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Pandemic Disease Swine Flu: H1N1 Virus Clinical and Prevention Aspects

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Review Article

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ABSTRACT

The influenza pandemic caused by the new H1N1 virus has by now affected all the continents of the world. However, the extent and likely impact are still uncertain. Like seasonal flu, the illness is mild and self-limiting in a great majority of cases, with only 1%–2% of patients requiring hospitalization. In a few cases, the clinical course can deteriorate in a matter of hours, leading to severe complications and eventually death. The risk of complications is higher among those who have preexisting diseases, such as asthma, heart disease and kidney disease, and among pregnant women. In such cases, antiviral treatment should not be delayed pending laboratory confirmation. The preferred antiviral drug is oseltamivir, and zanamivir is an alternative. Antiviral treatment is not necessary for those who are otherwise healthy, and have mild or uncomplicated illness. It is beneficial for patients with progressive lower respiratory tract disease or pneumonia, and those with underlying medical conditions and pregnant patients. As the supply of antivirals is limited, they should be used judiciously and where appropriate. There is a limited supply of pandemic influenza vaccine available in a few countries and efforts to produce it in India are presently underway. Effective personal preventive measures include shielding one's mouth and nose while coughing and sneezing, frequent washing of hands with soap, avoiding mass gatherings and voluntary isolation by symptomatic individuals. While at present the virus is causing a mild disease, the next wave may be more severe. Hence, enhanced surge capacity of health services is required for the clinical management of an increased patient load.

Introduction

The H1N1 subtype of Influenza A virus is the causative agent of swine flu. The 2009 outbreak caused by subtype H1N1 in humans is due to transfer of Swine Influenza Virus from pig to human. Thus to analyze the origin of this novel virus we compared the nucleocapsid sequences of H1N1 viruses of different origins. Phylogenetic analysis of these sequences was carried out along with bootstrap analysis of 100 replicates. The phylogenetic tree constructed revealed that Indian H1N1 strain showed the highest homology with Iowa H1N1 strain and also with Wisconsin H1N1 strain. Further the H1N1 strains analyzed using NP sequences of different Indian origins showed highly close sequence similarity. Hence, in future this study will be helpful for knowing the taxonomy and evolution of influenza viruses. Cases of swine flu have been reported in India, with over 31,156 positive test cases and 1,841 deaths till March 2015. Swine flu outbreaks was reported in India in late 2014 and early 2015. As of March 19, 2015 the disease has affected 31,151 people and claimed over 1,841 lives.[3] The largest number of reported cases and deaths due to the disease occurred in the western part of India including states like Delhi, Madhya Pradesh, Rajasthan, and Gujarat. Researchers of MIT have claimed that the swine flu has

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mutated in India to a more virulent version with changes in Hemagglutinin protein[2].This has however been disputed by Indian researchers

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Three such pandemics occurred in the previous century, in 1918, 1957 and 1968. The 1918 pandemic was the most devastating, taking a toll of 30–40 million lives worldwide. The subsequentpandemics were relatively milder, each killing around 1 million people.1 The year 2003 witnessed the appearance of a novel avian influenza A subtype (H5N1), which caused 438 cases and 262 deaths in 15 countries. It remains endemic in poultry populations in many countries, including some countries of the Southeast Asia region, in particular, Indonesia, and occasionally leads to the occurrence of human cases.

TABLE I. Sources of genes in the influenza A (H1N1) virus of 2009

Gene	Source
Polymerase basic 2 (PB2)	Avian influenza virus
Polymerase basic 1 (PB1)	Human influenza A virus
Polymerase acidic (PA)	Avian influenza virus
Haemagglutinin (HA)	Classical swine influenza A virus (triple reassortant swine influenza)
Nucleoprotein (NP)	Classical swine influenza A virus (triple reassortant swine influenza)
Non-structural proteins (NS)	Classical swine influenza A virus (triple reassortant swine influenza)
Neuraminidase (NA)	Swine in Eurasia
Matrix protein (M)	Swine in Eurasia

TABLE II. Characteristics of seasonal and pandemic influenza

Characteristics	Seasonal influenza	Pandemic (H1N1) 2009
Causative agent	Influenza A H1, or H2 or H3 Influenza B	Influenza A H1N1
Seasonal preponderance	Autumn/winter	Summer
Age group at higher risk	Extremes of age	Young adults
Resistance to amantadine	No	Yes
Susceptibility to oseltamivir	Yes (?)	Yes
Natural immunity	May be present	Absent
Availability of specific vaccine	Yes	No
Symptoms pertaining to the GIT	No	25%–50% of cases
Pregnancy a high risk factor	No	Yes

GIT gastrointestinal tract

Two hundred fourteen abstracts and 87 full texts regarding pregnant women infected with pandemic influenza A(H1N1) 2009 virus were systematically reviewed by using a PubMed search and assessing

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pandemic, clinical, laboratory test, vaccine, and control experiences. Both policy and health education were excluded. This review counted the total number of pregnant cases from different countries and analyzed their epidemic features, including trimester distribution, morbidity, hospitalization, intensive care unit admissions, maternal mortality, underlying diseases, complications, high-risk factors for death, pregnancy outcome, and clinical symptoms compared with the previous pandemic seasonal influenza A/H1N1 as compared with the general population. Early identification and treatment were the most important factors in different countries and areas examined. The vaccine and antiviral drugs that have been the most efficient means to control the novel virus appear to be safe but require more extensive study. In the future, the focus should be placed on understanding vertical transmission and the severe mechanisms[4].

Clinical presentation, diagnosis and Treatment:

Clinical presentation The data available indicate that the clinical spectrum of infection with the H1N1 virus is broad, and ranges from mild upperrespiratory tract illness to severe complications such as pneumonia resulting in respiratory failure, acute respiratory distress syndrome (ARDS), multi-organ failure and death. Like seasonal flu, a great majority of cases have fever, cough, sore throat and a runny nose. Gastrointestinal symptoms such as diarrhoea have been reported in 20%–50% of patients, and do not require hospitalization.What is critically important, however, is that in a small proportion of patients, the clinical course tends to deteriorate rapidly, leading to complications and death. Such
patients require immediate hospitalization and treatment with antivirals without delay; most deaths during influenza outbreaks have been associated with delayed administration of antivirals. In some countries, the main reason for hospitalization is primary viral pneumonia or viral pneumonitis. Among fatal cases,
microbiological evidence of a secondary bacterial or fungal infection has been observed. In the USA, >70% of hospitalized patients and approximately 80% of fatal cases have had underlying
conditions considered to put them at high risk for complications.

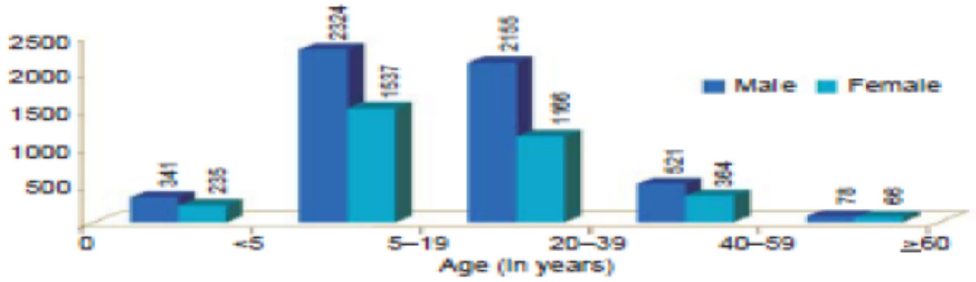

Fig3. Age and sex distribution of laboratory confirmed pandemic (H1N1) cases n=8787 in India (data unavailable for 836 cases)

Preventive Measures:

From a public health standpoint, for a vast majority of populations in developing and resource-constrained countries, pharmacological interventions such as vaccines and antivirals are not likely to play
a major role at present, due in part to limited supply, lack of access and the high costs involved. Such countries will have to depend on various non-pharmaceutical interventions. Non-pharmacological interventions Non-pharmacological or simple public health interventions include the use of personal protective measures such as shielding one's mouth and nose while coughing or sneezing, frequently washing one's hands with soap, avoiding mass gatherings and voluntary isolation by symptomatic individuals. A full understanding of the risks involved, what precautions to take and whom to consult
when one has symptoms is critical. The media plays an important role in communicating risks/targeted messages to the general population. Some of the measures such as the mandatory isolation of cases or quarantine of close contacts, have not been successful in containing the virus. They could even be

counterproductive in controlling the outbreak as those who are symptomatic may go underground, or such measures can lead to a false sense of complacency among the general population. Personal hygiene, including hand hygiene, if observed properly, can be effective in preventing respiratory viral infections, as shown by empirical studies.18,19 Media strategies should aim at advising people to observe the basic rules of hygiene. Interventions for social distancing, such as the cancellation of social events and
closure of cinemas and schools, may not be effective, and could create social disruption and panic in the community. In Japan, though such an intervention was effective in controlling an outbreak of the infection in a school, social distancing did not seem to have any effect on transmission in the community. Screening at the port of entry could not prevent entry of the virus in India, Thailand and several other countries. Hence, these measures can be considered only in specific situations. Healthcare workers have acquired H1N1 in occupational settings. Laboratories that process clinical samples should have adequate biosafety facilities (enhanced BSL2).

Pharmacological measures:

Currently, vaccine is starting to become available in a few countries. Antivirals are also available in limited supply, and should be used judiciously and where appropriate. Chemoprophylaxis. If the likelihood of complications is low, antiviral chemoprophylaxis should not be offered to individuals
at risk for infection or to healthcare workers. If the likelihood of complications is high (either due to the strain or baseline risk of the exposed group), oseltamivir or zanamivir may be used as postexposure
chemoprophylaxis for affected individuals, especially healthcare workers. Vaccination. Vaccine against the H1N1 virus is presently available in a few countries. WHO and its partners, both in the public and private sectors, are working to produce a vaccine against the pandemic virus as early as possible in developing countries too. Substantial progress has already been made and commercial production is about to commence. However, the capacity to produce the vaccine is limited in devoping countries. In India, five manufacturers are striving to have this vaccine in the market, but given the technological and regulatory requirements, limited doses of the vaccine are likely to be available only a few months later.
Three objectives that countries could adopt as part of their vaccination strategy include:21 (i) protecting the integrity of the healthcare system and the country's critical infrastructure; (ii) reducing the morbidity and mortality; and (iii) reducing transmission of the virus within communities. The first priority of all countries should be to immunize their healthcare workers (1%–2% of the world's population) in order to
protect the essential health infrastructure. Significant pandemicrelated morbidity in such workers will compromise the capacity of the health services to care for patients. Despite low rates of hospitalization and case fatality, as the virus invades new territories, the number of people infected, as well as of those developing disease, requiring hospitalization and succumbing to the illness will be many times more than is the case with seasonal flu, thereby stretching the local health services. The next priority should be pregnant women (2% of the world's population), who appear to be at increased risk for severe disease, especially during the second and third trimesters of pregnancy. Inactivated non-adjuvant vaccines similar to most seasonal influenza vaccines are considered the preferred option, given the extensive safety data on their use in pregnant women. Next in priority could be persons who are above the age of 6 months and have one of several chronic underlying medical conditions, in order to reduce morbidity and mortality. Next in order of priority could come healthy young adults (above 15 years of age to below 49 years of age).

CONCLUSION

The 2009 influenza pandemic has affected most countries of the world within a short span of time. Though at present, the pattern of illness does not differ from that of seasonal influenza, the sheer volume of cases that is expected to occur could easily overstretch the already fragile and overburdened health services, and cause considerable suffering in human populations around the world. It is a matter of much concern that while the novel virus is at present causing a mild disease in most cases, the next wave may be more severe. Larger numbers of severely ill patients requiring intensive care are likely to be the most urgent burden on health services, creating pressures that could overwhelm intensive care units and
possibly disrupt the provision of care for other diseases. This calls for an enhanced surge capacity of health or medical services in each country to enable the health facilities to clinically manage an

increased patient load in the future and keep the rate of fatality low. Although, the role of antivirals and vaccines is indisputable, the limited supply and lack of access in most developing countries can undermine the response capacity of the region and hence, enhance these countries' vulnerability in an emergency situation. Traditional non-pharmacological approaches to the prevention and control of disease have stood the test of time. Modern communication tools, the enhanced availability of antivirals and community awareness regarding the desirable behavioral changes may attenuate the effects of this pandemic. As new information about the virus and/or technologies (such as for a vaccine) become available, the opportunity should be taken to further strengthen prevention and control strategies, and minimize the overall health, social and economic effects of the pandemic in the coming years.

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