Review Articles

Swine Flu: An Old Virus with a New Face

*Wail A. Hayajneh, *[1] Azmi M. Mahafzah [2]*

Abstract

This review is describing the current world status of the recently identified swine origin influenza virus A (H1N1) outbreak with special focus on Jordan. This recent outbreak originated in Mexico and spread to more than 40 countries including USA and has been caused by a novel swine origin influenza virus A(H1N1). This virus is thought to be a result of a genetic reassortment process that took place in pigs. This disease affects mostly young people with symptoms that are similar to those of seasonal influenza. Sustained human-to-human transmission has been documented and the virus is so far resistant to both amantadine and rimantadine but susceptible to oseltamivir and zanamivir. The World Health Organization (WHO) has raised the level of influenza pandemic to phase 5 and future speculations seem to be uncertain. Laboratory diagnosis is confirmed using a swine virus real-time, reverse transcriptase PCR test. No cases have been confirmed in Jordan. Nevertheless, Jordanian health authorities have started a very serious cascade of actions based on a comprehensive preparedness plan and supported by the already available infrastructure, increasing stockpiles of medications and protective equipments, and strengthening infection control preparedness of health care facilities.

Keywords: Swine flu, influenza, oseltamivir, zanamivir, pigs.

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Background

On March 18, 2009, the Mexican health authorities started reporting influenza-like illnesses in humans. These cases were then identified to be caused by Swine-origin Influenza Virus (S-OIV) A(H1N1). Soon later after reporting the Mexican cases, the United States Government reported the first seven confirmed human cases of swine flu. [1]

Interestingly enough, the isolated A(H1N1) viruses from Mexican cases were genetically identical to those isolated from the American cases in California. Subsequently, confirmed human cases of swine flu have been reported from different countries. As of May 24, 2009, more than 40 countries have officially reported more than 12,000 cases of influenza A (H1N1) infection. Majority of cases have been reported in USA, followed by Mexico, Canada, and Japan, respectively.

1- Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan.
2-Faculty of Medicine, University of Jordan, Amman, Jordan.
**** Correspondence should be addressed to:***
Wail A. Hayajneh, M.D.
Faculty of Medicine, Jordan University of Science and Technology.
P. O. Box: 3030, Irbid, Jordan 22110.
E-mail: wailh@just.edu.jo

Death toll has also reached 86 cases. [2] Confirmed cases in our region have been reported only from Turkey and Israel.

This current outbreak seems to be the realization of an old prophecy for authors who had hypothesized that a new pandemic would be secondary to a swine influenza virus. They had based their speculations upon the theory that pigs are the mixing vessel for reassortment of avian, human and swine viruses. [3] However, previously reported cases of human infections with swine influenza virus, were much milder than those seen with avian influenza A (H5N1). [4] Actually, they were similar to infections with low pathogenic avian influenza viruses. [5]

Nevertheless, this is not the first outbreak of human infections caused by S-OIV A(H1N1). In 1976 an outbreak of swine influenza virus infections occurred among military recruits in Fort Dix, New Jersey in the United States, in which human-to-human transmission was documented. That outbreak resulted in over 200 infections and one death.[6]

In response to pending possible threats of an evolving new pandemic, the World Health Organization (WHO) has raised the level of influenza pandemic to phase 4 on 27 April, 2009, then to phase 5 in just 2 days after that.[7]

This means that we might be a brink away from the dreadful long-awaited pandemic. At this moment of time, speculations regarding the evolution of this outbreak are vague at most. Things to remember are the unique genetic profile of this virus (never isolated before in humans or pigs), the proven persistent human-to-human transmission, and the little or no benefits of seasonal influenza vaccine against this virus.

Case Definitions and Clinical Patterns

Case definitions have been recently proposed by the US CDC and WHO. [8, 9] These case definitions are extremely important for public health authorities to standardize their surveillance and reporting systems. Case definitions have been formulated to reflect the need for early warning of virus spread and laboratory confirmation. They can also be used to direct strengthening of existing surveillance and laboratory infrastructures. In this review, we are proposing case definitions as detailed in table (1).

Clinical presentations are usually similar to those with seasonal influenza. Epidemiological characteristics for a subgroup of 47 American patients showed that the median age was 16 years, 38 (81%) were aged <18 years; and 51% of cases were males. [9, 10]

A recent descriptive study of more than 3,500 Mexican cases has shown that more than a quarter of cases are in the age group 0-9 years. On the other hand, case fatality was the highest in the age group of 20-29 years. Most reported cases appear to have uncomplicated, typical influenza-like illness and did recover spontaneously. The most commonly reported symptoms include cough, fever, sore throat, malaise and headache.[11]

Laboratory Diagnosis

There are no known approved tests to detect S-OIV A (H1N1) in human clinical samples. Viral culture provides definitive diagnosis but relatively few laboratories may provide such services. Available rapid diagnostic tests can detect the presence of influenza A virus in human specimens, but cannot differentiate human from swine strains. A positive Rapid influenza diagnostic test means that the patient might have novel H1N1 virus infection (S-OIV A (H1N1)), seasonal influenza A virus infection, or the patient might have a false positive test result. However, information about the sensitivity and specificity of such tests in detecting S-OIV A(H1N1) are not yet available. On April 27, 2009, the US FDA has issued a EUA to use the Swine Influenza RT-PCR Detection Panel (rRT-PCR Swine Flu Panel) to test for the presumptive presence of swine influenza virus in human clinical specimens collected from nose or nasopharynx. [12]

A positive PCR test result indicates presumptive infection but does not indicate stage of disease. On the other hand, a negative test result does not necessarily rule out infection and other clinical observations have to be considered.

Management

Management of confirmed, probable, or suspected cases consists mainly of basic supportive care and antiviral medications. Admission to hospitals should be reserved for patients with signs of respiratory distress who require oxygen supplement, mechanical ventilation, or intravenous hydration.

Available antiviral medications are amantadine, rimantadine (adamantanes), oseltamivir (Tamiflu) and zanamivir (Relenza) (neuraminidases). However, the use of adamantanes is discouraged because of documented resistance. In fact, all CDC tested S-OIV A (H1N1) isolates are resistant to amantadine and rimantadine but are susceptible to oseltamivir and zanamivir. [13-15]

In response to the emerging current flue pandemic, the US Food and Drug Administration (FDA) has on April 27th 2009 used its rights [16] and issued Emergency Use Authorizations (EUAs) to modify uses of antivirals oseltamivir and zanamivir toward lowering age limits, providing alternate dosing recommendations, and distributing medications to larger segments of population. [17] In accordance with these EUAs and previous recommendations, [18] we are proposing the use of these antiviral medications as shown in table (2). Treatment with antiviral medications is reserved for confirmed, probable, or suspected cases and it is usually for 5 days. Optimal clinical benefits are obtained of antiviral medications if initiated within the first 48 hours of symptoms. However, this should not deter physicians from using these medications after that if needed. Prophylaxis with either oseltamivir or Relenza [19] should be offered to the following individuals:

1. Household close contacts of a suspected case and who are at high-risk for complications of influenza. Examples are:
   A- Persons with chronic medical conditions
   B- Persons 65 years or older
   C- Children younger than 5 years old
   D- Pregnant women.
2. Health care workers working in an area of the healthcare facility that contains patients with confirmed S-OIV A (H1N1) cases and who are at high-risk for complications of influenza. Examples are:
   A- Persons with chronic medical conditions.
   B- Persons 65 years or older.
   C- Pregnant women.
3. Travelers to areas (i.e. Mexico) with confirmed S-OIV A (H1N1) cases and who are at high-risk for complications of influenza. Examples are:
   A- Persons with chronic medical conditions.
   B- Persons 65 years or older.
   C- Children younger than 5 years old.
   D- Pregnant women.
4. First responders who are at high-risk for complications of influenza and who are working in areas with confirmed cases of S-OIV A (H1N1) infection. Examples are:
   A- Persons with chronic medical conditions.
   B- Persons 65 years or older.
   C- Pregnant women.

Prophylaxis is usually continued for a period of 10 days from the last known contact with an infectious case.

It is worth mentioning that Jordanian health authorities do have a stockpile of oseltamivir enough to treat 300,000 persons and they are in the process in getting more supplies.

Infection Control Precautions in Hospitals

Key elements for effective infection control within hospitals to decrease transmission of S-OIV A (H1N1) include effective use of administrative controls, environmental/hygienic controls, and effective use of personal protective equipments. Certain interventions to be emphasized are hand hygiene, and use of standard and droplet precautions when caring for a patient with an acute, febrile, respiratory illness.[20]

Table (1): Case Definitions for Infection with Swine-Origin Influenza A (H1N1) Virus.

A. A **confirmed** case of swine-origin influenza A (H1N1) virus infection is defined as an acute febrile respiratory illness in a person and laboratory-confirmed swine-origin influenza A (H1N1) virus infection by either of the following tests:

1- Real-time reverse transcription–polymerase chain reaction (rRT-PCR), or
2- Viral culture.

B. A **probable** case of swine-origin influenza A (H1N1) virus infection is defined as acute febrile respiratory illness in a person who is

Positive for influenza A, but negative for H1 and H3 by influenza rRT-PCR.

C. A **suspected** case of swine-origin influenza A (H1N1) virus infection is defined as acute febrile respiratory illness in a person:

1- with onset within 7 days of close contact with a person who has a confirmed case of swine-origin influenza A (H1N1) virus infection, or
2- with onset within 7 days of travel to a community, which has one or more confirmed swine-origin influenza A (H1N1) cases, or
3- who resides in a community in which one or more confirmed swine-origin influenza cases have occurred.

Table (2): Recommended regimens of antiviral medications for S-OIV A(H1N1) infected or exposed persons.

Agent	*Weight or Age*	*Treatment*	*Prophylaxis*
Oseltamivir			
Adults		*75 mg twice per day for 5 days*	*75 mg once per day*
Children ≥ 12 months	*< 15 kg*	*30 mg twice per day for 5 days*	*30 mg once per day*
	15-23 kg	*45 mg twice per day for 5 days*	*45 mg once per day*
	24-40 kg	*60 mg twice per day for 5 days*	*60 mg once per day*
	>40 kg	*75 mg twice per day for 5 days*	*75 mg once per day*
Children < 12 months	*< 3 months*	*12 mg twice per day for 5 days*	*Not recommended*
	3-5 months	*20 mg twice per day for 5 days*	*20 mg once per day*
	6-11 months	*25 mg twice per day for 5 days*	*25 mg once per day*
Zanamivir			
Adults		*10 mg (two inhalations) twice per day*	*10 mg (two inhalations) once per day*
Children ≥ 7 years		*10 mg (two inhalations) twice per day*	*10 mg (two inhalations) once per day*
Children 5-6 years		*Not recommended*	*10 mg (two inhalations) once per day*
Children < 5 years		*Not recommended*	*Not recommended*

Community Precautions

In areas where swine flu cases are confirmed, The US Centers for Disease Control and Prevention (CDC) recommend that a combination of actions may help to reduce the risk for infections. [21] These actions include:

1- Frequent handwashing.
2- Covering coughs.
3- Keeping ill persons at home.
4- Voluntary home quarantine of members of households with confirmed or probable swine influenza cases.
5- Reduction of unnecessary social contacts.
6- Avoidance of crowded settings whenever possible.

The CDC also recommends the use of facemask or an N95 respirator upon entering crowded areas. However, we refrain from recommending this for our community at this time because of absent confirmed cases and limited evidence for this practice.

Vaccine Status

The current available seasonal influenza vaccine is not expected to offer any protection against the new S-OIV A (H1N1). The work to develop a specific vaccine against S-OIV A (H1N1) has started. However, developing this completely new influenza vaccine can take five to six months at least.

The Epidemic Status in Jordan

No confirmed cases have been reported in Jordan and no unusual clinical trends have been observed since the beginning of the outbreak. However, we need to keep high level of vigilance with the presence of few confirmed cases across the Jordan River. Management of such outbreaks in Jordan is overseen by Disease Control Directorate-Ministry of Health in consultation with National Committees. These authorities do have in place now a comprehensive action plan that assigns, regulates, coordinates, documents and monitors all activities related to the total management process of the current status. This plan has also identified certain referral hospitals, delineated the available diagnostic services, and rationalized the use of antivirals among other important elements.

Summary

In view of established human-to-human transmission of S-OIV A (H1N1) virus infections, the long awaited influenza pandemic might be in action. The current outbreak situation is not showing signs of stabilization. However, no cases have been confirmed in Jordan. Fortunately, the Jordanian experience in the last two epidemics of SARS and avian flu has strengthened the basic infrastructure needed now to manage this current outbreak.

Nevertheless, any level of complacency should be discouraged. Jordanian Public Health authorities and other concerned ones are expected to put in place a comprehensive, integrated and practical plan. This plan is expected to help in effective screening all ports of entry to Jordan, diagnosing and managing suspected cases, and raising the preparedness level of recognized hospitals. Another important element of this plan is to raise the community awareness about the disease and possible community-based infection control practices.

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أنفلونزا الخنازير: فيروس قديم بوجه جديد

وائل أحمد هياجنة،[1] عزمي محافظة [2]

1- **كلية الطب، جامعة العلوم والتكنولوجيا، إربد، الأردن؛ 2- كلية الطب، الجامعة الأردنية، عمان، الأردن**

الملخص:

هدف هذه الدراسة إلى وصف الوضع العالمي الحالي لظاهرة انتشار وباء أنفلونزا الخنازير، مع التركيز على وضع الأردن.

كانت بداية الوباء في المكسيك، ثم انتشر وبسرعة إلى أكثر من أربعين دولة أخرى بما فيها الولايات المتحدة الأمريكية، وقد أرجع العلماء سبب هذا الوباء إلى ظهور فيروس جديد من سلالة الأنفلونزا نتيجة لتمازج جيني لسلالات مختلفة من فيروسات الأنفلونزا داخل أجسام الخنازير. ومن الصفات المقلقة لهذا المرض ثبوت انتقاله المباشر من الإنسان إلى الإنسان، واستجابته فقط لصنفين من مضادات الفيروسات (أوسيلتامفير وزانامفير). علماً أن تأكيد التشخيص يتم بوساطة تفاعل البلمرة المتسلسل. وقد دفعت هذه الأسباب "منظمة الصحة العالمية" إلى رفع الحالة الوبائية لمرض الأنفلونزا إلى الدرجة الخامسة، مع العلم أن التطورات المستقبلية لهذا الوباء لا تزال غير واضحة.

أما بخصوص الوضع في الأردن، فإنه لم تسجل لغاية الآن أية حالات، ومع ذلك فإن مديرية رقابة الأمراض قد بدأت باتخاذ إجراءات جدية للتعامل مع احتمالية ظهور هذا الوباء من خلال "خطة جاهزية" شاملة معتمدة على بنية تحتية متكونة سابقاً (في أثناء وباء أنفلونزا الطيور) و هدف إلى زيادة المخزون الاستراتيجي من الأدوية ووسائل الوقاية الشخصية، وتدعيم وسائل ضبط العدوى في المرافق الصحية الأردنية.

الكلمات الدالة: وباء أنفلونزا الخنازير، الأنفلونزا، مضاد الفيروس (أوسيلتامفير)، مضاد الفيروس (زانامفير)، الخنازير.