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Inside

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Swine influenza: an overview

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Introduction

In the late March and early April 2009, the first influenza pandemic of the 21st century was declared with the emergence of a novel Influenza A (H1N1) strain in the Mexico and USA[1]. To date this virus has been detected in about 214 countries killing at least 18,001 persons[2]. A modeling study suggested that by late July 2009, the number of individuals infected with pandemic H1N1(H1N1 P) influenza A in the United States may have been up to 140 times greater than the reported number of confirmed cases[3]. The World Health Organization (WHO) on 11th June 2009, raised the pandemic to phase six. In India samples from 1,34,271 persons have been tested for Influenza A H1N1 P in government laboratories and a few private laboratories across the country and 30,613 (22.79%) of them have been found positive with 1,504 deaths of lab confirmed cases[4].

Brief history

During 1918 flu pandemic Swine influenza was first proposed to be a disease related to human influenza as, the pigs became sick at the same time as humans, but swine influenza virus was first isolated from a human in 1974[5-6]. In the year 1976, in Fort Dix, New Jersey 13 soldiers were diagnosed infected by swine influenza. The virus caused a respiratory illness with one fatality. Subsequent studies showed that 230 soldiers had this infection[7-8]. Between 1958 and 2005, 37 cases of swine influenza among civilians were reported. Six cases (17%) resulted in death. Forty-four percent of infected individuals had known exposure to pigs.

The disease

The incubation period ranges from 1-7 days. The influenza virus uses surface proteins consisting of sialic acid linked to galactose for cell entry. The pathology is due to direct cell and tissue damage and innate immunity. The respiratory symptoms are due to cell death and inflammation. The virus mainly harms trachea and upper respiratory track, resulting in to viral pneumonia, pulmonary edema and acute

respiratory disease syndrome (ARDS). In few cases multi organ failure may occur that can lead to death. Like seasonal influenza, swine influenza begins with all or one of the symptoms such as fever, cough, nasal discharge sore throat, headache, nausea, body aches, chills and malaise. Gastrointestinal symptoms such as diarrhea and vomiting are reported more frequently than seasonal influenza. Low blood pressure; shortness of breath and/or labored breath, high grade of fever with any of above symptoms is alarming. Usually the disease is self-limiting and patient recovers within a week[9]. In this pandemic pregnant women, infants and children under age two, people of any age with certain chronic health conditions such as asthma or lung disease, heart disease, diabetes, kidney disease or some neurological condition and immuno compromised people appeared to be at higher risk. The people above age 65 are the least likely to be infected but those who do get sick are also at high risk[10]. Hospitalization rates have been highest for children under the age of 5 years[11], especially those under the age of 1 year, and lowest for persons 65 years of age or older[12]. The case fatality ratio 0.86% for H1N1 P was significantly higher than that of seasonal influenza A (0.13%)[13].

The principal clinical syndrome leading to hospitalization and intensive care is diffuse viral pneumonitis associated with severe hypoxemia, ARDS, and sometimes shock and renal failure. This syndrome has accounted for approximately 49 to 72% of ICU admissions for 2009 H1N1 P virus infection[14].

The causative agent

The H1N1 swine flu virus is influenza A virus belonging to family Orthomyxoviridae. The virus can be subdivided into different serotypes based on the antibody response to theseviruses. The shape is generally spherical with size of 80-120 nm in diameter. The virus genome contains 8 single-stranded RNA molecules. The influenza A genome contains[11] genes encoding for 11 proteins, hemagglutinin (HA), neuraminidase (NA), nucleoprotein (NP), M1, M2, NS1, NS2(NEP),PA,

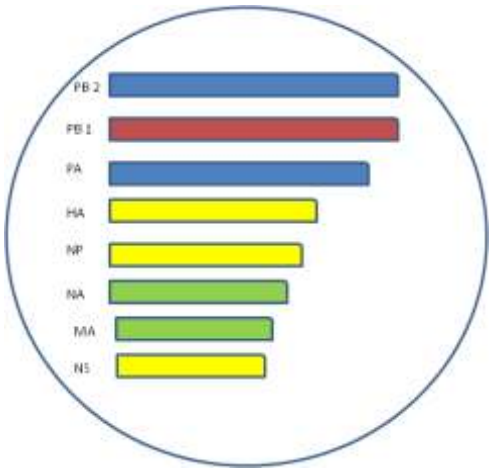

Figure 1: The gene assortment of novel Influenza H1N1 2009 virus, the presently circulating H1N1 virus possesses the polymerase basic-2 (PB2) and polymerase A (PA) genes of North American avian virus origin (Blue), the polymerase basic-1 (PB1) gene of human H3N2 virus origin(Red), the hemagglutinin (HA), nuclear protein (NP) and non-structural (NS) genes of classical swine origin (Yellow) and the neuraminidase (NA) and matrix (MA) genes of Eurasian swine virus origin (Green[15]).

PB1, PB1-F2 and PB2. The presently circulating H1N1 P virus possesses the polymerase basic-2 (PB2) and polymerase A (PA) genes of North American avian virus origin, the polymerase basic-1 (PB1) gene of human H3N2 virus origin, the hemagglutinin (HA), nuclear protein (NP) and non-structural (NS) genes of classical swine origin and the neuraminidase (NA) and matrix (M) genes of Eurasian swine virus origin[15] (Figure 1). The human-like PB1 gene and avian-like PB2 and PA genes however have been circulating in pigs since 1997-98 in the form of a triple reassortant swine virus[16]. The 2009 H1N1 P virus is antigenically distinct from other human and swine influenza A (H1N1) viruses[15], and the A/California/7/2009 strain, selected for pandemic influenza vaccines worldwide is antigenically similar to nearly all isolates that have been examined to date[17]. The study based on whole genome revealed that the virus is diversified in to 7 lineages. The study conducted on Indian isolates by Potdar *et. al.* indicated that the dominant H1N1 P lineage in India belong to clade 7, though both clades 6 and 7 are co-circulating[18].

Transmission

The infected person starts shedding virus, a day before the onset of symptoms, and continues to do so for 5-7 days. Children are more infectious and shed more amount of virus for longer periods. The virus can spread mainly by three ways direct transmission where the infected person's body fluids like sneeze directly infect the mucus membrane of healthy individual, in case of the airborner oute the healthy individual inhales the aerosol expelled by infected patient and through direct contact when they come in contact with patients by hands shakes *etc*. The virus can survive outside the body and can be transmitted by infected table tops, light buttons, door handles, banknotes *etc*[19-20].

Laboratory diagnosis

The traditional influenza diagnosis is made by HA-HAI test, virus isolation, and antigen detection by indirect florescence tests, RT PCR etc. For theH1N1 P influenza WHO adapted CDC devised Taqman based real time RT PCR assay is used. For molecular diagnosis this virus is placed in Risk group 2 with requirement of biosafety level 2, GLP based laboratory. This assay is designed in such a way that it can distinguish seasonal Influenza A virus from the H1N1 P virus, and could give accurate diagnosis within hours. The nasopharyngeal, endotracheal, bronchoscopic aspirates, throat swab taken early after the onset of symptoms are suitable samples. The samples collected in virus transport medium, stored and transported to diagnostic laboratory as described in guidelines[4] are excellent for detection of viral RNA by Taqman real time RT PCR[21]. In India initially only few laboratories (NIV, Pune and NICD New Delhi) were equipped for this diagnosis, but soon with Government of India and ICMR's initiatives the staff from various regional laboratories was trained at NIV and the network of diagnostic laboratories was established all over the country.

Antiviral treatment

Neuraminidase inhibitors such as Oseltamivir oral dose of 75 mg twice daily for adults, 3mg/kg/dose twice daily for children and Zanamavir 10 mg (two 5-mg inhalations) twice daily for adults and children can be administered under medical supervision for treatment or prophylaxis[22]. However sound medical judgment and proper understanding of pros and cons are to be considered before start of treatment. The currently circulating 2009 H1N1 P virus is resistant to amantadine and rimantadine[9]. Early therapy with oseltamivir in patients with 2009 H1N1 P virus infection may reduce the duration of hospitalization and the risk of progression to severe disease requiring ICU admission or resulting in death[14]. The oseltamivir-resistant isolates have been found in patients without known exposure to oseltamivir and in limited clusters of cases associated with person- to-person transmission in otherwise healthy patients and those with immunosuppression. In India NIV is vigilantly monitoring the oseltamivir drug resistance in the isolates as well as lab confirmed positive clinical samples.

Vaccine

Vaccine is an effective tool to prevent the spread of the current H1N1 P influenza pandemic. Two types of vaccines i.e. injectable and nasal sprays are available. Nasal spray is not recommended for the children below the age of two. The FDA of USA and European Medicine Agency (EMEA) have approved two types of vaccines. To produce the killed vaccine the virus is grown in chick embryos, purified by centrifugation and is inactivated. Both adjuvanted and unadjuvanted vaccine formulations are available. The data indicate that both the vaccines are effective and safe, however the people with egg allergies should not take the vaccine without proper medical supervision.

The common side effects of the vaccination include swelling, redness, or pain at the injection site, which usually resolves spontaneously a short time after vaccination. Rarely fever, headache, fatigue, and muscle aches, occurring shortly after vaccine administration, have also been reported. WHO has also received few reports, of the suspected cases of

Guillain-Barre syndrome after vaccination. But the overall data suggest that the vaccine used match the safety profile of seasonal influenza vaccines,which have been used for more than 60 years[23]. CDC's Advisory Committee on Immunization Practices (ACIP) recommends that the vaccine should be given on priority to pregnant women, household contact and caretakers of children younger than 6 months of age, healthcare and medical services personnel, all children and young adults from 6 months to 24 years of age and the persons in age group of 25-64 who have health condition associated with higher risk swine influenza[24].

Swine flu samples tested at RMRCT Jabalpur

The swine flu diagnosis laboratory was established at this centre and the testing started in the end of October 2009. Till March 2010, 488 samples were tested. Out of those tested 94 were positive for H1N1 P virus. Maximum samples were received in the month of January (200 nos.). Adults in the age group of 18-60 were most affected. There was not much difference in infection to male and female. City of Indore was most affected with 52 cases followed by Jabalpur (20) and Bhopal (11). Fifty-three seasonal flu (Influenza A) cases were also detected during this investigation. The data suggested that all though in Madhya Pradesh the number of cases were not as high as Maharashtra with 6202 and 449 deaths and some other states like Delhi (9696 cases) and Karnataka (2330 cases)[4] the percent positivity of samples referred to the laboratory from Madhya Pradesh (19.3%) was similar to that of national figures.

Acknowledgment:

Author is thankful to Dr. VA Potdar, NIV, Pune and Dr. JT Bhat, RMRCT, Jabalpur for their critical comments.

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Dr. Pradip V. Barde, Scientist 'C' (Microbiology)

Publications

1. Jain V, Singh PP, Silawat N, Patel R, Saxena A, Bharti PK, Shukla M, Biswas S, **Singh N**. A preliminary study on pro- and anti-inflammatory cytokine profiles in Plasmodium vivax malaria patients from central zone of India. Acta Trop. 2010 Mar;113(3):263-8.
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Foreign Visits

Dr. Neeru Singh visited Washington D.C., USA to attend the 58th Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH) during 18-22 Nov. 2009 and presented a paper.

Conference/Workshop/Meeting attended

Dr. Neeru Singh

- Attended international conference on 'Medicine Advancement in Last 10 Years' at Department of Medicine, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly during 2nd -4th October 2009 and delivered a lecture.
- Attended international conference on 'Current Trends in Advanced Biomedical Technology (CTAB-2009)' at Department of Microbiology & Biotechnology, Nehru Arts and Science College Coimbatore on 14th and 15th October 2009 and delivered a plenary lecture.
- Attended Public Health Foundation of India (PHFI) meeting on 'Expert Consultation on Disease Control in India', at New Delhi during 26th-28th October 2009.
- Attended X international symposium on Vectors and Vector Borne Diseases organized by Goa University and National Institute of Malaria Research at Goa during 4th-6th November 2009 and delivered a lecture.
- Attended a workshop "WHO Collaborating Centres in India" at New Delhi organized by WHO on 12th-13th November 2009.
- Attended 58th Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH) during 18th-22nd November 2009 in Washington D.C., USA and presented a paper.

Dr. V. G. Rao

- Presented a paper in Research Dissemination Workshop III, Jointly Organized by Tuberculosis Research Centre (ICMR) & World Health Organization) at Chennai on 9th and 10th December 2009.
- Presented a paper in 64th National conference on Tuberculosis & Chest Diseases (NATCON 2009) held at Kolkata during 26th-29th December 2009.

Dr. Jyothi Bhat

- Attended Sir Dorabji Tata Symposium on Newer diagnostics at SDTC, Bangalore on 10th & 11th March 2010.
- Attended training on laboratory techniques for diagnosis of STI's/RTI's at State Regional Centre, GMC, Nagpur on 18th & 19th January 2010.
- Attended a meeting for the project 'Epidemiology of Viral Hepatitis in Tribal Population of M.P., Chattisgarh, Orissa & Jharkahand' at NIV, Pune on 25th March 2010.

Dr.Pradip Barde

- Attended Sir Dorabji Tata Symposium on Newer diagnostics at SDTC, Bangalore on 10th & 11th March 2010.

Dr. Rajiv Yadav

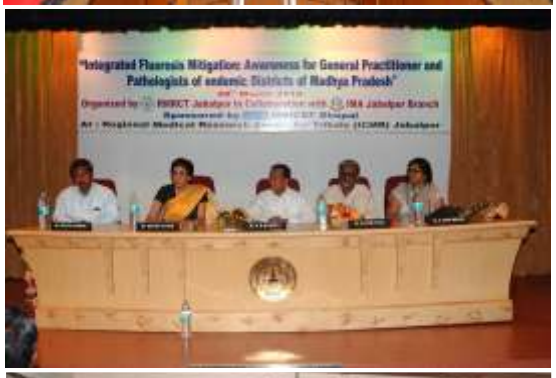
- Presented a paper in 64th National Conference on Tuberculosis & Chest Diseases (NATCON 2009) held at Kolkata during 26th-29th December, 2009.

Workshops/Symposium/Training/Meeting conducted

- 22nd Scientific advisory committee meeting held on 3rd and 4th December 2009.

- Three training workshops on vector borne diseases for Medical Officers of various districts of Madhya Pradesh were organized during 21st to 23rd December 2009, 6th to 8th January 2010 and 25th to 27th March 2010. The workshops were organized jointly by NIMR FS Jabalpur and Directorate of Health Services Bhopal under Enhanced Vector Borne Disease Control Programme (EVBDCP) at RMRCT, Jabalpur.

- A workshop on Integrated Fluorosis Mitigation: Awareness for General Practitioner and Pathologists of endemic Districts of Madhya Pradesh was organized on 28th March 2010. The Workshop was organized jointly by RMRCT Jabalpur and IMA Jabalpur Branch and sponsored by UNICEF Bhopal.



- A workshop on Tuberculosis was organized on 28th March 2010 at RMRCT Jabalpur.

- A Press Conference on Swine Flu was organized on 18th December 2009 at RMRCT Jabalpur. The Conference was organized jointly by RMRCT Jabalpur and Joint Director of Health Services Jabalpur.

Joining/Promotion/Retirement

Joining

Dr. R.K.Sharma joined as Scientist 'C' on 21st December 2009.
Dr. Jyothi Bhat joined as Scientist 'D' on 21st January 2010.
Dr. Pradip Barde joined as Scientist 'C' on 22nd February 2010.
Dr. Pravin Kumar Bharti joined as Scientist 'C' on 16th March 2010.
Mr. Narendra Kumar Jharia joined as Hindi typist on 5th January 2010.

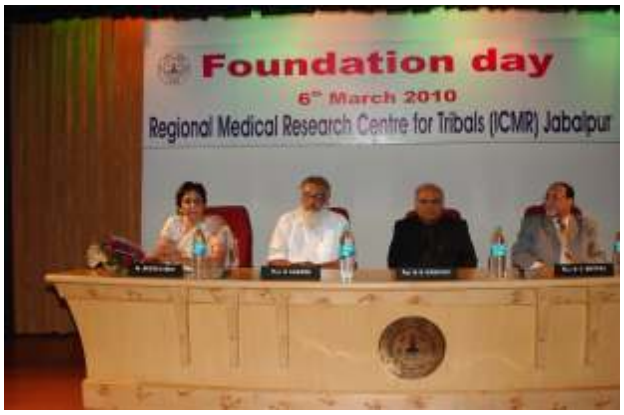
Promotion

Mr. D.P. Lodhi promoted as Section officer on 17th February 2010.
Mr. P.K. Bhalerao promoted as Section officer on 31st March 2010.

Retirement

Mr. B.K.Mazumdar retired as Accounts officer on 31st January 2010.
Mr. Ramnaresh Dube voluntary retired as Lower division clerk on 2nd February 2010.

Events



- The centre celebrated its Foundation Day on 6th March 2010. Dr. N. K. Ganguly, Ex-Director General ICMR delived the foundation day lecture.

- Lt. Gen. D. Raghunath, Principal Executive, Sir Dorabji Tata Centre for Research in Tropical Diseases, Bangalore laying Foundation Stone of new Guest House on 3rd December 2009.

- Shri A. K. Shrivastava, IAS Commisioner Jabalpur and Shri Hariranjan Rao, Collector Jabalpur visited the centre on 30th January 2010.