Mathematical Modelling of Effectiveness of H1N1

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Abstract: The Influenza a H1N1 virus is a highly contagious pathogen which caused the influenza pandemic. Here, we have used the Mathematical model (S.I.R) that could provide critical insights for informing preparedness and planning to deal with future epidemics of infectious disease.

Index Terms—H1N1, SIR Model, Excel 2007.

I. INTRODUCTION

H1N1 influenza (swine influenza or swine flu) is a respiratory disease of pigs caused by type A influenza virus that regularly causes outbreaks of influenza in pigs. H1N1 virus causes high levels of illness and low death rates in pigs (Centres for Disease Control and Prevention [CDC], 2009a). The classical swine flu virus (influenza type A H1N1 virus) was first isolated from a pig in 1930 (CDC, 2009a). Like all influenza viruses, H1N1 viruses change constantly. Pigs can be infected by avian influenza and human influenza viruses as well as H1N1 viruses (CDC, 2009a). As of June 2009, the CDC has identified that influenza viruses from different species infect pigs, thus the viruses can reassort (i.e. swap genes) and new viruses that are a mix of swine, human and/or avian influenza viruses can emerge. At this time, there are four main influenza type A virus subtypes that have been isolated in pigs: H1N1, H1N2, H3N2, and H3N1. Most of the recently isolated influenza viruses from pigs, however, have been H1N1 viruses (CDC, 2009a). H1N1 viruses do not normally infect humans. But, sporadic human infections with swine flu have occurred. Initially, these cases occur in persons with direct exposure to pigs [e.g. children near pigs at a fair or workers in the swine industry] (World Health Organization [WHO], 2009a).

Seasonal influenza occurs every year and the viruses change each year. Many people have some immunity to the circulating virus that helps limit infections. Some countries also use seasonal influenza vaccines to reduce illness and deaths. But influenza A (H1N1) is a new virus and one to which most people have no or little immunity to, therefore, this virus could cause more infections than are seen with seasonal flu (WHO, 2009a). By June 2009, the WHO has identified that the new influenza A (H1N1) appears to be as contagious as seasonal influenza, and is spreading fast, particularly among young people (ages ten to 45 years). The severity of the disease ranges from very mild symptoms to severe illnesses that can result in death. Most people who contract the virus experience the milder disease and recover without antiviral treatment or medical care. Of the more serious cases, more than half of hospitalized people had underlying health conditions or weak immune systems (CDC, 2009a).

This virus was originally referred to as “swine flu” because laboratory testing showed that many of the genes in this new virus were very similar to influenza viruses that normally occur in pigs (swine) in North America. Further study (CDC, 2009a) has shown that this new virus is very different from what normally circulates in North American pigs. It has two genes from flu viruses that normally circulate in the pigs of Europe and Asian continents and it has close resemblance with both bird (avian) genes and human genes (WHO, 2009a). Scientists call this a “quadruple reassortant” virus.

Flu viruses are spread mainly from person to person through coughing or sneezing by people with influenza. Sometimes people may become infected by touching something, such as a surface or object with flu viruses on it and then touching their mouth or nose. The symptoms of 2009 H1N1 flu virus in people include fever, cough, sore throat, runny or stuffy nose, body aches, headache, chills and fatigue (WHO, 2009b). Some people may have vomiting and diarrhea (WHO, 2009b). People may be infected with the flu, including 2009 H1N1 and have respiratory symptoms without a fever. Severe illnesses and death has occurred as a result of illness associated with this virus (WHO, 2009b).

II. PANDEMIC MODELING APPROACHES

The researcher uses models to examine the expected impact of various government imposed and voluntary interventions on the progression of an influenza pandemic. Past pandemics are one approach to evaluating the effect of different interventions. However, solely relying on past outbreaks is not sufficient since influenza strains continuously mutate and take on different characteristics. Also, the past provides us with a limited set of scenarios that actually occurred and does not give us any insight into what would have happened if the control measures were different. Models allow us to systematically assess different scenarios as well as pandemics of varied severity. With the help of mathematical models we can consider and resolve many different "what if" questions.
The types of models that have been used to describe the spread of infection range from basic differential equations to detailed stochastic agent-based models. Compartmental models of various complexities are the most common approach to modeling influenza.

Yet as computing capabilities and memory have increased over the past decade, very complex simulations have also become more prevalent in literature. Another widely used approach relies on one specific parameter for the description of infection spread - the basic reproductive number $R_0$: the average number of infections a typical infectious individual will generate in a fully susceptible population (Diekmann et al., 1990).

### III. DETERMINISTIC COMPARTMENTAL MODELS

The basic compartmental models are contained within a series of three papers by W.O. Kermack and A.G. McKendrick (Kermack, 1927, 1932, 1933). This most prominent epidemiology modeling approach is based on dividing the host population into several compartments based on their status with respect to the disease. It also incorporates the underlying assumptions about the nature and rate of transfer amongst the compartments. The simplest, yet applicable compartmental model, known as the SIR model divides the total population of N into three distinct groups:

1. Susceptible (S): people who have no immunity to the virus, and so have the potential to get infected,
2. Infectious (I): people who are currently infected and can transmit the virus to the susceptible individuals,
3. Removed/Recovered (R): people who are immune to the infection because they have recovered from the disease.

### IV. MATERIALS AND METHODS

In this study the patients suspected as well as confirmed cases of swine flu from month of July 2009 to March 2010. A complete data of all the patients visiting these OPDs and swine Flu wards had been kept on the daily basis right from the month July. Each and every patient visiting either swine flu OPD or swine flu ward, who are suspected clinically H1N1 positive were categorized in three categories according to the guidelines provided by Ministry of Health and Family welfare in August, 2009. They were as follows:

**Category A:**
Mild fever plus cough / sore throat with or without bodyache, headache, diarrhea and vomiting. No testing for H1N1 is required in such patients.

**Category B:**

i. Above signs and symptoms plus high grade fever and severe sore throat

ii. Addition of above symptoms and signs plus one or more of the following conditions:

- Children less than 5 years
- Pregnant women
- Age above 65 years
- Having lung, heart, liver or kidney diseases, blood disorders,
- diabetes, neurological disorders, cancer and HIV
- Long term cortisone

**Category C:**

In addition to symptoms and signs of A and B if patients have one or more of the following:

- Breathlessness, chest pain, drowsiness, low BP, sputum mixed with blood, bluish discolouration .
- Irritability among small children, refusal to accept feeds .
- Worsening of underlying chronic conditions .

Those falling in category C, as per the guidelines are confirmed by viral isolation (Polymerase chain reaction, QIAGENT™) in WHO reference laboratory by using throat and nasopharyngeal swabs are included in our study. Only those patients who fell in category C were subjected to viral isolation tests, while category B and Category A individuals were empirically given Oseltamivir and Azithromycin respectively, and are not included in the study. The patients are then classified according to age, gender, location, approach to either government or private hospital, duration of symptoms on admission, associated co morbid conditions, the final outcome, duration of death after symptoms and the district wise distribution of sale of Oseltamivir. The incidence ratio for cases and deaths per 10 lakh population is calculated and compared with other states.

The mathematical model described by Kermack and McKendrick was used for prediction of epidemic curve and number of H1N1 cases. The model is also known as the Susceptible Infectious Recovered (SIR) model.
The model assumes that when an infectious disease strikes a community, the disease often partitions the community into three categories: individuals that are yet to be infected (susceptible people and denoted by \( S \)); infected individuals (assumed to be infectious and denoted by \( I \)); and those recovered and possess immunity to or killed by this disease (denoted by \( R \)).

One infected individual is introduced into a closed population where everyone is susceptible, and each infected individual transmits influenza with probability \( \beta \), to each susceptible individual they encounter. The severity of the epidemic and the initial rate of increase depend upon the value of the basic reproduction number (\( R_0 \)) which is defined as an average number of new infections that one case generates, in an entirely susceptible population, during the time they are infectious.

The model assumes that if \( R_0 > 1 \), the disease will occur in an epidemic form; however, if \( R_0 < 1 \), the outbreak will die out. \( R_0 \) for H1N1 influenza is equal to \( \beta \) times average duration of the infectious period.

The model consists of a system of three coupled nonlinear ordinary differential equations,

\[
\begin{align*}
\frac{dS}{dt} &= -\beta SI \\
\frac{dI}{dt} &= \beta SI - \gamma I \\
\frac{dR}{dt} &= \gamma I
\end{align*}
\]

where, \( \beta \) is the infection rate which determines the number of susceptible persons infected per day by the infected person, \( \gamma \) is the recovery rate and \( 1/\gamma \) is the expected infectious period or the time until recovery.

We have used the data of Mexico outbreak for \( R_0 \) as 1.4 to 1.6, and for the expected infection period, \( 1/\gamma \), as 3 days. We iterated the model for various values of \( R_0 = 1.2, 1.3, 1.4, 1.5 \) and 1.6 to determine the effect of variations in \( R_0 \) on the potential size and time course of the epidemic, while keeping the value of \( 1/\gamma \) constant at 3 days. We further simulated the model using varying values of \( 1/\gamma \) ranging from 2 to 6 days, while keeping the value of \( R_0 \) constant at 1.4. The mathematical models were created and run in Microsoft Office Excel 2007.

The total number of patients who have visited swine flu OPD and ward were 27860. Out of these 13250 and 7621 belonged to category B and A respectively. The individuals, who were falling in category C, were 6989. Out of all those suspected the individuals who turned out positive were 1586 while 4125 turned out negative.

The simulation of the epidemic by SIR model, showed that the susceptible population decreases as the incidence (i.e., the number of individuals infected per unit time) increases. At a certain point of time, the epidemic curve reached its peak and subsequently declined, because infected individuals recover and cease to transmit the virus.

**The Infection Rate - \( \beta \) (beta)**

If we now think about how the disease is passed on in a model like this, we will have a flow of people - from the susceptible group to the infected group to the recovered group.

Susceptible → Infected → Recovered

The only way a person leaves the susceptible group is if they get infected. We assume that the number in the susceptible group depends on: the number of people already susceptible, the number of people already infected, and the amount of contact between susceptible people and people infected.

Assume that each infected person has a fixed number ‘\( b \)’ of contacts per day that can spread the disease. But, not all these contacts are with people who are susceptible.

Since there is homogeneous mixing of the population, we define the susceptible fraction of the population as \( S(t)/N \). Therefore, each infectious person, on average, will generate \( b*S(t)/N \), new infected people per day. The quantity \( b/N \) is called the infection rate and will be denoted as \( \beta \).

**The Recovery Rate - \( \gamma \)(gamma)**

The number of people who move from the infected group to the recovered group will be calculated using the recovery rate which is called \( \gamma \). The value of \( \gamma \) can be estimated in terms of the average number of days a person is infectious, (able to pass on the virus or disease). If this is equal to \( d \), then the fraction of the population that will recover on a given day is \( d/\gamma \), therefore \( \gamma = 1/d \).

**The Basic Reproductive Number**

One important characteristic determining the dynamics of the spread of a disease is the Basic Reproductive Number (\( R_0 \)). This number is the average number of new infections caused by a single infectious person in a totally susceptible population during the time the person is infectious.

Based on the definition given above,
\[ R_0 = \frac{\beta X S_0}{\gamma} \]

Where \( S_0 \) represents the maximum number of possible susceptible people.

The difference equation for the number of susceptible people is given as,

\[ S(t + 1) = S(t) - \beta S(t) I(t) \]

The two other difference equations required for each of \( R(t + 1) \), and \( I(t + 1) \) are,

\[ R(t + 1) = R(t) + \gamma I(t) \]

\[ I(t + 1) = I(t) + \beta S(t) I(t) \gamma I(t) \]

Model 1: \( 1/\gamma \) constant, \( R_0 \) variable
Model 2: $R_0$ constant, $1/\gamma$ variable

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<th>$\beta$</th>
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References


