Demographic and Clinical Characteristics of Patients Admitted to "Almaza Military Fever Hospital" with Influenza A Virus (H1N1) Infection

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H1N1	H1 (hem agglutinin type 1) and N1 (neuraminidase type1)
WHO	World Health Organization
CDC	Centers for Disease Control and Prevention
(rRT)-PCR	real-time reverse transcriptase-PCR
TIV	trivalent inactivated vaccine
LAIV	live attenuated influenza vaccine
GBS	Guillain-Barre syndrome
NHS	National Health Service
O.P	Oseltamavir Phosphate
CTL	Cytotoxic T Lymphocytes
N.K	Natural Killer
NAI	Neuraminidases Inhibitor
CV-N	Cyanovirin-N
dsRNA	double stranded RNA
siRNA	Small interfering RNAs
Roc curve	Receiver operating characteristic curve

Introduction

Influenza is caused by a virus that attacks mainly the upper respiratory tract (the nose, throat, bronchi) and rarely also the lungs. In addition to humans, they infect pigs, horses, sea mammals, and birds. The virus had three genera namely Influenza virus A, B and C. Viruses of the C types are common but usually cause no or mild symptoms. Type B viruses cause sporadic outbreaks of more severe respiratory disease. Type A viruses are of greatest concern as they may cause severe and fatal respiratory illness (attributed to its high affinity for mutation) ***(Lamb and Krug, 1996).***

Influenza viruses are subtyped by 2 different surface antigenic protein components. Haemagglutinin (H) and Neuraminidase (N) components.Haemagglutinin (H) component governs virus binding and entry into cells. There are 15 H subtypes, designated H1 to H15. Neuraminidase (N) component governs the release of newly formed virus from infected cells into the host's body. There are 9 N subtypes, designated N1 to N9. An individual virus strain is identified by the subtypes of H and N proteins. It is named by the letters H and N, each followed by the number of the subtype ***(Lamb and Krug, 1996).***

Swine influenza is known to be caused by influenza A subtypes H1N1, H1N2, H3N1, H3N2 and H2N3 ***(Matsuzaki et al., 2002 and Bouvier&Palese, 2008).***

The analysis of incidence occurred in the past revealed that H1N1 influenza virus was responsible of a big pandemic in1918–1919. Around 500 million persons at that time affected and caused 50 million deaths ***(Lopez et al., 2006).***

The first reported human case infected with H1N1 of 2009 outbreak was in April 2009 and since then, has prompted the World Health Organization (WHO) to raise its pandemic alert to the highest level ***(WHO updates, 2009).***

By the 10th January 2010, worldwide more than 208 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including at least 13554 deaths.

The most intense areas of pandemic influenza virus transmission are in parts of North Africa, South Asia, and East and Southeastern Europe ***(WHO updates, 2009).***

In North Africa, limited data suggest that transmission of pandemic influenza virus remains active throughout the region, particularly in Morocco, Algeria, and Egypt.

In Egypt, the Cumulative Total number of confirmed cases is 15036 cases from June 2009 till 15/1/2010, 5388 of them were in schools and 835 in universities. Cured cases are 14607 and 219 deaths were recorded ***(Ministry of Health Egypt, 2010).***

Aim of the Work:

- The aim of this work is to review the situation of influenza A H1N1 in the world and our situation in Egypt during the period from June 2009 to May2010.
- To study the demographic and clinical characteristics of patients admitted to Almaza Military Fever Hospital with proved infection with Influenza A H1N1 during the period from June 2009 to May2010.

Chapter I: Influenza

Influenza commonly referred to as the flu, is an infectious disease caused by RNA viruses of the familyOrthomyxoviridae (the influenza viruses), that affects birds and mammals. The most common symptoms of the disease are chills, fever, sore throat, muscle pains, severe headache, coughing, weakness/fatigue and general discomfort, sore throat, fever and coughs are the most frequent symptoms. In more serious cases, influenza causespneumonia, which can be fatal, particularly for the young and the elderly. Although it is often confused with other influenza-like illnesses, especially the common cold, influenza is a much more severe disease than the common cold and is caused by different types of virus. Influenza may produce nausea and vomiting, particularly in children**(*Brankston et al., 2007*).**

Typically, influenza is transmitted through the air by coughs or sneezes, creating aerosols containing the virus. Influenza can also be transmitted by direct contact with bird droppings or nasal secretions, or through contact with contaminated surfaces. Airborne aerosols have been thought to cause most infections, ***(Krisima, 2007).***

Influenza viruses can be inactivated by sunlight, disinfectants and detergents As the virus can be inactivated by soap, frequent hand washing reduces the risk of infection.***(Suarez et al., 2003&Brankston et al., 2007).***

Influenza spreads around the world in seasonal epidemics, resulting in the deaths of many people every year and millions in pandemic years. On average 41,400 people died each year in the United States between 1979 and 2001 from influenza **(Eccles,2005).**

Three influenza pandemics occurred in the 20th century and killed tens of millions of people, with each of these pandemics being caused by the appearance of a

new strain of the virus in humans. Often, these new strains appear when an existing flu virus spreads to humans from other animal species, or when an existing human strain picks up new genes from a virus that usually infects birds or pigs. An avian strain named H5N1 raised the concern of a new influenza pandemic, after it emerged in Asia in the 1990, but it has not evolved to a form that spreads easily between people **(Eccles,2005).**

The regression model attributes an annual average of 41,400 (95% confidence interval: 27.100, 55.700) deaths to influenza worldwide over the period 1979–1997 ***(Villegas, 1998).***

In April 2009 a novel flu strain evolved that combined genes from human, pig, and bird flu, initially dubbed "swine flu" and also known as influenza A/H1N1. It emerged in Mexico, the United States, and several other nations. The World Health Organization officially declared the outbreak to be a pandemic on June 11, 2009.The WHO's declaration of a pandemic level 6 was an indication of spread, not severity, the strain actually having a lower mortality rate than common flu outbreaks ***(Nava et.,al, 2009)*.**

Vaccinations against influenza are usually given to people in developed countries and to farmed poultry ***(WHO, 2009)(5).***

The most common human vaccine is the trivalent influenza vaccine (TIV) that contains purified and inactivated material from three viral strains. Typically, this vaccine includes material from two influenza A virus subtypes and one influenza B virus strain ***(Villegas, 1998).***

The TIV carries no risk of transmitting the disease, and it has very low reactivity. A vaccine formulated for one year may be ineffective in the following year, since the influenza virus evolves rapidly, and new strains quickly replace the older ones.

Antiviral drugs can be used to treat influenza, with neuraminidase inhibitors being particularly effective***(Villegas, 1998).***

H1N1 influenza is a respiratory disease of pigs caused by type A influenza virus that regularly causes outbreaks of influenza in pigs. H1N1 virus causes high levels of illness and low death rates in pigs. The classical swine flu virus (influenza type A H1N1 virus) was first isolated from a pig in 1930 Like all influenza viruses, H1N1 viruses change constantly. Pigs can be infected by avian influenza and human influenza viruses as well as H1N1 viruses At that time there are four main influenza type A virus subtypes that have been isolated in pigs: H1N1, H1N2, H3N2, and H3N1. Most of the recently isolated influenza viruses from pigs, however, have been H1N1 viruses.As of June 2009, the CDC has identified that influenza viruses from different species infect pigs, thus the viruses can reassort (i.e. swap genes) and new viruses that are a mix of swine, human and/or avian influenza viruses can emerge***(CDC, 2009)(1).***

H1N1 viruses do not normally infect humans. But, sporadic human infections with swine flu have occurred. Initially, these cases occur in persons with direct exposure to pigs [e.g. children near pigs at a fair or workers in the swine industry] ***(WHO, 2009)(1).***

This virus was originally referred to as “swine flu” because laboratory testing showed that many of the genes in this new virus were very similar to influenza viruses that normally occur in pigs (swine) in North America. Further study has shown that this new virus is very different from what normally circulates in North American pigs. It has two genes from flu viruses that normally circulate in the pigs of Europe and Asian continents and it has close resemblance with both bird (avian) genes and human genes. Scientists call this a "quadruple reassortant" virus ***(WHO, 2009)(1).***

On April 17, 2009, officials at the CDC confirmed two cases of swine influenza in children living in neighboring countries in California ***(WHO, 2009)(1).***

American health officials declared a public health emergency as cases of swine flu were confirmed in the U.S. Health officials across the world fear this could be the leading edge of a global pandemic emerging from Mexico, where seven people are confirmed dead as a result of the new virus***(WHO, 2009)(1).***

On Wednesday April 29th, the (WHO) raised its pandemic alert level to five on its six-level threat scale, which means they've determined that the virus is capable of human-to-human transmission. The initial outbreaks across North America reveal an infection already traveling at higher velocity than did the last official pandemic strain, the 1968 Hong Kong flu ***(WHO, 2009)(2).***

Phase 5 had never been declared since the warning system was introduced in 2005 in response to the avian influenza crisis. Phase 6 means a pandemic is under way.

Several nations have imposed travel bans, or made plans to quarantine air travellers that present symptoms of the swine flu despite the fact that WHO now openly states it is not possible to contain the spread of this infection and recommends mitigation measures, not restricting travel or closing borders ***(WHO,2009) (2)***.

Regular swine flu is a contagious respiratory disease, caused by a type-A influenza virus that affects pigs. The current strain, a (H1N1), is a new variation of H1N1 virus -- which causes seasonal flu outbreaks in humans -- that also contains genetic material of bird and pig versions of the flu ***(WHO,2009)***.(2)

As of June 12, 2009, 74 countries have officially reported 29,669 cases of influenza A(H1N1) infection and only 145 deaths in the entire world from this illness. The United States has had 13217 confirmed cases, and 27 deaths. Mexico has had less cases but still has the majority of the deaths at 108 ***(***CDC***, 2009)(2).***

It is important to note that nearly all suspected new cases by that time have been reported as mild. Preliminary scientific evidence is also pointing out that this virus is not as potent as initially thought ***(CDC, 2009)(4).***

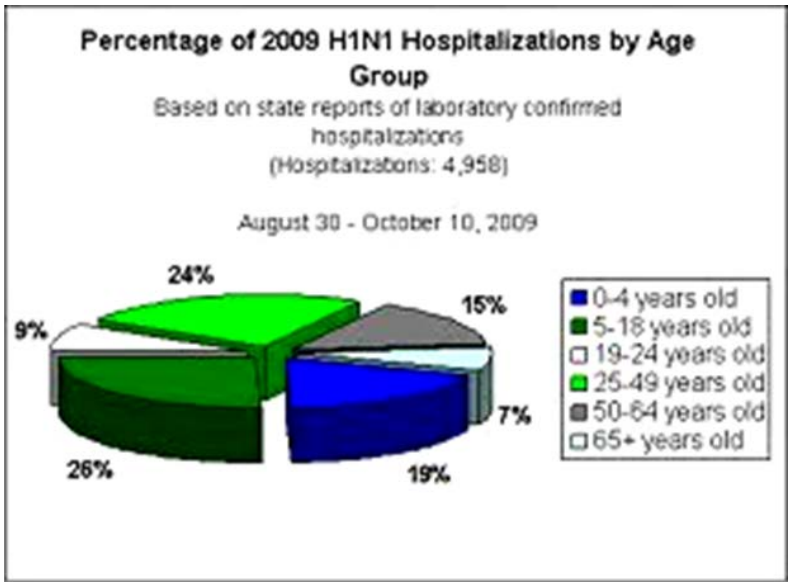

Figure (1): Percentage of 2009 H1N1 Hospitalizations by age Group(WHO,2009)(2).