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Calculation of Reproductive Number Using Data from H1N1 Patients in Fars Province, Southern Iran

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Abstract

Background: Effective reproductive number (Re) is an index which considers the proportion of susceptible people in a community. There are different methods for calculation of basic reproductive number. The aim of this study was to evaluate the reproductive number using data from H1N1 patients in Fars Province, southern Iran.

Methods: According to the data obtained, 233 cases were confirmed between July 15th and December 3rd, 2009. Two waves were observed during this period with a peak in October 21st in Fars Province.

Results: In the first wave, the highest amount of R_0 was 3.22 and the lowest amount was 2.12 and in the second wave, the highest and lowest amounts of R_0 were 3.42 and 2.42, respectively.

Conclusion: Effective reproductive number could not be more than 1.54. Thus in order to maintain R_0 below 1, using preventive measures like vaccination, only 70% of population should be immune. As 54.9% of Fars population were immune against H1N1 if only 15.1 of them take part in vaccination program, the disease will not reach an epidemic level.

Keywords: Reproductive number; H1N1; Epidemic; Influenza; Iran

Introduction

When a communicable disease is going to be epidemic, all susceptible individuals are at risk of the disease, thus the disease will spread rapidly among populations, will reach a peak and it slows down and eventually will be disappeared later. In absence of preventive measures, epidemic waves will be repeated for 2 or several times. Having data regarding this pattern, next epidemic of the disease is predictable. The transmissibility of the disease can be shown quantitatively by calculating basic reproductive number and epidemic curves of the disease. Basic reproductive number is the average number of individuals directly infected by a primary infected case during his or her infectious period without any preventive measure during the epidemic and when the infected person enters a totally susceptible population. This index (R_0) is useful in assessing the past preventive measures and needs assessment for prevention and prediction for future. If R_0 is less than 1, the disease will eventually die out. If R_0 is equal to 1, the disease is endemic and when R_0 is above 1, there will be an epidemic and increasing number of infected persons.[1] Effective reproductive number (Re) is an index which considers the proportion of susceptible people in a community. When, due to immunization or health education and increasing awareness, all people are not susceptible, the transmissibility of the disease will be better explained by calculation of Re using R_0.[1] Influenza type A (H1N1) is a communicable disease and became pandemic and a major health problem in 2009. A great deal of studies on influenza H1N1 has been conducted worldwide.[2-5] There are some antigenic similarities between seasonal influenza and influenza type A. Therefore, because of cross reactions, some individuals are immune against influenza H1N1 and susceptibility decreased in the population.[6]

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The aim of this study was to evaluate various methods of estimation of transmission factors and effective and basic reproductive number in Fars population in southern Iran. All necessary parameters for calculation of the above indexes have been taken into account. However, data from other studies has been used too.[7,8]

Materials and Methods

Between July 15th and December 3rd, 2009, an epidemic of influenza H1N1 with two obvious waves was observed in Fars Province, southern Iran with about 4 millions and 3 hundred thousands population. In this epidemy, 297 patients were diagnosed and confirmed by RT-PCR.[7] All patients were referred to public health centers by private and public sector physicians throughout Fars Province. In case of a severe respiratory problem, the patients were referred to local hospitals. In both public health centers and hospitals, a questionnaire including demographic data and history of travel during the week before the disease onset was completed for each patient.[7] Seventh reference of this paper describes the method of data collection in details. Then all necessary samples were sent to the Central Specialized Laboratory of Shiraz University of Medical Sciences. During this epidemy, a sero-epidemiologic study was conducted and its data was used in estimation of parameters of this study.[8] There are different methods for calculation of basic reproductive rate, which the simplest methods are as following:

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

In this formula, beta (β) shows the probability of the disease transmission from an infected person to a healthy person. Some texts called it force of infection. Using Favier method, it can be calculated by epidemic data.[9] Gama (γ) is recovery rate or one divided by average period of infection. In previous studies, the average period of infection has been reported as 7 days.[6,10] The second method for calculation of R_0 is as follows:[11]

$$R_0 = \frac{\beta}{\gamma + \delta}$$

In this formula, beta shows the probability of the disease transmission from an infected person to a healthy person. Gama is recovery rate or one divided by average period of infection. Delta (δ) is the mortality rate which is calculated by the following formula.[11]

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

In Shiraz study, the mortality rate was 4.4%.[7] Using the above formula, the delta was 0.006.
The third formula for calculation of R_0 is as follows:

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

There are different methods for calculation of Re. In this study the following formula was used.

$$R_e = \frac{S_t}{N} R_o$$

In this formula, (S_t) shows the number of susceptible individuals at the time t and N shows the total number of population. Another study in Fars Province showed that 59.4% of population were immune against H1N1.[8]

Results

According to the data obtained from Shiraz study, 253 cases were confirmed between July 15th and December 3rd [7], 2009. However, data of 233 cases were used for this study. Two waves were observed during this period, the first between July 15th and August 19th with a peak in August 5th (summer) and the second wave was seen from September 23rd to the end of November with a peak in October 21st (autumn), two ovals in Figure 1 indicating two waves. The slope of line in the highlighted parts with ovals considered as force of infection in the calculation of R_0 and the slopes in linear regression were 0.318 and 0.228, respectively. Also in Shiraz study, the mortality rate was 4.4%. Using the results of Shiraz study, the basic reproductive number for the two waves has been calculated by different methods and presented in Table 1. In Table 1 in the first wave, the highest amount of R_0 was 3.22 and the lowest amount was 2.12, and in the second wave, the highest and lowest amounts of R_0 were 3.42 and 2.42, respectively. Considering this result, effective reproductive number could not be more than 1.54.

Discussion

Calculations of R_0 and Re for projection of disease spread in future are main strength of this study.

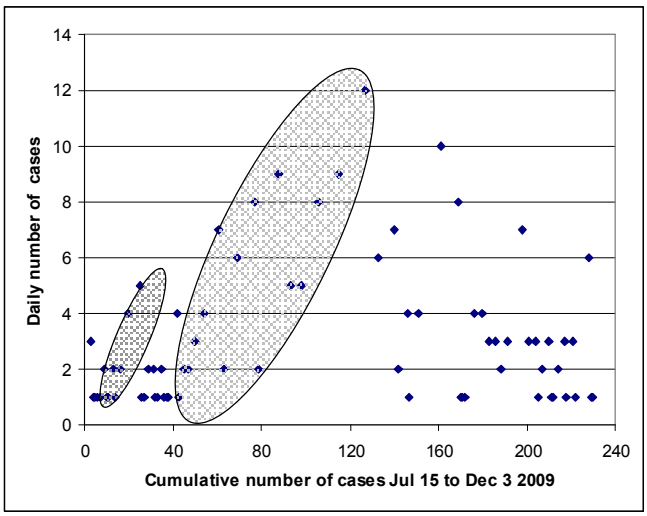

Fig. 1: Plot of the daily number of case declarations against the cumulative number of cases for the two successive epidemics in Fars province. The ellipses indicate the growing linear parts of the plots corresponding to the initial exponential growth of the epidemics.

Table 1: The basic reproductive number and R_e calculation according to three scenarios in Fars Province 2009.

	B	R_o	95% confidence interval		R_e	95% confidence Interval	
Scenarios (ref.)			**Low**	**High**		**Low**	**High**
Cintron – Arias et al (6)	0.318	2.22	1.88	4.18	1.00	0.85	1.89
Chowell G, et al (11)	0.318	2.12	1.80	4.00	0.96	0.81	1.81
Favier, C. et al (9)	0.318	3.22	2.88	5.18	1.45	1.30	2.34
Cintron – Arias et al (6)	0.346	2.42	2.00	4.38	1.09	0.91	1.98
Chowell et al (11)	0.346	2.32	1.92	4.19	1.04	0.87	1.89
Favier, et al (9)	0.346	3.42	3.01	5.38	1.54	1.36	2.43

There are various methods for calculation of R_0 and Re but they need more patients' information. In this study, the R_0 and Re were calculated using data obtained by previous studies. Different methods of calculation of R_0 have been reported so far.[1] Based on available data for those methods only 3 of them were used in this study. According to the results of two studies in Fars Province, in the highest level R_0 was 3.42. Therefore, it can be concluded that in the worst situations the progress of epidemic is not so worrying. Other studies reported R_0 from 1.2 to 7.5,[3,11,12-17] and majority of them are less than 3. However, some studies like our study reported R_0 above 3.[13,15] When duration of infectivity considered 7 days and severe cases of the disease are included in study, R_0 can be overestimated. We selected 7 days because in one study in Iran, 7 days was considered too.[10] In another study, duration of infectivity was reported 2 days.[6] Even with this overestimated R_0, the epidemy was not so problematic because a high proportion of population was immune. A study from Shiraz confirmed high proportion of immunity against H1N1 that could be due to antigenic similarities between this virus and other influenza viruses and previous use of seasonal influenza vaccine.[8]

In particular, it was shown that 45.1% of the population were susceptible to disease and also R_e was 1.54 which is not worrying. However, this amount was calculated based on 4.4% mortality rate in Fars Province which is overestimated. Even when mortality rate is about 1 per 1000, the amount of R_0 will not be above 3.5. Thus in order to maintain R_0 below 1, using preventive measures like vaccination, only 70% of population should be immune. As 54.9% of Fars population were immune against H1N1, if only 15.1 of them take part in vaccination program, the disease

will not reach an epidemic level.[8] Here, the role of health education when the cost of vaccination is high is of great importance because following health regulations and isolation of infected individuals have important roles in preventive meaures during the infectious period.

Conflict of interest: None declared.

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