Estimation of Basic Reproductive Number of Flu-like Syndrome in a Primary School in Iran

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Date of Submission: Oct 04, 2011

Date of Acceptance: Jan 15, 2012

How to cite this article: Haghdoost A, Baneshi MR, Zolala F, Farvahari S, Safizadeh H. Estimation of basic reproductive number of flu-like syndrome in a primary school in Iran. Int J Prev Med 2012;3:408-13.

Original Article

ABSTRACT

Introduction: Iran, similar to other countries, had faced H1N1 flu outbreak in 2009. In order to assess its transmission dynamic, we estimated its force of infection (β) and basic reproductive number (R_0).

Methods: Within a middle size primary school in Iran, we actively followed students and detected flu-like syndrome among students and their families in the first three months of academic year; October through December 2009. We estimated the probability of disease transmission within families (β) fitting random effects Poisson regression model. Moreover, R_0 within the school was computed based on the number of detected cases.

Results: In 452 students, 204 influenza-like syndromes were detected. The estimated β within families was 0.10; increasing one infectious member within each family was associated with 30% increase in this number. The estimated R_0 for the first month was 1.21 (95% C.I.: 0.99, 1.47); corresponding numbers for the first two and first three months were 1.28 (95% C.I.: 1.05, 1.54) and 1.32 (95% C.I.: 1.11, 1.59), respectively.

Conclusion: It seems that the dynamic transmission of H1N1 virus was more or less comparable with that in other seasonal species. Our findings showed that the virus mainly circulated among students within schools. In addition, it seems that the transmission rate within families was relatively high.

Keywords: Basic reproductive number, force of infection, H1N1, influenza, R_0

INTRODUCTION

Influenza A (H1N1) virus was the most common cause of human influenza in 2009, which was declared as a pandemic by the World Health Organization (WHO). By mid 2010, more than 214 communities reported laboratory confirmed cases of pandemic influenza H1N1 2009 including over 18,138 deaths.[1]

Although it is difficult to estimate the burden of this new type of influenza (such as the number of death and inpatient and

outpatient cases) without any doubt preparedness against such a pandemics is necessary.[2] This enables the policy makers to implement appropriate plans so as to prevent the rapid spread of the virus in the society.

In this regard, mathematical dynamic models are used frequently to show how fast the virus may transmit within and among the communities.[3] As an example, Haghdoost AA *et al*. modeled the epidemic curve of H1N1 in a middle and a large cities in Iran.[4] The results of these models may be used by policymakers in different levels to design the national and sub-national programs accordingly; however, because of the lack of key information about many influential parameters in these models, the uncertainty around their results is a point of concern.

Among these parameters, basic reproductive number (R_0) plays a central role. This parameter shows the average number of new infections that a single patient generates in a fully susceptible population.[5] Clearly severe and mild outbreaks are associated with high and low R_0 values, respectively.[6] Therefore, the results of a model, to a great extent, depend on the R_0 value.

There is a considerable variability in the estimated R_0 for influenza virus, possibly due to the location of study, the stage of epidemic curve, or the used methodology.[6] As an example, the estimated R_0 for the 1918 Spanish flu for different regions of the world varies from 1.5 to 5.4.[7,1,2,8,9] In another study, to develop the Canadian pandemic plan for the heath sector, R_0 value is estimated to be between 1.4 and 1.8.[10] Corresponding figure in other parts of the world were 1.4 to 2.4 in the US, 1.28 to 2 in the UK, and 1.68 to 1.89 in the Netherlands, respectively.[11-15]

In May 2009, just after the report of the epidemic in Mexico, Iran launched a new surveillance system to detect H1N1 suspected cases nationally. Between June and November 2009, 2662 confirmed H1N1 cases were reported in this system. The peak of this epidemic was in October, just after the start of new academic year.[16] In other words, by opening schools and colleges, because of the huge effective contacts among students, virus transmitted much faster in the Iranian community.

In order to estimate R_0, we decided to monitor the number of flu-like cases in one of the primary schools in Kerman closely.

Although "confirm cases detection" and "case based surveillance" systems are key components in disease control program, now-a-days there is a special attention to the syndromic surveillance as well.[17] Confirmation of cases is a time consuming step which needs considerable human and financial recourses. Therefore, for early epidemic detection scheme, particularly at national level, syndromic surveillance is recommended.[18] This type of surveillance system for flu-like syndrome is implemented in other countries as well.[19-22]

Based on the above explanation, in this study, we aimed to estimate R_0 for the flu-like syndrome in one of the primary schools in Iran in the peak of H1N1 transmission, particularly among the students. At the same time, we estimated the force of infection (β) among family of these students to show how fast the infection might transmit among the family members of students.

METHODS

This study was carried out in Kerman city, located in the South East of Iran. We selected a primary boys' school with 452 students that voluntarily participated in our study.

Having explained the main objectives in a parent-teacher conference, we sought maximum contribution of the school and families.

We adopted a syndromic surveillance approach for our data collection. Flu-like syndrome was described as "a cluster of symptoms and findings including fever and cold symptoms, cough, nausea, vomiting, body aches, and sore throat".[17]

In three months period, i.e., from October through December 2009, the absence of students and their flu-like syndromes were carefully recorded on a daily basis.

We actively approached families of sick students during and after their diseases to check the signs and clinical presentations of the disease in all family members.

Data analysis

Estimation of the force of infection (β)

We defined the family of each student as a cluster. The numbers of susceptible and infectious family members were computed based on the collected information where we allowed these two numbers to vary if one of the susceptible subjects contracted the infection during the study period.

Using a random effects Poisson regression model, we estimated β. This model, taking into account the correlation between household members, estimated the risk of infection for each susceptible family member as the result of his/her contacts with one infectious subject in that family. We also estimated the risk ratio for the number of infectious cases in a family to show the increasing trend of infection risk by increasing the number of infectious cases in the family.

Estimation of basic reproductive number (R_0) within the school

We then estimated R_0 using the following formula.[23,24]

$$R_0 = \frac{N-1}{C} \sum_{i=N-C+1}^{N-1} \frac{1}{i}$$

In this formula, N and C show the total population at risk and total number of infections, respectively, in the first phase of a new epidemic in a fully susceptible community.

We estimated R_0 in the first month, in the first two months, and in the first three months of epidemic within the selected school independently. In addition, R_0 in the first three months was estimated in 14 classes one by one; then the arithmetic mean and Huber's M-estimator across classes was calculated. In arithmetic mean, an equal weight would be applied for all of R_0 in different classes, while in M estimator extreme R_0s would be got lower weights.

In addition, we created a model to predict the optimum weights for R_0 of different classes in a way to minimize the sum of squares of the differences between the weighted mean of R_0 and R_0 in each class.

For all statistics, a 95% confidence interval (95% CI) was derived through Monte Carlo simulation using 1000 iterations. All computations were done in STATA version 10 and Excel software.

RESULTS

The selected school had 14 classes; in average each class had 32 students. Among 452 followed students, 204 flu-like syndrome were detected, 153 in the first, 33 in the second, and 18 in the third months.

The mean (±SD) age of students was 9.65 ± 1.31 years. Corresponding figure for their family size was 4.06 ± 0.76. Among 767 total family members, 141 flu-like syndromes were detected in 85 families.

FORCE OF INFECTION

The risk of contracting infection for each family member as the results of contact with one infectious member (β) was 0.10. The results of the random effects Poisson model showed that by increasing one infectious member, the risk of infection of every susceptible member would increase around 30% [Table 1].

Basic reproductive number

The estimated R_0 in different months and classes are summarized in [Tables 2 and 3], respectively. R_0 for flu-like syndrome in the first three months was 1.32 (95% CI: 1.32, 1.59). The estimated R_0s based on the data of the first month and the first two months were more or less close to each other (in the first month: 1.21 (95% CI 0.99, 1.47); in the first two months: 1.28 (95% CI: 1.05, 1.54) [Table 2].

The estimated R_0 in different classes was ranged between 0.93 and 1.95. In four classes, the estimated R_0 was less than 1.1, and in two classes, it was more than 1.6 [Table 3].

The mean of R_0s of classes using different formulae were more or less comparable. The simple arithmetic mean for R_0s and its Huber's M-estimator was 1.26 and 1.22, respectively. The

Table 1: Risk of infection for family members based on number of infectious in the family

Number of infectious subjects within family members	Risk of infection for each susceptible family member
1	0.1
2	0.13
3	0.17
4	0.22

Table 2: Estimation of the basic reproductive number (R_0) in different months among students

Time	R_0 (95% CI)
First month	1.21 (0.99, 1.47)
First and second month	1.28 (1.05, 1.54)
First, second, and third month	1.32 (1.11, 1.59)

Table 3: Estimation of R_0 in different classes

ID of class	Number of susceptibles	Number of patients	R_0 (95% CI)
1	32	15	1.22 (0.58, 2.54)
2	28	17	1.38 (0.69, 3.85)
3	33	16	1.24 (0.63, 2.52)
4	33	15	1.95 (0.58, 2.47)
5	31	19	1.41 (0.68, 3.46)
6	32	7	0.93 (0.28, 2.26)
7	37	20	1.32 (0.62, 2.67)
8	40	25	1.46 (0.78, 3.11)
9	30	22	1.64 (0.73, 5.27)
10	28	7	0.97 (0.28, 2.35)
11	28	7	0.97 (0.28, 2.35)
12	28	8	0.98 (0.38, 2.52)
13	37	15	1.15 (0.58, 2.28)
14	35	11	1.05 (0.78, 2.19)
Arithmetic mean of R_0 across classes			1.26
Weighted mean of R_0 in a way to minimize the sum of square of residuals (MLE)			1.26
Huber's M estimates of Mean			1.22

weighted mean of R_0 using optimum weights for the information of different classes also was 1.26 [Table 3].

In addition, we estimated R_0 at different grades. values varied from 1.18 (grade 5) to 1.41 (in grade 4). Corresponding figures for those in the first, second, and third grade were 1.36, 1.28, and 1.21, respectively.

DISCUSSION

For modeling of infectious diseases both R_0 and β are very important parameters. Both of these two parameters show how fast an infection may transmit from infectious to susceptible subject.[4] However, β mainly depends on the biology of agent and presents its infectivity. On the other hand, R_0 is a number which shows the combined effects of effective contacts in a community and the infectivity of an agent.[23]

The estimated β in our study within a family was around 0.10. There would be 30% increase in risk by increasing one infectious person in the family. In a similar study in Pennsylvania, impact of social network on transmission of H1N1 influenza has been addressed.[22] Within a class, child-to-child transmission probability was 0.035. Furthermore, the child-to-adult transmission probability varied from 0.096 to 0.026 in households of size two to six, respectively. The inverse association between transmission probability and household size might be due to higher chance of past-exposure to agents in extended families.

In addition, our results showed that R_0 for flu-like syndrome in the peak of H1N1 transmission in a primary school in Iran was around 1.32. This indicates that each infected student might spread the disease to 1.32 of students in average. The estimated average of R_0 across 14 classes was also 1.26 indicating robustness of our estimate.

In Pennsylvania study, the global reproduction number of a typical case was 1.3 (95% C.I. 1.2, 1.4) in the first two weeks of the outbreak.[22] However, our figure (i.e., 1.32) was slightly lower than that estimated in other countries. For example, the corresponding figure in the Canada was between 1.4 to 1.8.[6,10] It is important to mention that our R_0 was only for students within a school, while they may transmit infection to others outside of their school as well. Therefore, a grand R_0 is more than an R_0 limited to a school which we purposed to measure.

We only selected one primary school in a middle size city, so the generalizability of the results to the whole country is a point of concern. However, we have to mention that Kerman is located in the center of Iran and from the socio-economical and climate point of views it is in average.

We adopted a syndromic surveillance scheme to detect the influenza cases. This indicates that we did not confirm H1N1 infection in our cases using any serology or virology tests. However, H1N1 was the dominant species in Iran between October and December of 2009.[16] Therefore, we may suppose that almost all of cases were infected by H1N1.

Although our estimation for R_0 within the school was lower than that of the whole community; their differences was not considerable. This means that in children the transmission of virus mainly occurs within schools. Students spend many hours within schools and have very close direct and indirect contacts. Therefore, the chance of transmission between students is considerable.

Having accepted the high risk of transmission within schools, it is easy to accept the logic behind of big surge of H1N1 epidemic in the beginning of academic year in Iran similar to many other

parts of the world.[25,26,20] It has been shown that late closure of schools when around one-fourth of students had symptoms could not affect the spread.[22] Therefore, closure of schools in very special scenarios might be a justified solution to control influenza epidemics.

Both parameters which were estimated in our study are very important in modeling and quantify the transmissibility of H1N1. Generally, it seems that the transmissibility of H1N1 was more or less similar to transmissibility of seasonal influenza. Therefore, our findings might be used in modeling of seasonal influenza as well.

Therefore, we can imply that the huge number of H1N1 cases in 2009 was mainly because of susceptibility of people, but not because of its infectivity. This means that the higher proportion of infected people in a pandemic can be mainly explained with limited immunity to the new strain.[27]

CONCLUSION

It seems that the transmissibility of H1N1 virus was more or less comparable with that in other seasonal species. Our findings quantified the transmissibility of H1N1 within school and within families. Based on our findings, we showed that the virus mainly circulated among students within schools.

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Source of Support: Nil **Conflict of Interest:** None declared.