Bulletin of Applied Mathematics and Mathematics Education
Volume 3, Number 1, 2023 pp. 1-14
https://dx.doi.org/10.12928/bamme.v3i1.9475
e-ISSN 2776-1029, p-ISSN 2776-1002

A mathematical model of meningitis with antibiotic effects

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ARTICLE INFO

Article History
Received 2 December 2023
Revised 29 December 2023
Accepted 29 December 2023

Keywords
Basic reproduction number
Global stability
Local stability
Meningitis

How to cite this article:
Ginting, R. S., & Adi, Y. A. (2023). A mathematical model of meningitis with antibiotic effects. *Bulletin of Applied Mathematics and Mathematics Education*, *3*(1), 1-14.

ABSTRACT

The mathematical model in this study is a SCIR-type meningitis disease spread model, namely susceptible (S), carrier (C), infected (I), and recovery (R). In the model used, there are two equilibrium points, namely the disease-free equilibrium point (E^0) and the endemic equilibrium point (E^*). The conditions and stability of the equilibrium point are determined by the basic reproduction number ($\Re_0$), which is the value that determines whether or not the spread of meningitis infection in a population. The results of this study show that the stability of the disease-free equilibrium point and the endemic equilibrium point are locally asymptotically stable and by using the Lyapunov Function method it is found that the disease-free equilibrium point will be globally stable when ($\Re_0 \leq 1$), while the endemic equilibrium point will be globally stable when ($\Re_0 > 1$). Numerical simuations perform to support the theoretical results.

Introduction

Meningitis is an infectious disease characterized by infection and inflammation of the brain's lining, making it one of the ten most dangerous diseases in the world (Hardiyanti et al., 2017). This infection is usually caused by several microorganisms, such as bacteria, viruses, and fungi, but can also be caused by chemical irritation, cancer, and drug allergies. The spread of meningitis caused by bacteria or viruses is very easily transmitted from one person to many people through the air, such as coughing, sneezing, or close contact with people who carry the pathogen (Asamoah et al., 2020). Bacterial meningitis causes death in children around 5-40% and in adults around 20-50% if not treated. Even if diagnosed early and treated adequately, 8-15% of patients will die within 24 to 48 hours after the onset of symptoms. Furthermore, 10-20% of people susceptible to meningitis infection will have permanent sequelae, namely brain damage. Patients who survive meningitis will experience neurological disorders and even if they receive proper treatment, they will still cause health problems such as partial vision impairment, hearing impairment, and learning disabilities (Hadning et al., 2020). One treatment that can be done to reduce morbidity and mortality due to infectious diseases such as bacterial meningitis is by administering antibiotics.

Patients infected with bacterial meningitis can survive with antibiotic treatment. Antibiotics are a treatment to fight infections caused by bacteria, which can reduce the risk of severe complications and brain damage in bacterial meningitis patients. One standard treatment for bacterial meningitis is intravenous administration of antibiotics injected directly into a vein (Sheehan, 2019; Asamoah et al., 2020). Every year, more than 250,000 patients are successfully treated with IV (intravenous) antibiotics at home. Even though the availability of antibiotics and hospital care is now guaranteed, bacterial meningitis still has high morbidity and mortality rates. Around 10% of the cases reported are the mortality rate in treated patients, while the mortality rate in untreated patients reaches 50% - 90% (Yanuar et al, 2019).

Mathematical modeling of the spread of meningitis that has been carried out previously can be studied, among others, in (Afifah et al, 2019; Asamoah et al, 2018; Asamoah et al, 2020; Kotola et al, 2022; Peter et al, 2022; Turkun et al, 2023). In this study, the effect of antibiotic efficacy is analyzed using the mathematical model. The SCIR-type meningitis epidemic model in this study will be analyzed by determining the disease-free equilibrium point, endemic equilibrium point, basic reproduction number, local stability analysis of the equilibrium point, global stability analysis of the equilibrium point, and numerical simulation of the stability analysis obtained. To calculate the basic reproduction number we used the next generation matrix method (Van-den-Driessche & Watmough, 2002; Martcheva, 2015). Meanwhile, to show the global stability of the equilibrium point, we use the Lyapunov function which has been commonly used in previous studies (Vargas, 2009).

Mathematical model

The establishment of a mathematical model of the spread of meningitis is done by considering the following assumptions.

(1) Each individual in the population (at time t) is always in one of the populations namely susceptible (S), carrier (C), infected (I), and recovered (R). The population size of S, C, I, R is in the form of proportion, so $N(t) = S(t) + C(t) + I(t) + R(t)$.
(2) Every new individual, immune-compromised individual, and surviving individual belongs to the susceptible population (S).
(3) There is an average recruitment process of new individuals in the sub-population with an average recruitment rate $\Lambda > 0$. There is a natural mortality process in each sub-population with a natural mortality rate $\mu > 0$.
(4) The rate of disease transmission from susceptible (S) to carrier (C) through interaction between susceptible and infected individuals is expressed by $\beta > 0$.
(5) The transition rate of disease transmission from carrier class (C) to fully infected (I) is expressed by $\alpha > 0$.
(6) The number of operators that switch to the recovered class due to defense or natural cure is expressed by $\omega > 0$.
(7) The rate of disease recovery from infected (I) to cured (R) is expressed by $\rho\gamma(I)$ with γ the minimum recovery rate and ρ the rate of change in antibiotic efficacy assumed to be $0 < \rho \leq 1$.
(8) The death rate due to disease is expressed by $\delta > 0$
(9) The transition rate from being cured (R) and becoming susceptible to the disease again (S) is expressed by the immunity loss rate $\theta > 0$.

Based on the above assumptions, the following bacterial meningitis disease spread model was formed (Figure 1).

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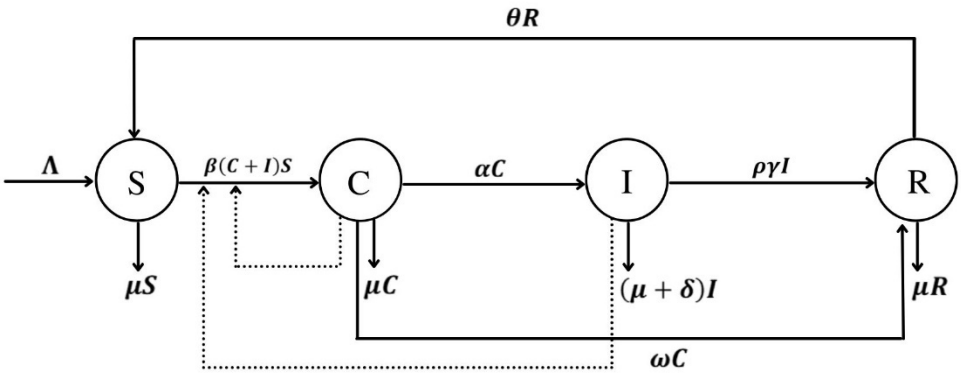

Figure 1. Compartment diagram of SCIR model for transmission dynamics of bacterial meningitis with antibiotic recovery

(1) Susceptible sub-populations (S)

The increase of individuals in the susceptible sub-population is caused by the presence of new individuals denoted by Λ. The population size (S) will also increase due to the presence of θR which is individuals who lose immunity after recovery and will decrease with the transmission process with infected individuals, carrier individuals, and with natural death denoted $[\beta(C+I)+\mu]S$.

$$\frac{dS}{dt} = \Lambda - [\beta(C+I)+\mu]S + \theta R$$

(2) Carrier sub-population (C)

The number of individuals in the carrier sub-population will increase as susceptible individuals develop into infected $[\beta(C+I)]S$ individuals. It will then decrease with natural mortality μC, individuals recovering from disease due to natural cure ωC,, and individuals in the carrier class becoming fully ill αC or progression of infection to symptomatic infection.

$$\frac{dC}{dt} = [\beta(C+I)]S - (\mu+\omega+\alpha)C$$

(3) Infected sub-population (I)

The number of individuals in the infected sub-population is due to the transition rate of individuals from the carrier class to fully sick αC. It then decreases due to natural mortality μI, death from infection δI, and recovery rate $\rho\gamma I$. To study the rate of change of antibiotic efficacy, this study uses the ideas proposed by [4] which incorporates the effect of effective antibiotic change in its model where ρ is the rate of change of antibiotic efficacy and γ is the recovery rate. Antibiotic efficacy, $\rho = 1$ indicates 100% antibiotic efficacy and it is assumed that $0 < \rho \leq 1$. Thus the population of infected individuals will decrease due to the recovery process that relies on antibiotic efficacy.

$$\frac{dI}{dt} = \alpha C - [(\mu+\delta)I + \rho\gamma I]$$

(4) Recovered sub-population (R)

The number of individuals in the Recovered sub-population increases with the presence of sick individuals undergoing recovery $\rho\gamma I$ and with the rate of individuals experiencing natural recovery ωC. The number of individuals in the Recovered sub-population will

decrease due to the presence of individuals who lose immunity after recovery θR as well as the presence of natural mortality μR.

$$\frac{dR}{dt} = \rho\gamma I + \omega C - (\theta + \mu)R$$

Thus, the following system of differential equations is obtained:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - [\beta(C + I) + \mu]S + \theta R \\
\frac{dC}{dt} &= \beta(C + I)S - (\mu + \omega + \alpha)C \\
\frac{dI}{dt} &= \alpha C - [(\mu + \delta)I + \rho\gamma I] \\
\frac{dR}{dt} &= \rho\gamma I + \omega C - (\theta + \mu)R
\end{aligned} \qquad (1)$$

which fulfils the initial conditions $S(0) \geq 0, C(0) \geq 0, I(0) \geq 0, R(0) \geq 0$. The total disease dynamics of the model is obtained by summing up the system of equations (1), namely $\frac{dN}{dt} = \frac{dS}{dt} + \frac{dC}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = \Lambda - \mu N - \delta I$, which $N = S + C + I + R$.

Results and discussion

Analysis of local stability at equilibrium points

The equilibrium point of the system in equation (1) is obtained when $\boldsymbol{\frac{dS}{dt} = 0, \frac{dC}{dt} = 0, \frac{dI}{dt} = 0}$, dan $\boldsymbol{\frac{dR}{dt} = 0}$. Thus, the disease-free equilibrium point $\boldsymbol{E^0 = (S^0, C^0, I^0, R^0) = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right)}$. Analysis of stability at the equilibrium point requires a basic reproduction number ($\boldsymbol{\Re_0}$). Basic reproduction number is the average number of infections carried out by infected individuals. The basic reproduction number is obtained using the next generation matrix method (Martcheva, 2015). The basic reproduction number is $\boldsymbol{\Re_0 = \frac{\beta\Lambda((\mu+\delta)+\rho\gamma+\alpha)}{\mu(\mu+\omega+\alpha)((\mu+\delta)+\rho\gamma)}}$.

Theorem 1

The equilibrium point is E_0 locally asymptotically stable if $\Re_0 < 1$.

Proof

The Jacobian matrix of system (1) at point$E_0 := (S^0, C^0, I^0, R^0) = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right)$ is as follows:

$$J(S, C, I, R) = \begin{bmatrix} -(\beta(C + I) + \mu) & -\beta S & -\beta S & \theta \\ \beta(C + I) & \beta S - (\mu + \omega + \alpha) & \beta S & 0 \\ 0 & \alpha & -(\mu + \delta + \rho\gamma) & 0 \\ 0 & \omega & \rho\gamma & -(\theta + \mu) \end{bmatrix}$$

The disease-free stability point $E_0 := (S^0, C^0, I^0, R^0) = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right)$ is substituted into the Jacobian matrix to obtain

$$J(S^0, C^0, I^0, R^0) = \begin{bmatrix} -\mu & -\beta\left(\frac{\Lambda}{\mu}\right) & -\beta\left(\frac{\Lambda}{\mu}\right) & \theta \\ 0 & \beta\left(\frac{\Lambda}{\mu}\right) - (\mu + \omega + \alpha) & \beta\left(\frac{\Lambda}{\mu}\right) & 0 \\ 0 & \alpha & -(\mu + \delta + \rho\gamma) & 0 \\ 0 & \omega & \rho\gamma & -(\theta + \mu) \end{bmatrix}$$

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From the Jacobian matrix, we will find the characteristic equation using

$$|J(E_0) - \lambda I| = 0$$

thus,

$$\begin{bmatrix} -\mu-\lambda & -\beta\left(\frac{\Lambda}{\mu}\right) & -\beta\left(\frac{\Lambda}{\mu}\right) & \theta \\ 0 & \beta\left(\frac{\Lambda}{\mu}\right)-(\mu+\omega+\alpha+\lambda) & \beta\left(\frac{\Lambda}{\mu}\right) & 0 \\ 0 & 0 & R-\lambda & 0 \\ 0 & 0 & 0 & -(\theta+\mu+\lambda) \end{bmatrix} = 0$$

The characteristic equation of the Jacobian matrix is obtained as follows

$$(-\mu-\lambda)\left(\beta\left(\frac{\Lambda}{\mu}\right)-(\mu+\omega+\alpha+\lambda)\right)\left(\frac{-\alpha\beta\left(\frac{\Lambda}{\mu}\right)}{\beta\left(\frac{\Lambda}{\mu}\right)-(\mu+\omega+\alpha)}-(\mu+\delta+\rho\gamma)-\lambda\right)(-\theta-\delta-\lambda) = 0$$

From this characteristic equation, the eigenvalue is found to be

$\lambda_1 = -\mu < 0$

$$\lambda_2 = \beta\left(\frac{\Lambda}{\mu}\right)-(\mu+\omega+\alpha)$$

$$= (\mu+\omega+\alpha)\left(\frac{\beta\left(\frac{\Lambda}{\mu}\right)}{(\mu+\omega+\alpha)}-1\right)$$

for, $\frac{\beta\left(\frac{\Lambda}{\mu}\right)}{(\mu+\omega+\alpha)} < 1$, maka $\lambda_2 = \beta\left(\frac{\Lambda}{\mu}\right)-(\mu+\omega+\alpha) < 0$

$$\lambda_3 = \frac{-\alpha\beta\left(\frac{\Lambda}{\mu}\right)}{\beta\left(\frac{\Lambda}{\mu}\right)-(\mu+\omega+\alpha)}-(\mu+\delta+\rho\gamma)$$

$$= \frac{(\mu+\delta+\rho\gamma)}{\left(-\frac{\Lambda\beta}{\mu(\mu+\omega+\alpha)}+1\right)}(\Re_0-1)$$

for, $\Re_0 = \frac{\beta\Lambda((\mu+\delta)+\rho\gamma+\alpha)}{\mu(\mu+\omega+\alpha)((\mu+\delta)+\rho\gamma)} < 1$, Maka

$$\lambda_3 = \frac{-\alpha\beta\left(\frac{\Lambda}{\mu}\right)}{\beta\left(\frac{\Lambda}{\mu}\right)-(\mu+\omega+\alpha)}-(\mu+\delta+\rho\gamma) < 0$$

$\lambda_4 = -\theta-\mu < 0$

Since the eigenvalues $(\lambda_1, \lambda_2, \lambda_3, and\ \lambda_4)$ are negative in all real parts, based on the characteristic roots (eigenvalues), the equilibrium point E_0 of the nonlinear system is locally asymptotically stable and the disease-free equilibrium point is stable for $\Re_0 < 1$.

Furthermore, we have endemic equilibrium point $\boldsymbol{E}^* = (\boldsymbol{S}^*, \boldsymbol{C}^*, \boldsymbol{I}^*, \boldsymbol{R}^*)$ are obtained as follows.

$$S^* = \frac{(\mu+\omega+\alpha)\left((\mu+\delta)+\rho\gamma\right)}{\beta\left((\mu+\delta)+\rho\gamma+\alpha\right)}$$

$$C^* = \frac{\Lambda\left((\mu+\delta)+\rho\gamma\right)(\Re_0-1)(\theta+\mu)}{(\iota-\theta\kappa)\Re_0}$$

$$I^* = \frac{\Lambda\alpha(\Re_0 - 1)(\theta + \mu)}{(\iota - \theta\kappa)\Re_0}$$
$$R^* = \frac{\Lambda(R_0 - 1)(\alpha\rho\gamma + [(\mu + \delta) + \rho\gamma]\omega)}{(\iota - \theta\kappa)\Re_0}$$

With $\iota = (\mu + \omega + \alpha)(\mu + \delta + \rho\gamma)(\theta + \mu)$ and $\kappa = \alpha\rho\gamma_0 + (\mu + \delta + \rho\gamma)\omega$.

The local stability of the endemics equilibrium point is state in Theorem 2 as follow.

Theorem 2
The equilibrium point E_1 is locally asymptotically stable if $\Re_0 > 1$.

Proof
The Jacobian matrix of system (1) at point $E_1 = (S^*, C^*, I^*, R^*)$ is as follows:

$$J(E_1) = \begin{bmatrix} T & -\frac{(\mu+\omega+\alpha)\left((\mu+\delta)+\rho\gamma\right)}{\left((\mu+\delta)+\rho\gamma+\alpha\right)} & -\frac{(\mu+\omega+\alpha)\left((\mu+\delta)+\rho\gamma\right)}{\left((\mu+\delta)+\rho\gamma+\alpha\right)} & \theta \\ U & \frac{-\alpha(\mu+\omega+\alpha)}{(\mu+\delta+\rho\gamma+\alpha)} & \frac{(\mu+\omega+\alpha)\left((\mu+\delta)+\rho\gamma\right)}{\left((\mu+\delta)+\rho\gamma+\alpha\right)} & 0 \\ 0 & \alpha & -(\mu+\delta+\rho\gamma) & 0 \\ 0 & \omega & \rho\gamma & -(\theta+\mu) \end{bmatrix}$$

with,
$$T = \frac{-\beta\Lambda(\Re_0 - 1)(\theta + \mu)(\mu + \delta + \rho\gamma + \alpha) - \Re_0\mu(\iota - \theta\kappa)}{(\iota - \theta\kappa)\Re_0}$$
$$U = \frac{\beta\Lambda(\Re_0 - 1)(\theta + \mu)(\mu + \delta + \rho\gamma + \alpha)}{(\iota - \theta\kappa)\Re_0}$$

The characteristic equation of the Jacobian matrix is obtained as follows

$$(T - \lambda)(V - \lambda)(X - \lambda)(Z - \lambda) = 0$$

From this characteristic equation, the eigenvalues are obtained

For the value of T

$$T = -\frac{\beta\Lambda(\Re_0 - 1)(\theta + \mu)(\mu + \delta + \rho\gamma + \alpha) - \Re_0\mu(\iota + \theta\kappa)}{(\iota - \theta\kappa)\Re_0}$$
$$= -\left(\frac{\beta\Lambda(\Re_0 - 1)(\theta + \mu)(\mu + \delta + \rho\gamma + \alpha) + \Re_0\mu(\iota + \theta\kappa)}{(\iota - \theta\kappa)\Re_0}\right)$$

Thus, $\lambda_1 = T < 0$

For the value of V

$$\mathrm{V} = \frac{U}{T}\left(\frac{(\mu+\omega+\alpha)(\mu+\delta+\rho\gamma)}{(\mu+\delta+\rho\gamma+\alpha)}\right) - \frac{\alpha(\mu+\omega+\alpha)}{(\mu+\delta+\rho\gamma+\alpha)}$$
$$= \frac{\left(\frac{\beta\Lambda(\Re_0 - 1)(\theta + \mu)(\mu + \delta + \rho\gamma + \alpha)}{(\iota - \theta\kappa)\Re_0}\right)}{\left(\frac{-\beta\Lambda(\Re_0 - 1)(\theta + \mu)(\mu + \delta + \rho\gamma + \alpha) - \Re_0\mu(\iota - \theta\kappa)}{(\iota - \theta\kappa)\Re_0}\right)}\left(\frac{(\mu+\omega+\alpha)(\mu+\delta+\rho\gamma)}{(\mu+\delta+\rho\gamma+\alpha)}\right)$$
$$- \frac{\alpha(\mu+\omega+\alpha)}{(\mu+\delta+\rho\gamma+\alpha)}$$

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$$= -\frac{\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\omega+\alpha)(\mu+\delta+\rho\gamma)}{\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\delta+\rho\gamma+\alpha) + \Re_0\mu(\iota-\theta\kappa)} - \frac{\alpha(\mu+\omega+\alpha)}{(\mu+\delta+\rho\gamma+\alpha)}$$

$$= -\left(\frac{\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\omega+\alpha)(\mu+\delta+\rho\gamma)}{\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\delta+\rho\gamma+\alpha) + \Re_0\mu(\iota-\theta\kappa)} + \frac{\alpha(\mu+\omega+\alpha)}{(\mu+\delta+\rho\gamma+\alpha)}\right)$$

Thus $\lambda_2 = V < 0$

For the value of X

$$\text{X} = \frac{-\alpha W}{V} - (\mu+\delta+\rho\gamma)$$

$$= -\alpha\left(\frac{\frac{-\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\omega+\alpha)(\mu+\delta+\rho\gamma)}{\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\delta+\rho\gamma+\alpha) + \Re_0\mu(\iota-\theta\kappa)} + \frac{(\mu+\omega+\alpha)(\mu+\delta+\rho\gamma)}{(\mu+\delta+\rho\gamma+\alpha)}}{\frac{-\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\omega+\alpha)(\mu+\delta+\rho\gamma)}{\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\delta+\rho\gamma+\alpha) + \Re_0\mu(\iota-\theta\kappa)} - \frac{\alpha(\mu+\omega+\alpha)}{(\mu+\delta+\rho\gamma+\alpha)}}\right)$$

$$- (\mu+\delta+\rho\gamma)$$

$$= -\alpha\left(\frac{(\mu+\delta+\rho\gamma)[\Re_0\mu(\iota-\theta\kappa)]}{(\mu+\delta+\rho\gamma+\alpha)\,[\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\delta+\rho\gamma) + \alpha\beta\Lambda(\Re_0 - 1)(\theta+\mu)] + \alpha\mu\Re_0(\iota-\theta}\right.$$

$$- (\mu+\delta+\rho\gamma)$$

Thus $\lambda_3 = X < 0$

For the value of Z

$$\text{Z} = \frac{-Y}{X}\frac{\alpha\theta U}{TV} + \frac{\theta\omega U}{TV} - (\theta+\mu)$$

$$= -\frac{U}{TV}\left(\alpha\theta\frac{Y}{X} - \theta\omega\right) - (\theta+\mu)$$

$$= -\frac{U}{TV}\left[\alpha\theta\left(\frac{-\omega\left(\frac{(\mu+\delta+\rho\gamma)[\Re_0\mu(\iota-\theta\kappa)]}{(\mu+\delta+\rho\gamma+\alpha)\,[\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\delta+\rho\gamma) + \alpha\beta\Lambda(\Re_0 - 1)(\theta+\mu}\right.}{-\alpha\left(\frac{(\mu+\delta+\rho\gamma)[\Re_0\mu(\iota-\theta\kappa)]}{(\mu+\delta+\rho\gamma+\alpha)\,[\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\delta+\rho\gamma) + \alpha\beta\Lambda(\Re_0 - 1)(\theta+\mu)] +}\right.}\right.$$

$$\left.\left.- \theta\omega\right] - (\theta+\mu)\right]$$

$$= -\frac{U}{TV}\left[\alpha\theta\left(\frac{\omega\left(\frac{(\mu+\delta+\rho\gamma)[\Re_0\mu(\iota-\theta\kappa)]}{(\mu+\delta+\rho\gamma+\alpha)\,[\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\delta+\rho\gamma) + \alpha\beta\Lambda(\Re_0 - 1)(\theta+\mu)}\right.}{\alpha\left(\frac{(\mu+\delta+\rho\gamma)[\Re_0\mu(\iota-\theta\kappa)]}{(\mu+\delta+\rho\gamma+\alpha)\,[\beta\Lambda(\Re_0 - 1)(\theta+\mu)(\mu+\delta+\rho\gamma) + \alpha\beta\Lambda(\Re_0 - 1)(\theta+\mu)] + \alpha}\right.}\right.$$

$$\left.\left.- \theta\omega\right] - (\theta+\mu\right]$$

Thus $\lambda_4 = Z < 0$

Since the eigenvalues $(\lambda_1, \lambda_2, \lambda_3, dan\ \lambda_4)$ are negative in all real parts, based on their characteristic roots, the equilibrium point E_1 of the nonlinear system is locally asymptotically stable.

Global stability of equilibrium points

Theorem 3

The disease-free equilibrium point $E_0 = (S^0, C^0, I^0, R^0)$ in system (4.1) is globally asymptotically stable if $\Re_0 \leq 1$.

Proof

Suppose the Lyapunov function for the SCIR model at the disease-free equilibrium point with positive constants k_1, k_2, and k_3 as follows:

$$V(S,C,I,R) = \left(S - S^0 - S^0 \ln\left(\frac{S}{S^0}\right)\right) + k_1 C + k_2 I + k_3 R \qquad (4.19)$$

Investigate whether $V(S,C,I,R) = 0$ for $(S,C,I,R) = (S^0, C^0, I^0, R^0)$ and $V(S,C,I,R) \geq 0$ for $(S,C,I,R) \neq (S^0, C^0, I^0, R^0)$ as follows:

for $(S,C,I,R) = (S^0, C^0, I^0, R^0)$,

$$V(S,C,I,R) = \left(S - S^0 - S^0 \ln\left(\frac{S}{S^0}\right)\right) + k_1 C + k_2 I + k_3 R$$

$$= \left(S - S^0 - S^0 \ln\left(\frac{S}{S^0}\right)\right) + 0 + 0 + 0$$

$$= \frac{\Lambda}{\mu}(1 - 1 - \ln 1)$$

$$= 0$$

for $(S,C,I,R) \neq (S^0, C^0, I^0, R^0)$, $\frac{S}{S_0} \neq 1$, thus

$$\frac{S}{S_0} - 1 - S_0 \ln\left(\frac{S}{S_0}\right) \neq 0$$

Thus,

$$V(S,C,I,R) = \left(S - S_0 - S_0 \ln\left(\frac{S}{S_0}\right)\right) + k_1 C + k_2 I + k_3 R$$

$$= S_0\left(\frac{S}{S_0} - 1 - \ln\frac{S}{S_0}\right) + k_1 C + k_2 I + k_3 R$$

It can be seen that $V(S,C,I,R)$ will be positive if $S_0\left(\frac{S}{S_0} - 1 - \ln\frac{S}{S_0}\right) > 0$. Suppose $\frac{S}{S_0} = x$, then suppose there is a function $g(x) = x - 1 - \ln x$, function $g(x)$ will reach a global minimum at $x = 1$ and $g(1) = 0$. Therefore, $g(x) > 0$ for all $x > 0$ and $x \neq 1$. Then $V(S,C,I,R)$ is positive for $\frac{S}{S_0} > 0$ and $\frac{S}{S_0} \neq 1$.

The derivative of the V function in equation (4.19) is as follows:

$$\frac{\partial V(S,C,I,R)}{\partial t} = \frac{dV}{dS}\cdot\frac{dS}{dt} + \frac{dV}{dC}\cdot\frac{d}{dt} + \frac{dV}{dI}\cdot\frac{dI}{dt} + \frac{dV}{dR}\cdot\frac{dR}{dt}$$
$$= \left(1 - \frac{S_0}{S}\right)\cdot\frac{dS}{dt} + k_1\cdot\frac{dC}{dt} + k_2\cdot\frac{dI}{dt} + k_3\cdot\frac{dR}{dt} \qquad (4.20)$$

Substitute $\frac{dS}{dt}, \frac{dC}{dt}, \frac{dI}{dt}$, and $\frac{dR}{dt}$ from equation (4.1) into equation (4.20) to obtain

$$\frac{\partial V(S,C,I,R)}{\partial t} = \left(\left(1 - \frac{S_0}{S}\right)(\Lambda - (\beta(C+I) + \mu)S + \theta R) + k_1(\beta(C+I)S - (\mu + \omega + \alpha)C)\right.$$
$$\left. + k_2(\alpha C - (\mu + \delta)I - \rho\gamma I) + k_3(\rho\gamma I + \omega C - (\theta + \mu)R)\right)$$

It will be investigated whether $\frac{\partial V(S,C,I,R)}{\partial t} = 0$ for $(S,C,I,R) = (S^0, C^0, I^0, R^0)$ and $\frac{\partial V(S,C,I,R)}{\partial t} \leq 0$ for $(S,C,I,R) \neq (S^0, C^0, I^0, R^0)$ as follows :

For $(S,C,I,R) = (S^0, C^0, I^0, R^0)$,

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$$\frac{\partial V(S,C,I,R)}{\partial t} = \left(\left(1-\frac{S_0}{S}\right)(\Lambda-(\beta(C+I)+\mu)S+\theta R) + k_1(\beta(C+I)S-(\mu+\omega+\alpha)C) + k_2(\alpha C-(\mu+\delta)I-\rho\gamma I) + k_3(\rho\gamma I+\omega C-(\theta+\mu)R)\right)$$

$$= 0$$

For $(S,C,I,R) \neq (S^0,C^0,I^0,R^0)$, When $S \leq S_0$, so

$$\frac{\partial V(S,C,I,R)}{\partial t} = \left[k_1\left(\beta(C+I)\left(\frac{\Lambda}{\mu}\right)-(\mu+\omega+\alpha)C\right)+k_2(\alpha C-(\mu+\delta)I-\rho\gamma I) + k_3(\rho\gamma I+\omega C-(\theta+\mu)R)\right]$$

$$= \left[k_1\frac{\beta\Lambda}{\mu}C+k_1\frac{\beta\Lambda}{\mu}I-k_1(\mu+\omega+\alpha)C+k_2\alpha C-k_2(\mu+\delta+\rho\gamma)I + k_3\rho\gamma I+k_3\omega C-k_3(\theta+\mu)R\right]$$

$$= \left[\left(k_1\left(\frac{\beta\Lambda}{\mu}-(\mu+\omega+\alpha)\right)+k_2\alpha+k_3\omega\right)C + \left(k_1\frac{\beta\Lambda}{\mu}-k_2(\mu+\delta+\rho\gamma)+k_3\rho\gamma\right)I-k_3(\theta+\mu)R\right]$$

Suppose

$$\left(k_1\frac{\beta\Lambda}{\mu}-k_2(\mu+\delta+\rho\gamma)+k_3\rho\gamma\right)=0$$

$$k_1\frac{\beta\Lambda}{\mu}=k_2(\mu+\delta+\rho\gamma)-k_3\rho\gamma$$

Chosen $k_1=(\mu+\delta+\rho\gamma)-\rho\gamma$, $k_2=\frac{\beta\Lambda}{\mu}(1-\rho\gamma)$, and $k_3=\frac{\beta\Lambda}{\mu}\left(1-(\mu+\delta+\rho\gamma)\right)$, thus

$$\frac{\partial V(S,C,I,R)}{\partial t} \leq \left[\left(\left((\mu+\delta+\rho\gamma)-\rho\gamma\right)\left(\frac{\beta\Lambda}{\mu}-(\mu+\omega+\alpha)\right)+\left(\frac{\beta\Lambda}{\mu}(1-\rho\gamma)\right)\alpha + \left(\frac{\beta\Lambda}{\mu}\left(1-(\mu+\delta+\rho\gamma)\right)\right)\omega\right)C - \left(\frac{\beta\Lambda}{\mu}\left(1-(\mu+\delta+\rho\gamma)\right)\right)(\theta+\mu)R\right]$$

$$= \left[\left((\mu+\delta+\rho\gamma)(\mu+\omega+\alpha)(\Re_0-1) - \frac{\beta\Lambda}{\mu}\left((\alpha+1)\rho\gamma+(\mu+\delta+\rho\gamma-1)\omega\right) + (\mu+\omega+\alpha)\rho\gamma\right)C - \frac{\beta\Lambda}{\mu}(\theta+\mu)\left(1-(\mu+\delta+\rho\gamma)\right)R\right]$$

It is obtained that $\frac{\partial V(S,C,I,R)}{\partial t} \leq 0$ if $\Re_0 \leq 1$.

Since the model fulfils the Lyapunov property, the meningitis epidemic model at the disease-free equilibrium point is globally asymptotically stable.

Theorem 4

The endemic equilibrium point $E_1 = (S^*, C^*, I^*, R^*)$ in system (4.1) is globally asymptotically stable if $\Re_0 > 1$.

Proof

Define the Lyapunov function at the endemic equilibrium point as follows:

$$V(S,C,I,R) = \frac{1}{2}[(S-S^*) + (C-C^*) + (I-I^*) + (R-R^*)]^2$$

It will be investigated wheter $V(S,C,I,R) = 0$ for $(S,C,I,R) = (S^*, C^*, I^*, R^*)$ and $V(S,C,I,R) \geq 0$ for $(S,C,I,R) \neq (S^*, C^*, I^*, R^*)$ as follows:

For $(S,C,I,R) = (S^*, C^*, I^*, R^*)$,

$$\begin{aligned} V(S,C,I,R) &= \frac{1}{2}[(S-S^*) + (C-C^*) + (I-I^*) + (R-R^*)]^2 \\ &= \frac{1}{2}[(0) + (0) + (0) + (0)]^2 \\ &= 0 \end{aligned}$$

For $(S,C,I,R) \neq (S^*, C^*, I^*, R^*)$,

$$V(S,C,I,R) = \frac{1}{2}[(S-S^*) + (C-C^*) + (I-I^*) + (R-R^*)]^2 > 0$$

It is obtained that $V(S,C,I,R)$ is positive.

The time derivative of $V(S,C,I,R)$ is as follows

$$\frac{dV(S,C,I,R)}{dt} = [(S-S^*) + (C-C^*) + (I-I^*) + (R-R^*)]\frac{d(S+C+I+R)}{dt}$$

It is obtained that $\frac{dV(S,C,I,R)}{dt} = 0$ for $(S,C,I,R) = (S^*, C^*, I^*, R^*)$ and $\frac{dV(S,C,I,R)}{dt} \leq 0$ for $(S,C,I,R) \neq (S^*, C^*, I^*, R^*)$ sebagai berikut:

For $(S,C,I,R) = (S^*, C^*, I^*, R^*)$,

$$\begin{aligned} \frac{dV(S,C,I,R)}{dt} &= [(S-S^*) + (C-C^*) + (I-I^*) + (R-R^*)]\frac{d(S+C+I+R)}{dt} \\ &= 0 \end{aligned}$$

For $(S,C,I,R) \neq (S^*, C^*, I^*, R^*)$, It is known that $N = S + C + I + R$ and $\frac{dN}{dt} = \Lambda - \mu N - \delta I$. Thus, the

$$\frac{dV(S,C,I,R)}{dt} = [(S-S^*) + (C-C^*) + (I-I^*) + (R-R^*)][\Lambda - \mu(S+C+I+R) - \delta I]$$

Suppose $\Lambda = \mu(S^*, C^*, I^*, R^*) + \delta I^*$, so

$$\begin{aligned} \frac{\partial V}{\partial t} &= [(S-S^*) + (C-C^*) + (I-I^*) + (R-R^*)][\mu(S^*, C^*, I^*, R^*) + \delta I^* \\ &\qquad - \mu(S+C+I+R) - \delta I] \\ &= [(S-S^*) + (C-C^*) + (I-I^*) + (R-R^*)][-\mu(S-S^*) - \mu(C-C^*) \\ &\qquad - \mu(I-I^*) - \mu(R-R^*) - \delta(I-I^*)] \end{aligned}$$

$$\frac{\partial V}{\partial t} = -\begin{pmatrix} \mu(S-S^*)^2 + 2\mu(S-S^*)(C-C^*) + \mu(C-C^*)^2 + (\mu+\delta)(I-I^*)^2 + \mu(R-R^*)^2 \\ +(2\mu+\delta)(I-I^*)\big((S-S^*) + (C-C^*) + (R-R^*)\big) \\ +[\mu(S-S^*)(R-R^*) + \mu(C-C^*)(R-R^*)] \end{pmatrix}$$

Next, substitute the value of E^*, obtained

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$$S - S^* = S - \left(\frac{(\mu+\omega+\alpha)\big((\mu+\delta)+\rho\gamma\big)}{\beta\big((\mu+\delta)+\rho\gamma_0+\alpha\big)}\right) > 0$$

$$C - C^* = C - \left(\frac{\Lambda[(\mu+\delta)+\rho\gamma](R_0-1)(\theta+\mu)}{(\iota-\theta\kappa)\Re_0}\right) > 0$$

$$I - I^* = I - \left(\frac{\Lambda\alpha(R_0-1)(\theta+\mu)}{(\iota-\theta\kappa)\Re_0}\right) > 0$$

$$R - R^* = R - \left(\frac{\Lambda(R_0-1)(\alpha\rho\gamma+[(\mu+\delta)+\rho\gamma]\omega)}{(\iota-\theta\kappa)\Re_0}\right) > 0$$

If $\Re_0 > 1$, then $\frac{\partial V}{\partial t}$ is negative. Therefore, the model fulfils the Lyapunov property and the meningitis epidemic model at the endemic equilibrium point is globally asymptotically stable.

Simulation of meningitis disease spread model

Simulations were conducted to get an idea of the spread of meningitis by giving values for each parameter according to the $\Re_0$ condition.

Table 1. Parameter for meningitis spread disease simulation model

Parameter	Description	Parameter Value	
Λ	Average recruitment rate of the vulnerable population	20	20
β	Disease transmission rate (disease transmission)	0.002	0.0005
α	Transition rate of disease transmission from carrier class to fully ill	0.02	0.02
ω	Natural healing rate	0.1118	0.1118
ρ	Rate of change of antibiotic efficacy	$[0.1-0.9]$	$[0.1-0.9]$
γ_0	Minimum recovery rate	$(0\,,1)$	$(0\,,1)$
μ	Natural mortality rate	0.045	0.089
δ	Death rate due to disease	$[0.05-0.2]$	$0.05-0.2$
θ	Immunity loss rate	0.0839	0.0839
$\Re_0$	Basic reproduction	4.6160	0.5588

By using the parameters in Table 1, the following graph is obtained.

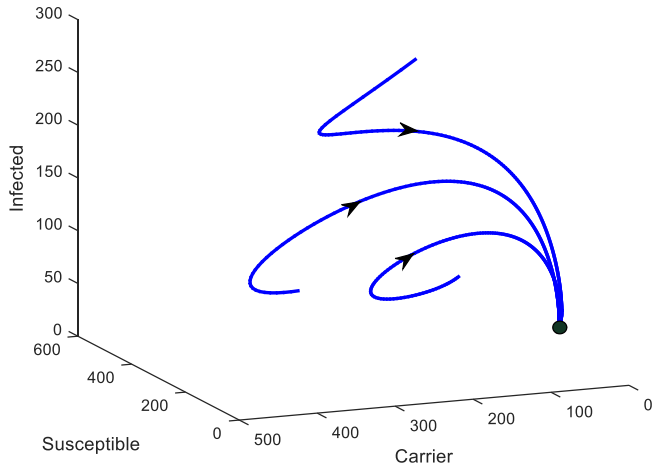

Figure 2. Phase portraits of Susceptible, Carrier, and Infected populations with different initial values

It can be seen in Figure 2 that the stable condition is reached when$(S^* = 95.61, C^* = 55.58, I^* = 48.37, R^* = 0)$ for the basic reproduction number is $\Re_0 = 4.6160 > 1$ with three different numbers of initial states of the population Susceptible, Carrier, and Infected the population will be stable at a point close to point E^*. This will be clarified in Figure 3 where the population will be stable at $(S^* = 95.61, C^* = 55.58, I^* = 48.37, R^* = 49.14)$ which is an endemic equilibrium point with four different initial states.

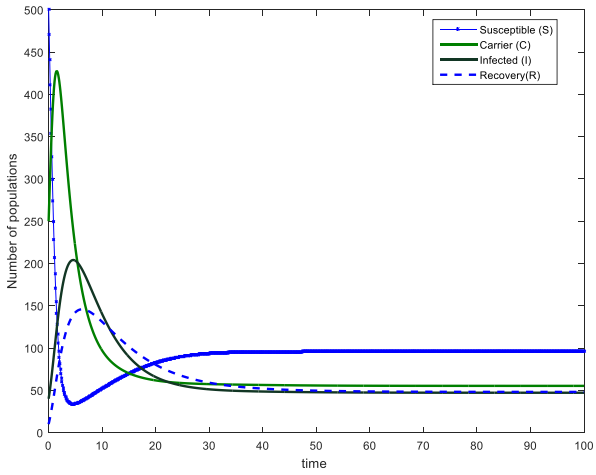

Figure 3. Graph of population size for $\Re_0 > 1$

While in Figure 4 the stable condition is achieved when $(S^0 = 224.7, C^0 = 0, I^0 = 0, R^0 = 0)$ for the basic reproduction number is $\Re_0 < 1$ with three different numbers of initial states of the Susceptible, Carrier, and Infected populations the population will be stable at a point close to the point E_0. Numerical simulation results are in accordance with analytical calculations that show if $\Re_0 = 0.5588 < 1$ and for local asymptotic stability conditions $\frac{\beta\left(\frac{\Lambda}{\mu}\right)}{(\mu+\omega+\alpha)} = 0.28034 < 1$ then the disease-free equilibrium point is fulfilled. So that in the condition $\Re_0 < 1$, the average infected population will decrease or there will be no spread of the disease because there are individuals in the Recovered population who can cure meningitis infection and the effect of the efficacy of antibiotics given. This will be clarified in Figure 5 where the population will be stable at $(S^0 = 224.7, C^0 = 0, I^0 = 0, R^0 = 0)$ which is a disease-free equilibrium point with four different numbers of initial states.

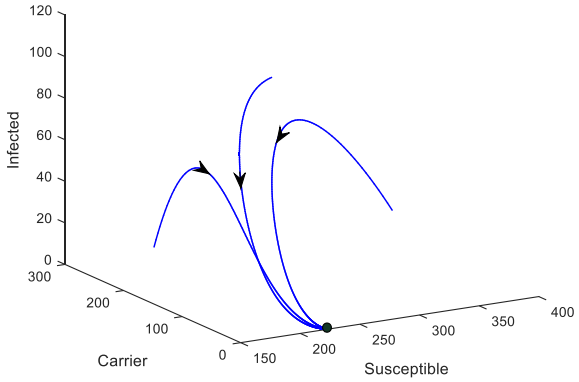

Figure 4. Phase portraits of Susceptible, Carrier, and Infected populations with different initial values

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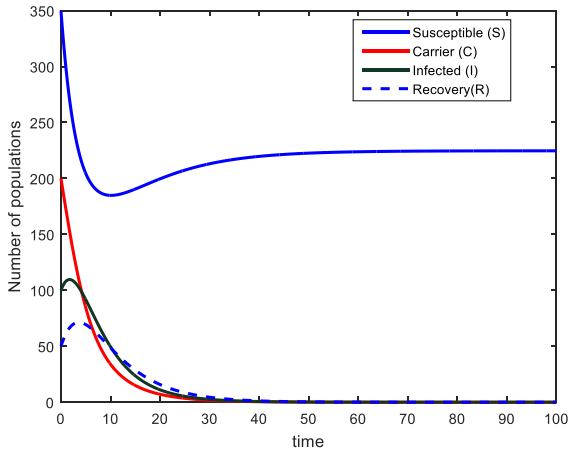

Figure 5. Population change graph for $\mathfrak{R}_0 < 1$

Conclusion

In this paper, the spread of meningitis can be modelled in the form of a system of differential equations. The equilibrium points obtained from the model are the disease-free equilibrium point (E_0) and the endemic equilibrium point (E^*). The disease-free equilibrium point is locally asymptotically stable and globally asymptotically stable when $\mathfrak{R}_0 < 1$, while the endemic equilibrium point is locally asymptotically stable and globally asymptotically stable when $\mathfrak{R}_0 > 1$ and from numerical simulations, if $\mathfrak{R}_0 < 1$ in the long run the spread of bacterial meningitis infection will disappear from the population, and the number of individuals infected with bacterial meningitis will decrease until it reaches the disease-free equilibrium point E^0, which identifies that meningitis will experience extinction. Meanwhile, if $\mathfrak{R}_0 >$ in the long run, meningitis infection will always exist, in a certain epidemic level.

Acknowledgement

We thank to Universitas ahmad Dahlan to support this research.

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