Mathematical Modelling of Transmission Dynamics of Meningitis

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Abstract: *The most effective ways to control the transmission of most infectious diseases are vaccination and treatment, while vaccination and treatment helps to reduce the disease burden. In this papera mathematical model is formulated based on the transmission dynamics of Meningitis. The model has a locally asymptotically stable disease-free equilibrium (DFE) whenever, the basic reproduction number ($\mathcal{R}_0$) that is a certain epidemiological threshold, is less than unity. Using a Lyapunovfunction and Lasalle Invariance Principle, it is also shown that the DFE of the co-infection model is globally –asymptotically stable (GAS) whenever $\mathcal{R}_0 < 1$. Numerical simulation indicates that the reduction of the effective contact rate and increase in the treatment rate and vaccination efficacy rate can reduce the disease burden of co-infection.*
Keywords: *Equilibrium, Local and Global stability.*

I. Introduction

Meningitis is an acute inflammation of the protective membranes covering the brain and spinal cord, known collectively as the meninges and the inflammation may be caused by infection with viruses, bacteria, or other microorganisms, and by certain drugs which is less common[1]. Some other forms of meningitis are preventable by immunization with the meningococcal, mumps, pneumococcal, and Hib vaccines.People with significant exposure to certain types of meningitis can be given antibiotics which is useful. In acute meningitis the first treatment consists of promptly giving antibiotics and sometimes antiviral drugs[3]. Corticosteroids can also be used to prevent complications from excessive inflammation. If not treated quickly, meningitis can lead to serious long-term consequences such as deafness, epilepsy, hydrocephalus, or cognitive deficits [1].

Meningococcus vaccines exist against groups A, B, C, W135 and Y. A quadrivalent vaccine now exists, which combines four vaccines with the exception of B; immunization with this ACW135Y vaccine is now a visa requirement for taking part in Hajj [5]. Routine vaccination against Streptococcus pneumoniae with the pneumococcal conjugate vaccine (PCV), which is active against seven common serotypes of this pathogen, significantly reduces the incidence of pneumococcal meningitis. Short-term antibiotic prophylaxis is another method of prevention, particularly of meningococcal meningitis. In cases of meningococcal meningitis, preventative treatment in close contacts with antibiotics (e.g. rifampicin, ciprofloxacin or ceftriaxone) can reduce their risk of contracting the condition, but does not protect against future infections. Bacterial meningitis occurs in about 3 people per 100,000 annually in Western countries. Population-wide studies have shown that viral meningitis is more common, at 10.9 per 100,000, and occurs more often in the summer. In Brazil, the rate of bacterial meningitis is higher, at 45.8 per 100,000 annually. Sub-Saharan Africa has been plagued by large epidemics of meningococcal meningitis for over a century, leading to it being labeled the "meningitis belt". Epidemics typically occur in the dry season (December to June), and an epidemic wave can last two to three years, dying out during the intervening rainy seasons. Attack rates of 100–800 cases per 100,000 are encountered in this area, which is poorly served by medical care. These cases are predominantly caused by meningococci [9].

The study of transmission dynamics of meningitis is of great interest asmeningitis can be life-threatening because of the inflammation's proximity to the brain and spinal cord, which drives to use mathematical modelling to acquire knowledge about it's transmission dynamics and from which we can identify effective control strategies.By studying some model[3,10,11], a mathematical model is formulated based on transmission dynamics of meningitis. In section II the model is formulated and analyzed (for the stability of the disease-free equilibrium equilibrium) in section IV,V and VI and in section VII numerical simulations are carried out.

II. Formulation of Model

The total populations at time t, which is denoted by $N(t)$, is subdivided into six mutually exclusive compartments, namely susceptible class ($S(t)$), carrier class ($C(t)$) of individuals, who are able to infect others without suffering from the disease, infected individuals without symptoms at time t ($I_N(t)$), infected individuals

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with symptoms at time t ($I_S(t)$), individuals who are taking treatments ($T(t)$) and recovered class ($R(t)$) of individuals who are recovered from the disease and those who are vaccinated. So that the the total population ($N(t)$) at time t is, $N(t) = S(t) + C(t) + I_N(t) + I_S(t) + T(t) + R(t)$.

The susceptible population is increased at a rate $(1 - \xi)v\pi$ either by birth or immigration or by the loss of immunity, acquired through natural infection and at a rate γ_1. The susceptible individuals acquire meningitis at a rate λ, where,

$$\lambda = \frac{\beta(\theta_1 C + \theta_2 I_N + \eta I_S)}{N} \; ; 0 < \theta_1 < 1, 0 < \theta_2 < 1, \eta > 1, \qquad (1)$$

Where λ is the force of infection for meningitis, β is the transmission rate for meningitis and the parameter $\eta(\eta > 1)$ indicates that an individual with symptomatic meningitis is more infectious than carrier and asymptomatic meningitis ($0 < \theta_1 < 1, 0 < \theta_2 < 1$). The population of C(t) class is reduced by the development of symptomatic meningitis at a rate $p\alpha$, asymptomatic meningitis at a rate $(1 - p)\alpha$, by natural death at a rate of μ and by γ_1. The population in $I_S(t)$ class is reduced by the natural death at a rate of μ, by disease induced mortality at a rate of μ_1 and by taking treatments at a rate of σ. $I_N(t)$ class is reduced by the natural death at a rate of μ and also reduced at a rate of γ_2, as individuals move from $I_N(t)$ to $R(t)$ at a rate of γ_2. Vaccinated individuals enter into the class $R(t)$ at a rate of $\xi v\pi$ and individuals from the treatment class enter into the same class at a rate of γ_2. Recovered class of populations $(R(t))$ are reduced at a rate of μ (natural mortality rate). Combining all the aforementioned assumption and definitions, the model becomes:

$$\frac{dS}{dt} = (1 - \xi)v\pi + \gamma_1 C - (\lambda + \mu)S,$$

$$\frac{dC}{dt} = \lambda S - (\mu + \gamma_1 + p\alpha + (1 - p)\alpha)C,$$

$$\frac{dI_N}{dt} = p\alpha C - (\mu + \gamma_2)I_N, \qquad (2)$$

$$\frac{dI_S}{dt} = (1 - p)\alpha C - (\mu + \mu_1 + \sigma)I_S,$$

$$\frac{dT}{dt} = \sigma I_S - (\mu + \gamma_2)T,$$

$$\frac{dR}{dt} = \gamma_2 I_N + \xi v\pi + \gamma_2 T - \mu R.$$

III. Positivity and Boundedness of Solution:

Lemma 1. The region $\boldsymbol{\Omega} = \{(\boldsymbol{S}, \boldsymbol{C}, \boldsymbol{I_N}, \boldsymbol{I_S}, \boldsymbol{T}, \boldsymbol{R}) \in \mathbb{R}_+^6 : \boldsymbol{S} + \boldsymbol{C} + \boldsymbol{I_N} + \boldsymbol{I_S} + \boldsymbol{T} + \boldsymbol{R} \le \frac{v\pi}{\mu}\}$ is positively invariant and attracting with respect to the basic model (2).

Proof: Adding all the equations in the model, gives:

$$\frac{dN}{dt} = (1 - \xi)v\pi - \mu N - \mu_1 I_S + \xi v\pi \qquad (3)$$

Since $\frac{dN}{dt} < v\pi - \mu N$, it follows that $\frac{dN}{dt} < 0 \; if \; N > \frac{v\pi}{\mu}$. Thus a standard comparison theorem [8] can be used to show that $N(t) \le N(0)exp^{-\mu t} + \frac{v\pi}{\mu}[1 - exp^{-\mu t}]$. In particular, $N(t) \le \frac{v\pi}{\mu}$ if $N(0) \le \frac{v\pi}{\mu}$. Hence, $\boldsymbol{\Omega}$ is positively invariant. Further if $N(t) > \frac{v\pi}{\mu}$ then either the solution enter $\boldsymbol{\Omega}$ in finite time or $\boldsymbol{N(t)}$ approaches $\frac{v\pi}{\mu}$ and the infected variable $C(t), \boldsymbol{I_N(t)}, \boldsymbol{I_S(t)}$ approaches zero. Therefore, $\boldsymbol{\Omega}$ is attracting. Thus in $\boldsymbol{\Omega}$ the model (2) is well-posed epidemiologically and mathematically[2]. Therefore it is sufficient to study the dynamics of the model in $\boldsymbol{\Omega}$.

IV. Disease Free Equilibrium (DFE):

The model (2) has a DFE , which is given by,

$$\boldsymbol{E_0} = (\boldsymbol{S^*}, \boldsymbol{C^*}, \boldsymbol{I_N}^*, \boldsymbol{I_S}^*, \boldsymbol{T^*}, \boldsymbol{R^*})$$

$$= (\frac{(1 - \xi)v\pi}{\boldsymbol{\mu}}, \boldsymbol{0}, \boldsymbol{0}, \boldsymbol{0}, \boldsymbol{0}, \frac{\xi v\pi}{\boldsymbol{\mu}})$$

V. Local Stability of the Disease-Free-Equilibrium point

We calculate the basic reproduction number, which depends on the associated non-negative matrix, $\boldsymbol{F}$, for the new infection terms, and the non- singular M-matrix $\boldsymbol{V}$, for the remaining transfer terms, are given below,

$$F = \begin{bmatrix} \frac{\beta S\theta_1}{N} & \frac{\beta S\theta_2}{N} & \frac{\beta S\eta}{N} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}, V = \begin{bmatrix} k_1 & 0 & 0 & 0 & 0 \\ -k_2 & k_3 & 0 & 0 & 0 \\ -k_4 & 0 & k_5 & 0 & 0 \\ 0 & 0 & -\sigma & k_3 & 0 \\ 0 & -\gamma_2 & 0 & -\gamma_2 & \mu \end{bmatrix} \text{ and}$$

$$FV^{-1} = \begin{bmatrix} \frac{\beta S\eta k_4}{Nk_1 k_5} + \frac{\beta S\theta_1}{Nk_1} + \frac{k_2\beta S\theta_2}{Nk_1 k_3} & \frac{\beta S\theta_2}{Nk_3} & \frac{\beta S\eta}{Nk_5} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

Where $k_1 = \mu + \gamma_1 + p\alpha + (1-p)\alpha$, $k_2 = p\alpha$, $k_3 = \mu + \gamma_2$, $k_4 = (1-p)\alpha$, $k_5 = \mu + \mu_1 + \sigma$

The associated basic reproduction number , denoted by, $\mathcal{R}_0$, is then given by, $\mathcal{R}_0 = \rho(FV^{-1})$, where ρ is the spectral radius of FV^{-1}. It follows that

$$\mathcal{R}_0 = \frac{\beta S(\eta k_3 k_4 + k_3 k_5 \theta_1 + k_2 k_5 \theta_2)}{Nk_1 k_3 k_5}$$

Lemma 2[4]: The DFE, E_0, of the system (2), is locally-asymptotically stable (LAS) if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$.

The threshold quantity, $\mathcal{R}_0$, measures the average number of secondary cases generated by a single infected individual in a completely susceptible population [6].

VI. Global Stability of the DFE of Model (2)

Theorem 1: The DFE, E_0, of the model (2), is globally asymptotically stable (GAS) in Ω if $\mathcal{R}_0 < 1$.
Proof: Consider the lyapunov function

$$\mathcal{F} = f_1 C + f_2 I_N + f_3 I_S$$

Where

$$f_1 = \frac{\eta k_3 k_4 + k_3 k_5 \theta_1 + k_2 k_5 \theta_2}{\eta k_1 k_3}$$

$$f_2 = \frac{k_5 \theta_2}{\eta k_3},$$
$$f_3 = 1$$

withLyapunov derivative given by (where a dot represents differentiation with respect to *t*)

$$\dot{\mathcal{F}} = f_1 \dot{C} + f_2 \dot{I_N} + f_3 \dot{I_S}$$

$$= \frac{\eta k_3 k_4 + k_3 k_5 \theta_1 + k_2 k_5 \theta_2}{\eta k_1 k_3}\left[\frac{\beta S(\theta_1 C + \theta_2 I_N + \eta I_S)}{N} - k_1 C\right] + \frac{k_5 \theta_2}{\eta k_3}(k_2 C - k_3 I_N) + k_4 C - k_5 I_S$$

$$= \frac{\beta S(\eta k_3 k_4 + k_3 k_5 \theta_1 + k_2 k_5 \theta_2)k_5 N}{\eta k_1 k_3 k_5 NS\beta}\left[\frac{\beta S(\theta_1 C + \theta_2 I_N + \eta I_S)}{N} - k_1 C\right] + \frac{k_5 \theta_2}{\eta k_3}(k_2 C - k_3 I_N) + k_4 C - k_5 I_S$$

$$= \frac{\mathcal{R}_0 k_5}{\eta}(\theta_1 C + \theta_2 I_N + \eta I_S) - \frac{\mathcal{R}_0 k_5 Nk_1 C}{\beta \eta S} + \frac{k_2 k_5 \theta_2 C}{\eta k_3} + k_4 C - \frac{k_5 \theta_2 I_N}{\eta} - k_5 I_S$$

$$= \frac{k_5 \theta_1 C}{\eta}(\mathcal{R}_0 - 1) + \frac{\theta_2 I_N k_5}{\eta}(\mathcal{R}_0 - 1) + k_5 I_S(\mathcal{R}_0 - 1)$$

Thus, $\dot{\mathcal{F}} < 0$ if $\mathcal{R}_0 < 1$ with $\dot{\mathcal{F}} = 0$ if and only if $C = I_N = I_S = 0$ and $\mathcal{R}_0 = 1$. It follows, from the Lasalle Invariance Principle [7] that $C \to 0, I_N \to 0$ and $I_S \to 0$ as $t \to \infty$ (i.e., the disease dies out). Thus (C, I_N, I_S)=(0,0,0) as $t \to \infty$. That is the disease will be eliminated. Now, from the first and sixth equations of the model with $C = I_N = I_S = T = 0$, it follows that $S \to S^*$ and $R \to R^*$ as $t \to \infty$.
Thus, $\lim_{t\to\infty}(S, C, I_N, I_S, T, R) = (S^*, 0,0,0,0, R^*) = E_0$ for $\mathcal{R}_0 \le 1$. Therefore the DFE, E_0 is GAS in Ω if $\mathcal{R}_0 \le 1$.
Epidemiological significance of the above theorem is that the meningitis disease will be eliminated permanently from the community if we can reduce the threshold quantity ($\mathcal{R}_0$) to less than one.

Table 1. Description of variables of the model(2)

Variables	Descriptions
$S(t)$	Susceptible population
$C(t)$	HIV positive individuals
$I_N(t)$	AIDS class of individuals
$I_S(t)$	Diabetic class of individuals
$T(t)$	Treatment class of individuals
$R(t)$	Treatment class of individuals

Table 2. Description of the parameters of the model(2)

Parameter	Description
π	Recruitment rate of humans
β	Effective contact rate
σ	Treatment rate
η	Modification parameter
θ_1	Modification parameter
θ_2	Modification parameter
ν	Proportion of unvaccinated individuals.
ξ	Vaccination efficacy
α	Infection rate of carriers
p	Fraction of carriers
γ_2	Recovery rate
μ	Natural mortality rate
μ_1	Disease induced mortality rate
γ_1	Rate at which carriers return to susceptible class

VII. Numerical Simulations and Discussions:

Different parameter values are used to simulate the model (2). Figure (1) indicates that if the vaccination efficacy ξ and the treatment rate σ increases then the total number of infected human population decreases rapidly ($\mathcal{R}_0 < 1$). Figure (2) and (3) presents that if the treatment rate σ decreases then the total number of infected human population increases rapidly ($\mathcal{R}_0 > 1$) and the disease burden will increases. Figure (4) presents that if the effective contact rate β increases then the total number of infected human population increases rapidly ($\mathcal{R}_0 > 1$) and the disease burden will increases.
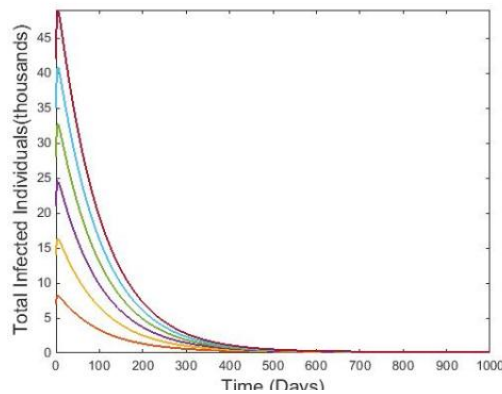

Figure 1: Simulations of the model (2) showing the total number of infected human population as a function of time. Here $\mathcal{R}_0 =0.7193, \xi = 0.81, \sigma = 0.73, \pi = 0.12, p = 0.32$
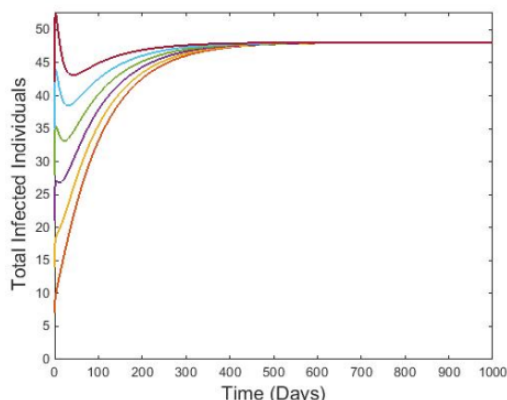
Figure 2: Simulations of the model (2) showing the total number of infected human population as a function of time. Here $\mathcal{R}_0$ =2.238, $\xi = 0.15, \sigma = 0.59, \pi = 0.12, p = 0.48$
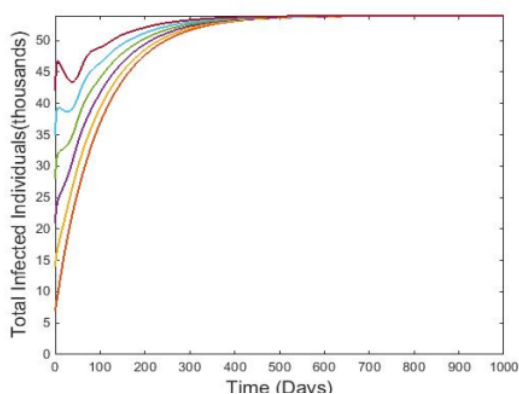

Figure 3: Simulations of the model (2) showing the total number of infected human population as a function of time. Here $\mathcal{R}_0$ =2.6612, $\xi = 0.15, \sigma = 0.24, \pi = 0.12, p = 0.48$

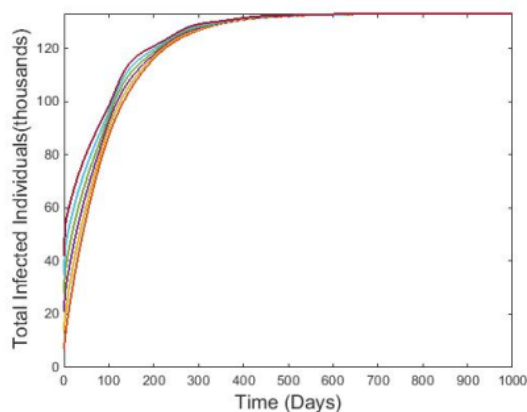**Figure 4**: Simulations of the model (2) showing the total number of infected human population as a function of time. Here $\mathcal{R}_0$ =3.6913, $\xi = 0.15, \sigma = 0.24, \pi = 0.12, p = 0.48, \beta = 0.62$

VIII. Conclusion

In summary, the main findings are given below:

(i)   Reduction of the effective contact rate (β) can reduce the disease burden .

(ii)   Increasing the treatment rate (σ) and vaccination efficacy rate (ξ), disease elimination is possible.

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