SIR Model of Swine Influenza Epidemic in Abu Dhabi:

Estimation of Vaccination Requirement

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***Abstract*- Mathematical models could be used to analyse dynamics of epidemic infections and create better insights into the measures that could prevent future epidemics. In this paper, we developed a basic SIR model which was fit to data from recent influenza A (H1N1) epidemic in Abu Dhabi. We estimated values for the threshold reproductive number $\Re_\circ$ which prevent outbreak of swine influence infection. Results suggest that vaccination of 59% of population could achieve 'herd immunity' and prevent spread of the disease. The results could guide future public health measures in the Emirate of Abu Dhabi.**

Keywords*- *Influenza A (H1N1); ODEs; Parameter Estimation Simulation; Stability; Steady States

I. INTRODUCTION

In March 2009, the State of Mexico announced first confirmed cases of influenza A (H1N1) infection. Within a month, eleven other countries reported 331 cases of the disease and the World Health Organization (WHO) declared a state of pandemic. Many countries throughout the world set up the measures to monitor and control the outbreak of the disease. The Abu Dhabi Government set up a surveillance system in May 2009 comprising hospitalization and vaccination measures. In July 2009, the numbers of confirmed infections and fatalities reported by WHO were 94,512 and 429 respectively [5].

The spreading of influenza can be prevented or reduced by various control measures like vaccination (immunization) and timely use of specific antiviral agents. Vaccination reduces the pool of susceptible individuals and could be either constant (conventional) or intermittent (seasonal). If an adequate percentage of susceptible population is immunized, infectious disease cannot spread within the population. This is due to the fact that vaccination does not only protect immunized person but confers protection of other members of the population.

Post- epidemic analysis in Abu Dhabi showed a relatively low fatality rate of 1.4 per 100,000 of population [1]. This occurred despite some resistance to vaccination which was observed during epidemic in some segments of population. In addition, considerable amount of expensive vaccine was not utilized. These observations have created a need for a better estimation of the fraction of the population that needs to be vaccinated and the amount of vaccine to be ordered in the event of similar future outbreak.

This paper presents a mathematical model of influenza A (H1N1) epidemic in Abu Dhabi in 2009-2010. The main objective of the study is to estimate the fraction of the population that needs to be vaccinated in order to achieve adequate control of disease in similar future epidemic.

II. THE MODEL

We used basic SIR model which relies on three epidemiological classes: i) portion of population that is susceptible and not yet infected, S(t); ii) portion that is infected and able to spread the diseases by contact to susceptible individual, I(t); and iii) portion of those removed by immunization, recovery or death, R(t). The simplest SIR model of Kermack and Mckendrick [8] computes the theoretical number of people infected with a contagious illness in a closed population over time. Transmission of a disease is a dynamical process driven by the interaction between susceptible and infective. The behaviour of the SIR models are greatly affected by the way in which transmission between infected and susceptible individuals are modelled.

In case of swine influenza, it is reasonable to assume that a much larger proportion of the population is susceptible than is the case for the seasonal influenza. However, the average duration of infectivity and other relevant epidemiological characteristics of swine influenza are assumed to be similar to that of seasonal influenza. The model has the following postulates: (i) Susceptible individuals are born at a rate μN, (ii) β is the fixed-average number of adequate contacts of a person per unit time and does not depend on the population size N or vary seasonally, (iii) the death rates in the three epidemiological classes are μS, μI and μR, the deaths balance the births, so that the population size N is constant, (iv) the model uses standard incidence and has recovery rate γI. Then the model takes the form

$$\begin{aligned} S'(t) &= \mu N - \mu S(t) - \beta S(t) I(t), & S(0) &= S_0, \\ I'(t) &= \beta S(t) I(t) - \mu I(t) - \gamma I(t), & I(0) &= I_0, \\ R'(t) &= \gamma I(t) - \mu R(t), & R(0) &= R_0, \end{aligned} \quad (1)$$

with $S(t)+I(t)+R(t)=N$. Dividing the equations in (1) by the constant total population size N such that $s(t)=S(t)/N;\ i(t)=I(t)/N;\ r(t)=R(t)/N$ yields

$$\begin{aligned} s'(t) &= \mu-\mu s(t)-\beta s(t)i(t), \\ i'(t) &= \beta s(t)i(t)-(\mu+\gamma)i(t), \end{aligned} \quad (2)$$

with $r(t)=1-s(t)-i(t)$. This model has then two equilibria:

$$E_0=(1,0),\quad E_+=(s^*,i^*)=\left(\frac{1}{\Re_\circ},\frac{\mu}{\beta}(\Re_\circ-1)\right), \quad (3)$$

where $\Re_\circ=\dfrac{\beta}{\mu+\gamma}$ is the Reproduction Number; it denotes the number of individuals infected by a single infected individual placed in a totally susceptible population.

The first equilibrium represents the case where none of the individuals are infected (free-infection). The second equilibrium represents the case where a fraction of the individuals are infected (infected equilibrium, or endemic equilibrium), when $\Re_\circ>1$ (Each infected individual infects more than one other member of the population and a self-sustaining group of infectious individuals will propagate).

The Jacobian matrix of the lineated system at the equilibrium point (s^*,i^*) is

$$J=\begin{pmatrix} -\mu-\beta i^* & -\beta s^* \\ \beta i^* & \beta s^*-(\mu+\gamma) \end{pmatrix} \quad (4)$$

The characteristic equation for the infection-free equilibrium $E_0=(1,0)$ is then

$$(\lambda+\mu)[\lambda-\beta+(\mu+\gamma)]=0. \quad (5)$$

While characteristic equation of the endemic equilibrium $E_+=(1/\Re_\circ,\mu(\Re_\circ-1)/\beta$ is

$$\lambda^2+\mu\Re_\circ\lambda+\frac{\mu\beta}{\Re_\circ}(\Re_\circ-1)=0. \quad (6)$$

From this simple analysis and the fact that the seedy state (s^*,i^*) is stable if and only if all the roots of its characteristic equation have negative real parts. Therefore, we arrive at the following Proposition.

Proposition:

The disease-free equilibrium E_0 is asymptotically stable and the infection will die out if $\Re_\circ=\dfrac{\beta}{\mu+\gamma}<1$ and unstable if $\Re_\circ>1$. Conversely, the endemic equilibrium E_+ is stable when $\Re_\circ>1$ and $\Re_\circ^{\#}=\dfrac{\mu\Re^3_\circ}{4\beta(\Re_\circ-1)}<1$.

Thus over the entire duration of the infection an infected individual will infect $\dfrac{\beta}{\mu+\gamma}$ proportion of individuals [6, 8, 11].

Figures 1 displays the qualitative behaviour of SIR model when $\Re_\circ<1$ (infection-free steady state). While Figure 2 shows the behaviour when $\Re_\circ>1$ (endemic steady state).

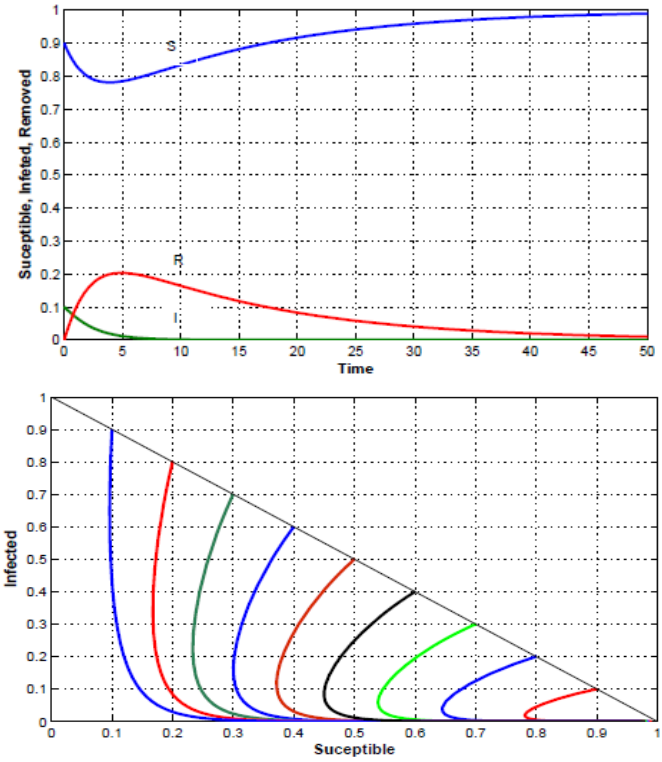
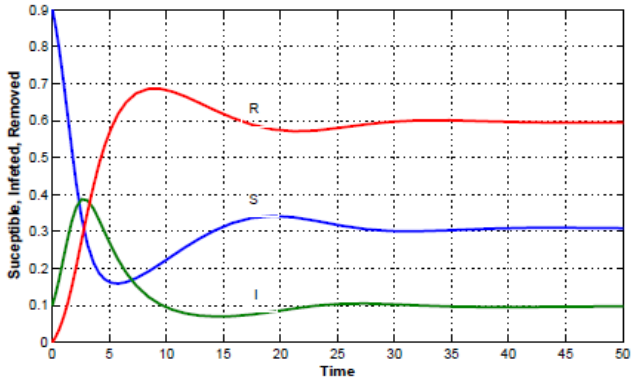


Fig. 1 (Top) shows the numerical simulations of epidemic model (1); (Bottom) the trajectories of the system approach to the infection-free steady state E_0, when

$\mu=1/14,\ \beta=1.2,\ \gamma=1.4,\ \Re_\circ=0{:}8180<1$



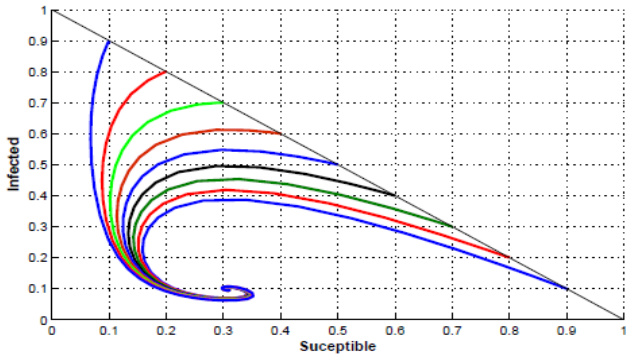


Fig. 2 (Top) shows the numerical simulations of endemic model (1); (Bottom) the trajectories of the system approach to the infection-free steady state E_+, when $\mu = 1/14,\ \beta = 1.66,\ \gamma = 0.44,\ \Re_\circ = 3.2458 > 1$

III. VACCINATION

To estimate fraction of immunized population which will suffice for prevention of infectious disease epidemic, let us consider an epidemic for which a portion of population is vaccinated (with a vaccine giving life-long immunity) at a protective rate $P \in (0,1)$. If the vaccination transfers individuals directly from the susceptible to the immunized class, how much we have to reduce s^* in population to prevent spread of disease? Here $s^* = \dfrac{1}{\Re_\circ}$ is the population of susceptible individuals at the infected equilibrium, and the threshold condition is given by $\Re_\circ = 1$ (see [2, 4, 3]). Thus the critical proportion of individuals that need to be vaccinated is given by

$$P_v = 1 - s^* = 1 - \frac{1}{\Re_\circ}. \qquad (7)$$

Hence, the higher the reproductive number, the higher the fraction of individuals that need to be vaccinated in order to eradicate the disease. Once the population of susceptibles falls below a critical level ($P_v N$), the entire population is protected against infection. This concept is called herd immunity, which is not a property of the individual, but a property of the population only [8]. In case of epidemic infection when $\Re_\circ = 4$, 75% of the population needs to be immunized to prevent epidemic. This value depends on form of SIR epidemic models. The difficulty is that S_0, and $\Re_\circ$ are rarely known, and are often difficult to estimate. Yet without accurate information on both of these, it is impossible to predict the proportion of the population infected, or attack rate[1] of the epidemic. The attack rate is defined by $A = \dfrac{Z}{\Re_\circ}$, where Z is fraction of susceptible that is infected during the pandemic (or epidemic).

Although there are various vaccination strategies, a constant flow of individuals to the susceptible population is assumed. Similarly, certain percentage of susceptible individuals is continuously vaccinated. An important task is to determine the effect of the extent of such vaccination on the spread of the disease.

IV. PARAMETER ESTIMATIONS: CASE STUDY

Parameters for the described model were estimated using 858 cases of H1N1 influenza reported over 12 month period (May 2009 – April 2010) (Table 1 and Figure 3) and supplied by the Health Authority of Abu Dhabi (HAAD); this institution has mandated laboratory testing and reporting of all suspected cases of H1N1 infection [1, 7, 10].

TABLE I
NUMBER OF INFECTED PERSONS IN ABU DHABI OVER 12 MONTHS [1, 9]

Months	Confirmed cases	Recovered
9-May	1	1
9-Jun	11	11
9-Jul	172	172
9-Aug	233	228
9-Sep	134	128
9-Oct	194	189
9-Nov	178	171
9-Dec	16	14
10-Jan	8	7
10-Feb	12	12
10-Mar	5	5
10-Apr	2	2
Total	858	839

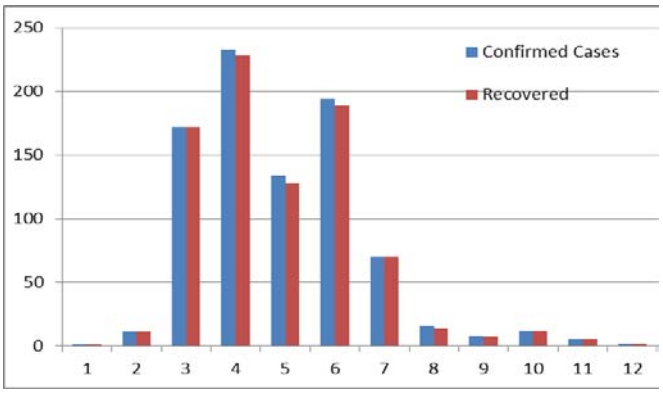


Fig. 3 Number of confirmed and recovered persons from H1N1 infection over 12 months (from May 2009 till April 2010) in Abu Dhabi

Fitting of model to data and parameter estimations strongly depend on the statistical nature of the data, sensitivity, and nonlinearity of the model. Given a set of real data $\{t_j, Y_j\}_{j=1}^{M}$ in Table 1 and our mathematical model (1), the objective function (weighted least squares function)

$$\Phi_w(P) = \sum_{i=1}^{3}\sum_{j=1}^{M} w_{ij}[y^i(t_j, P) - Y_j^i]^2 \qquad (8)$$

[1] The proportion of an exposed population at risk who become infected during a defined period of time (or fraction of a region's population infected over the entire influenza season).

is being minimized. Here y^i, $i=1,2,3$, represent the variables S, I, R, respectively; P is the set of model parameters to be estimated. The optimum parameter $\hat{P}$ is taken such that $\Phi_w(\hat{P}) \le \Phi_w(P)$ (The weighting function w_{ij} depends on the statistical nature of the data).

Fitting the ODEs model (1) to data and using Least Squares Approach involves the following steps:

Provide an initial guess P_0 for the parameter estimates;

Solve the model equations with the current values of the parameters and calculate the corresponding objective function $\Phi(P)$;

The parameter values are then adjusted by a minimization routine

When no further reduction in the value $\Phi(P)$ is possible, the best-fit parameter values have been found;

Determine whether the chosen set of parameter values is acceptable or not (8).

As the model is nonlinear, selection of local minima should be based on meaningful biological parameters. The above technique is adopted to fit the model by providing estimates for the parameters μ, β and γ. The initial values $S(0); I(0)$ could be parameters to be estimated.

The most important parameters that need to be estimated are S_0, and $\Re_o$. A reasonable assumption is to assume a fairly large number of initial susceptible percentages of the population. This assumption is conservative from public health perspective and will assist in assessing control scenarios in case that a large percentage of the population is infected. Upon a decision on the values of S_0, and $\Re_o$ is made, the model prediction is verified and validated to fit the available data for the particular influenza incidence.

The standard approach for fitting epidemic models is to use detailed data from epidemic curves as obtained through surveillance. However, we believe that the type of rough fitting proposed here is useful as a complement, with the advantage that it depends only on robust characteristics of influenza epidemics and is thus less sensitive to the uncertainties involved in the surveillance process.

Having estimated the key parameters $\Re_o$, and the fraction that is infected from S_0 during the period of infection, we then proceed to make projections for the expected attack rate of pandemic influenza. We assume that pandemic influenza differs from seasonal influenza mainly in terms of the larger initial percentage of susceptibles in the population. Although, 100% of susceptible in the population may be unreal, this estimate described the worst case scenario from the aspect of public health measures that may need to be considered. The effect of such a large pool of susceptibles on the size of the epidemic, is estimated using results derived from the SIR model.

The unknowns to be estimated in the underlying model are the fundamental parameters that govern the epidemic behaviour, $\Re_o$ the incident rate β, recovery rate γ and the death rate μ. The fitting of model to data (see Figure 4), result in following estimates: $\hat{\beta}=3.0698$, $\hat{\gamma}=1.1564$, $\hat{\mu}=0.0755$ and $\hat{\Re}_o=2.4919$. The proportion of individuals to be vaccinated in this case is $P_v=1-1/\Re_o=59\%$. The attack rate is then $A=0.1$.

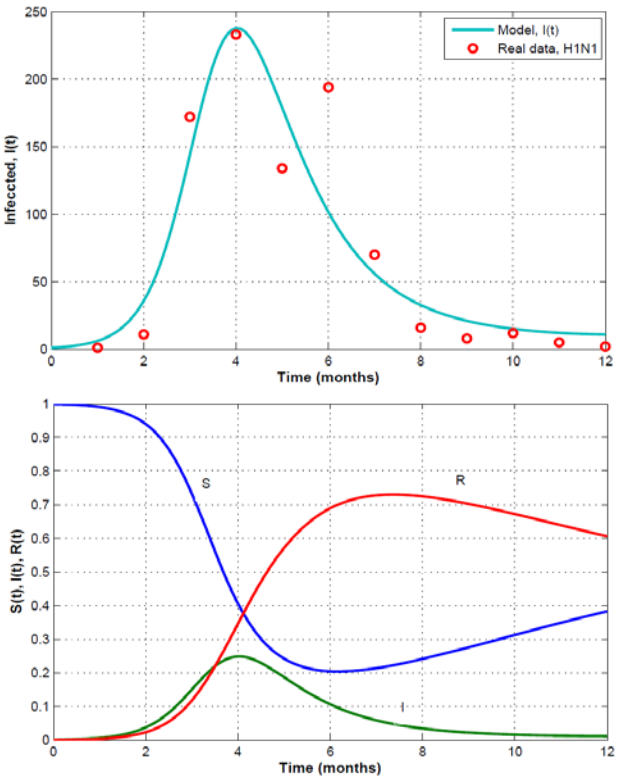


Fig. 4 (Top) shows the fitting of the SIR model with real data of confirmed-H1N1 cases in Abu Dhabi epidemic, May 2009 to April 2010,. (Bottom) shows the numerical simulation of the SIR endemic model with the estimate $\hat{\Re}_o = 2.4919$

This occurs after vaccination of 59% of population.

V. DISCUSSION AND CONCLUDING REMARKS

In this paper, we studied the qualitative behaviours of SIR model. We also deduced the conditions, in terms of threshold $\Re_o$, that guaranteed the asymptotic stability of the infection-free and endemic equilibria. It has been noted that when $\Re_o > 1$, the infection dies out and when $\Re_o > 1$, the disease becomes endemic and infection is maintained in the population. We collected real data as a case study from Abu Dhabi (for the spread of Influenza H1N1 to fit such data with the suggested model).

Pandemic or epidemic influenza has a major impact on services and the economy, through illness, absenteeism, lost

production and increased mortality. In addition to the characteristic symptoms, which may necessitate several days of bed rest; pandemic influenza may be complicated by a higher frequency of serious sequelae, such as primary viral or secondary bacterial pneumonia, which may require hospitalization and can be fatal. The cases reached a first peak in August 2009 and subsequently the number of cases peaked for a second time in October. The overall case fatality rate was 1.4/100,000 population. It is believed that this rated is considered to be rather low if compared with rates reported in other countries.

To prevent an epidemic, we need to reduce $\Re_o$ by increasing γ (transfer of the number of susceptible S into recovered R by decreasing the average of infectious period, improving the medical treatment and immunization), and reducing β (isolate the known infective).

We used the SIR model and data from Abu Dhabi epidemic to estimate model parameters. Assuming that only 30% of the susceptables were infected, then the attack rate for the pandemic influenza was approximately 10% or $A = 0.1$. The duration of that pandemic was 2:5-3 months. The average infectious period of a sick individual was between 2−3 weeks. Results of our simulation and analysis indicate that around 55-60% of population should be vaccinated to make infections die out.

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