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Impact of vaccination and treatment on SIRS model with Non-linear incidence rate

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ABSTRACT

In this paper, an epidemic model consisting of susceptible, vaccination, infected and removal is formulated mathematically. The proposed model deals with incorporating the vaccination factor, treatment factor and non-linear incidence rate. Non negative for the model Solutions are proved, a simplex attractor invariant set is found, the basic reproduction number of the model is calculated using the method of the next-generation matrix, and the model equilibrium points performed a local stability analysis, we have collected the infected cases COVID-19 real data in Kurdistan region from Iraq to estimate the model parameters and sensitivity of the basic reproduction number and the model variable to the parameters of the model was studied.

تأثير التطعيم والعلاج على نموذج SIRS مع معدل الحدوث غير الخطي

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قسم الرياضيات ، كلية التربية ، جامعة السليمانية ، السليمانية ، العراق

الملخص

في هذا البحث ، تمت صياغة نموذج وبائي يتكون من القابلين للإصابة والتطعيم والمصابين والإزالة رياضياً. يتعامل النموذج المقترح مع دمج عامل التطعيم وعامل العلاج ومعدل الوقوع غير الخطي. تم إثبات الحلول غير السالبة للنموذج ، وتم العثور على مجموعة ثابتة للجاذب البسيط ، وتم حساب رقم التكاثر الأساسي للنموذج باستخدام طريقة مصفوفة الجيل التالي ، وأجرت نقاط توازن النموذج تحليل الاستقرار المحلي ، وقمنا بجمعها تمت دراسة البيانات الحقيقية للحالات المصابة COVID-19 في إقليم كردستان من العراق لتقدير معلمات النموذج وحساسية رقم التكاثر الأساسي ومتغير النموذج لمعاملات النموذج

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1- Introduction

There are various methods to control epidemic disease like, medicine, vaccination, vector population, reductions, or behavioral, modifications and finding the correct strategy using mathematics. Compartmental models have become essential methods for investigating the transmission and treatment of infectious diseases [1,2]

Usually, compartmental model SIRS can be used to mathematically describe the transmission of infectious diseases. (where S(t) is the overall number of susceptible individuals, I(t) is the overall number of individuals they infected, and R(t) is the overall number of removed individuals who have temporary immunity against the disease;, A variety of compartmental models, including COVID-19 applied to infectious diseases, have been emerged in recent years.[3,4,5,6,7] Vaccination is the process of administering weakened to help the immune system develop the immunity from disease, Thus, several simple compartmental mathematical models with vaccinated populations have been used in the literature to assess the effect of vaccination in the last few years or potential impact of imperfect vaccines for combatting the transmission, of diseases [8,9,10,11]

The incidence rate which in epidemiology show the number of individuals who acquire an infection per unit of time. Play an important role on the dynamics of the transmission of diseases. There are various types of incidence rates, the simple linear form of incidence rate which are defined by the form αSI where α stands for infection rate [12]. The non-linear incidence rate defined as $\frac{\alpha_1 SI}{1+\beta I}$. Where α_1 is the transmission rate I and β is stand for Saturation factor or "inhibitory impact,", this type of incidence rate due to the crowding of infected individuals or due to the protective measures taken by the susceptible individuals [12].

It is well known that treatment is an important method to control the spread of diseases. In classical epidemic models, the treatment due to impact vaccination the above verifies, as well as for controlling the disease to founded Basic reproduction number authors have demonstrated that the disease's basic reproduction number R_0 determines the model's dynamics, Which is the boundary between forwarding invariant and the attraction for stable equilibrium point.

In this paper, the impact of both vaccination and treatment on the dynamics of the spreading of infectious disease is modeled and the proposed model considered the non-linear transmission rate.

This work is arranged as follows: The details of the mathematical model formulation and description of the parameters and variable given in Section 2. The non-negative and boundedness properties of the solution of the model are proved in Section 3. The basic reproduction number for the model parameters is also discussed Numerical simulations of the model in Section 4, its stability analysis is studied in section 5, and then estimating the parameters are given the SIRS model with data of coronavirus (coved -19) in Kurdistan region in section 6, The sensitivity of the basic reproduction number for the parameters of the model is also discussed in Section 7, Conclusions of the study are given in Section 8

2-Model formulation

In this section, we propose an epidemic model which based on SIRS model for the disease transmission dynamics on infectious model, the model population divided into four classes: (Susceptible, vaccination, Infected, Recovered) the numbers of Susceptible, vaccination, Infected, Recovery at any time are denoted by S(t), V(t), I(t), R(t) respectively, and the model based on the following, assumption have been considered:

1. There is a fixed number of the susceptible populations added to the system with recruitment rate $\Lambda > 0$.
2. The diseases is transmitted from the infected people to the Susceptible people and vaccinated people by contact according to the nonlinear incidence rate of the from $\frac{\alpha_1 SI}{1+\beta I}, \frac{\alpha_2 VI}{1+\beta I}$, respectively [9] ,where $\alpha_1 I$, $\alpha_2 I$ respectively measures the infection force of the disease and $\frac{1}{1+\beta I}$ measures the inhibition effect from the crowding effect of the infected individuals.
3. The infected people are facing death due to the disease (virus) with infection death rate d > 0 and they get temporary immunity with a recovery rate p > 0.
4. The people in the R and V compartments are losing the immunity against the virus and return back to be susceptible again with losing immunity rate $0 \leq r < 1$ and $0 \leq$? < 1 respectively.
5. There is a natural death rate $\mu > 0$ for the individuals in the susceptible population
6. The Susceptible individuals Vaccinated with the rate kS
7. the infected population treated with the nonlinear treatment rate $\frac{aI}{1+bI}$ where a represent the maximum treatment rate and b the measure of inhibition recovered rate due to the long time responded of infected individual to the treatment.[12]

According to the above assumption the mathematical model can be described by the diagram given in Fig. (1).

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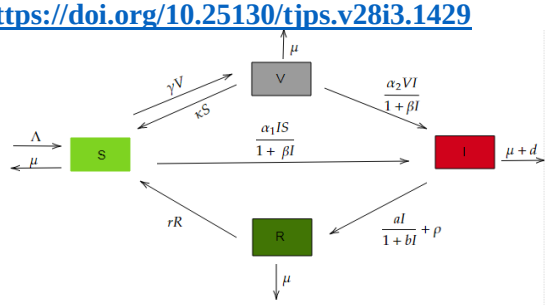

Fig. 1: model diagram and interaction individual's components

The chemical reactions of the model can be expressed as follows:

null $\xrightarrow{\Lambda}$ S, S $\xrightarrow{\mu S}$ null, S $\xrightarrow{\square V}$ V, V $\xrightarrow{kS}$ S, S $\xrightarrow{\frac{\alpha_1 SI}{1+\beta I}}$ I, V $\xrightarrow{\frac{\alpha_2 VI}{1+\beta I}}$ I,

V $\xrightarrow{\mu V}$ null, I $\xrightarrow{\frac{aI}{1+bI}+p}$ R , I $\xrightarrow{(\mu+d)I}$ null, R $\xrightarrow{rR}$ S, R $\xrightarrow{\mu R}$ null.

In addition all constants and initial conditions can be found by using the concept of standard chemical kinetics and mass action law to formulate the model; we can be modeled mathematically by the following set of first-order non-linear ordinary differential equations.

$$\frac{dS}{dt} = \Lambda + rR - \frac{\alpha_1 SI}{1+\beta I} - kS - \mu S + \square V$$
$$\frac{dV}{dt} = kS - \mu V - \frac{\alpha_2 VI}{1+\beta I} - \square V$$
$$\frac{dI}{dt} = \frac{\alpha_1 SI + \alpha_2 VI}{1+\beta I} - \frac{aI}{1+bI} - \mu I - dI - pI \quad ...(1)$$
$$\frac{dR}{dt} = \frac{aI}{1+bI} + pI - (\mu + r)R$$

In addition, since the number of the population cannot be negative then the model variable of the system (1) is initial in $R_+^4 \cup \{0\}$

In the following theorem, forward invariant and attractor set is founded

Theorem 1: The simplex set $\Omega = \left\{(S,V,I,R)\epsilon R_+^4;\ S+V+I+R \leq \frac{\Lambda}{\mu}\right\}$ is forward invariant and attractor.

Proof: Assume $N(t) = S(t) + V(t) + I(t) + R(t)$, holds for $t \geq 0$ then we obtain

$$\frac{dN}{dt} = \Lambda - \mu N - dI \leq \Lambda - \mu N$$

Applying the comparison theorem for solving first-order differential inequality, we get

$$N(t) \leq \frac{\Lambda + (N(0)\mu - \Lambda)e^{-\mu t}}{\mu}; \forall\, t \geq 0$$

If the solution of system (1) initiate in Ω, then

$N(0) \leq \frac{\Lambda}{\mu}$, and hence the following inequality is get

$$N(t) \leq \frac{\Lambda}{\mu}; \forall\, t \geq 0$$

Thus Ω is forward invariant.

If the trajectory of system initiates at the exterior of Ω, then

$\lim_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu}$ Which is means Ω is attractor set.

3- Basic reproduction number

Basic reproduction number is the most important thresholds in the studying infectious disease models because is the expected number of newly infected peoples produced by an infected individual and usually it denote by R_0 [13,14,16].

This threshold characteristic of R_0 helps epidemiologists to make the following assumptions:

(a) If R_0, less than one it means that disease will die out with time

(b) If R_0 greater than one it means that disease will be endemic

We used Next Generation Matrix [11] find, R_0 of the system (1). The suggested model here includes one infected state I and three uninfected states S, V and R. Suppose that A be a vector infected class and B be a vector uninfected class. They can be shown below:

A=$[I]$, B= $\begin{bmatrix} S \\ V \\ R \end{bmatrix}$

Suppose H=$\left[\frac{\partial F_i}{\partial X_j}\right]_{P_0}$ and W= $\left[\frac{\partial V_i}{\partial X_j}\right]_{P_0}$ for i = 1, 2, 3, m and j = 1, 2, 3, m

We have:

P_0 is the disease equilibrium point.

m is the number of infectious compartment.

$X_j$is number of infected individuals in the ith infected in the ith Infected compartment.

F_i= represent the rate of appearance of new infectious.

V_i= rate of transfer of individuals out of the compartment.

The next generating matrix is HW^{-1} and the basic reproduction number is the spectral radius of HW^{-1}

In our model, we have one infection compartment with our infected individuals. Which can be written as:

So F_1=$\frac{\alpha_1 SI + \alpha_2 VI}{1+\beta I}$

V_1= $-\frac{aI}{1+bI} - (\mu + d + p)I$

d(I)= F(S,V,I,R) – V(S,V,I,R)

Therefore the Jacobian of matrices (F_1) and (V_1) at the disease free equilibrium can be written as:

D $F_1(E_1)$ =$\left[\alpha_1\left(\frac{\Lambda(\mu+\square)}{\mu(\mu+k+\square)}\right) + \alpha_2\left(\frac{k\Lambda}{\mu(\mu+k+\square)}\right)\right]$

DV $(E_1) = a + \mu + d + p$

It is easy to find the inverse of W and given by

W^{-1}=$\left[\frac{1}{a+\mu+d+p}\right]$

According to the next generation matrix method, the basic reproduction number is the maximum eigenvalues of the matrix. Thus

$$R_0 = spect(HW^{-1}) = \frac{\Lambda[\alpha_1(\mu+\square)+\alpha_2 k]}{\mu(\mu+k+\square)(a+\mu+d+p)}$$

Theorem 1: The disease-free equilibrium $E_1$is locally asymptotically stable if $R_0 < 1$

And it is Unstable if$R_0 > 1$.

Proof: The Jacobian system (1) at the free disease equilibrium point

= ($\frac{\Lambda(\mu+\square)}{\mu(\mu+k+\square)}$, $\frac{k\Lambda}{\mu(\mu+k+\square)}$,0,0) is

J (E_1) =

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$$\begin{bmatrix} -(k+\mu) & ⍰ & -\alpha_1\frac{\Lambda(\mu+⍰)}{\mu(\mu+k+⍰)} & r \\ k & -(\mu+⍰) & -\alpha_2\frac{k\Lambda}{\mu(\mu+k+⍰)} & 0 \\ 0 & 0 & (a+\mu+d+p)(R_0-1) & 0 \\ 0 & 0 & a+p & -(\mu+r) \end{bmatrix}$$

Thus the Eigen values in I-direction is $\lambda_I = (a+\mu+d+p)(R_0-1)$ which s negative f $R_0 < 1$and Thus the Eigen values in I-direction is $\lambda_R = -(\mu+r) < 0$

The Eigen values in SV-Plane satisfies the following equation

λ^2+Aλ +B =0, Where

A= (k+2μ + ⍰)(1- R_0)

and B= $(k+\mu)(\mu+⍰)(1-R_0)$

Then, by Routh-Hurwitz criteria which required that $B_1 > 0$ and $B_2 > 0$ if and only if $R_0 < 1$, and hence the disease free equilibrium point is locally asymptotically stable if $R_0 < 1$ otherwise it is unstable.

5-Applyng the model in Kurdistan region

In this section we applied the opposed model at Kurdistan region in Iraq, therefore we must estimate the model parameters firstly we assume Λ = 300, represent number of new daily , $\mu = \frac{1}{35+360} =$ 0.00008,Gobal median age of population half average of individuals life span ,r =$\frac{1}{6+30} = 0.005$: average time of recovery periods, , ⍰ = 0.005 efficacy of the vaccine= 0.02: Death rate due to the virus, p= 0.08: rate of recovery , k=$\frac{V}{S} = \frac{1000}{6000000} =$ 0.00016

In order to estimate the other parameters, the COVID-19 confirmed cases[Table 3, 4] were used.

We want to find the vector of least-square estimators $\boldsymbol{\theta}$ that minimizes $\sum_{i=1}^{n} E_i{}^2 = \sum_{i=1}^{n}(y_i - w_i)^2$ …(2)

Here $E_i\}_{i=1}^{n}$ represent the difference between the observed value y_i and the corresponding fitted value w_i

To estimate the model parameters we must find an optimization algorithm to update the parameters based on equation (2)

The process of updating the parameters continues until no significant improvement (convergence) in the objective function is observed. We use estimation procedure in the Metropolis–Hastings (MH) [15] algorithm is replaced by comparing the minimum of the sum squared errors between the proposed parameter and the previously assigned parameter.$\boldsymbol{\theta}$ = [$\boldsymbol{\theta}_1$, $\boldsymbol{\theta}_p$], where, p is the number of parameters to be estimated. In our case, the number of parameters is p=12, we take one parameter at a time and consider the other parameters held constant in the objective function,

i.e.$\sum_{i=1}^{n} E_i{}^2 \left(\boldsymbol{\theta}_j \mid \boldsymbol{\theta}_1, \ldots, \boldsymbol{\theta}_{j-1}, \ldots, \boldsymbol{\theta}_p\right) = \sum_{i=1}^{n}(y_i - w_i)^2$ …(3)

First, we have to initialize the model parameters and propose the next parameter value by sampling from $\boldsymbol{\theta}_i{}^{prop} = \boldsymbol{\theta}_i \pm U\,[\boldsymbol{\theta}_i - \boldsymbol{d}_1, \boldsymbol{\theta}_i + \boldsymbol{d}_1]$

Where $\boldsymbol{d}_1$ is a small quantity to move the parameter $\boldsymbol{\theta}_i$ up and down process of estimation the model parameter.

A rough outline of the algorithm is given in Algorithm[15]

Algorithm 1: MH algorithm with Least square

Input: P (iteration numb), $\boldsymbol{\theta}_i{}^0$(initial value of mdl parameters) , Y (Observed data)

Step 1. For i = 0, 1, . . ., P

Step 2. Solve ode's for Equation (1) at $\boldsymbol{\theta}_i{}^n$ and compute the sum of squared errors for Equation (3)

Step 3. Select new parameter $\boldsymbol{\theta}_i{}^{prop}$ ∽g $\boldsymbol{\theta}_i{}^{prop}$ ∽ \$\boldsymbol{\theta}_i{}^n$).

Step 4. Solve Ode's at $\boldsymbol{\theta}_i{}^{prop}$and Compute Equation (9)

Step 5. If the sum of squared errors in Step 4 is less than in Step 2

$\boldsymbol{\theta}_i{}^{n+1} = \boldsymbol{\theta}_i{}^{prop}$

eles,

$\boldsymbol{\theta}_i{}^{n+1} = \boldsymbol{\theta}_i{}^{n}$.

Step 6. n=n+1.

The best fitting parameters based on the real data in Kurdistan are Table 1 as follows:

Table 1: Results of model fitting

α_1	β	α_2	a	B
0.0002	0.64	0.0006	0.34	0.0005

More interestingly, the parameter of basic reproduction number for our data collection is about R_0=1.808. The result shows that R_0 more than one new infection, the disease (COVID-19) will be transmitted between among people and it requires more preventions and interventions.

7-Sensitivity indices of R_o with respect to ach parameters

With the development of the application of the biological system, the methods of sensitivity analysis mostly used in the study of biological systems can give worthy insights into the strangeness of the biological replays with the consideration of biological parameter changes that the main causes are model inputs which influenced the model outputs. However, sensitivity analysis is important to find data that have a high impact on R_0,

The studies of local sensitivity analysis interchanges in the model output variable input parameter differences all over the parameter area in the local point, which are consisted of sensitivity coefficients.

Mathematically, the sensitivity coefficients are the first-order derivatives of the model

Outputs with an agreement to the model parameters, as follows see [13]. , $⍰_p^{R_0} = \frac{\partial R_0}{\partial p} * \frac{p}{R_0}$

where p is the set of all parameters, we calculate the sensitivities index of R_0 for each model parameter. They are given below:

$⍰_{\Lambda}^{R_0} = \frac{\partial R_0}{\partial p} * \frac{\Lambda}{R_0} = 1$

$⍰_{\alpha_1}^{R_0} = \frac{\partial R_0}{\partial \alpha_1} * \frac{\alpha_1}{R_0} = \frac{\alpha_1(\mu+⍰)}{\alpha_1(\mu+⍰)+\alpha_2 k}$

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$$\square_k^{R_0} = \frac{\partial R_0}{\partial k} * \frac{k}{R_0} = \frac{k[\alpha_2(\mu+k+\square)]-(\alpha_1(\mu+\square)+\alpha_2 k)]}{(\alpha_1(\mu+\square)+\alpha_2 k)(\mu+k+\square)}$$

$$\square_\mu^{R_0} = \frac{\partial R_0}{\partial \mu} * \frac{\mu}{R_0} = \frac{-2\,\mu-(a+d+p)}{(\alpha_1(\mu+\square)+\alpha_2 k)(a+d+p+\mu)}$$

$$\square_\square^{R_0} = \frac{\partial R_0}{\partial \square} * \frac{\square}{R_0} = \frac{\square[\alpha_1(\mu+k+\square)]-(\alpha_1(\mu+\square)+\alpha_2 k)]}{(\alpha_1(\mu+\square)+\alpha_2 k)(\mu+k+\square)}$$

$$\square_{\alpha_2}^{R_0} = \frac{\partial R_0}{\partial \alpha_2} * \frac{\alpha_2}{R_0} = \frac{\alpha_2 k}{\alpha_1(\mu+\square)+\alpha_2 k}$$

$$\square_a^{R_0} = \frac{\partial R_0}{\partial a} * \frac{a}{R_0} = \frac{-\,\mathrm{a}}{(a+\mu+d+p)}$$

$$\square_d^{R_0} = \frac{\partial R_0}{\partial d} * \frac{d}{R_0} = \frac{-\,\mathrm{d}}{(a+\mu+d+p)}$$

$$\square_p^{R_0} = \frac{\partial R_0}{\partial p} * \frac{p}{R_0} = \frac{-\,\mathrm{p}}{(a+\mu+d+p)}$$

Using the estimated parameters in Kurdistan region, we can compute sensitivity indices of R_o with respect to each parameter; see Table 2.

The values of the sensitivity indices for the parameters values of Table 1 are given in Table 2.

Table 2: sensitivity value of R_0 regarding to model parameters

Parameters	$\square_p^{R_0}$
Λ	1
α_1	0.912
k	0.056
μ	-899444
$\square$	-0.055
α_2	0.086
A	-0.772
d	-0.045
p	-0.182

Results given in Table 2 show the positive and negative signs for the model sensitivity. These give us the direct or indirect relation between R_0 and the model parameters. For example, this coefficient is positive for the set of parameters { α_1,k, α_2}. This means that when { α_1,k, α_2} are increased, the value of R_0 is increased too and this virus spreads further. On the other hand, the sign of {$\square$, α,d ,p,μ} are negative. It means that the value of basic reproduction number can be reduced by increasing such parameters.

8- Sensitivity of the model variables to each parameter

In this section, we study the Sensitivity of the model variables to each parameter [13]. Assume that there are $\boldsymbol{n}$ compartments c_i for i = 1,2,..., $\boldsymbol{n}$ and m parameters p_j for j = 1,2,..., m in an infectious disease model. The model balanced equations are represented by the following system of differential equations: $\frac{dC_i}{dt}=g_i(C,p)$ (10)

Where C $\in R^n$, p $\in R^m$, to find Sensitivity of the model variables to each parameter we used three different techniques: non normalizations, half normalizations and full normalizations;

The non-normalization sensitivities are defined as follows:

$$S_{p_i}^{C_i} = \frac{\partial C_i(t)}{dp_i}$$

The half-normalization sensitivities are defined as follows:

$$S_{p_i}^{C_i} = \frac{1}{c_i(t)} * \frac{\partial C_i(t)}{dp_i}$$

The full-normalization sensitivities are given as follows:

$$S_{p_i}^{C_i} = \frac{p_i}{C_i(t)} * \frac{\partial C_i(t)}{dp_i}$$

where $S_{p_i}^{C_i}$ are described as sensitivity for each variables $C_i$with respect to the parametersp_i. We apply the idea of local sensitivity for our proposed COVID-19 model equations (System 1). The model initial populations S_0 = 6×10^6, V_0 = 1000, I_0 = 18311, R_0 = 1500 and the model parameters from Table 2 are used in the computational cases. SimBiology Toolbox for MATLAB are used to compute the results, which includes three different methods: non-normalizations, half normalizations, and full normalizations[7].

see Figure 2-4. The results give us a better knowledge of the model and help us to identify the key critical model parameters.

According to the non-normalization technique, indicate that the most sensitive parameter for all model states (α_1)Transmission Rate . As well as the susceptible and Recovered individuals are also very sensitive to the set of parameters {r, β} {Recovery Rate and Inhibitory impact} respectively.

Vaccination rate (k) is the most sensitive parameter for only Vaccinate individuals in the suggested model; see Figure 2a. In addition, all model states are also very sensitive to these parameters {$\gamma, \alpha_2, a, r, \beta$}{ Vaccination efficacy, Recovery Rate due to the Vaccination, maximum treatment rate, Recovery Rate and Inhibitory impact} respectively;*see* Figure 2b.

In this technique the set of parameters is very sensitive compared to the other parameters thus two Figures are computed, (Figure 3a) the sensitivity of all variables with respect to all parameters, the vaccination, infected and Recovered individuals are also very sensitive to the set of parameters { k, α_1, b }{ Vaccination rate, Transmission Rate and the measure of inhibition recovered rate}respectively.

(Figure 4) shows the sensitivity of all variables with respect to the set of parameters {μ, α_2,p {Natural death, Recovery Rate due to the Vaccination and rate of recovery} respectively.

Figure 2, Figure 3 shows that parameters {Λ, p} {Rate of recruitment, rate of recovery} respectively, are the less critical model parameters whereas the remaining model parameters are the most sensitive to the model.

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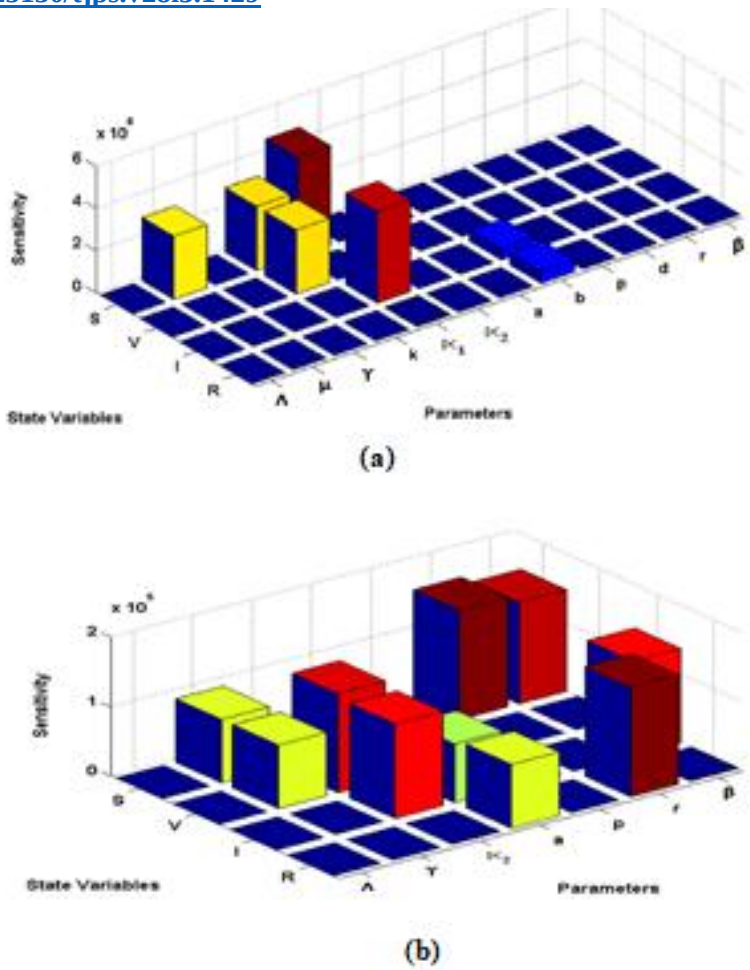

Fig. 2: Local sensitivity analysis with non-normalizations for the data given in Table 1.

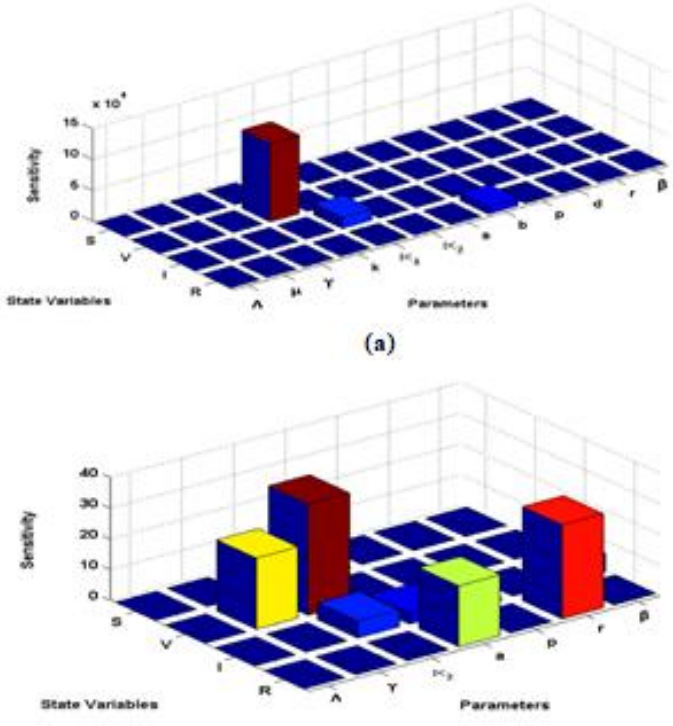

Fig. 3: Local sensitivity analysis with half-normalizations for the data given n Table 1.

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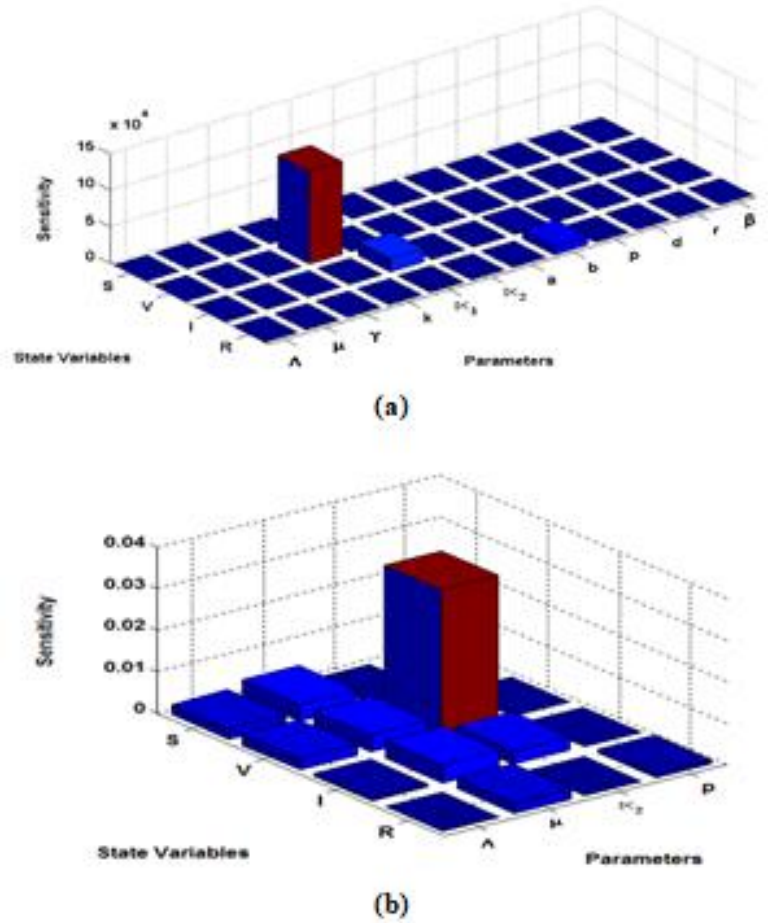

Fig. 4: Local sensitivity analysis with full-normalizations for the data given in Table 1.

9- Conclusion

In this paper, we investigate a non-linear incidence rate SIRS epidemic model

Solutions' positives and boundedness, computation of the disease-free equilibrium point, and calculate the model's basic reproduction number, we carried out a local stability analysis of the disease-free equilibrium point, demonstrates that the disease-free equilibrium point is locally asymptotically stable if $R_0 < 1$, Unstable if $R_0 > 1$.

The parameters are estimated using the combination of least square and Mat lab codes for the combination of the MH algorithm with the least square. The estimation results of the model of the COVID-19 disease and we suggested the SIRS model with four spices and twelve parameters to predict the spreading of this disease in Kurdistan. The daily infections and deaths recorded from 22th August 2021 to 30th September 2021.

In addition, R_0 was computed for real data in Kurdistan, it was about 1.808. This value is larger than unity; it means that the COVID 19 will be spread further and required some healthcare strategies to control this disease. Furthermore, we used the concept of local sensitivity to calculate the sensitivity of the model state with the model parameters.

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