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Mathematical Modeling of Meningitis

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Abstract

Meningitis is acute inflammation of the brain and spinal cord coverings, caused by viral or bacterial infections, or occasionally, medications. It poses a severe risk to life due to its proximity to vital neurological structures. Symptoms include headache, neck stiffness, fever, confusion, vomiting, and sensitivity to light or sound. In children, symptoms like irritability and drowsiness are common, and the presence of a rash may indicate specific causes such as meningococcal infection. Mathematical modeling, especially SIR modeling, helps understand disease dynamics and informs intervention strategies. This paper examines meningitis models and methods for find the basic reproduction number ($\mathcal{R}_0$).

Keywords: Mathematical Modeling, Meningitis, Reproduction Number, SCIR Model, Vaccination.

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Introduction

Meningitis is an acute inflammation of the protective membranes covering the brain and spinal cord, known as the meninges. The inflammation can be caused by various factors including viral, bacterial, or other microbial infections, and less commonly by certain medications. Meningitis can be life-threatening due to its proximity to the brain and spinal cord; hence, it is classified as a medical emergency. The most common symptoms of meningitis are headache and neck stiffness associated with fever, confusion or altered consciousness, vomiting, and photophobia (aversion to light) or phonophobia (aversion to sound). In children, non-specific symptoms such as irritability and drowsiness often predominate. The presence of a rash may indicate a specific cause of meningitis. For example, meningitis caused by meningococcal bacteria may be accompanied by a distinctive skin rash.

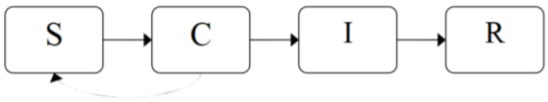
Individuals worldwide are susceptible to meningitis [4]. The highest burden of this disease is recorded in a region in sub-Saharan Africa called the African Meningitis Belt [3]. Bacteria and germs can be transmitted from person to person through exposure to respiratory droplets when sneezing, kissing, or coughing. Some types of germs can also be transmitted to individuals through food. Therefore, there is a strong need to study this disease, and from a medical perspective, various studies can be conducted to prevent it. To strengthen these medical studies, it is necessary to resort to mathematical modeling of meningitis. Some academic mathematicians interested in studying this disease have classified individuals into several categories based on SIR modeling and added other categories to delve deeper into meningitis analysis [1].

In this paper, some mathematical models of meningitis will be presented and a comparison will be made in methods for producing the basic reproduction number $\mathcal{R}_0$.

Mathematical Modeling of Meningitis

Modelling without the R Class

In a scientific study, Vereen modeled meningitis based on classifying individuals into four compartments: Susceptible (S), Infected (I), Carriers (C), and Recovered (R) [5]. Individuals in the carrier category are capable of infecting others without experiencing the disease themselves. They will then become infected or return to the susceptible category. Individuals in the Infected category directly come from the carrier category.



Based on this scheme, a system of 4D differential equations was formulated.

$$\frac{d\tilde{S}}{dt} = (1-p)vN - \frac{\beta}{N}\tilde{C}\tilde{S} + \gamma_1\tilde{C} - \mu_1\tilde{S} \text{ (3.1)}$$

$$\frac{d\tilde{C}}{dt} = \frac{\beta}{N}\tilde{C}\tilde{S} - \gamma_1\tilde{C} - \alpha\tilde{C} - \mu_1\tilde{C} \text{ (3.2)}$$

$$\frac{d\tilde{I}}{dt} = \alpha\tilde{C} - \gamma_2\tilde{I} - \mu_2\tilde{I} - \mu_1\tilde{I} \text{ (3.3)}$$

$$\frac{d\tilde{R}}{dt} = pvN + \gamma_2\tilde{I} + \mu_2\tilde{I} - \mu_1\tilde{R} \text{ (3.4)}$$

To simplify the above SCIR model, the following mathematical terms were taken into consideration:

$$\frac{dS}{dt} = \frac{1}{N}\frac{d\tilde{S}}{dt}.\frac{dC}{dt} = \frac{1}{N}\frac{d\tilde{C}}{dt}.\frac{dI}{dt} = \frac{1}{N}\frac{d\tilde{I}}{dt} \text{ and } \frac{dR}{dt} = \frac{1}{N}\frac{d\tilde{R}}{dt}$$

Considering that $1 = S + C + I + R$, the model was simplified by eliminating $\mathcal{R}_0$, resulting in three differential equations:

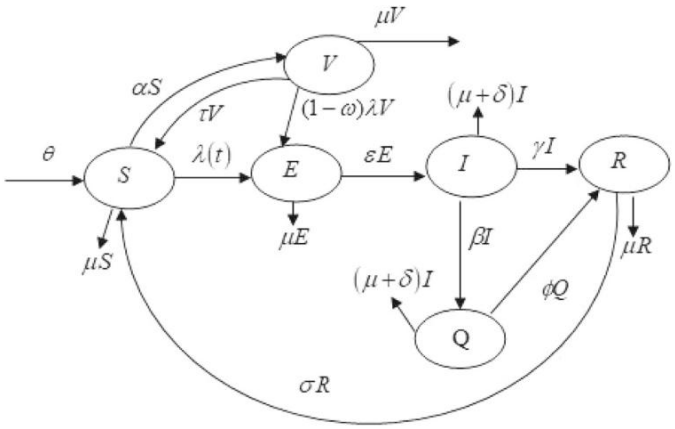
$$\frac{dS}{dt} = (1-p)v - \beta CS + \gamma_1 C - vS \text{ (3.5)}$$

$$\frac{dC}{dt} = \beta CS - \gamma_1 C - \alpha C - vC \text{ (3.6)}$$

$$\frac{dI}{dt} = \alpha C - \gamma_2 I - \mu_2 I - vI \text{ (3.7)}$$

Modeling with Categories (V) and Medical Intervention (Q)

Prevention of this disease primarily occurs through vaccination. Mass vaccination of susceptible populations and early detection of infected individuals have contributed significantly to mitigating the meningitis epidemic [9]. Similar to many other diseases, vaccination has been proven to reduce the spread of meningitis in numerous regions . Therefore, Peter and others argue that it is essential to add another compartment between individuals, namely the vaccinated individuals compartment (those who have received the vaccine), followed by the hospitalized individuals compartment [7].



The classification is based on Susceptible (S), Vaccinated individuals (those who have received vaccination) (V), Exposed (E) (when a healthy individual susceptible to a certain disease comes into contact that might transmit the disease, this individual becomes exposed to the disease. These individuals may or may not become infected. They are typically non-infectious. In mathematical models, it is often assumed that all exposed individuals eventually become infected [6]), Infected (I), Hospitalized (Q), and Recovered (R) individuals. It is important to note that researchers have assumed that the vaccinated layer decreases due to infection at rates of $(1-\omega)\lambda(t)$ where $0 \leq \omega \leq 1$. Here, ω determines the effectiveness of the vaccine.

$$\frac{dS}{dt} = \theta - (\mu + \lambda(t))S + \sigma R + \tau V - \alpha S \quad (3.8)$$

$$\frac{dV}{dt} = \alpha S - (1-\omega)\lambda(t)V - (\tau + \mu)V \quad (3.9)$$

$$\frac{dE}{dt} = \lambda(t)S - (\varepsilon + \mu)E + (1-\omega)\lambda(t)V \quad (3.10)$$

$$\frac{dI}{dt} = \varepsilon E - (\delta + \beta + \gamma + \mu)I \quad (3.11)$$

$$\frac{dQ}{dt} = \beta I - (\phi + \delta + \mu)Q \quad (3.12)$$

$$\frac{dR}{dt} = \gamma I + \phi Q - (\sigma + \mu)R \quad (3.13)$$

Modeling with Treatment and the Effect of Treatment Discontinuation

Some types of meningitis are primarily treated using intravenous antibiotics. Additionally, close family members of infected patients are usually given prophylactic antibiotics to prevent infection and transmission[2]. The duration of treatment typically depends on the type of bacteria and ranges from 10-14 days or 14-21 days. Many researchers have worked on mathematical modeling of bacterial meningitis. In their work, Asamoah et al. presented a model that looked at the dynamics of meningitis with control measures such as vaccination and treatment. None of these mathematical models, however, considered the impact of treatment discontinuation on the dynamics of bacterial meningitis transmission. Therefore, a basic model for the spread of bacterial meningitis in the presence of treatment discontinuation is developed. The proposed model assumes an SCITR modeling framework, which is an extension of previous models [8].

They have created a system of differential equations in which individuals are divided into five compartments: Susceptible individuals (S), Carrier individuals (C), Infected individuals (I), Treated individuals (Medical Intervention) (T), and Recovered individuals (R).

$$S' = \Pi + \phi R - (\lambda(S,C,I,T) + \mu)S \quad (3.14)$$
$$C' = \lambda(S,C,I,T)S - (\alpha + \mu + \omega + \theta)C \quad (3.15)$$
$$I' = \alpha C + \rho T - (\psi + \mu + \delta_1)I \quad (3.16)$$
$$T' = \theta C + \psi I - (\mu + \gamma + \rho + \delta_2)T \quad (3.17)$$
$$R' = \omega C + \gamma T - (\phi + \mu)R \quad (3.18)$$

The Basic Reproduction Number

Finding the value of the basic reproduction number $\mathcal{R}_0$ is essential in disease modeling as it helps identify the presence of the disease (or epidemic). It also enables the study of equilibrium points, which are divided into two main categories: disease-free equilibrium point and endemic equilibrium point. There are several methods that can be used to find $\mathcal{R}_0$, including the Jacobian method, the Van den Driessche and Watmough Approach, the Routh–Hurwitz Criteria, among others. Mathematicians typically choose an appropriate and straightforward method to find $\mathcal{R}_0$. In the above models, the value of the basic reproductive number was determined using the Van den Driessche and Watmough Approach.

$\mathcal{R}_0$ for the First Model

In this method, the basic reproductive number depends on $\mathcal{R}_0 = \rho(FV^{-1})$, where,

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0)\right] \text{ and } V = \left[\frac{\partial \boldsymbol{V}_i}{\partial x_j}(x_0)\right] \text{ with } 1 \le i,j \le m$$

and for the first model,

$$\mathcal{F}_i(x) = \begin{pmatrix} 0 \\ \beta CS \\ 0 \end{pmatrix}$$
$$\mathcal{V}_i(x) = \begin{pmatrix} -(1-p)v - \gamma_1 C + vS \\ \alpha C + \gamma_1 C + vC \\ -\alpha C + \gamma_2 I + \mu_2 I + vI \end{pmatrix}$$
$$F = \begin{pmatrix} \beta & 0 \\ 0 & 0 \end{pmatrix}$$
$$V = \begin{pmatrix} \gamma_1 + \alpha + v & 0 \\ -\alpha & \gamma_2 + \mu_2 + v \end{pmatrix}$$
$$V^{-1} = \begin{pmatrix} \frac{1}{\gamma_1 + \alpha + v} & 0 \\ \frac{\alpha}{(\gamma_1 + \alpha + v)(\gamma_2 + \mu_2 + v)} & \frac{1}{\gamma_2 + \mu_2 + v} \end{pmatrix}$$

therefore,

$$FV^{-1} = \begin{pmatrix} \frac{\beta}{\gamma_1 + \alpha + v} & 0 \\ 0 & 0 \end{pmatrix}$$

this leads to $\mathcal{R}_0 = \frac{\beta}{\gamma_1 + \alpha + v}$

$\mathcal{R}_0$ for the Vaccination Model

At first $\mathcal{F}(X)$ and $\mathcal{V}(X)$ were determined.

$$\mathcal{F}(X) = \begin{pmatrix} 0 \\ 0 \\ \lambda(t)S + (1-\omega)\lambda(t)V \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

$$\mathcal{V}(X) = \begin{pmatrix} \mu S + \alpha S - \theta - \sigma R - \tau V \\ (\tau + \mu)V - \alpha S \\ (\varepsilon + \mu)E \\ (\delta + \beta + \gamma + \mu)I - \varepsilon E \\ (\phi + \delta + \mu)Q - \beta I \\ (\sigma + \mu)R - \gamma I - \phi Q \end{pmatrix}$$

Using the Jacobian method, the following was calculated:

$$\mathrm{F} = \begin{pmatrix} \frac{\psi\rho S_0 + (1-\omega)\psi\rho V_0}{S_0 + V_0} & \frac{\psi S_0 + (1-\omega)\psi V_0}{S_0 + V_0} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$\mathrm{V} = \begin{pmatrix} (\varepsilon + \mu) & 0 & 0 \\ -\varepsilon & (\delta + \beta + \gamma + \mu) & 0 \\ 0 & -\beta & (\phi + \delta + \mu) \end{pmatrix}$$

Finally, \(R_0 \) was calculated.

$$\mathcal{R}_0 = \frac{\psi\big((\delta + \beta + \gamma + \mu)\rho + \varepsilon\big)(S_0 + (1-\omega)V_0)}{(S_0 + V_0)(\varepsilon + \mu)(\delta + \beta + \gamma + \mu)}$$

$$\mathcal{R}_0 = \frac{\psi\big((\delta + \beta + \gamma + \mu)\rho + \varepsilon\big)(\tau + \mu + (1-\omega)\alpha)}{(\delta + \beta + \gamma + \mu)(\varepsilon + \mu)(\alpha + \tau + \mu)}$$

$\mathcal{R}_0$ for the Last Model

$$F = \begin{bmatrix} \frac{\beta S_0}{1 + \alpha_1 S_0} & \frac{\beta S_0 \eta_1}{1 + \alpha_1 S_0} & \frac{\beta S_0 \eta_2}{1 + \alpha_1 S_0} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}. V = \begin{bmatrix} f & 0 & 0 \\ -\alpha & g & -\rho \\ -\theta & -\psi & h \end{bmatrix},$$

Whereas,

$$f = (\alpha + \mu + \omega + \theta), g = (\psi + \mu + \delta_1), \text{ and } h = (\mu + \gamma + \rho + \delta_2).$$

and the value of \(R_0 \) is,

$$\mathcal{R}_0 = \rho(FV^{-1})\frac{\beta S_0}{(1 + \alpha_1 S_0)}\left[\frac{1}{f} + \frac{\eta_1(\alpha h + \theta\rho)}{f[(\mu + \delta_1)h + \psi(\mu + \gamma + \delta_2)]} + \frac{\eta_2(\alpha\psi + g\theta)}{f[(\mu + \delta_1)h + \psi(\mu + \gamma + \delta_2)]}\right]$$

Conclusion and Discussion

Through our review of previous studies, we have confirmed the necessity of presenting other scientific papers with a mathematical focus to study meningitis. Mathematical modeling of diseases provides insights into future outcomes and guides medical specialists in understanding the spread of the disease and when viruses become active during the disease stages. Moreover, studies on stochastic differential equations systems should be conducted alongside deterministic differential equation systems. Finding the value of $\mathcal{R}_0$ and whether it exceeds or is less than one determines the fate of the disease and governs equilibrium points. In the future, it may not be necessary to use the same approach to find $\mathcal{R}_0$, but alternative methods could be chosen. Additionally, parameter estimation and data fitting are crucial to understanding the disease behavior and mitigating its impact.

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