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H1N1: UNDERSTANDING THE ENIGMA

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ABSTRACT
Some months ago, Swine flu was spreading like wildfire affecting people from all walks of life. Swine flu, which was unheard before, is suspected to be the mutated virus of Avian, Classical Swine and Human influenza. Its virulence is very strong leading to respiratory failure and death. There were several hundred lives lost due to H1N1 infection recently. The H1N1 appeared as a blitz, which caught the public unaware and caused nightmare throughout the country. The Health care emergency was declared to effectively control and contain the spread of H1N1. The threat of emergence looms over our head in coming seasons of winter.

Keywords: *H1N1, Swine Flu, Oseltamivir, H1N1 Vaccine, N95 Mask.*

INTRODUCTION

The H1N1 viral infection inflicted in the last three months among humans often is called “swine flu”, because initial testing of the infected patients confirmed that genes in the virus were similar to the genes present in influenza viruses, usually occurring in North American swine. But further research has demonstrated that the outbreak is due to a new strain of H1N1, which was not previously reported in pigs. The H1N1 virus is a type of influenza virus, mainly existing as influenza A subtype. Till now, it is known that influenza virus strains include influenza C and subtypes of influenza A known as H1N2, H2N3, H3N1 and H3N2. The H1N1 virus encloses an enveloped ribonucleic acid (RNA) as its genetic material and it belongs to the family of orthomyxoviridae. The virus is capable of undergoing continuous genetic variation, which is based upon two important features:

1) It consists of a segmented genome which is composed of 8 RNA segments, which are genetically independent of each other; and

2) It has a high frequency of mutation.

These unique molecular features coupled with the ability of the virus to multiply rapidly, cause widespread infection. H1N1 viruses have two kinds of surface proteins, which help them to bind with the host cell and also are responsible for their mutation. The name of the virus originated from the types of surface proteins present in it, i.e. type 1 haemagglutinin(H1) and type 1 neuraminidase(N1).[1]

The compilation of the study was performed in the Health Sciences Library of Manipal University during the months of August, September and October, 2009. The methodology comprised of systematic search for relevant information in various virology, medical microbiology and health sciences journals available, in the library and on the internet. Since the swine flu has emerged as a difficult challenge for the medical world, it was decided to take up the task of studying the disease in depth, its emergence, pathophysiology and available treatment with risk factors (Fig. 1). The curve shows a rapid progression of the disease towards a pandemic.[2]

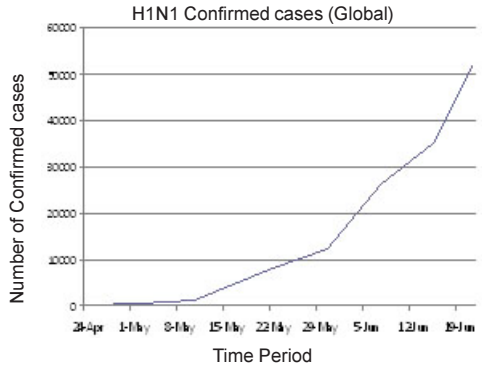

***Fig. 1**: Number of confirmed cases around the world between April and June, 2009.*

Emergence

The emergence of H1N1 virus is said to be caused by reassortment process, which took place between classical swine virus, avian influenza virus and human influenza virus resulting in the reassortant strain of influenza virus in the pig (host). This strain again underwent reassortment with the Eurasian avian like influenza virus (triple reassortment) and generated novel influenza H1N1 virus in swine, which further spreads to human[3] (Fig. 2).

Pathophysiology

It is said that infection is chiefly caused due to the reaction of sialic acid and haemagglutinin. Sialic acid, also known as neuraminic acid, is a glycoprotein which

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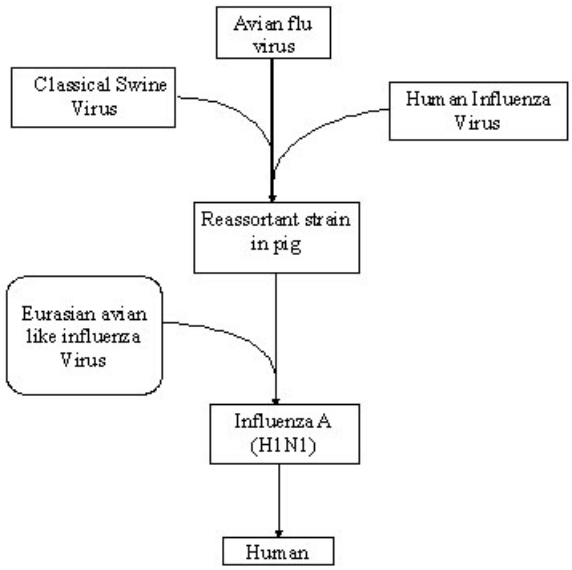

Fig.2: *Evolution of Influenza H1N1 virus by triple reassortment*

is present on the surface of human erythrocytes and on the cell membranes of the upper respiratory tract whereas, haemagglutinin is a surface protein of virus. When the virus gains entry into the host cell through the respiratory pathway, the surface protein haemagglutinin binds to sialic acid and leads to the agglutination of red blood cells. Upon binding to the receptor, haemagglutinin changes shape and results in fusion of viral and the host cell. It also mediates viral entry in to the RBCs and causes infection of the upper respiratory track[4]. Large surface area of respiratory system makes it the most vulnerable site of infection.

Signs and Symptoms

As per the reports of Centers for Disease Control and Prevention- USA (CDC), patients suffering from swine flu show symptoms which are similar to the general indications of influenza and of influenza-like illness. These general indications include fever, cough, sore throat, bodyaches, headache, chills and fatigue. The novel 2009 H1N1 virus infection has reported increased incidence of vomiting and diarrhoea, along with the general influenza symptoms. Most of the deaths reported, have been caused by respiratory failure, along with others like pneumonia (leading to sepsis), high fever (leading to neurological problems), dehydration (from excessive vomiting and diarrhoea) and electrolyte imbalance. Fatalities are more common in young children and the elderly.[5]

Diagnosis

World Health Organization (WHO) recommends that suspected clinical cases of novel H1N1 influenza A virus infection are confirmed by:

1. Specific real time RT-PCR (reverse transcriptase-polymerase chain reaction) assay
2. Isolation and identification of swine like influenza virus.[3]

Treatment

According to WHO Guidelines, treatment of infected patients of swine flu is carried out with antiviral drugs. Among these, oseltamivir and zanamivir are used in treatment of infection caused by novel H1N1 virus in humans.[6] It is known that antiviral drugs oseltamivir and zanamivir, which are neuraminidase enzyme inhibitors, act as transition state analogues inhibitors of influenza neuraminidase and thereby prevent the progeny virion to detach from infected cells. As neuraminidase enzyme is also responsible for viral mutation, the virus is not able to acquire resistance against these drugs. However amantadine and rimantidine, which are M2 blockers, are not useful against novel H1N1 virus, as it has acquired resistance against those drugs.[7]

Vaccines

In USA, the Food and Drug Administration (FDA) has approved four vaccines against the novel H1N1 virus and they will be introduced in the market by middle of the year 2010.[8] The CDC recommends that initial doses should go to priority groups such as:

1. **Travelers**, as they are the major cause for spreading the infection from one country to another.
2. **Children** between 6 months to 5 years, as they have low immunity and are more prone to infection.
3. **Elderly>65**
4. **People with long-term illnesses** such as cardiac patients, diabetic patients, asthmatic patients.
5. People with **depressed immunity.**
6. **Pregnant women** in 2nd-3rd trimester, as they are at high risk of low immunity during this period.
7. **Health care workers,** as they are in close contact with the patients admitted in the hospital.

Prevention of transmission

Influenza spreads among humans through coughing, sneezing and air borne droplets carrying the viruses. As the virus is not transmitted through food, the infection does not spread by pork containing dishes. Swine flu is highly contagious during first five days of acquiring the infection, but in children it can remain contagious up to ten days. Steps to prevent spreading of the infection among humans include use of standard infection control measures against influenza. This includes washing of hands with alcohol or alcohol based sanitizers, every time after coming back from crowded places.

General precautions which can be useful in prevention of disease are:

1. Avoid handshake with people having flu like symptoms
2. Maintenance of personal hygiene
3. Avoid close contact with ill people
4. Regular exercise
5. Avoid going to crowded places
6. Cover the mouth and nose while coughing or sneezing

Even hospitals should take certain safety measures:

- Suspected and confirmed patients of H1N1 infections should be quarantined.
- Health workers should advise the patients to wear N95 mask.

N95 masks

The N95 masks have a basic purpose of preventing the spreading of the infection. To use the exact medical terminology, they work by preventing snot, spit or other virus-carrying particles from becoming air borne.[5] Thus, if the wearer sneezes, coughs, drools, spits or talks excitedly, his/her infected fluids will be trapped in the mask and will not infect others. The mask is made up of three layers:

Inner Layer - It is usually made of non woven polypropylene cloth that is hypoallergenic and comfortable against the face.

Filter Layer - It is the middle layer, made of blown web of fabric that blocks 95 percent of particulates.

Outer Layer - It contains active carbon that absorbs harmful vapors.

CONCLUSION

Swine flu is spreading across the globe at an alarming rate and threat of it becoming pandemic, is imminent. The H1N1 virus is genetically most capable, among its subtypes, of showing resistance to various antiviral drugs. It will be very difficult to contain the virus unlike the case of SARS, chicken guinea or bird flu. The governments and medical fraternity of the world should take appropriate steps to face this powerful threat to mankind.

According to the information provided by government of India, as on 25th of August 2009, a total of 6050 confirmed cases of swine flu were diagnosed in the country, and majority of them were identified in Delhi, Mumbai and Pune[9] (Fig. 3 and 4). By the first week of September, the number of infected cases had already crossed 5000 mark, and was still on the rise.[10] Maximum number of deaths were reported in western Indian cities (Mumbai, Pune) followed by southern and northern Indian cities (Bangalore, New Delhi). No deaths were reported from Eastern India.[11]

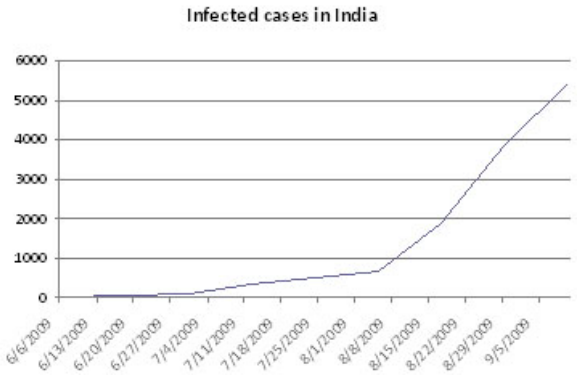

Fig. 3: *Rapid increase in reported cases of swine flu in India.*

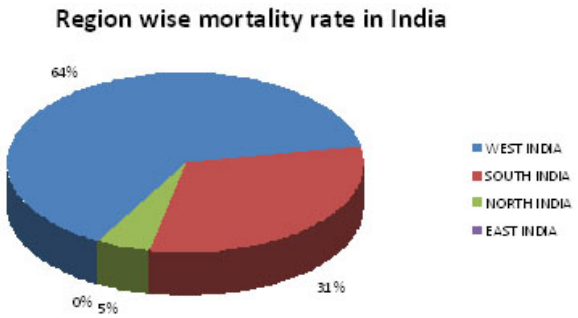

Fig. 4: *Region wise mortality due to swine flu*

The metropolitan cities have maximum number of travelers arriving from other countries, and these travelers are acting as carrier for the influenza virus, hence resulting in large scale infection. To prevent this situation, the existing screening at various airport terminals should be made more stringent and care should be taken to prevent any lapses in the checking of the suspected cases arriving from infected countries. Media should be advised to restrain from making exaggerating news related to the ill effects of swine flu as it creates unnecessary panic in the public, which can be quite harmful for people suffering from cardiovascular and respiratory illnesses. Awareness regarding disease and its spread vis-à-vis preventive measures should be widely advertised in mass media and people should be educated about the precautions, which can prevent the virus to spread further.

Though the US FDA has approved four new vaccines for H1N1 influenza, search is underway for a more immunogenic vaccine in various research labs around the world. It has become indispensable to discover more drugs with effective cure, as the cases of resistance against oseltamivir have been reported worldwide.[12] The recently approved vaccines are prepared from chicken eggs and show adverse effects like soreness at the site of injection, mild fever, body aches and fatigue, but nevertheless they have shown promising results in clinical trials. The vaccines elicit an effective immune response in healthy adults, but clinical research is in progress for establishing an optimum dose for children, who are usually worst affected.[8]

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