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Modelling of The Spread of Meningitis Disease Using SEIR Model

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Abstract

The inflammation of the meninges, the three membrane tissue layers that protect the brain and spinal cord, causes meningitis illness. The purpose of this study is to examine the underlying dynamics and properties of meningitis disease by using the Suspected-Exposed-Infected-Recovered SEIR model, which is based on infectious disease compartmental dynamics. The model is developed using the system of Ordinary Differential Equations (ODEs). The disease-free equilibrium point (DFEP) and endemic equilibrium point (EEP) are the equilibrium points studied in this study, and their stability properties are analysed by using Descartes Rule of Signs. The basic reproduction number, R_0 of the meningitis disease distribution model is investigated using the Next-Generation Matrix approach to determine whether an infectious disease tends to fade out quickly or spread to epidemic proportions. If $R_0 > 1$, some preventive steps must be taken to control transmission. Lastly, the SEIR model is simulated in MATLAB using the ODE45 built-in function. The parameter values are changed to examine how they affect the outputs.

Keywords Meningitis; SEIR model; Ordinary Differential Equations; Stability analysis; Descartes Rule of Signs

1. Introduction

A study of 48 elderly patients with bacterial meningitis in Jutland, Denmark, from 1976 to 1988 indicated that diagnostic delay, defined as community-acquired bacterial meningitis (CABM) identified more than 2 days after admission, was related with a 50 percent increase in mortality and a purely non-meningitis epidemiology [1]. Any inflammations of the meninges, the three membrane tissue layers that cover the brain and spinal cord are referred to as meninges which form the blood-brain barrier. The meninges and the cerebrospinal fluid that is produced in and circulated in the meninges have the primary role of protecting, cushioning, nourishing, and supporting the brain and spinal cord.

It is essential to correctly diagnose the type of meningitis to receive potentially life-saving treatment as soon as possible as delay in diagnosis can contributes to poor outcomes There are many types of meningitis such as viral meningitis, fungal meningitis and bacterial meningitis but most common types is bacterial meningitis. While fungal meningitis which is a very rare type of meningitis that is caused by breathing cryptococcus, a common environmental fungus. Lastly, the most common type of meningitis is bacterial meningitis which is a dangerous type.

In the initial stage, it is hard to study meningitis disease when it was initially discovered as it was hardly reported. Before the introduction of a meningitis vaccine, meningitis serogroup A accounted for 80–85 percent of meningitis epidemics in the African meningitis belt. However, outbreaks and cases of meningitis caused by meningitis serogroups continue to be reported. To eliminate bacterial meningitis epidemics in the African Meningitis Belt, the rollout of multivalent meningitis conjugate vaccines is a

public health priority [2]. Due to fatal cases reported, the mortality rate can be overestimated when compared to the disease occurrence rate. Hence, the understandings about meningitis may help to prevent and control the transmission of meningitis. Therefore, by applying mathematical modelling and data analysis such as Suspected-Exposed-Infected-Recovered (SEIR) model is used to implement the meningitis disease prevention strategies as this approach can reduce death rates and the socio-economic impacts.

This study may help to determine how the transmission of meningitis disease occurs and thus can help to prevent the spread of the disease. The SEIR model is based on the Ordinary Differential Equations (ODEs) system. This research also generates insights to control the value of R_0 to be less than 1 via some preventive measures. The numerical simulations of SEIR model are also carried out by using MATLAB software to study the dynamical behaviour of the system at the equilibrium points. The significance of this research is to gain a better knowledge of the dynamics of meningitis disease by studying the stability analysis of the model.

This research aims to study a Suspected-Exposed-Infected-Recovered (SEIR) model for Meningitis disease and to perform the stability analysis of the proposed SEIR Model. Lastly, we aims to perform numerical simulation of the proposed model using MATLAB.

2. Literature Review

2.1. Introduction

The inflammation of meninges that surround membranes of the spinal cord and brain is called meningitis. Meningitis disease can affects both children and adults as it spreads quickly in an isolated place [3]. The disease can be caused by a variety of pathogens, including bacteria, fungi, and viruses. Without living in complete isolation, it is difficult to prevent the spread of infection between people [4]. Vaccines are important to protect against meningitis as well as prevent bacteria from surviving in the nose and throat [5].

2.2. Origin of meningitis

The history of meningitis is mentioned by Dr. Gaspard Viesseux as oubreak of a Swiss epidemic that began in 1805 [6]. According to Dr. Vieusseux, the outbreak began in a peculiar and terrifying manner a short distance from the city in a filthy sector populated by poor people and others vulnerable to the spread of any contagious disease. Several other epidemics in Europe and the U.S. were described after that. In 1840, the first outbreak in Africa was documented [7]. Gaspard Vieusseux and Andre Matthey in Geneva, as well as Elisa Northin in Massachusetts who documented epidemic meningitis [8].

Anton Vaykselbaum, an Austrian bacteriologist, first described bacterial meningitis in 1887 [9]. Heinrich Quincke performed the first cerebrospinal fluid investigation in 1842 by using his innovative lumbar puncture technique (CSF) [10]. The introduction of serum therapy for meningitis disease in the twentieth century marked the beginning of modern medicine [11]. Vaccines against meisseria meningitis which is created in the early twentieth century and are still utilised in modern medicine [12].

2.3. Mathematical modelling approach on Meningitis

Mathematical modelling is important in understanding the transmission mechanisms, structures and aspects of meningitis disorders [13]. Mathematicians and epidemiologists have used a variety of mathematical models to predict the trajectory of an epidemic. Modelling methodologies are critical for understanding and anticipating the potential and severity of a meningitis disease epidemic. They also give crucial information for determining the severity of the activity in the illness [14].

2.3.1. Deterministic mathematical model

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A deterministic mathematical model was used by Dr. Getachew Teshome Tilahun for pneumoniameningitis co-infection. The results reveals that implementing prevention controls has a significant influence on reducing the spread of pneumonia, meningitis and associated coinfections [15].

2.3.2. Compartmental Model For Meningitis

Several studies have used compartmental models to observe the pathophysiological mechanisms underlying the seasonal dynamic and epidemic occurrence of bacterial meningitis in the African region. Meningitis has a predictable seasonal pattern which is important to understand for better prevention and modelling. The two main explanations for hyperendemicity during the dry season imply a greater risk of invasive disease due to asymptomatic carriage of bacteria [16].

2.3.3. Application of Atangana Baleanu Caputo (ABC) derivative

Meningitis dynamics studied by Swati Yadav and co-authors using a new mathematical model. They used the Atangana Baleanu Caputo–Fabrizio derivative to solve the Advection–Diffusion equation. They demonstrated how fractional calculus can be used to simulate real-world problems. Backward bifurcation occured in the model, where the locally stable disease-free equilibrium coexists with an endemic equilibrium [17].

2.3.4. Application of SIR model

A SIR model was used by Kalimah Vereen to assess the influence of a vaccination campaign on the health for population in epidemic-prone countries. The model is numerically solved using the Euler method. In conclusion, in order to prevent disease spread in a densely populated area, vaccination rates must rise [18].

2.3.5. Application of SEIR model

A study of SEIR model by Hurit aims to solve the spread of meningitis. Computer programming and simulations were employed as research methods. Numerical solutions created using the Euler, Heun and RK4 methods are shown. It can be inferred that vaccination can be used to stop the spread in humans [19].

2.3.6. Application of Next-Generation Matrix (NGM) Method

A study of the basic reproduction number, R_0 using Next-Generation Matrix (NGM) approach by Diekmann. They clarify up some ambiguity in the literature about how to construct this matrix. They provide a step-by-step method for building the NGM using simple materials obtained directly from the model's parameters [20].

3. Methodology

3.1. System of Ordinary Differential Equations (ODEs)

An ordinary differential equation (ODE) is an equation that consists of one or more functions of one independent variable, as well as their derivatives. Differential equations are required for a mathematical representation of nature because they form the basis for many physical theories [21].

The ODE is defined as a relationship with one independent variable x, a real

dependent variable *y* and no intermediate variables, with some of its derivatives such as *y*, *y'*, *y"*, ..., *yⁿ* with respect to *x*. Levermore said that first-order systems of n-th ordinary differential equations for functions $x_i(t)$, i = 1, 2, ..., n that can be put into the normal form [22]

$$\frac{dx^{1}}{dt} = f_{1} (t, x_{1}, x_{2}, ..., x^{(n)}),$$

$$\frac{dx^{2}}{dt} = f_{2} (t, x_{1}, x_{2}, ..., x^{(n)}),$$

$$\vdots$$

(1)

$$\frac{dxn}{dt} = f_n (t, x_1, x_2, ..., x^{(n)}).$$

3.2. Stability Analysis of ODEs

3.2.1. Equilibrium Points

An equilibrium point is a constant solution to a differential equation in differential equations. Therefore, the first derivatives of the first order ODE equilibrium point are zero. The dimensional system is considered as follows

$$\frac{df_1}{dt} = f_1(x, y),$$

$$\frac{df_2}{dt} = f_2(x, y).$$
(2)
(3)

Thus, we let equilibrium points of Equation (3.2) and Equalion (3.3) equal to zero as follows:

$$f_1(x, y) = 0, (4) f_2(x, y) = 0. (5)$$

Then, the stability and properties of non-linear systems are studied using Jacobian linearization, a standard notion in control theory. The Jacobian Matrix, J is defined as follows:

$$J = \begin{bmatrix} \frac{\partial F_1}{\partial x_1} & \frac{\partial F_1}{\partial x_2} & \cdots & \frac{\partial F_1}{\partial x_n} \\ \frac{\partial F_2}{\partial x_1} & \frac{\partial F_2}{\partial x_2} & \cdots & \frac{\partial F_2}{\partial x_n} \\ \cdots & \cdots & \ddots & \cdots \\ \frac{\partial F_m}{\partial x_1} & \frac{\partial F_m}{\partial x_2} & \cdots & \frac{\partial F_m}{\partial x_n} \end{bmatrix}.$$
 (6)

Then, we need to find the eigenvalues where we first need to identify the eigenvectors where eigenvector is a vector result in the original vector multiplied by some factor when multiplied by a $n \ge n$ matrix. With I as an identity matrix, we may find the eigenvalues λ as the values that satisfy the following equation, where *det* is the determinant matrix is obtained as follows:

$$det(\lambda I - A) = 0, \tag{7}$$

where A is the Jacobian matrix A.

After the λ is determined, we may obtain the characteristics polynomial equations and determine the number of positive and negative real zeros for polynomial by Descartes Rule of Sign method. For positive roots, we need to let the f(x) is equal to or less than the number of changes in the sign of the coefficients and arrange the function in descending powers of the variable and count number of changes in sign for the coefficients of f(x). While, we need to let f(-x) is equal to or less than the number of changes changes in the sign of the coefficients and arrange the function in ascending powers of the variable and count number of changes in the sign of the coefficients and arrange the function in ascending powers of the variable and count number of changes in the sign for the coefficients of f(-x) to determine the negative roots.

3.3. Basic Reproduction Number

The basic reproduction number (R_0) is an epidemiological statistic for describing contagiousness or transmissible of infectious agents. The value of the parameter determines the severity of a disease in terms of mortality and morbidity and is summarized into two situations as follows [23]:

- $R_0 > 1$ represents that each infected person creates more than one new infectionon average and the disease can spread across the population.
- $R_0 < 1$ represents that over the period of its infectious phase, an infected individual generates less than one new infected individual on average and the virus cannot spread.

4. SEIR Model

In SEIR model, there are four classes: population of suspected people affected by the disease is denoted by the Suspected class S(t) over time t. The population of people who have been exposed to a disease but have not yet been affected is referred as the exposed class E(t). The Infected class, I(t) define the population of people who have been infected with the disease while the recovered class, R(t) denotes the population of people who have been cured of the sickness [19].

4.1. Assumption and Formulation for Meningitis Disease

Major assumptions of the SEIR model are

- Meningitis disease has a long incubation period.
- The natural birth and death rates are included.
- The environment is unsupportive.
- individuals may enter the subpopulation after done with the treatment.

Consider the system of differential equations with size of population, N as follows

$$\frac{dS}{dt} = \mu - \mu S - \beta SI - \nu S, \quad (4.1)$$

$$\frac{dE}{dt} = \beta SI - (\mu + \sigma)E, \quad (4.2)$$

$$\frac{dI}{dt} = \sigma E - (\mu + \gamma)I, \quad (4.3)$$

$$\frac{dR}{dt} = \gamma I - \mu R + \nu S. \quad (4.4)$$

Table 1: Definition of parameters

Parameters	Definition
β	The rate between $S(t)$ and $E(t)$
σ	The rate between $E(t)$ and $I(t)$
γ	The rate between $I(t)$ and $R(t)$
μ	Birth\Death rate of population
ν	Vaccination rate of population

4.2. Stability Analysis of SEIR Model for Meningitis

4.2.1. Equilibrium Points

To determine the equilibrium points for SEIR model, Equations (1) -(4) must be equated to zero as $\frac{ds}{dt}$ =

$$0, \frac{dE}{dt} = 0, \frac{dI}{dt} = 0, \text{ and } \frac{dR}{dt} = 0.$$

After solving the Equations, we may obtain (S^*, E^*, I^*, R^*) as follows

$$(S^*, E^*, I^*, R^*) =$$

$$=\left(\frac{(\mu+(\mu+\sigma))2}{(\mu+\nu)(\mu+\gamma)(\mu+\sigma)^{2}},\frac{\mu}{\mu+\nu)(\mu+\gamma)(\mu+\sigma)}+\frac{1}{\mu+\nu)(\mu+\gamma)},\frac{\mu\sigma+\sigma((\mu+\sigma)}{(\mu+\gamma)^{2}(\mu+\gamma)(\mu+\sigma)},\frac{\gamma\sigma^{2}}{\mu^{2}(\mu+\gamma)(\mu+\sigma)}+\frac{\nu(\mu+\nu)}{\beta\mu^{2}}\right)$$
(5)

4.2.2. Disease Free Equilibrium Point (DFEP) and its stability

At disease-free equilibrium point (DFEP), there is no disease infection in the population, and hence the disease is eradicated.

Therefore, by letting E = I = 0 in Equations (4.1) - (4.2) with assumption and obtain the (S^*, E^*, I^*, R^*) as follows

$$(S^*, E^*, I^*, R^*) = \left(\frac{\mu}{(\mu + \nu)}, 0, 0, \frac{\nu}{(\mu + \nu)}\right)$$
(6)

Next, to determine the stability analysis point at DFEP, we need to find Jacobian matrix based on Equations (4.1) - (4.2) as follows

$$J = \begin{bmatrix} -\mu - \beta I - \nu & 0 & -\beta S & 0\\ \beta I & -(\mu + \sigma) & \beta S & 0\\ 0 & \sigma & -(\mu + \gamma) & 0\\ \nu & 0 & \gamma & -\mu \end{bmatrix}.$$
 (7)

Thus, after obtaining the polynomial characteristic, we may use Descartes rule of signs by finding the real roots and obtain the negative roots which leads to a conclusion that the disease-free equilibrium point (DFEP) of SEIR model is locally asymptotically stable whenever $R_0 < 1$.

4.2.3. Endemic Equilibrium Point (EEP) and its stability

By using the Equation (4.5) and use the same method as the disease-free equilibrium point (DFEP), we may determine the Jacobian matrix and obtain the polynomial characteristic. By using Descartes rule of signs, the characteristic polynomial has five negative roots which leads to a conclusion that endemic equilibrium point (EEP) of SEIR model is locally asymptotically stable whenever $R_0 < 1$.

4.3. Basic Reproduction Number,

To obtain the basic reproduction number, $R_{0,}$, we need to determine the $det(FV^{-1} - \lambda I)$ where matrix F represents the rate of appearance of new infections in compartments, while matrix V represents the rate of transfer of individuals from one compartment to another.

Thus, we obtain

$$F = \begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} \mu + \sigma & 0 \\ \sigma & \mu + \gamma \end{pmatrix}.$$
 (8)

Next, we need to find $det(FV^{-1} - \lambda I)$

$$R_0 = det(FV^{-1} - \lambda I) = \begin{vmatrix} \frac{\beta\sigma}{(\mu+\sigma)(\mu+\gamma)} - \lambda & \frac{\beta(\mu+\gamma)}{(\mu+\sigma)(\mu+\gamma)} \\ 0 & 0 - \lambda \end{vmatrix} = 0$$

and obtain

$$|\lambda_1| = \lambda_1 = \frac{\beta\sigma}{(\mu+\sigma)(\mu+\gamma)}, \ \lambda_2 = 0$$

Since λ_1 is the dominant eigenvalue, thus we conclude the R_0 are as follow

$$R_0 = \frac{\beta\sigma}{(\mu+\sigma)(\mu+\gamma)}$$

5. Results and discussion

5.1. Parameters Values of SEIR Model

The simulation of the models is obtained by using MATLAB. Several simulations are carried out by adjusting the parameters to understand the transmission dynamics of the meningitis disease. Each parameter is changed at a time to see how it affects the results. The initial parameter values of the model used in this simulation are presented in Table 2.

Parameters	Definition	Estimated value
β	The rate between <i>S</i> (<i>t</i>) and <i>E</i> (<i>t</i>)	0.90
σ	The rate between <i>E(t)</i> and <i>I(t)</i>	0.20
γ	The rate between <i>I(t)</i> and <i>R(t)</i>	0.50
μ	Birth\Death rate of population	0.12
ν	Vaccination rate of population	0.50

Table 2: Definition of initial parameters

5.2. Simulation Results of SEIR Model

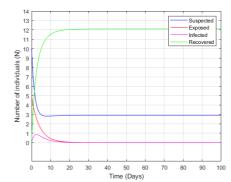


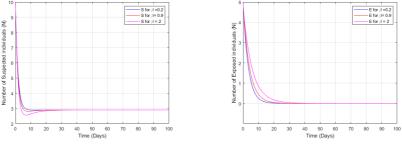
Figure 1 Simulation of SEIR model for β = 0.9, σ = 0.5, γ = 0.2, μ = 0.12 and v = 0.5.

Figure 1 shows all four classes of SEIR model with initial parameters. The suspected S(t) population shows decline curve at the first 10 days and increases gradually over time, after day 10. This decreasing curve is likely as they become infected due to the high rate between suspected and infected individually. All four classes show a similar curve after day 20 as the curve began to flatten.

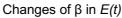
5.3. Result of changes in parameters

5.3.1. Changes in beta

The changes in the infection rate, β is explained in Figure 2 where the parameter value of β varies from 0.9 to 0.2 and then increase to 2.



Changes of β in S(t)



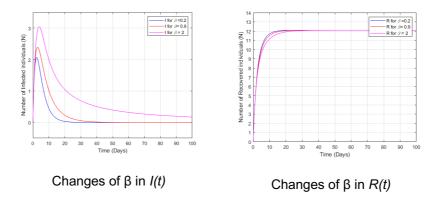


Figure 2 Variation in the number of populations for different β values.

The rate of change of the suspected *S*(*t*) population is inversely proportional to the infection rate as the curve shows that this relationship changes with higher number of suspected individuals at the first 10 days compared to the original values for a given period of time. The rate of change of the exposed population is directly proportional to the infection rate as the simulation results for exposed *E*(*t*) population. Next, the simulation results for infected *I*(*t*) population shows the size of the exposed when β =2, compared to the original β =0.9 in infected population. As the value of the infection rate increases, the number of infected individuals increase over time. Lastly, the simulation results for *R*(*t*) show that as the value of the infection rate increases, the number of infected individuals increase over time. This shows that the rate of change of the infected population is inversely proportional to the size of the size of the size over time. This shows that the rate of change of the infected population is inversely proportional to the size of the population.

5.3.2. Changes in sigma

The changes of the transfer rate between E(t) and I(t) classes, σ is explained in Figure 3 where the parameter value of σ varies from 0.5 to 0.1 and then increases to 2.

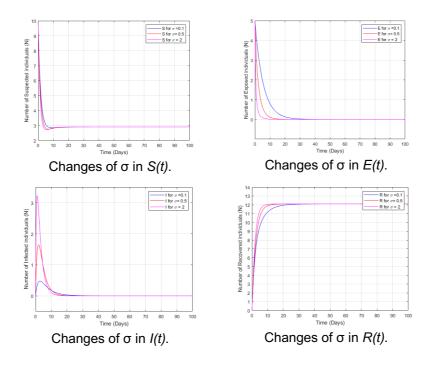


Figure 3 Variation in the number of populations, for different σ values.

The suspected S(t) population shows that as the value of the transfer rate between E(t) and I(t) classes, σ decreases, the population of suspected individuals decreases over time. The rate of change of the suspected population is directly proportional to the size of suspected class. Next, the population of exposed individuals decreases over time. It shows that the rate of change of the population is directly proportional to the transfer rate between E(t) and I(t) classes. The curve with lowest transfer rate has the lowest number of infected individuals compared to other classes. Lastly, the recovered R(t) curve shows that the rate of change of the transfer rate as the value of the σ increases, the number of recovered individuals increases over time.

5.3.3. Changes in gamma

The changes in the recovery rate, γ is explained in Figure 4 where the parameter value of γ varies from 0.2 to 0.1 and then increases to 1.

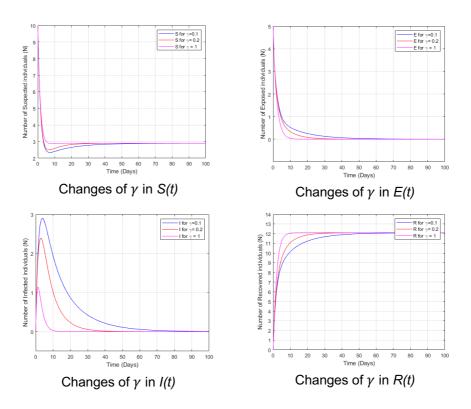


Figure 4 Variation in the number of populations for different γ values.

The suspected S(t) simulation results shows the rate of change of the suspected population is inversely proportional to the recovery rate, γ . As the value of γ increases, the population of suspected individuals decreases over time. Next, as the value of γ increases, the population of exposed individuals decreases over time. Moreover, the infected I(t) simulation results shows that the rate of change of the infected population is inversely proportional to the recovery rate, γ due to the lowest recovery rate, $\gamma = 0.1$ has the lowest number of infected individuals compared to other γ . Lastly, when the value of the γ increases, the number of recovered R(t) individuals increases over time. This shows that the rate of change of the recovered population is directly proportional to the recovery rate.

Conclusion

The SEIR compartmental model is used to investigate the transmission spread of meningitis disease. The SEIR model is an extended model of SIR model for infectious disease research. It is divided into four classes which are suspected, exposed, infected and recovered populations. The SEIR model is used as a reference model for meningitis disease transmission. The simulation results showed that immunizations would enhance the healing of meningitis and provide a forecast of future instances of the disease. Findings also can be considered as a reference for future pandemic prevention of

meningitis disease. In the future, more research into this model should be done to see if it can forecast cases based on time and location, and if other considerations should be made for other Malaysian states.

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