

# NOVEL H1N1 INFLUENZA EPIDEMIC: Lessons From A Tertiary Centre In Bangalore

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## Abstract

In the new millennium, the world has seen the emergence of three novel human respiratory viruses; SARS virus (a novel Corona virus) in 2003, Influenza H5N1 ('Avian flu') in 2004 and now an international outbreak caused by a new strain of Novel 2009 Influenza virus A/H1N1[1]. This novel Influenza 2009 A/H1N1 virus contains a combination of swine, avian, and human influenza virus genes. In sharp contrast to SARS and Avian Influenza H5N1 viruses which emerged from the Asian continent, Influenza 2009 A/H1N1 virus emerged from North America. We review this virus outbreak.

## INTRODUCTION

In the new millennium, the world has seen the emergence of three novel human respiratory viruses; SARS virus (a novel Corona virus) in 2003, Influenza H5N1 ('Avian flu') in 2004 and now an international outbreak caused by a new strain of Novel 2009 Influenza virus A/H1N1[1]. This novel Influenza 2009 A/H1N1 virus contains a combination of swine, avian, and human influenza virus genes. In sharp contrast to SARS and Avian Influenza H5N1 viruses which emerged from the Asian continent, Influenza 2009 A/H1N1 virus emerged from North America. In mid April 2009, the World Health Organization (WHO)[2], Geneva, and Centers for Disease Control (CDC)[3], USA, initially recognized a dramatic increase in the number of influenza cases being reported from Mexico. In less than sixty days the novel Influenza 2009 A/H1N1 virus has rapidly spread across 66 countries in the world and caused over 17,000 infections across the globe [2]. Amongst them, three North American countries- USA (8975 cases), Mexico (5029 cases) and Canada (1336 cases) accounted for 88 % of the total number of global cases reported [2]. Unlike the SARS and Avian Influenza H5N1 viruses, which never were reported in human beings from India, the novel Influenza 2009 A/H1N1 virus has already been detected in patients in India. All of them acquired the infection abroad and were detected to be positive upon arrival in our country. Indeed, one of the notable features of the current strain of Influenza 2009 A/H1N1 virus is the high efficiency of human-to-human transmission. This probably explains the alarming spread of the virus across the globe in a very short time and therefore

poses a serious pandemic threat.

Influenza virus is an enveloped RNA virus of the Orthomyxoviridae family. It is endowed with an inherent capacity for genetic variation that is based on two important features; (i) the presence of a segmented genome, with eight RNA segments that are genetically independent of each other and (ii) a high rate of mutation, especially in the surface haemagglutinin (H) and neuraminidase (N) proteins. These unique molecular features coupled with the ability of the virus to cause infection in a wide host range of humans, domestic animals and birds renders it a potential pandemic agent. Domestic pigs and birds because of their proximity to humans provide a great opportunity for the occurrence of mixed influenza infections. Consequently, these two species (pigs and birds) act as 'melting pots' for the generation of reassortment of viruses and thus play a crucial role in evolution of influenza pandemics. The current outbreak of Influenza 2009 A/H1N1 is a rare recombination of gene segments from swine with avian and human influenza strains. Phylogenetic analysis of sequences of all genes of A/California/04/2009, the virus isolated from a patient in the recent outbreak in USA, showed that its genome represents a quadruple reassortment of two swine strains, one human strain, and one avian strain of influenza [4]. The virus contained six gene segments (PB2, PB1, PA, HA, NP, and NS) that were similar to ones previously found in triple-reassortant swine influenza viruses circulating in pigs in North America [5]. The North American triple-reassortant virus is itself a combination of the haemagglutinin (HA),

nucleoprotein (NP), and nonstructural protein (NS) genes, originating from classic swine influenza A viruses; the polymerase PB2 (PB2) and polymerase (PA) genes from avian influenza viruses from the North American lineage; and the polymerase PB1 (PB1) gene from human influenza A viruses [5]. The genes encoding neuraminidase (NA) and M protein (M) however were most closely related to those in influenza A viruses circulating in swine populations in Eurasia [6]. The largest proportion of genes in this novel virus comes from swine influenza viruses (30.6 percent from North American swine influenza strains, 17.5 percent from Eurasian swine influenza strains), followed by North American avian influenza strains (34.4 percent) and human influenza strains (17.5 percent) [6]. This particular genetic combination of influenza virus segments had not been seen before in the United States or elsewhere [1,4].

There are several key epidemiological features that determine the occurrence of a pandemic influenza. According to Miller et al (2009)[7] who have recently analyzed the “signature features” of three previous influenza pandemics (A/H1N1 in 1918, A/H2N2 in 1957 and A/H3N2 in 1968) four important factors emerge as key determinants- (i) occurrence of a shift in the virus subtype, (ii) shifts of the highest death rates to younger populations, (iii) successive pandemic waves, and (iv) higher transmissibility than that of seasonal influenza. The current outbreak of Influenza 2009 A/H1N1 has fulfilled two of these four conditions viz. occurrence of shift in the virus subtype (Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team) and higher transmissibility than that of seasonal influenza [8]. Coming months would determine whether the remaining two conditions would also be met. However based on the initial descriptions of the clinical manifestations reported from cases in USA there is sufficient cause for concern at this stage. The age of the 642 confirmed cases Influenza A 2009/H1N1 reported from USA, ranged from 3 months to 81 years although a majority (60%) were younger than 18 years suggesting thereby that children and young adults may be more susceptible to this infection than older persons[1,4]. This not a surprise finding as most older adults probably have substantial immunity to H1 variants that have circulated among humans from 1918 through 1957 and then again from 1977 through the present. It is not clear though; whether cross-reacting antibodies from previous H1N1 infections will provide protection against the novel Influenza A 2009/H1N1 virus but the epidemiologic features of the confirmed cases from USA suggest that there may be partial protection from multiple previous influenza infections [1].

The salient clinical manifestations noted in the laboratory confirmed cases [1] of the current outbreak include a self-limiting, uncomplicated febrile respiratory illness and typical symptoms similar to those of seasonal influenza (cough, sore throat, rhinorrhoea, headache, and myalgia). However 38% of cases have also reported vomiting or diarrhea, neither of which is typical of seasonal influenza.

The recommended procedure for laboratory diagnosis of Influenza 2009 A/ H1N1 virus infection is real-time reverse-transcriptase PCR or culture [9]. These facilities are at present available in India only at The National Institute of Virology (NIV), Pune, and The National Institute of Communicable Diseases (NICD), New Delhi. To establish the diagnosis of Influenza 2009 A/ H1N1 in the laboratory, an upper respiratory sample (nasopharyngeal swab, nasal swab, throat swab, combined oropharyngeal/nasopharyngeal swab, or nasal aspirate) should be collected [9]. In intubated patients, an endotracheal aspirate should also be obtained. Swabs with a synthetic tip (eg, polyester or Dacron) and an aluminum or plastic shaft should be used. Swabs with cotton tips and wooden shafts are not recommended. Swabs made of calcium alginate are not acceptable. The collection vial in which the swab is placed should contain 1 to 3 ml of viral transport media. Specimens should be placed in viral transport media and placed on ice (4°C) or refrigerated immediately for transportation to the laboratory [9]. Once the samples arrive in the laboratory, they should be stored either in a refrigerator at 4°C or in a -70°C freezer. If a -70°C freezer is not available, they should be kept refrigerated, preferably for ≤1 week. Specimens should be shipped on dry ice to the designated laboratories in clearly labeled containers and should include all information requested by the state health laboratory [9]

The H1N1 epidemic took the health care delivery system in India by surprise. The avian influenza pandemic prompted and also probably prepared for a better preparedness.

We present the analysis of 72 RTPCR confirmed cases of H1N1 cases in SDS &RGICD BANGALORE which is tertiary care hospital was attached to Bangalore medical college and research center which is recognized center for H1N1 by government of India During the period of May 09 to September 2009 286 patients were admitted with ILI (influenza like illness). In India initially surveillance was started at airports, and then extended to community level. In order to make the testing facility more accessible at large and due to onset of seasonal flu in the country, the guidelines were revised and persons presenting like flu like symptoms

were categorized into three categories

Category A (patients with mild fever plus cough/sore throat with or without body ache, headache, diarrhea and vomiting) ,category B ( in addition to signs and symptoms of category A if the patient has high grade fever and severe sore throat or having one or more of the following high risk conditions- children less than 5 yrs old ,pregnant women ,persons aged 65 years or older ,patients with lung diseases ,heart diseases liver diseases kidney disease ,blood disorders diabetes neurological disorders cancer and HIV and AIDS and patients on long term cortisone therapy) and category C ( in addition to the above symptoms and signs of category A and B ,if the patient has breathlessness chest pain drowsiness ,fall in blood pressure, irritability among small children ,refusal to accept food worsening of underlying chronic condition) testing is done for category C and pharmacological treatment is given for category B and C(6)

Majority of the confirmed cases were 42 males (58.3%) and were adults (26 to 40 years - 52.8%). The youngest patient was 2 years and the oldest 66 year old. 28 patients (38%) had at least one associated co morbid illness (chronic respiratory illness, DM, neurological disease and pregnancy). Key clinical presentations were cough (90%) followed by fever (89%) and sore throat (29%). Other respiratory symptoms (Shortness of Breath (SOB), Rhinitis) and gastrointestinal symptoms (either vomiting or diarrhea) were seen in 20% and 15% of the patients respectively. 3 patients developed insignificant hemoptysis during the course of their hospitalization which improved with simple conservative treatment. Of the 56 patients (77%) who were radiographed 31 (55.3%) displayed a normal chest X ray. Of those with abnormal radiographic findings, 17 (68 %) had bilateral pneumonia while 8 (32%) had unilateral pneumonia.

On arrival at the hospital, all patients were started on antiviral therapy: average 4.5 days from the start of symptoms. Two thirds (69%, 50 pts) received 75mg bid oseltamivir for 5 days. Of the remaining, 18 patients needed an extended duration (for 8 – 10 days) and 4 adult patients who initially presented with severe illness were given 150mg twice daily for 7 days. Twenty one patients (29.26%) required ICU care (average 3.8 days, min 1 day and maximum 10 days); 11 required mechanical ventilation (average 2.55 days).

## **MORTALITY**

15 of the 21 patients in ICU care died of the illness

accounting for 21% of the hospitalized patients, and 0.49% of the total positive cases detected in our institute.

However all mechanically ventilated patients had features consistent with ARDS and they did not recover.

## **LESSONS LEARNT**

1. There were 59 positive h1n1 patients who came from abroad from different countries all of them recovered and there were no complications but what we noticed was local people were affected in larger number than people who had traveled abroad the age group affected were between 20- 50 there were 14 deaths in this age group
2. once oseltamivir 75 mg 2 capsules twice a day was started there was faster recovery
3. During the present year h1n1 is not severe as compared to last year as there are less no deaths and patients who were on mechanical ventilator have recovered and gone home

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