.1.4. Asia

Information about swine flu in Asia is limited, especially for some regions, but H1N1, H3N2 and H1N2 viruses are known to circulate. Various North American and European lineage viruses belonging to these three subtypes have been reported. Some viruses have infected Asian pigs only transiently, and different swine influenza viruses may predominate in different regions (Choi *et al*., 2013). Influenza A (H1N1) pdm09 was reported in Asia with Widespread outbreaks occurred in the Indian subcontinent in 2015. Swine flu outbreak was reported in India in early 2015. The disease affected more than 20,000 people and claimed over a 1,000 lives (Tekle *et al*., 2015). In Asia, regional and widespread Influenza-A (H3N2) outbreaks were reported in February and March by Japan, and in March by Israel. Regional outbreaks were reported in June by China Hong Kong Special Administrative Region, June and July by Cambodia, and July and August by China (WHO, 2016).

5.1.5. Australia

Influenza virus infection has not been previously confirmed in Australian pigs until pandemic H1N1 was first identified in 2009 (Holyoake *et al*., 2011). Among the five countries with the highest total numbers of cases reported to the WHO, Australia has the third-highest rate of infection during H1N1 2009 swine flu outbreak. Out of 100,000 populations, 1694cases in chile, 2978 cases in Canada and 1307 cases in Australia (Senanayake, 2009).

The pandemic 2009 swine flu (H1N1) detected in commercial pigs in 2009 represented the first ever report of influenza in Australian swine. Three outbreaks of A(H1N1)pdm09 in commercial piggeries were reported in 2009 during the peak of human infections in Australia at that time, and one confirmed case was investigated in 2011 indicating more recent incidence of the virus in Australian pigs. With the exception of pandemic 2009 swine flu (H1N1), Australia is considered to be free from

SIV and there is no support for active surveillance (OIE, 2012).

5.1.6. Africa

The intensification of pig farming operations in urban and peri-urban areas favours circulation of pathogens at the human-animal interface (Matheka *et al*., 2013). Data on swine flu in sub Saharan Africa is scanty. This is not due to the absence of virus activity but poor surveillance and the absence of coordinated reporting and documentation systems (Clement, 2013). Out of 198 countries in the world, from 2009 to 2011, Africa countries had the lowest death cases of H1N1 of 116 while other countries worldwide had the highest (death of 19,544 peoples). Among the African countries affected by the H1N1 pandemic disease, Nigeria recorded the highest number of death cases of 15.38% followed by Mauritius 10.39%. Libya and Tanzania recorded the lowest number of death cases of 0.13% in Africa as shown in table 2 below (Adetunde *et al*., 2012).

Table 2: Swine flu deaths in some African countries (2009-2010.)

Selected Countries	Rate of Death
Namibia	1.32%
Nigeria	15.38%
Libya	0.13%
Ghana	0.44%
Sudan	3.33%
Tunisia	1.96%
Algeria	5.86%
South Africa	0.73%
Egypt	1.73%
Morocco	2.19%
Mauritius	10.39%
Mozambique	3.39%
Tanzania	0.13%

Source: Adetunde *et al*., 2012.

Kenya: the first case of 2009 pandemic influenza A (H1N1) virus was identified on 2009, and majority of influenza cases in the country were caused by H1N1. From July to November 2009, identified 690 patients with laboratory-confirmed pandemic (H1N1) 2009 (Osoro *et al.*, 2011). In 2012, there was a steady decline of pandemic H1N1 influenza cases among the sentinel surveillance sites in Kenya. Out of 745 samples collected between January 2012 and May 2012, only 92 were positive for influenza viruses. From these 80 samples positive for influenza A (73 samples were H3N2 and 7 samples were H1N1). 12 samples were influenza B (Matheka *et al*., 2013).

Nigeria: the first case of Swine influenza was reported in Nigeria, in 2009 and involved an American child returning to Lagos from holidaying abroad. The first death from the infection was also recently announced, a woman resident in Lagos, who had returned from the USA 3 months earlier (Sar *et al*., 2010). A study conducted from 2014-2015 in Ibadain city, Nigeria from 125 swine specimens reveals 8% prevalence of swine flu (2009 pandemic H1N1) (*Adeola,* 2015).

Ethiopia: the ministry of health of Ethiopia reported Ethiopia has confirmed its first case of H1N1 (swine flu) virus on June 19, 2009 in Addis Ababa. Both of the cases were girls that arrived back in the country for a summer break from their US high school (Reuters, 2016). In February 5, 2016 the Ethiopian health ministry confirmed a new case of H1N1 (or Swine Flu) virus outbreak in the capital Addis Ababa and its surrounding areas with a confirmed death of four people so far. Sources from Addis Ababa indicates the virus has been first detected earlier one week of February 5, 2016 in three major referral hospitals in Addis Ababa with a total confirmed cases exceeding 32 people so far (Andegna.com, 2016). Both Influenza A and B was detected but not Influenza C. The virus is severe on children under two years old, people older than 60 years old and those peoples who have a chronic disease (TesfaNews**,** 2016)

5.2. Reservoir

Water birds, especially ducks which are reservoirs of influenza-A virus, provide a genetic pool for the generation of the new influenza subtypes capable of infecting mammals. Migratory water fowls distribute the virus across the international borders. Human influenza pandemic have been attributed to the close association of concentrated human populations with domestic fowl and swine. The frequency of genetic reassortment in this animal population can lead to the generation of virulent influenza virus subtypes which are capable of infecting peoples, and initiating pandemics (Quinn and Markey, 2003).

Influenza-A viruses are common pathogens of horses, pigs, humans, and domestic poultry throughout the globe, but they also are the cause of sporadic infections and diseases in seals, mink, whales, and dogs. Influenza B viruses are pathogens of humans. Influenza C viruses infect humans and swine (Machlachelan and Dubovi, 2011). The pig has receptors for both avian and mammalian influenza viruses, and is uniquely important as a mixing vessel for genetic reassortment and evolution of influenza viruses (Ma *et al*., 2009). This dual infection could generate reassortants between pigs and avian/human viruses. These reassortant viruses could then be transmitted to humans (Ma *et al*., 2008).

5.3. Risk factors

Host factor*:* young, growing swine are most susceptible. The influenza infection is commonly complicated by bacterial infection due to *Haemophilus parasuis*, *Actinobacilus pleuropneumoniae*, and possibly other opportunists of the upper respiratory tract of the swine. The agent also contributes to the porcine respiratory disease complex (Radostits *et al*., 2007).

Agent factor: the virus has the ability to emerge and evolve easily. The emergence of variant viruses depends not only on genetic drift, but also on genetic shift. This has now revealed the antigenic diversity of the influenza-A virus (Machlachelan and Dubovi, 2011).

Environmental factor: epidemics occur mainly during the cold month of the year, starting in the early winter and terminating with a few out breaks in early spring. Several days of inclement weather often precede an outbreak. The virus likes cool and less humid atmosphere (Murray *et al*, 2002).

5.4. Transmission

The primary route of infection is via swine to swine contact through the nasopharyngeal route. The rapid spread of infection from swine to swine occurs by inhalation of infective droplets (Radostits *et al*., 2007). While horizontal transmission is common vertical transmission is also described in natural conditions (Lefevere *et al*., 2010).

The swine influenza virus can be transmitted to humans via contact with infected pigs or environments contaminated with swine influenza viruses, otherwise it is uncommon. Once a human becomes infected, he or she can then spread the virus to other humans via coughing or sneezing (Mahore, *et al.,* 2011). The bidirectional transmission of influenza viruses between pigs and human has been documented (Fig. 3). This allows the possibility of reverse zoonosis (Thacker and Janke, 2008).Humans who work with poultry and swine, especially those with intense exposures, are at increased risk of zoonotic infection with influenza A virus (Rewar *et al*., 2015).

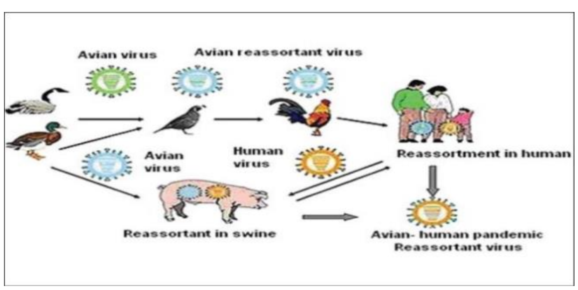
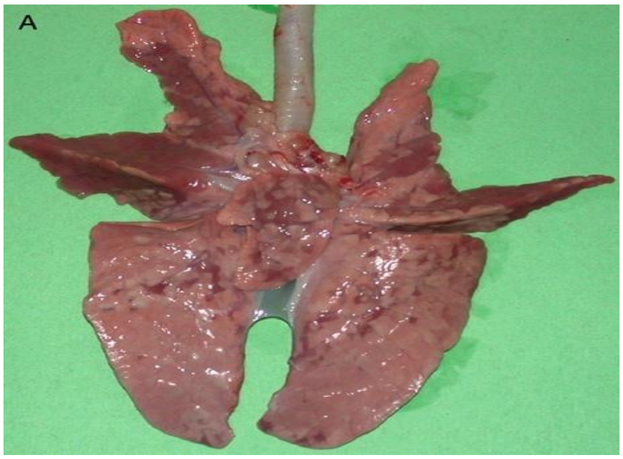


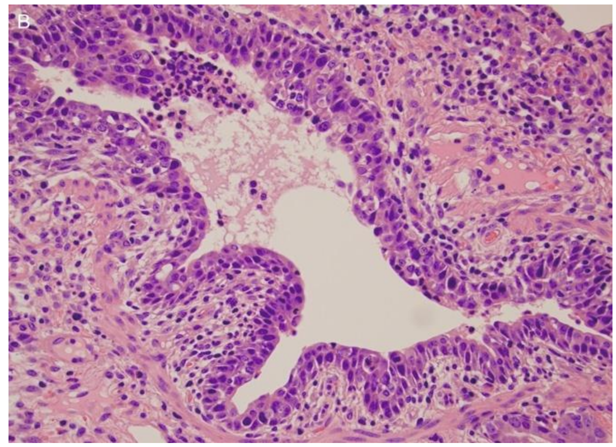
Figure 3: Transmission cycle of swine flu (Source : Rewar *et al*., 2015).

6. Pathogenesis And Necropsy Finding

6.1. Pathogenesis and necropsy findings in pigs

Swine flu virus infection follows the typical pattern for respiratory viral infections: virus entry is through aerosol or contact, and there is a rapid progression of the infection in the epithelium of the nasal cavity and large air ways in just a few hours. Animal develop bronchointestinal pneumonia that is characterized by sharply demarcated lung lesions in the apical and cardiac lobes, with hyperemia and consolidation, and the presence of inflammatory exudates in airways (Machlachelan and Dubovi, 2011). Macroscopically, Bronchial and mediastinal lymph nodes are often enlarged (Lefevre *et al*., 2010). SIV-infected lungs display a purple-red color that contrasts with the soft, light pink color of the healthy area and the lungs are consolidated as shown below (Fig. 4A). Microscopic changes in the lung consist of necrosis of bronchiolar epithelial cells and sloughing of these cells into airway lumen, which contains proteinaceous fluid and a few leukocytes (Fig. 4B) **(**Vincent *et al*. 2008).





A) Macroscopic B) Microscopic

Figure 4: A). Macroscopic pneumonia associated with swine H1N1 influenza virus characterized as purple-red consolidation located primarily in cranial and middle lung lobes.
B). Necrotizing bronchiolitis associated with swine H1N1 influenza virus
(Source**:** Vincent *et al*. 2008).

6.2. Pathogenesis and necropsy findings in humans

First the virus enter into the respiratory tract, then the virus replicates in cells of both the upper and lower respiratory tract. Then, after viral replication the infection lead to destruction and loss of cells lining the respiratory tract. Influenza complications of the upper and lower respiratory tract includes sinusitis, otitis media, bronchitis, and croup. Pneumonia is among the more severe complications of influenza-A infection most commonly seen in children or adults. Combined viral-bacterial pneumonia is common. The most common bacteria causing influenza-associated pneumonia are *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Haemophilus influenza* (Tekle *et al*., 2015). Respiratory failure, pneumonia and cytokine storms (overreacting immune system) often lead to deaths (Sar *et al*., 2010). Common necropsy finding includes mononuclear cell infiltration, thick alveolar septae, and intra alveolar hemorrhage, congested pulmonary blood vessels, pulmonary edema, and collapse of alveolar cells (Prasad, *et al.*, 2011). On the other hand, if there is recovery, it is associated with the production of interferon and the mounting of cell-mediated immune responses. T-cell responses are important for effecting recovery and immunopathogenesis. However, swine influenza infection depresses macrophage and T-cell function, hindering immune resolution (Murray *et al*, 2002).

7. Diagnosis

Diagnosis is based on history, clinical sign, viral isolation and detection, and using serological test. Virus isolation from nasal swab is obtained either through cultivation on emberyonated eggs or on cell lines such as Madin-Darby Canine Kidney (MDCK) or on primary cells susceptible to swine influenza virus (such as primary swine kidney cells and swine lung cells) the amplified virus is then revealed by haemagglutination test or by measuring a cytopatic effect respectively (Lefevere, *et al*., 2010).

Viral culture is the gold standard for diagnosing swine flu. The virus from the nasal secretion is grown and identified in the laboratory. The advantage of a viral culture is that the specific viral strain and type can be identified (Heinen, 2003). Culture is usually slow to help guide clinical management. A negative viral culture does not exclude pandemic S-OIV infection (Poon *et al*., 2009).

Isolated viruses can be subtyped using the haemagglutination inhibition (HI) and the neuraminidase inhibition tests, or by reverse transcription-polymerase chain reaction assays. Immunohistochemistry can be conducted on formalin-fixed tissue and a fluorescent antibody test can be conducted on fresh tissue. The serological test for detection of swine influenza virus includes HI test, agar gel immunodiffusion test, indirect fluorescent antibody test, virus neutralisation, and ELISA (OIE, 2009). Real-time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) is the recommended test to confirm the diagnosis of S-OIV for influenza A and B (CDC and WHO, 2009).

As a deferential diagnosis, the following diseases can commonly confused swine flu. These include Enzootic pneumonia, Hog cholera, and Atrophic rhinitis. Enzootic pneumonia is more insidious in its onset and chronic in its course. Hog cholera is manifested by less respiratory involvement and a high mortality rate. Atrophic rhinitis has a much longer course and is accompanied by characteristic distortion of the facial bones (Radostits *et al*., 2007).

8. Prevention And Control

Vaccination: Vaccination of People who work with poultry and swine, especially those with intense exposures, against influenza is an important public health measure (Gray *et al.*, 2007). The antigenic shift and drift nature of swine influenza virus makes the primary obstacle for successful influenza vaccination (Thacker and Janke, 2008). The two types of the influenza vaccines that are available includes trivalent influenza vaccine that contains A/H1N1, A/H3N2, and B and live attenuated influenza vaccine which also contains the same three strains of the flu viruses (Adetunde *et al*., 2012).

Biosecurity: it obiviously of paramount importance to prevent the introduction of the virus in to herds and to prevent contact between susceptible and infected animals. Pigs should be quarantine before introduced in to commercial herds. At the home- farm stage strict sanitary measures, such as age segregation, all- in/ all-out by building and appropriate hygiene routines can also inhibit the spread of infection (Lefevere *et al*., 2010).

Sanitation and hygiene: Protective measures for zoonotic influenza viruses include sanitation and hygiene (e.g., frequent hand washing), avoidance of contact with sick animals, and the use of personal protective equipment (PPE) when working with infected swine. Recommended PPE may include face masks, protective clothing and gloves (CFSPH, 2016). To prevent human to human transmission, there should be frequent washing of hands with soap and water or with alcohol-based hand sanitizers, Avoid Touching of the eyes, nose or mouth without washing hands, patient must be quarantined, patient must be stay at home from work, school and crowed places (Mahore, 2011).

Treatment**:** There is no effective treatment. Antiviral medications can make the illness milder and make the patient feel better faster. The US CDC recommends the use of oseltamivir (Tamiflu) or zanamivir (Relenza) for the treatment and/or prevention of infection with swine flu viruses. However, the majority of people infected with the virus make a full recovery without requiring antiviral drugs. The virus isolated in the 2009 outbreak has been found resistant to Amantadine and Rimantadine (Rewar *et al*., 2015). Supportive therapy includes parental nutrition, IV Fluids, Oxygen therapy, and Antibiotics for secondary infection (Lokwani *et al*., 2011).

9. Conclusion And Recommendations

Swine flu is an acute zoonotic respiratory viral disease of humans and animals characterized by high morbidity rate and low mortality rate. It is economically important in swine industry leading to significant loss of weight, poor growth rate and abortion in addition to high costs for the control and prevention of the disease. Currently H1N1, H3N2 and other influenza A virus subtypes are distributed throughout the world and causes pandemic and epidemic. Many countries in the world reported that swine flu can affect both humans and pigs and pigs serve as “mixing vessel”, since it has receptors for both human and avian influenza virus subtypes. People who work with poultry and swine, especially those with intense exposures, like veterinarians, swine farmers and meat processing workers are at increased risk on zoonotic infection with swine flu. The risk of diseases severity is high mainly in children, pregnant women and immune compromised persons. In general the presence of the receptors in pigs for both human, avian and swine flu viruses, the ability of the virus to mutate easily, the presence of weak biosecurity system, inhalational transmission ability of the agent and its contagious nature contribute for the pandemicity of the diseases and considerable loss in swine industry. Control and prevention of swine flu includes vaccination of humans and pigs, quarantine of newly introduced and infected pigs, treatment, and biosecurity. Even though a number of swine influenza vaccines are made commercially, all vaccines may not be protective to the diseases due to its great frequency mutation behavior.

Based on the above conclusion the following recommendations are forwarded:

- ✓ Since the virus can easily mutate and changes in its antigenic structure, vaccine producing institutes should modify the composition of the vaccines accordingly.
- ✓ Public health awareness should be created by giving primary attention on mode of transmission of the disease and prevention mechanisms.
- ✓ Good biosecurity including Quarantine should be encouraged to avoid contact among infected wild and domestic birds, pigs and humans.
- ✓ An ongoing research should be done to produce safe and effective therapy.
- ✓

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