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Research Article

ESTIMATION OF THE REPRODUCTION NUMBER OF THE NOVEL INFLUENZA A, H1N1 IN MALAYSIA

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ABSTRACT

In June 2009, the World Health Organization (WHO) confirmed that the novel influenza A, H1N1 as a pandemic. After six months, as of December 29, 2009, it was reported by WHO that more than 208 countries and territories were affected by the pandemic accounting for about 150,000 infected cases and at least 11,516 death. In Malaysia, during the first wave, there are about 14,912 cases were reported from May, 15, 2009 until June, 4, 2010 and a total number of 88 deaths were recorded across the country in 2010. The aim of this study is to assess the transmissibility of this pandemic in Malaysia by estimating the basic reproduction number, *Ro*, which is the average number of secondary cases generated by a single primary case. The value of *Ro* is a summary measure of the transmission potential in a given epidemic setting and has been estimated to range from 1.4 – 1.6 in Mexico, from 2.0 – 2.6 in Japan, 1.96 in New Zealand and 1.68 in China for this current pandemic.

INTRODUCTION

In June 2009, WHO raised the influenza pandemic alert level from phase 5 to phase 6, declaring that the influenza A, H1N1 had reached pandemic levels. As of December 29, 2009, it was reported by WHO that more than 208 countries and territories were affected by the pandemic accounting for about 150,000 infected cases and at least 11,516 death [1]. In Malaysia, during the first wave, there are about 14,912 cases were reported from May, 15, 2009 until June, 4, 2010 and a total number of 88 deaths were recorded across the country in 2010[2].

The H1N1 pandemic calls for action and the various mathematical models have been constructed to study the spread and control of H1N1. The transmissibility of the disease can be shown quantitatively by calculating basic reproduction number which is the average number of individuals directly infected by a primary infected case during infectious period without any preventive measure during the epidemic and when the infected person enters a totally susceptible population. It is a key concept in epidemiology and is inarguably one of the foremost and most valuable ideas that mathematical thinking has brought to epidemic theory [3]. This index is useful in assessing the necessary preventive measures and needs assessment for prevention and prediction for future. If *Ro* less than 1, it shows that the disease will eventually die out. However, if *Ro* is equal to 1, the disease is endemic and when *Ro* is greater than 1, then there will be an epidemic and increasing number of infected persons [4]. This threshold behavior is the most important and useful aspect of the *Ro* concept. In an endemic infection, the control measures and at what magnitude, would be most effective in reducing *Ro* below one can be determined and this will provide important guidance for public health initiatives [5].

The estimation of the basic reproduction number *Ro* in Mexico is in the range of 1.4 – 1.6 [6]. For Japan, the reproduction number *Ro* was estimated in the range 2.0 – 2.6[7]; 1.96 for New Zealand [8]; and 1.68 in China [9]. The main aim of this study is to calculate and determine the estimation of the reproduction number, *Ro* for Malaysia.

MATERIAL AND METHODS

During the first wave of influenza A, H1N1, 5,496 cases were reported between July, 26, 2009 and August 20, 2009 and a total number of 77 deaths in Malaysia as in Table 1 and the Figure 1 and Figure 2 [10a. 10b. 10c.]. All patients were referred to public and private hospital.

Confirmed Cases in Malaysia		Death Cases in Malaysia	
26/7/2009	1124	26/7/2009	2
27/7/2009	1219	27/7/2009	3
2/8/2009	1429	2/8/2009	6
3/8/2009	1460	3/8/2009	8
5/8/2009	1476	5/8/2009	12
6/8/2009	1492	6/8/2009	14
10/8/2009	1983	10/8/2009	32
11/8/2009	2250	11/8/2009	38
14/8/2009	2253	14/8/2009	56
16/8/2009	3857	16/8/2009	62
17/8/2009	4225	17/8/2009	64
20/8/2009	5496	20/8/2009	68

Table 1: The number of confirmed and death cases in Malaysia

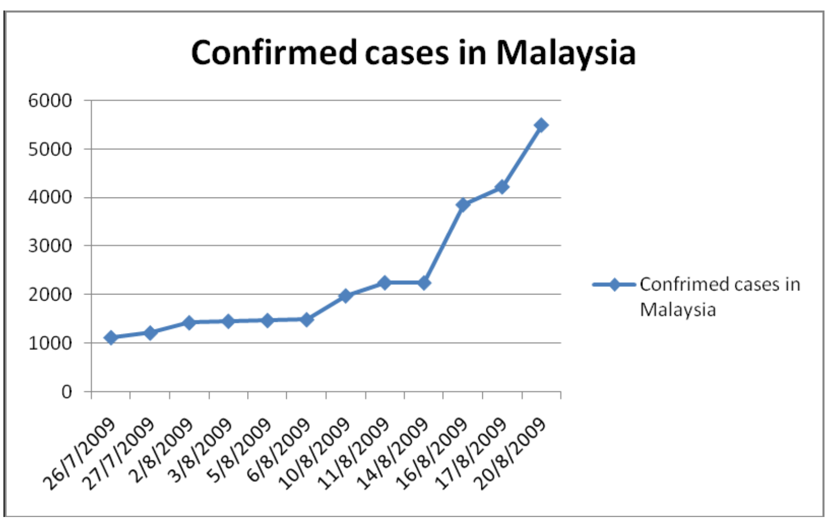

Figure 1: Confirmed cases in Malaysia

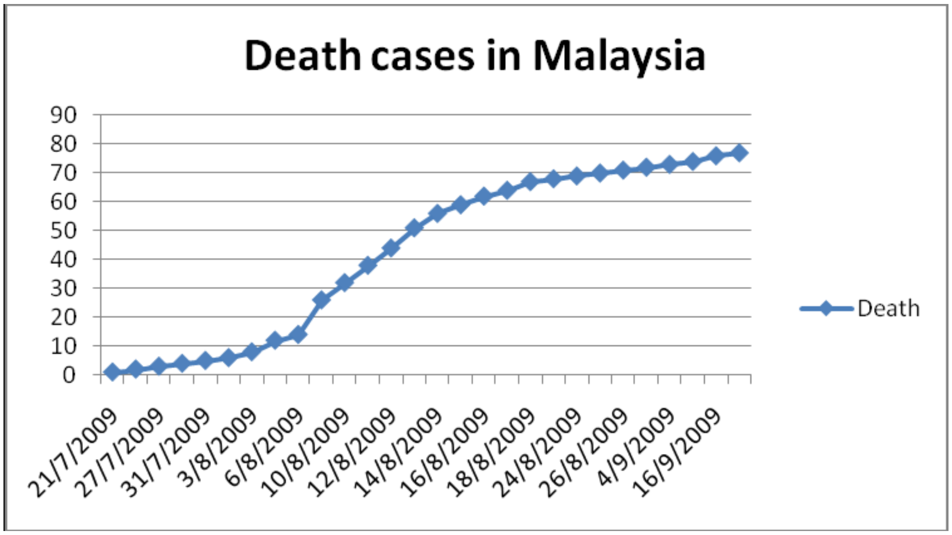

Figure 2: Death cases in Malaysia

During that time the study was conducted to develop a proposed mathematical modeling of this disease using SEIR model [11], where S is susceptible, E is exposed, I is infectious and R is recovered. The least-square fitting procedure in MATLAB using the build-in routine *cftools*in the optimization toolbox is implemented to the data and model can be estimated. Two models were fitted to the data for each case as in the Table 2 and Table 3.

	Boltzmann Model : $f(x)=\alpha_1+\frac{\alpha_2-\alpha_1}{1+\exp((x_1-x_0)/\alpha_3)}$	Double Exponent Model: $f(x)=\alpha_1\exp(\alpha_2 x)+\alpha_3\exp(\alpha_4 x)$
Parameters estimation	$\alpha_1 = 10744$, $\alpha_2 = 1214.1$, $\alpha_3 = 2.0421$, and $x_0 = 12.441$	$\alpha_1 = 1088$, $\alpha_2 = -0.03448$, $\alpha_3 = 120.4$, and $\alpha_4 = 0.3075$
The coefficient of determination, R^2	0.977	0.976

Table 2: The models for confirmed cases in Malaysia

Based on Table 2, because the R2 for Boltzmann model is greater than double exponent model then the fitting model for confirmed cases is a Boltzmann model as in the figure 3.

	Boltzmann Model : $f(x)=\alpha_1+\frac{\alpha_2-\alpha_1}{1+\exp((x_1-x_0)/\alpha_3)}$	Rational Function Model: $f(x)=\frac{\alpha_1 x^3+\alpha_2 x^2+\alpha_3 x+\alpha_4}{x^2+\beta_1 x+\beta_2}$
Parameters estimation	$\alpha_1=69.521$, $\alpha_2=3.175$, $\alpha_3=1.235$ and $x_0=7.591$	$\alpha_1=1.582$, $\alpha_2=-12.69$, $\alpha_3=51.41$, $\alpha_4=188.8$, $\beta_1=-21.3$ and $\beta_2=156.3$
The coefficient of determination, R^2	0.999	0.992

Table 3: The models for death cases in Malaysia

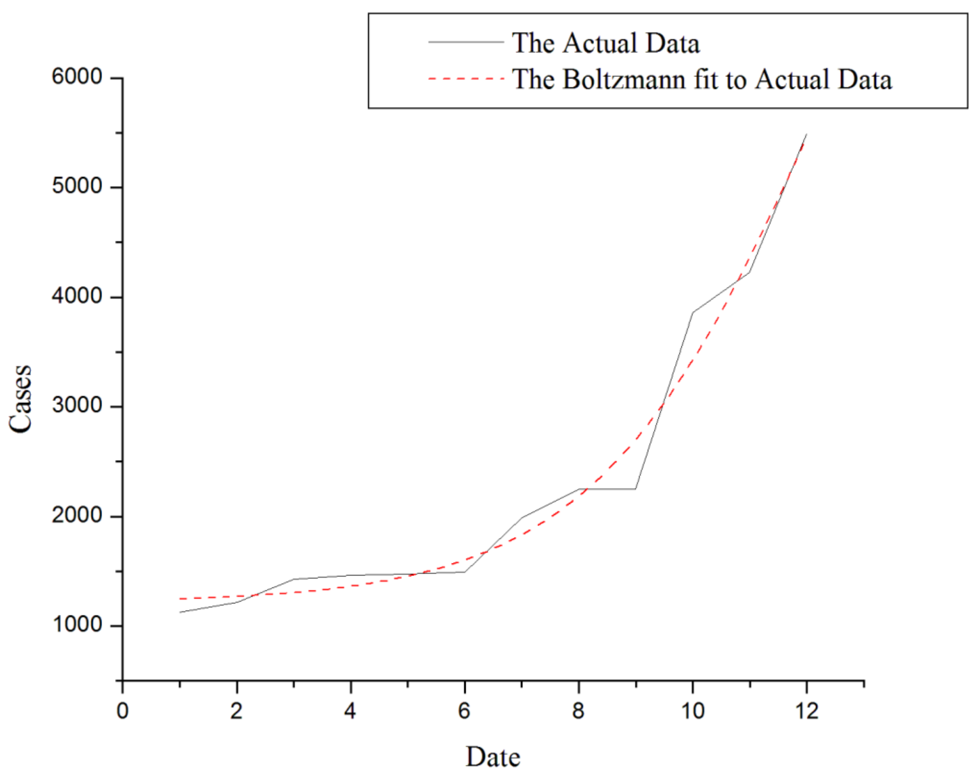

Figure 3: Fitting model for confirmed cases in Malaysia

Where *x* axis is the time and *f(x)* or *y* axis is the confirmed cases estimation

While based on Table 4, the fitting model for the death cases is a rational function since the R2 for Boltzmann model is greater than rational function as shown in the figure 4.

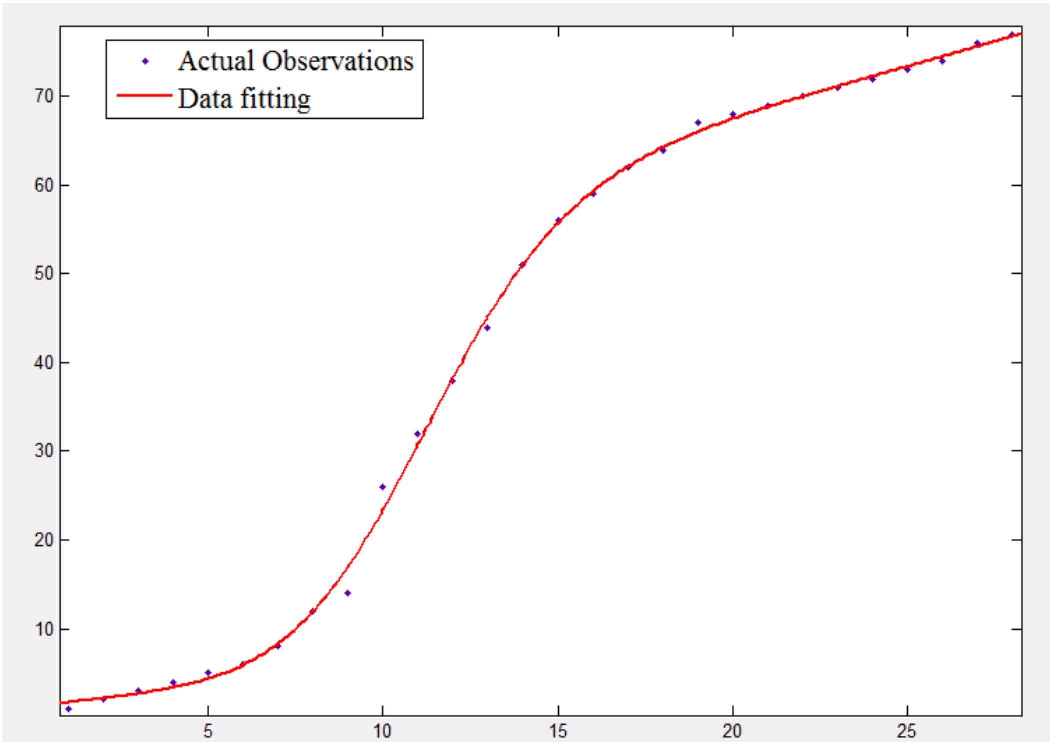

Figure 4: Fitting model for death cases in Malaysia

Where *x* axis is the time and *f(x)* or *y* axis is the death cases estimation.

The data from this study was use in estimation of reproduction number. There are different methods to calculate the basic reproduction number which the simplest method using SIR model is given by [12]:

$$R_o = \frac{\beta}{\gamma} \tag{1}$$

where β is the probability of the disease transmission from an infected person to a healthy person and γ is the recovery rate or one divided by average period of infection.

The second method for calculation of *Ro* using SEIR model is given by [13],

$$R_o = \frac{\beta}{\gamma + \delta} \tag{2}$$

where β is the probability of the disease transmission from an infected person to a healthy person, γ is the recovery rate or one divided by average period of infection and δ is the mortality rate which is calculated by the following formula [13]:

$$\delta = \gamma \left(\frac{CFP}{1 - CFP} \right) \quad (3)$$

Where*CFP* is the mean case fatality proportion.

The third method for calculation of *Ro* using the complex SEIR model is given by [13],

$$R_o = \left(1 + \frac{\beta}{\gamma} \right) \quad (4)$$

In our previous study, we proposed the model SEIR as our appropriate mathematical model for influenza A, H1N1 in Malaysia. So we will use the equation (2) and (4) to estimate the basic reproduction of the influenza A, H1N1 in Malaysia.

RESULT AND DISCUSSION

According to the data obtained in the first wave of influenza A, H1N1 in Malaysia, it is founded that the probability of the disease transmission from an infected person to a healthy person, β is 0.35. The recovery rate or one divided by average period of infection, γ is 1/6 days, and the mean case fatality proportion (CFP) is 0.003 hence the mortality rate, δ is 0.0005.

From equation (2), the basic reproduction number, *Ro* is 2.1. However if we use equation (4), the basic reproduction number, *Ro* is 3.1. So the range of basic reproduction number, *Ro* forMalaysia can be concluded is between 2.1 and 3.1. A value of *Ro* is determined which minimized the sum of squares differences between the simulated and observed data. The median estimate for *Ro* is 2.6. It is interesting to note that in this study, one of the most careful and a recent investigation of *Ro* in the literature, the result is relied on a very simple simulation and least squares fitting. Based on theory of reproduction number, if *Ro* >1, then the pathogen is able to invade the susceptible population. This threshold behavior is the most important and useful aspect of the *Ro* concept to determine which control measures and at what magnitude would be most effective in reducing *Ro* < 1, and providing important guidance for public health initiatives.

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