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Editorial

Influenza A (H1N1): responding to a pandemic threat

Influenza viruses by nature are highly unpredictable and unstable. They have the unique distinction of having segmented genome which permits them reassortment in their genetic structure resulting in evolution of new subtypes. This genetic restructuring occurs regularly in nature and at times provides the virus unusual capability to cause widespread disease in immunologically naïve population and swiftly move across geographical borders to cause pandemics or global scale epidemic.

The previous century saw three such pandemics, the first (Spanish flu) caused by influenza A (H1N1) killing around 20-50 million people and a loss in global GDP of around 16 per cent[1]. The other two in 1957 and 1968 were relatively milder but still killed nearly one million.

The current millennium saw the appearance of a novel subtype of influenza A (H5N1) in 2003. This virus had genes in human influenza virus from dreadful highly pathogenic avian influenza virus. Human infections occurred from poultry but human to human transmission has not been reported except in one situation. Till June 29, 2009 this virus had caused 433 cases and 262 deaths in 15 countries[2]. However, the presence of this virus in poultry in 63 countries[3] indicates persistence of a reservoir that continues to act as the source of highly pathogenic genetic components to other circulating influenza viruses. While the world was grappling with H5N1 avian flu and preparing for a pandemic that could emerge, another influenza virus made a dramatic appearance in Mexico in March 2009 in the form of a novel H1N1 subtype.

The new virus and the evolving pandemic situation: The novel influenza A (H1N1) virus has the genetic structure resulting from reassortment of genes from four influenza viruses *viz*., North American swine influenza, Asia/Europe swine influenza, human influenza and avian influenza (non H5). The virus has a unique genetic composition that has never been seen earlier. As a result of this, within a short period of two months the virus has spread to more than 110 countries, caused around 58,000 cases and 263 deaths[4].

The reported clinical presentation ranges broadly from asymptomatic infection to severe pneumonia resulting in death. The available data from Mexico and the USA show that clinical features of fever, cough and sore throat are similar to those of seasonal influenza. In addition, several patients have clinical features of gasterointestinal tract mainly nausea, vomiting and diarrhoea. In USA, of 642 confirmed cases of influenza 25 per cent had diarrhoea. Among the serious patients who were hospitalized in USA, only 50 per cent had infiltrates on chest radiographs. More than 50 per cent of those who were hospitalized had characteristics (pregnancy, chronic medical conditions, or an age of less than 5 yr) that conferred an increased risk of influenza[5]. The transmission is thought to occur in the same way as seasonal influenza which is mainly person-to-person transmission through coughing or sneezing of people infected with this virus. People may be infected by touching something with flu viruses on it and then touching their mouth or nose. The causative virus may have undergone reassortment in swines and does carry genes from swine and avian influenza viruses but transmission from non-human sources (pigs or birds) does not seem to play any role in current epidemiology of the disease. The available information also indicates that unlike seasonal influenza this event has primarily affected younger adults with median age in Mexico being 22 yr. In USA, 75 per cent of 532 cases belonged to the age group 10-50 yr[5]. This is in contrast to the fact that complications of seasonal influenza affect primarily the elderly or young children.

The pandemic of 1918 and 1957 both started with mild illness but followed later by more severe illness.

Lessons from the past pandemics: The H1N1 virus was responsible for Spanish Influenza Pandemic of 1918. The causative agent of current event seems to have evolved from H1N1 of 1918 pandemic[6]. However, it will be naïve to extrapolate the impact of 1918 pandemic to current event because of the effective tools that are available today including drugs, diagnostics and the level of preparedness in place in the countries such as infection control practices, case management facilities and mass media reach for public awareness and risk communication.

Advances in technology are now swiftly translatable into tools. This is evident from determination of genetic sequence of novel H1N1 and development of diagnostic reagents within a few days of isolation of causative agents as well as determination of susceptibility to currently available influenza drugs. The data also show that virus is resistant to amantadine and rimantadine but the organism continues to remain susceptible to oseltamivir and zanamivir. The access to these drugs and their rational use are critical in mitigating disease as well as prolonging the utility of the drugs by obviating emergence of resistance. To prevent deaths and morbidity due to secondary bacterial infections, a wide variety of antimicrobial agents are available globally. Presently vigorous process is underway in both developed and developing countries to develop the vaccine. A study conducted by the International Federation of Pharmaceutical Manufacturers and Associations[7] has shown that pandemic vaccine production capacity has increased by 300 per cent over the last two years, largely driven by improvements in production yields and dosage sparing technologies. It is believed that manufacturers could produce 2.5 billion doses of pandemic vaccine in 12 months following receipt of production strain and global demand can be met within 2-3 years. However, the supply of vaccine, at least during the first year of pandemic shall be finite and not easily accessible to vast majority of people living in developing countries. Intensive public education for adopting cost-effective non pharmaceutical interventions can yield substantial results[8]. Non pharmaceutical prevention through repeated hand washing and following cough/sneeze etiquettes can be easily employed at all levels in the communities and prevent spread of disease. Isolation of cases and proper case management including infection control are equally important to cut down on the transmission of the disease.

Preparedness and surge capacity is key: With rapid spread of infection from Mexico to other countries, WHO as a part of International Health Regulations (2005) declared the event as International Public Health Emergency of International Concern on April 25, 2009[9]. The risk level was further increased when sustained community based transmission was verified in two countries with which the world entered pandemic phase 5 for influenza which denotes that pandemic is imminent[10]. Occurrence of similar sustained community based transmission in another country in a different WHO region will, as per the current definition of WHO phases, mean that pandemic is underway thereby triggering the multisectoral response by the national authorities to not only mitigate the impact on health of the people but also minimize the social, and economic consequences.

While currently we are at phase 6 of the pandemic, global community is in a good state of preparedness than anytime in the past. In the South East Asia (SEA) Region, all countries have prepared their National Influenza Pandemic Preparedness Plans and are gearing up to implement these plans in right earnest and through a coherent global collaboration to mitigate the impact of pandemic. The need of the hour is to launch swift action at all fronts by triggering the surge capacity at all levels both within the countries and at global levels.

The WHO is closely monitoring the influenza situation which is evolving rapidly. As an intergovernmental UN agency with mandate for health sector response, WHO is co-ordinating global response through information sharing, provision of critical supplies especially diagnostics and drugs, technical support in strengthening national response and dissemination of technical guidelines to assist national authorities in mounting an effective response.

Since 2003 when influenza A H5N1 emerged as potential influenza pandemic, the global community and national authorities have been engaged in strengthening their response efforts with assistance from WHO and other developmental partners. The national influenza pandemic preparedness plans have provided valuable framework of action and with minor modifications can be activated to launch effective response to current event.

The global response to the spread of avian influenza A (H5N1) that began in 2003 has helped shaped a number of significant public health advances. During the past six years, the world has been strengthening its preparedness while trying to understand the virus and its mode of spread. Generation of proper evidence will help reformulation of policy and strategy in combating this new threat to public health in the Region.

Jai P. Narain* **& Rajesh Bhatia**
Communicable Diseases Department
WHO Regional Office for South-East Asia
New Delhi 110 002, India
**For correspondence*:
narainj@searo.who.int

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