A SIR Model for Measles Disease Case for Albania

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ABSTRACT

Many models for the spread of infectious diseases in populations have been analyzed mathematically and applied to specific diseases. In this paper we have used SIR model to study the outbreak of measles epidemic in Albania during the year 2018. Two basic parameters of SIR model are determined using least square principle and other numerical techniques. The model can be used to predict in advance the dynamics of the disease and this can help finding the best possible strategies to control its spread.

Keywords

Measles Mpidemic, SIR Model, Susceptible Population, Reproduction Function, Differential Equation, Least Square Principle.

1. INTRODUCTION

Infectious diseases like influenza, measles, tuberculosis, to name a few, have been a great concern of humankind since the very beginning of the history [3]. Nowadays, they are still the major causes of mortality in many countries [4], [5]. Mathematical models provide helpful tools in studying a large range of such diseases. One of them, known as Susceptible-Infected-Removed (SIR) model, was firstly developed in [4]. It is used in epidemiology to compute the number of susceptible, infected, and recovered people in a closed population at any time. The whole population is divided into three classes, S: the number of susceptible, I: the number of infective and R: the number of recovered during an epidemic. The dynamic of the SIR model is greatly affected by the modeling way of the disease transmission mechanism from infective to susceptible individuals. Many different epidemic models are related to different kinds of these transmission mechanisms. In this paper we study the SIR model related to measles disease and some specific and reasonable assumptions related to this last. The basic and analytic discussion of the model, terminology and biological meaning of parameters and variables used, are given in section 2. A brief description of measles disease history in Albania and especially the epidemic of year 2018, hereafter EpAL18, is given in section 3. Facts, data and helpful conclusions of this section are used in section 4. In this section we collate measles SIR model with EpAL18 and implement it in Matlab using a range of numerical and computer techniques. The results are presented and analyzed graphically. Relevant conclusions are drawn in section 5.

2. MEASLES SIR MATHEMATICAL MODEL

When a disease is modeled, it is needed to understand the way this disease is spread, to be able to predict the progression of the disease and to understand how it's spread may be controlled. The following model is used to study population dynamics of susceptible, infected and recovered individuals from measles disease and to describe the temporal evolution in the number of individuals in need of medical care during this illness. The compartments used for the SIR model consist as usually of three classes:

Infective ($I(t)$): denotes the number of individuals at time t (days) who have been infected with the disease and can spread the disease to those in the susceptible category. Overall, measles usually resolves after statistically 21 days, but it is supposed, like in [2], that an ill individual spreads its illness only in 3-4 days before the characteristic measles rash and 3-4 days after it. We have selected the onset of rash as reference time in our model for the important fact that individuals are able to report this event exactly to their best. Each other moment would be probably reported wrong. So symbolically, an individual is considered infective only in the time interval (t(rash)-3.5, t(rash)+3.5).

Susceptible ($S(t)$): denotes the number of individuals at moment t, not yet infected with the disease, i.e., not able to spread the illness to other individuals.

Recovered ($R(t)$): denotes the individuals who have been infected from the disease, then recovered, and not able to be infected again or to transmit the infection to others.

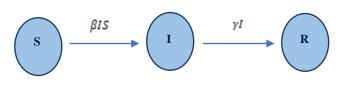Measles SIR model is presented schematically in Figure 1.

Figure 1: Kermack-McKendrick Schematic Model.
Individuals move in direction from class S to class I and R.

The above model is subject of the assumptions:

- The rate of infection and recovery is much faster than the time scales of births and deaths and therefore the last factors are ignored, so the population size is fixed.

-Absence of interventions aimed at controlling the infection during epidemic.

-Age, sex, race and social status do not affect the probability of a person being affected.

-The susceptible population is reduced through infection (moving to class I); The only way a person can leave the susceptible group is to become infective.

-The population of infective class is increased by a fraction of susceptible individuals becoming infective;

-The population of infective individuals is reduced by recovery from the disease; The only way a person can leave the infective group is to become recovered.

-The recovered population gets increased with the recovered individual from infective class. Once a person is recovered, this person is no longer susceptible, he is immune.

-There is no inherited immunity.

From the above assumptions it follows that S(t) + I(t) + R(t) = N = constant. N denotes the total number of susceptible individuals just 1 day before epidemic begins, or the total number of individuals under consideration. For best numerical performance we normalize the last sum by dividing each of the variables by N, and still we denote the new variables by the same letters. So, S + I + R = 1, at any time t. It is reasonable to assume that the rate of decreasing of S(t) is proportional to the product of S(t) * I(t). For the same reason I(t) is increased with the same rate and decreased (recovered) with a rate proportional to I(t). Based on the above assumptions the system of differential equations governing the disease can be written as

$$
\begin{cases}
\frac{dS(t)}{dt} = -\beta S(t)I(t) & (1) \\
\frac{dI(t)}{dt} = \beta S(t)I(t) - \gamma I(t) & t_0 < t < t_f \quad (2) \\
\frac{dR(t)}{dt} = \gamma I(t) & (3)
\end{cases}
$$

Above, t_0 and t_f denote respectively the first and the last day of epidemic or $[t_0\, t_f]$ denotes the study time interval. From the assumptions done it follows that $S(t_0) = S_0 > 0$, $I(t_0) = I_0 > 0$ and $R(t_0) = R_0 = 0$, are initial conditions. Typical value for I_0 is $I_0 = 1/N$ (typically each epidemic starts with 1 first imported case). Therefore, the typical value for S_0 is $S_0 = (N-1)/N$. N is important data of the model, so its value needs careful discussion. As the statistic time of an infective individual (the period of infection) is supposed to be 7 days, the rate of recovery γ is expected to be approximated: $\gamma \approx 1/7 \approx 0.143$. A more detailed table for the parameters above and their biological meaning is given below.

Table 1: Biological meaning of all parameters and state variables

Parameter	Biological meaning
S	Proportion of susceptible population
S_0	Number of susceptible individuals at time $t = t_0$
I	Proportion of infective population
I_0	Proportion of infective individuals at time $t = t_0$
R	Proportion of recovered population
R_0	Number of recovered individuals at time $t = t_0$, $R_0 = 0$
N	Total population
β	Successful contact rate (infection rate)
γ	Recovery rate
$1/\gamma$	Mean recovery time for clinically ill
RR	The basic reproduction function (the average number of persons infected by one case)

Since population is constant and R does not appear in the first two differential equations, the last equation can be omitted, so the system (1-3) can be reduced into a system of two equations:

$$
\begin{cases}
\frac{dS(t)}{dt} = -\beta S(t)I(t) \\
\frac{dI(t)}{dt} = \beta S(t)I(t) - \gamma I(t)
\end{cases}
\quad (4)
$$

The nonlinear term in the above dynamical system makes it difficult to find analytically its solution, but we can perform some qualitative analysis in order to understand the system.

At time $t = t_0$, the equation (2) can be written as

$$
\frac{dI(t)}{dt} = I_0(\beta S_0 - \gamma)
\begin{cases}
> 0, if\ S_0 > \frac{\gamma}{\beta} \\
< 0, if\ S_0 < \frac{\gamma}{\beta}
\end{cases}
\quad (5)
$$

From equation (1), at time t

$$
\frac{dS(t)}{dt} < 0, S \le S_0
$$

Therefore

$$
\frac{dI(t)}{dt} = (\beta S(t) - \gamma)I(t) \le 0, if\ S_0 < \frac{\gamma}{\beta} \quad (6)
$$

Therefore $I_0 > I(t)$ and $\lim_{t \to \infty} I(t) = 0$. On the other hand

$$
\frac{dI(t)}{dt} = (\beta S(t) - \gamma)I(t) \ge 0, \quad if\ S_0 > \frac{\gamma}{\beta} \quad (7)
$$

In that case the number of infective individuals increases. Therefore, if $S_0 > \frac{\gamma}{\beta}$ there is an epidemic, if $S_0 < \frac{\gamma}{\beta}$ the disease dies out. The key parameter in SIR model is the basic reproduction function $RR(t)$, sometimes called the basic reproduction ratio [1]. RR characterizes the transmission intensity

of a disease in a population and its role is very important. In model (1-3), if the initial number of susceptible individuals at the beginning of a disease is S_0, the dynamics of infectious depends on the initial value of the basic reproduction function, $RR_0 = RR(t_0) = S_0 \frac{\beta}{\gamma}$. If at time t, $RR(t) < 1$ then the number of infected individuals declines, the epidemic eventually disappears. If $RR(t) > 1$, the number of infected individuals increases first due to the infection and then decreases due to the recovery of infected individuals, then occurs outbreak and/or persistence of the disease.

3. MEASLES HISTORY CASE FOR ALBANIA

Measles is one of the most highly contagious diseases, usually affecting children. Despite the availability of a safe and effective vaccine, measles remains one of the leading causes of death among young children around the world and the disease is known as the greatest killer of them in the history [8]. Measles has an endemic character but can take epidemic outbreak in special circumstances when there is a large disease contingent in a population. In Albania, measles has been endemic, with rare outbreaks of small epidemics, but in the last 70 years five epidemics have exploded. The first epidemic occurred in 1948-1949 and affected around 40,000 children, expressed with many pathological complications. The second epidemic occurred in 1954-1955 and affected around 190,000 people, with high rates of complications and 1,712 deaths. The third epidemic in 1970-1971 affected 48, 156 people with a receptive population contingent of over 1 million. The fourth epidemic began in April 1989, where a widespread epidemic eruption spread from Tirana to the entire country after a case of measles imported from Turkey. The epidemic ended in 1990 with 168,636 reported cases and 44 reported deaths. Cases of measles were reported also during the 90s years and afterwards [6]. The last epidemic, EpAL18, occurred in 2018. During January-May 2018 Albania was involved in a measles outbreak. This epidemic was certainly correlated with severe situation of some European countries during 2018. There have been particularly serious outbreaks in countries such as Serbia, Ukraine, Georgia, Greece, Romania, Italy, and France [7]. The Figure 2 below shows the measles cases in Europe in period 2009-2018.
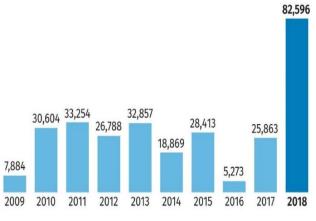

Figure 2: Measles cases in Europe in the period 2009- 2018 [7]

Vaccination coverage is one of the most important components which describe the immunization situation in a country. Albania is a country with high routine vaccination coverage levels that exceed 95%, as a basis for avoiding outbreaks. However, from database of EpAL18, it resulted [2], then 24.6% of confirmed cases had been previously vaccinated at least with one dose. For many complex reasons, not subject of this paper, the routine vaccination system had lost considerably its effectiveness. This situation allowed for a rapid and dangerous accumulation of susceptible children. Persons born before 1960 and a proportion of adults born after 1960, can be assumed to have been exposed to naturally circulating measles virus, [6], and thus be immune to the disease. By this fact and by the measles history, with simple calculation we found that about 18 % of Albanian had received natural immunization. From the last two figures it comes out that the percentage of the susceptible category at the kick off EpAL18 was $0.82*0.246 \approx 20\%$. More than 99% of confirmed cases infected in first 7 weeks of EpAL18 have been from 3 districts: Tirana, Kuksi, Lezha. Based on district population Albanian Table, we found that the total number of susceptible individuals in EpAL18 was approximately N = 163,000. This is a big number compared to the territory and the high population density of the three mentioned districts, factors that facilitated contact between persons infected with measles and susceptible persons. In Figure 3 and Figure 4 below are shown epidemic histograms of measles outbreak (positive and negative cases) and confirmed measles cases according to the start date of the rash. The initial figures and rates clearly demonstrate e rapid measles outbreak.
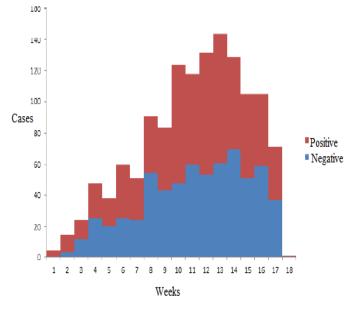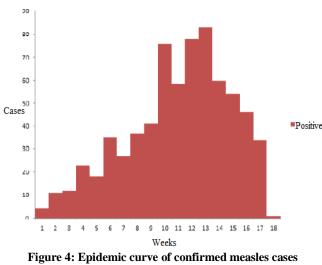

Figure 3: Epidemic curve of the measles outbreak according to the start date of the rash [2]

Figure 4: Epidemic curve of confirmed measles cases according to the start date of the rash [2].

The organization of data in 7 days bins, as in histograms above, is very useful and will facilitate the further computation. Remember the fact mentioned in section 2, that an ill individual spreads the infection, and he is considered infective, only in the time interval t(rash)±3.5 days. From the basic report of EpAL18, it results that during the first 8 weeks of epidemic, the effects of the control interventions, mainly routine vaccination, have been small. The mass campaigns, special vaccination and surveillance system have increased their effect after the first 8 weeks. So, we have used the first 8 weeks data just to collate the SIR model with EpAL2018. This is done in next section.

4. COLLATED SIR MODEL, MATLAB IMPLEMENTATION, AND NUMERICAL RESULTS

In this section, firstly we determine the rates β and γ of the measles SIR model (1-3) of section 2, using the basic data base of EpAL18, so we collate the measles SIR model with EpAL18. For the reasons mentioned in section 3, we are restricted only in period from 9 Jan 2018 to 6 Apr 2018 (8 weeks). During this period of time the effect of the interventions, aimed at controlling the infection, has been small.

In order to facilitate the computation and for performance of graph presentations, the time interval $[t_0 \ t_f]$ = [3.5 122.5], within the interval [0 126] of epidemic days, is discretized into 17 subintervals, each of width h = 119/17 = 7 days. Each epidemic week is presented by its middle point.

The following algorithm details the complete procedure.

Step 1: Input basic data: N, S_0.

Step 2: Guess initial values for β and γ. For γ we guessed the initial value 1/7 = 0.143

Step 3: Create meshes of time nodes: tt=3.5:7:52.5 and tr=59.5:7:122.5

Step 4: Integrate the system (4) by Matlab utility ode45 and get the two solution vectors SS = S(tt) and II =I(tt)

Step 5: Read the appropriate data from filtered database EpAL18, manipulate them statistically, build the histogram presented in Figure 4, and create vector i of ill individuals per each week

(numerical version of histogram). Matlab utilities: *xlsread, sort, histc,* and some other advanced Matlab commands needs to be used.

Step 6: Compute the empirical data-based vectors ss and ii, corresponding in time with vectors SS and II. The basic formula for the last computation, would be

ss(1) = S_0, ss(k) = ss(k-1) - i(k), k ≥ 2

ii(k+1) = ii(k) - i(k-1) + i(k + 1) for k= 2, 3,....

This formula must be modified for the computation of first initial and last values of ii

Step 7: Find those values for β and γ which minimize the function $D(\beta,\gamma) = \|SS - ss\|^2 + \|II - ii\|^2$ according to the principle of least square method. Adjust vectors SS and II of step 4 by reintegrating the system (4) for the new β and γ found.

Step 8: Graph in the same plot SS and ss vs. time t

Step 9: Graph in the same plot II and ii vs. time t

Step 10: Extend properly the graphs of steps 8 and 9 for t > 52.5 days, using different styles of color and line.

Step 11: Graph for comparison in the same plot the function I(t) (normalized for best performance) and the basic reproduction function RR(t)

The above algorithm is implemented in Matlab and the basic results are presented in the four graphs below. For Matlab utility *fminsearch* (step 5) some of its default parameters were changed to provide convergence, showing a flat minimum that is unfortunately typical for similar optimization problems.

From step 7 the values for β and γ result to be

β = 0.1638, γ = 0.1060

In Figure 5, in solid line is presented the graph of the function I(t) - the solution of system (4). We see what it would had happen with the proportion of infected individuals, in case of total absence of mass campaigns, routine and special vaccination, surveillance system, etc. The correlation coefficient between the two curves, for 3.5 ≤ t ≤ 52.5, is 0.97.
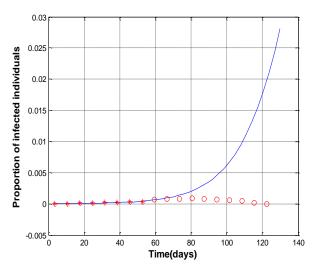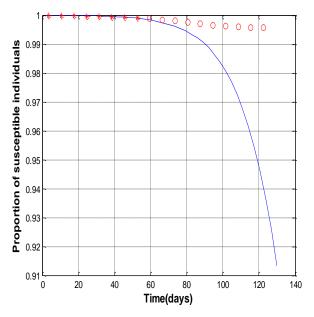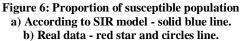

Figure 5: Proportion of infective individuals
a) According to SIR model - solid blue line
b) Real data - red star and circles line

In Figure 6 we have the same things as in Figure 5, this time for proportion of susceptible individuals, function S(t)

Figure 6: Proportion of susceptible population
a) According to SIR model - solid blue line.
b) Real data - red star and circles line.

In Figure 7 is presented the dynamic of function I(t) in a wider range of variable t. It can be seen that in total absence of disease control, EpAL18 would reach its peak approximately 170 days from its outbreak, and the disease would eradicated after about 300 days. This is almost double of the time of the real peak.
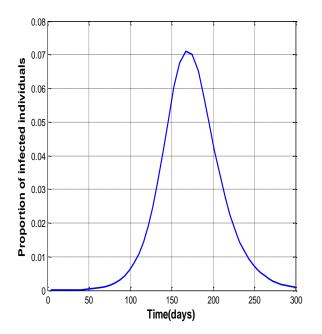

Figure 7: Proportion of infective population -function I(t).

In Figure 8, they are graphed in the same plot for comparison the function I(t) - here normalized for better performance of the graph, and the basic reproduction function RR(t). The description done for the relation of these two functions at the end of section 2 can be verified to be true in this Figure.
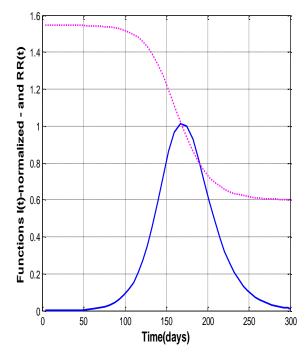

Figure 8: a) Proportion of infective population I(t) normalized
- blue solid line.
b) The basic reproduction function RR(t) – magenta

dotted line.

5. CONCLUSIONS

A SIR model is adopted for the study of measles epidemic. Two basic parameters of this model are determined using database of epidemic taken placed in Albania during the year 2018 and a range of numerical and computer techniques, such as numerical differential equations, least square principle, numerical optimization. Model is implemented in Matlab. It can be used in the future to predict in advance the dynamics of possible outbreaks of measles disease. This can help finding the best possible strategies to control the disease spread. Different kinds of control actions may be easily simulated and implemented in this model in order to see in advance their effects.

6. ACKNOWLEDGMENTS

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