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Mathematical Modelling Of H1N1

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***Abstract*— Inherent inter disciplinarily of mathematical biology necessarily brings about two contrasting approaches. On one hand, there are mathematicians that have a taste for biology and develop analytically tractable models for the sake of the analysis itself On the other hand, there are theoretically inclined biologists who use relatively simple models in support of their empirical findings or develop very complex models, but also systems of dozens of differential equations, to simulate complex biological systems .The niche in between these two worlds is the playground for mathematical biologists or biomathematicians who develop and analyze and/or numerically simulate relatively sophisticated mathematical models to primarily address a biological question, yet with the attendant aim to get from these models as much as possible also mathematically. In this study the patients suspected as well as confirmed cases of swine flu from month of July 2013 to March 2014. 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.**

I. INTRODUCTION

Mathematical models of population dynamics build on this empirical knowledge, attempt at linking such lower-level individual phenomena to upper-level population dynamics, help formulate ecological theories, and generate falsifiable hypotheses to be tested in the next round of empirical work (for a recent example, see Vercken et al, 2011). For a real progress to be made, empirical and mathematical approaches in biology have to be used complementarily The wealth of mathematical biology can also be seen on the journal market. A great many of articles published in biological journals use mathematics to help address their focal questions (e.g. Vercken et al, 2011). Conversely, a plenty of articles published in journals on applied mathematics use biology as a source of challenging nonlinear problems to solve (e.g. Sun and Saker, 2005).

Mathematical models of population dynamics are often expressed in terms of differential or difference equations, which describe how populations change with time, space, or stage of development (Murray, 1993; Case, 2000; Kot, 2001; Mangel,2006). Biological processes are, however, inherently complex. Given that mathematical models disconnected from biological reality are of a little use, this complexity has to show up in the models. Unfortunately, this is paid by the fact that although it is often not that complicated to write down an adequate system of dynamical equations, frequently it is virtually impossible to analyze such equations by standard mathematical methods, or at least not for the most part. Thus, formal analysis needs to often be complemented with numerical simulations or use of a numerical bifurcation tool that exemplify and often even reveal interesting, analytically intractable system behavior. Simulations can thus be incredibly helpful, allowing the reader to see what the equations predict and allowing the author to obtain results from even very complex models. On top of that, many models in current mathematical biology are by definition simulation models, consisting of a set of rules of how individuals behave and interact. This is in part because current ecology increasingly recognizes impacts of individual variability on population dynamics. These rules are repeatedly simulated for an ensemble of individuals with the aim to come up with dynamics of the population as a whole. Such models are often referred to as individual-based models (IBMs; e.g. Grimm and Railsback, 2005). Due to substantial complexity of IBMs, techniques have been developed that allow for approximating IBM dynamics by differential or difference equations, thus providing further insight into the systems under study (e.g. Dieckmann et al, 2000).

II. INFLUENZA

There are three distinct types of influenza virus that have been identified **A,** B, and **C.** These three antigenically distinct RNA viruses comprise the Orthomyxoviridae family. Flu types **A** and B are responsible for epidemics associated with increased hospitalization and death rates. Type B, which mutates at a slower rate than Type **A,** is found only in humans and seals. Consequently, a degree of immunity to Type B is maintained **by** a portion of the population. Because of this slower rate of antigenic change as well as limited host range, type B influenza never results in a pandemic (Zambon, **1999).** Influenza type **C** usually

manifests itself in a very mild illness, or is completely asymptomatic and has not caused widespread outbreaks. Types B and **C** do not present a large magnitude of public health concern, thus we will focus on type **A.**

Influenza virus **A** can be further divided into subtypes based on differences in two surface proteins called hemagglutinin (H) and neuraminidase (N). Hemagglutinin, making up approximately **80%** of the surface proteins, functions in the attachment of the virus to a host cell. The remaining 20%, the neuraminidase, is thought to facilitate the spread of the progeny virus. Antivirals function **by** blocking either the hemagglutinin or the neuraminidase to prevent the multiplication of the virus in the host. Both H and **N** are antigens to which the human body can raise antibodies. There are **16** known H and nine known **N** subtypes that, through various combinations, make up all the subtypes of influenza **A.** As virus cells replicate, various mutations of the surface antigens occur as a response to host immunity; this is termed "antigenic drift". These types of gradual mutations result in seasonal flu outbreaks, but do not lead to pandemics since partial immunity remains in the population. In order to deal with this gradual evolution of the virus the World Health Organization (WHO) selects and reformulates the strains of the flu virus into the annual influenza vaccine. Influenza A virus also experiences another more worrisome type of mutation called "antigenic shift". Antigenic shift is a reassortment of gene segments, and it can occur when two or more different subtypes of influenza A infect the same cell.

The unusually broad range of hosts susceptible to influenza **A,** especially birds, pigs and humans, appears to increase the likelihood of this event. Notably, in some parts of the world, humans live in close proximity to both swine and fowl, so antigenic shift is even more likely to effect the human population. It is not possible to predict the antigenic shift mutations, thus no vaccines can be produced for these emerging strains ahead of time. This emergence of a new and unpredictable strain to which humans have no immunity or effective vaccine, can cause a global pandemic in a very short amount of time.

Subtype	Name/Location	Time Period	Cases/Deaths
H1N1	Spanish Flu, global	1918-1919	50-100 million deaths
	Endemic in humans	Annual	Seasonal
H1N2	Endemic in humans	Annual	Seasonal
H2N2	Asian Flu , global	1957-1958	1-4 million deaths
	Russian Flu , global	1889-1890	~ 1 million deaths
H3N2	Hong kong Flu , global	1968-1969	~ 1 million deaths
	Endemic in humans	Annual	Seasonal
H5N1	Avian Flu , Asia - Turkey	2003-2009	405 cases , 254 deaths
H7N2	North America , UK	2002, 2003, 2007	6 cases
H7N3	Canada	2004	2 cases
H7N7	Netherlands	2003	89 cases , 1 death
H9N2	Hong Kong	1999, 2003 ,2007	4 cases
H10N7	Egypt	2004	2 cases

A non-exhaustive list of Influenza A subtypes that have infected the human population (CDC). The strains currently endemic in humans are included in the seasonal flu vaccine.

III. MATERIALS AND METHODS

In this study the patients suspected as well as confirmed cases of swine flu from month of July 2013 to March 2014. 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 body ache, 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, QIAGEN^{TM}) 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 β, 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 β times average duration of the infectious period.

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

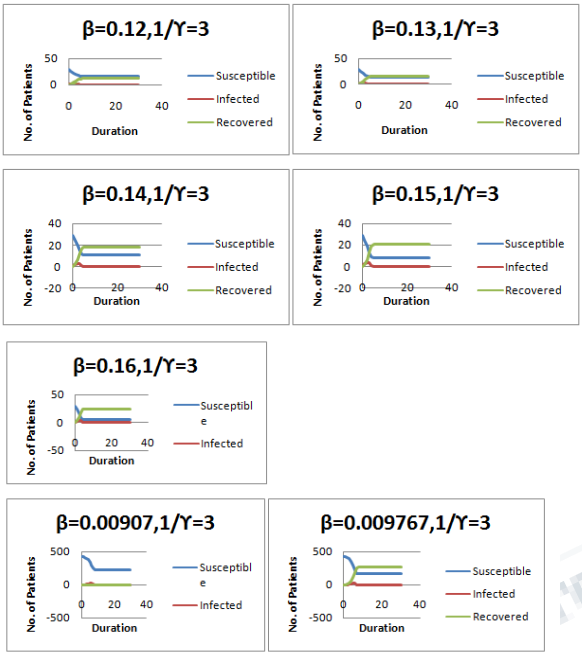
$$dS/dt = -\beta SI$$
$$dI/dt = \beta SI - \gamma I$$
$$dR/dt = \gamma I$$

	Suspected Cases(St)	Immu.,recovery/death(It)	Confirmed Cases(Rt)
Jul-13	30	1	2
Aug-13	10	0	2
Sep-13	7	1	2
Oct-13	24	4	4
Nov-13	430	14	190
Dec-13	812	48	348
Jan-14	437	13	85
Feb-14	359	0	55
Mar-14	42	0	0

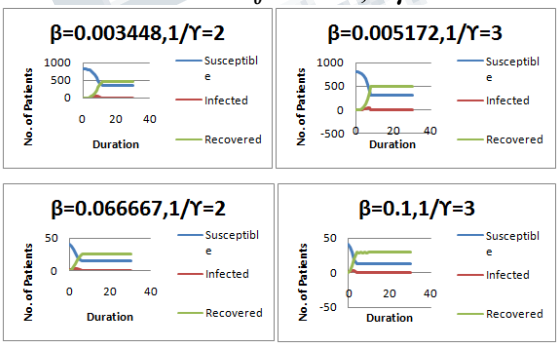
where, β is the infection rate which determines the number of susceptible persons infected per day by the infected person, γ is the recovery rate and 1/ γ is the expected infectious period or the time until recovery.

We have used the data of Mexico outbreak for R_0 as 1.4 to 1.6, and for the expected infection period, 1/γ, 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/γ constant at 3 days. We further simulated the model using varying values of 1/γ ranging from 2 to 6 days, while keeping the value of R_0 constant at 1.4.

Model 1: 1/γ constant, R_0 variable



Model 2: R_0 constant, 1/γ variable



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