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A MATHEMATICAL MODEL FOR CO-DYNAMICS OF LISTERIOSIS AND BACTERIAL MENINGITIS DISEASES

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Abstract. The co-infection of Listeriosis and Meningitis in humans is a public health burden globally with its endemicity mostly felt in the tropical and sub-tropical countries. In this study, we develop a novel deterministic model describing the Listeriosis-Meningitis co-infection dynamics. Two sub-models, namely the Listeriosis-only and Meningitis-only sub-models are presented and analysed. Mathematical analysis of each sub-model is carried out, as well as that of the co-infection model. We use Latin-hypercube sampling to determine the parameters affecting the severity of the infection co-dynamics. Results from the numerical simulations suggest that reduction in the Listeria pathogens in the environment and an increase in the Meningitis recovery rate decreases the rate of Listeriosis-Meningitis co-infections.

Keywords: Listeriosis-Meningitis model; co-infection; basic reproduction number; numerical simulation.

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1. INTRODUCTION

Listeriosis is a serious food-borne bacteria infection in humans, plants and animals, caused by the bacterium *Listeria monocytogene (L. monocytogene)* [1]. There are five strains of the bacterium, namely: Listeria innocua, Listeria seeligeri, Listeria welshimeri, Listeria ivanovii and Listeria monocytogenes which is the only strain that is pathogenic to both humans and animals. The food-borne pathogen L. Monocytogene survives and grows in environments with temperatures ranging from $30^{\circ}C$ to $37^{\circ}C$ and even in refrigerated environments with temperatures of as low as $4^{\circ}C$ [2]. Its primary habitats are soil and water, and it is transmitted to humans and animals by consumption of contaminated ready-to-eat (RTE) food products such as polony, cheese, ham, meat, raw milk, processed meats, fresh and frozen poultry, fresh produce including fruits and vegetables. After consumption, the bacteria enter the gastrointestinal tract and counteract changes in acidity, osmolarity, oxygen tension, or the challenging effects of antimicrobial peptides and bile [3]. It then crosses the epithelium barrier of the infected individual through the transcytosis and invades the mesenteric lymph nodes into the blood [4]. In pregnant women, the bacteria are transmitted to the foetus either during delivery or through the placenta, which can lead to premature labour, death of the newborn babies, serious illness, Meningitis, miscarriages, and stillbirth [5].

Bacterial Meningitis (BACMEN) is a disease that causes inflammation of the meninges (membranes that surround the spinal cord and the brain) and its causative agents are bacteria such as Listeria monocytogenes, Streptococcus pneumonia, Group B Streptococcus, Neisseria meningitides, and Haemophilias influenza. The disease is more common in children and young adults. It is transmitted through contact with infected an individual and it easily spreads in communities/societies in which people live in close quarters (e.g. police staff, college students, military staff, and prisons). Once infected, the bacteria attacks the brain of the individuals and infected individuals usually have the following symptoms: intense headache and fever, vomiting, sensitivity to light, and stiff neck, which result in convulsion, delirium, and death [6]. In fact, it is estimated that meningococcal Meningitis causes over 10,000 deaths annually in Sub-Saharan Africa [8]. Infections from BACMEN can cause permanent disabilities such as brain damage,

hearing loss, and learning disabilities [7]. BACMEN can be prevented by vaccination or avoiding contact with infected individuals, but vaccination is the most effective mode of prevention, especially in children.

Since both Listeriosis and BACMEN are caused by the L. Monocytogene bacteria, there is a possibility of people being infected by both diseases simultaneously. Therefore, we are motivated by the quest to understand how these diseases spread in the human population and to understand the best prevention or control programs that can be implemented in communities in which individuals are infected with both diseases.

In recent times, mathematical models have been widely used in the study of infectious diseases and their transmission dynamics. Many mathematical models have been developed to understand the transmission dynamics of Listeriosis [2,9–11] and Meningitis [12–16,20]. Nevertheless, none of these considered the co-infection dynamics of Listeriosis and BACMEN. In this paper, we develop a model to study the transmission dynamics of the Listeriosis-BACMEN co-infection, as well as the effects of the co-infection in humans.

The remainder of the paper is organized as follows: Section 1 is the introduction and in Section 2 we give a brief description of the Listeriosis-Meningitis co-infection model. In Section 3 we present sub-model analysis with their basic reproductive numbers, using the next generation matrix approach. In Section 4, we give the basic properties and analysis of the co-infection model with the respective stability analysis of the equilibrium points. Numerical simulations are done in Section 5. Finally in Section 6 we give a brief discussion and conclusions regarding the obtained results.

2. CO-INFECTION MODEL

The diseases under study sub-divides the human population into epidemiological compartments. The total human population is denoted by $N = S+C_M+I_M+I_L+I_{LM}+R_M+R_L+R_{LM}$, where S represents the susceptible humans, C_M represents Meningitis asymptomatic individuals, I_L, denotes the Listeriosis symptomatic, I_M denotes the Meningitis symptomatic individuals and I_{LM} represents individuals infected with both Listeriosis and bacterial Meningitis. R_M, R_L and R_{LM} consists of individuals who have recovered from Meningitis only, Listeriosis only and

from the coinfection respectively, while $L(t)$ denotes the Listeria contaminated environment. Individuals are recruited into the susceptible class at a rate Λ. Susceptible individuals becomes infected with Listeriosis and Meningitis at rates λ_L and λ_M respectively. Meningitis carriers become infectious at a rate α_M or recover at rate ω_M or die from natural causes at a rate μ. The Listeriosis and Meningitis infected individuals may become coinfected at rates ρ_L and ρ_M or recover at rates σ_L and σ_M respectively and become susceptible again. The coinfected can also recover at a rate σ_{LM} and become susceptible or die from the coinfection at a rate δ_{LM}. δ_L and δ_M are the Listerisois and Meningitis related death rates while γ and ε are the rates of removal of the pathogens in the environment by death and environmental hygiene respectively.

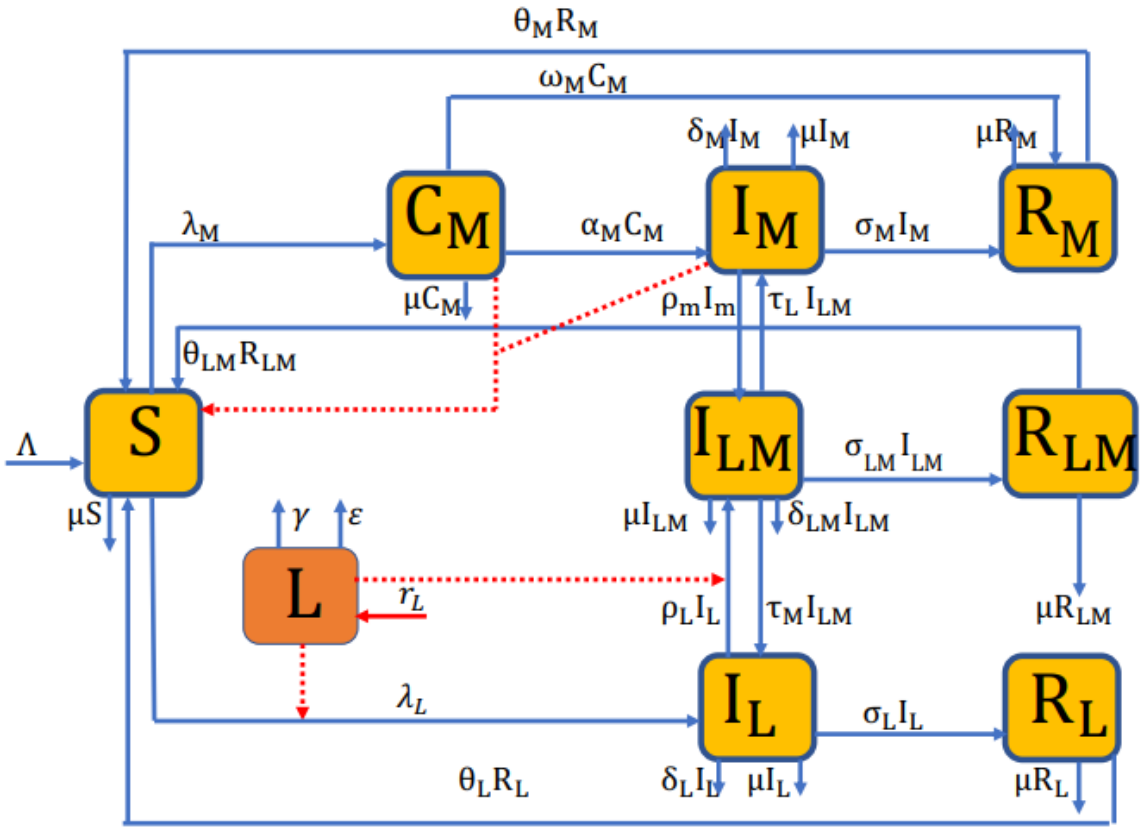


Figure 1. Listeriosis-Meningitis model diagram. The solid arrows represent transmissions from one compartment to another, while the dotted arrows represent the effects on the transmission arrows.

Combining the model Figure 1, assumptions, parameters and the model formulation description, gives the non-linear system of ordinary differential equations for Listeriosis-Meningitis co-infection in the human population is given by:

$$
\left\{
\begin{aligned}
\frac{dS}{dt} &= \Lambda + \theta_M R_M + \theta_L R_L + \theta_{LM} R_{LM} - (\lambda_L + \lambda_M + \mu)S, \\
\frac{dC_M}{dt} &= \lambda_M S - (\alpha_M + \omega_M + \mu)C_M, \\
\frac{dI_M}{dt} &= \alpha_M C_M + \tau_L I_{LM} - (\sigma_M + \rho_M + \delta_M + \mu)I_M, \\
\frac{dR_M}{dt} &= \sigma_M I_M + \omega_M C_M - (\theta_M + \mu)R_M, \\
\frac{dI_L}{dt} &= \lambda_L S + \tau_M I_{LM} - (\sigma_L + \rho_L + \delta_L + \mu)I_L, \\
\frac{dR_L}{dt} &= \sigma_L I_L - (\theta_L + \mu)R_L, \\
\frac{dI_{LM}}{dt} &= \rho_L I_L + \rho_M I_M - (\delta_{LM} + \tau_L + \tau_M + \sigma_{LM} + \mu)I_{LM}, \\
\frac{dR_{LM}}{dt} &= \sigma_{LM} I_{LM} - (\theta_{LM} + \mu)R_{LM}, \\
\frac{dL}{dt} &= r_L L\left(1 - \frac{L}{K_L}\right) - (\varepsilon + \gamma)L,
\end{aligned}
\right. \tag{1}
$$

where

$$
\lambda_M = \frac{\beta\left(I_M + \eta_1 I_{LM} + \eta_2 C_M\right)}{N} \quad \text{and} \quad \lambda_L = \beta_L L,
$$

subject to the initial conditions

(2)

$$
S(0) > 0, C_M(0) > 0, I_M(0) \geq 0, I_L(0) > 0, I_{LM}(0) \geq 0, R_L(0) \geq 0, R_M(0) \geq 0, R_{LM}(0) \geq 0, L(0) \geq 0.
$$

All parameters for model system (1) are assumed to be non-negative for all $t > 0$. We assume that upon infection no susceptible individual will directly enter the class I_{LM} but rather, we consider the class I_{LM} as a result of progression from either the class; I_L or I_M.

3. CO-INFECTION MODEL PROPERTIES

Here, we show that the model is bounded and dissipative.

3.1. Positivity of solutions. We show that model system (1) has positive solutions subject to the initial conditions by applying the following Lemma as in [17].

Lemma 1. *Suppose $\Omega \subset \mathbb{R} \times C^n$ is open, $f_i \in C(\Omega, \mathbb{R}), i = 1, 2, \ldots, n$. If*

$$f_i|_{x_i(t)=0, X_t \in C^n_{0+}} \geq 0,\ X_t = (x_{1t}, \cdots, x_{nt})^T\ i = 1, 2, \cdots, n,$$

then C^n_{+0} is the invariant domain of the following equations

$$\dot{x}_i(t) = f_i(t, X_t),\ t \geq \sigma,\ i = 1, 2, \cdots, n. \tag{3}$$

If $f_i|_{x_i(t)=0, X_t \in C^n_{-0}} \leq 0,\ X_t = (x_{1t}, \cdots, x_{nt})^T\ i = 1, 2, \cdots, n$, then C^n_{-0} is the invariant domain of equations (3).

We have the following Theorem on the invariance of model equation (1).

Theorem 1. *The solutions $\Big(S(t),\ C_M(t),\ I_L(t),\ I_M(t),\ R_M(t),\ R_L(t),\ I_{LM}(t),\ R_{LM}(t),\ L(t)\Big)$ of the model system (1) with the positive initial conditions (2) is positive for all $t > 0$.*

Proof. Let $X = \Big(S(t),\ C_M(t),\ I_L(t),\ I_M(t),\ R_M(t),\ R_L(t),\ I_{LM}(t),\ R_{LM}(t),\ L(t)\Big)$ and

$$g(X) = \Big(g_1(X),\ g_2(X),\ g_3(X),\ g_4(X),\ g_5(X),\ g_6(X),\ g_7(X),\ g_8(X),\ g_9(X)\Big)^T,$$

then we can re-write the model system (1) as follows $\dot{X} = g(X)$ where

$$g(X) = \begin{pmatrix} g_1(X) \\ g_2(X) \\ g_3(X) \\ g_4(X) \\ g_5(X) \\ g_6(X) \\ g_7(X) \\ g_8(X) \\ g_9(X) \end{pmatrix} = \begin{pmatrix} \Lambda - (\lambda_L + \lambda_M + \mu)S, \\ \lambda_M - (\mu + \alpha_M + \omega_M)C_M \\ \alpha_M C_M + \tau_L I_{LM} - (\sigma_M + \rho_M + \delta_M + \mu)I_M \\ \sigma_M I_M + \omega_M C_M - (\theta_M + \mu)R_M \\ \lambda_L S + \tau_M I_{LM} - (\sigma_L + \rho_L + \delta_L + \mu)I_L, \\ \sigma_L I_L - (\theta_L + \mu)R_L, \\ \rho_L I_L + \rho_M I_M - (\delta_{LM} + \tau_L + \tau_M + \sigma_{LM} + \mu)I_{LM}, \\ \sigma_{LM} I_{LM} - (\theta_{LM} + \mu)R_{LM}, \\ r_L L\big(1 - \frac{L}{K_L}\big) - (\mu + \varepsilon) \end{pmatrix}. \tag{4}$$

From (4), setting all the classes to zero, we have that

$$\begin{aligned}
\tfrac{dS(t)}{dt}|_{S=0} &= \Lambda + \theta_M R_M > 0,\ \tfrac{dC_M(t)}{dt}|_{C_M=0} = \lambda_M > 0, \\
\tfrac{dI_M(t)}{dt}|_{I_M=0} &= \alpha_M C_M + \tau_L I_{LM} > 0,\ \tfrac{dR_M(t)}{dt}|_{R_M=0} = \sigma_M I_M + \omega_M C_M > 0, \\
\tfrac{dL_L(t)}{dt}|_{I_L=0} &= \lambda_L S + \tau_M I_{ML} > 0,\ \tfrac{dR_L(t)}{dt}|_{R_L=0} = \sigma_L I_L > 0, \\
\tfrac{dI_{LM}(t)}{dt}|_{I_{LM}=0} &= \rho_L I_L + \rho_M I_M > 0,\ \tfrac{dR_{LM}(t)}{dt}|_{R_{LM}=0} = \sigma_{LM} I_{LM} > 0, \\
\tfrac{dL(t)}{dt}|_{L=0} &= -(\mu + \varepsilon) < 0.
\end{aligned}$$

Thus, it follows that from Lemma 1 that $\mathbb{R}^9_+$ is an invariant set and is positive. □

3.2. Uniqueness of solutions. We now show that the solutions of systems (1) are bounded. We thus have the following result.

Theorem 2. *The solutions of model system (1) are contained in the region* $\Omega \in \mathbb{R}^9_+$, *which is given by*

$$\Omega = \left\{ \Big(S(t),\, C_M(t),\, I_L(t),\, I_M(t),\, R_M(t),\, R_L(t),\, I_{LM}(t),\, R_{LM}(t),\, L(t)\Big) \in \mathbb{R}^9_+ : 0 \le N \le \frac{\Lambda}{\mu},\, 0 \le L \le K_L \right\},$$

for the initial conditions (2) in Ω.

Proof. Total change in human population is given by

$$\frac{dN}{dt} \le \Lambda - \mu N, \tag{5}$$

whose solutions of yields

$$N(t) \leq \frac{\Lambda}{\mu} - \left(\frac{\Lambda}{\mu} - N_0\right) e^{-\mu t}$$

for $N_0 = N(0)$. Also, from the last equation of (1), we have that

$$\frac{dL}{dt} \leq r_L \left(1 - \frac{L}{K_L}\right) L,$$

whose solution gives

$$L(t) \leq \frac{L(0) K_L e^{r_L t}}{K_L - L(0) + L(0) e^{r_L t}},$$

$$L(t) \leq \frac{L(0) K_L}{L(0) + K_L e^{-r_L t} - L(0) e^{-r_L t}}.$$

As t tends to infinity, $L(t)$ tends to K_L. The region Ω is thus positively-invariant. □

4. Sub-model Analysis

4.1. Listeriosis only model analysis.

The Listeriosis only sub-model is given by

$$\begin{cases} \dfrac{dS}{dt} = \Lambda + \theta_L R_L - (\mu + \beta_L L) S, \\ \dfrac{dI_L}{dt} = \beta_L L S - l_{g1} I_L, \\ \dfrac{dR_L}{dt} = \sigma_L I_L - l_{g2} R_L, \\ \dfrac{dL}{dt} = r_L L \left(1 - \dfrac{L}{K_L}\right) - l_{g3} L, \end{cases} \tag{6}$$

where $l_{g1} = \sigma_L + \delta_L + \mu$, $\quad l_{g2} = \theta_L + \mu$ and $l_{g3} = \varepsilon + \gamma$.

4.1.1. *The reproduction number for the Listeriosis only model.*

The disease-free equilibrium point for the Listeriosis only sub-model is given by $E_L^* = \left(\dfrac{\Lambda}{\mu},\ 0,\ 0,\ 0\right)$. Following the next generation matrix approach method by van den Driessche and Watmough [19], we obtain the

transition matrices for the rate of appearance of new infections and the net rate out of the matrices for the Listeriosis only sub-model as

$$F = \begin{pmatrix} \beta_L & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} l_{g3} - r_L & 0 & 0 \\ 0 & l_{g1} & 0 \\ 0 & -\sigma_L & l_{g2} \end{pmatrix}.$$

The reproduction number for the Listeriosis only sub-model ($\mathscr{R}_0^L$) is the spectral radius of the next generation matrix FV^{-1}. Thus,

$$\mathscr{R}_0^L = \frac{\beta_L}{l_{g3} - r_L}.$$

Note that, the existence of $\mathscr{R}_0^L$ is subject to $l_{g3} > r_L$. We call $\mathscr{R}_0^L$ the contamination threshold caused by Listeria from the environment, which is equivalent to reproduction number in epidemiology as defined in [18].

4.1.2. *The endemic equilibrium for the Listeriosis only model.* The endemic equilibrium point for the Listeriosis only sub-model is given by $E_L^{**} = (S^{**}, I_L^{**}, R_L^{**}, L^{**})$ where

$$\begin{aligned} S^{**} &= \frac{\Lambda l_{g1} l_{g2} r_L}{l_{g1} l_{g2} \left(k_L \beta_L \left(r_L - l_{g3}\right) + \mu r_L\right) + k_L \beta_L \theta_L \sigma_L \left(l_{g3} - r_L\right)}, \\ I_L^{**} &= \frac{\Lambda l_{g2} k_L \beta_L \left(l_{g3} - r_L\right)}{k_L \beta_L \theta_L \sigma_L \left(r_L - l_{g3}\right) - l_{g1} l_{g2} \left(k_L \beta_L \left(r_L - l_{g3}\right) + \mu r_L\right)}, \\ R_L^{**} &= \frac{\Lambda k_L \beta_L \sigma_L \left(r_L - l_{g3}\right)}{l_{g1} l_{g2} \left(k_L \beta_L \left(r_L - l_{g3}\right) + \mu r_L\right) + k_L \beta_L \theta_L \sigma_L \left(l_{g3} - r_L\right)}, \\ L^{**} &= k_L \left(1 - \frac{l_{g3}}{r_L}\right). \end{aligned} \tag{7}$$

It can be observed in equation (7) that, the existence of E_L^{**} is subject to $\mathscr{R}_0^L > 1$.

4.2. Meningitis only model analysis. The Meningitis only sub-model is given by

$$
\begin{cases}
\dfrac{dS}{dt} = \Lambda + \theta_M R_M - (\mu + \lambda_M)S, \\[2ex]
\dfrac{dC_M}{dt} = \lambda_M S - m_{g1} C_M, \\[2ex]
\dfrac{dI_M}{dt} = \alpha_M C_M - m_{g2} I_M, \\[2ex]
\dfrac{dR_M}{dt} = \sigma_M I_M + \omega_M C_M - m_{g3} R_M,
\end{cases} \tag{8}
$$

where $N_M = S + C_M + I_M + R_M$, $\lambda_M = \dfrac{\beta_M \left(I_M + \eta_2 C_M \right)}{N_M}$, $m_{g1} = (\mu + \alpha_M + \omega_M)$, $m_{g2} = (\mu + \sigma_M + \delta_M)$ and $m_{g3} = \mu + \theta_M$.

4.2.1. *The reproduction number for the Meningitis only model.* The disease-free equilibrium for the Meningitis only is given by, $E_M^* = \left(\dfrac{\Lambda}{\mu},\ 0,\ 0,\ 0 \right)$. We use the next generation matrix approach in [19] to determine the reproduction number $(\mathscr{R}_0^M)$ for the Meningitis only sub-model. Here, the transition matrices for the rate of appearance of new infections and the net rate out of the matrices are respectively given by

$$
F = \begin{pmatrix} \beta_M \eta_2 & \beta_M & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \qquad \text{and} \qquad V = \begin{pmatrix} m_{\mathrm{g1}} & 0 & 0 \\ -\alpha_M & m_{\mathrm{g2}} & 0 \\ -\omega_M & -\sigma_M & m_{\mathrm{g3}} \end{pmatrix}.
$$

The spectral radius is the maximum eigenvalue of the next generation matrix and is given by

$$
\mathscr{R}_0^M = \mathscr{R}_0^{C_M} + \mathscr{R}_0^{I_M} \quad \text{where} \quad \mathscr{R}_0^{C_M} = \frac{\eta_2 \beta_M}{m_{\mathrm{g1}}} \quad \text{and} \quad \mathscr{R}_0^{I_M} = \frac{\alpha_M \beta_M}{m_{\mathrm{g1}} m_{\mathrm{g2}}}.
$$

We represent $\mathscr{R}_0^M$ as a sum of two sub-reproduction numbers $\mathscr{R}_0^{C_M}$ and $\mathscr{R}_0^{I_M}$ showing the contribution of individuals in classes C_M and I_M respectively.

4.2.2. *The endemic equilibrium for the Meningitis only model.* The endemic equilibrium for the Meningitis only sub-model $E_M^{**} = (S^{**},\ C_M^{**},\ I_M^{**},\ R_M^{**})$ is obtained by setting the left hand

side of system (8) to zero. Thus, we solve the following system of equations:

$$\begin{cases} 0 = \Lambda + \theta_M R_M^* - (\mu + \lambda_M^*) S^*, \\ 0 = \lambda_M^* S^* - m_{g1} C_M^*, \\ 0 = \alpha_M C_M^* - m_{g2} I_M^*, \\ 0 = \sigma_M I_M^* + \omega_M C_M^* - m_{g3} R_M^*. \end{cases} \tag{9}$$

From the second, third and last equation of system (9) we express S^*, C_M^* and R_M^* in terms of I_M^* as follows:

$$\begin{aligned} S^{**} &= \frac{m_{\mathrm{g1}} m_{\mathrm{g2}} \mathrm{I}_M^* \left(m_{\mathrm{g2}} \left(m_{\mathrm{g3}} + \omega_M \right) + \alpha_M \left(m_{\mathrm{g3}} + \sigma_M \right) \right)}{m_{\mathrm{g3}} \alpha_M \left(\beta_M \left(\eta_2 m_{\mathrm{g2}} + \alpha_M \right) - m_{\mathrm{g1}} m_{\mathrm{g2}} \right)}, \\ C_M^{**} &= \frac{m_{\mathrm{g2}} \mathrm{I}_M^*}{\alpha_M}, \qquad R_M^{**} = \frac{\mathrm{I}_M^* \left(m_{\mathrm{g2}} \omega_M + \alpha_M \sigma_M \right)}{m_{\mathrm{g3}} \alpha_M}. \end{aligned} \tag{10}$$

Substituting expressions for S^*, C_M^* and R_M^* in (10) into the first equation of system (9) and solving for I_M^* gives $I_M^* = 0$ which corresponds to the Meningitis-free equilibrium or

$$I_M^{**} = \frac{\mathscr{L}_1}{\mathscr{L}_2} \tag{11}$$

where $\mathscr{L}_1 = \Lambda m_{\mathrm{g3}} \alpha_M \left(\beta_M \left(\eta_2 m_{\mathrm{g2}} + \alpha_M \right) - m_{\mathrm{g1}} m_{\mathrm{g2}} \right)$ and
$\mathscr{L}_2 = m_{\mathrm{g1}} m_{\mathrm{g2}} \left(m_{\mathrm{g2}} \left(m_{\mathrm{g3}} \left(\mu + \eta_2 \beta_M \right) + \omega_M \left(\mu + \theta_M \right) \right) + \alpha_M \Upsilon_0 \right) - m_{\mathrm{g1}}^2 m_{\mathrm{g2}}^2 m_{\mathrm{g3}} - \beta_M \theta_M \Upsilon_1$, for $\Upsilon_0 = \left(m_{\mathrm{g3}} \left(\mu + \beta_M \right) + \sigma_M \left(\mu + \theta_M \right) \right)$ and $\Upsilon_1 = \left(\eta_2 m_{\mathrm{g2}} + \alpha_M \right) \left(m_{\mathrm{g2}} \omega_M + \alpha_M \sigma_M \right)$. Thus, substituting I_M^* in (11) into expressions for S^*, C_M^* and R_M^* in (10) we obtain the Meningitis-endemic equilibrium $E_M^{**} = (S^{**}, C_M^{**}, I_M^{**}, R_M^{**})$. We have the following result on the existence of the Meningitis-endemic equilibrium.

Theorem 3. *The Meningitis only sub-model has a unique endemic equilibrium point* $E_M^* = (S^{**}, C_M^{**}, I_M^{**}, R_M^{**})$.

4.3. Listeriosis-Meningitis co-infection model. We consider the Listeriosis-Meningitis co-infection model given by (1).

4.3.1. *The reproduction number for the Listeriosis-Meningitis co-infection model.* The Listeriosis-Meningitis co-infection model system (1) has a disease-free equilibrium given by,

$$E^0 = \left(S^0,\, C_M^0,\, I_M^0,\, R_M^0, L^0,\, I_L^0,\, R_L^0,\, I_{LM}^0,\, R_{LM}^0\right) = \left(\frac{\Lambda}{\mu},\, 0,\, 0,\, 0,\, 0,\, 0,\, 0,\, 0\right).$$

We use the next generation matrix approach in [19] to determine the reproduction number $(\mathscr{R}_0)$ for the Listeriosis-Meningitis co-infection model. The new infections and the transfer matrices are given by

$$F = \begin{pmatrix} \beta_M\eta_2 & \beta_M & 0 & 0 & 0 & 0 & \beta_M\eta_1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_L & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} p_{\mathrm{m1}} & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\alpha_M & p_{\mathrm{m2}} & 0 & 0 & 0 & 0 & -\tau_L & 0 \\ -\omega_M & -\sigma_M & p_{\mathrm{m3}} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & p_{\mathrm{l3}} - r_L & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & p_{\mathrm{l1}} & 0 & -\tau_M & 0 \\ 0 & 0 & 0 & 0 & -\sigma_L & p_{\mathrm{l2}} & 0 & 0 \\ 0 & -\rho_M & 0 & 0 & -\rho_L & 0 & p_{\mathrm{lm1}} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\sigma_{\mathrm{LM}} & p_{\mathrm{lm2}} \end{pmatrix}.$$

The spectral radius is the maximum eigenvalue of the next generation matrix and is given by

$$\begin{aligned} \mathscr{R}_{FH} &= \max\left\{\mathscr{R}_{0F}, \mathscr{R}_{0H}\right\} \qquad \text{where} \\ \mathscr{R}_{0F} &= \frac{\beta_L}{p_{\mathrm{l3}} - r_L} \qquad \text{and} \qquad \mathscr{R}_{0H} = \mathscr{R}_{0H}^{C_M} + \mathscr{R}_{0H}^{I_M} + \mathscr{R}_{0H}^{I_{LM}} \qquad \text{with} \\ \mathscr{R}_{0H}^{C_M} &= \frac{\beta_M\eta_2}{m_{g1}}, \quad \mathscr{R}_{0H}^{I_M} = \frac{\beta_M\alpha_M}{m_{g1}Q_1}, \end{aligned} \tag{12}$$

$$\mathscr{R}_{0H}^{I_{LM}} = \frac{\beta_M\alpha_M\rho_M(Q_1\eta_1 + \tau_L)}{m_{g1}Q_1^2Q_4\left(1 - \Phi_1 - \Phi_2\right)},$$

$m_{g1} = \alpha_M + \omega_M + \mu, Q_1 = \sigma_M + \rho_M + \delta_M + \mu,\ Q_7 = \theta_M + \mu,\ Q_5 = \sigma_L + \rho_L + \delta_L + \mu,$
$Q_3 = \theta_L + \mu, \quad Q_8 = \varepsilon + \gamma,\ Q_4 = \delta_{LM} + \tau_L + \tau_M + \sigma_{LM} + \mu,\ Q_6 = \theta_{LM} + \mu,\ \Phi_1 = \dfrac{\rho_M \tau_L}{Q_4 Q_1},$
$\Phi_2 = \dfrac{\rho_L \tau_M}{Q_5 Q_4}$. $\mathscr{R}_{0F}$ represents the contribution of the Listeria contaminated environment $(L(t))$ in Listeriosis transmission while $\mathscr{R}_{0H}$ is the contribution of human to human Meningitis transmission. The sub-reproduction numbers $\mathscr{R}_{0H}^{C_M}$, $\mathscr{R}_{0H}^{I_M}$ and $\mathscr{R}_{0H}^{I_{LM}}$ show the contribution of individuals in classes C_M, I_M and I_{LM} to Meningitis transmission respectively.

5. Numerical Simulations

5.1. Model parameter values. In this subsection , we carry out numerical simulations using the parameter values given in Table 1. The parameter values were either obtained from existing literature or estimated. We use the following initial conditions $S(0) = 58000, C_M(0) = 2000,$ $I_M(0) = 10000, R_M(0) = 200, I_L = 4000, I_L = 400, R_{LM}(0) = 3500,\ R_{LM} = 350, L(0) = 0.001$ for the numerical simulation and illustrative purposes.

Table 1. Parameter values with $\mathscr{R}_0 = 1.6017$.

Parameter	Symbol	Point-value (day^{-1})	Source
Immigration rate	Λ	680000	Assumed
Mortality rate of humans	μ	0.04	Assumed
Infection rate of co-infection	β	0.8824	Assumed
Listeriosis infection rate	β_L	0.008[0.683]	[2]
Meningitis infection rate	β_M	0.88	[6]
Modification parameter due to I_{ML}	η_1	0.842	Assumed
Modification parameter due to C_M	η_2	[0.2-0.85]0.2	[6]
Growth rate of Listeria	r_L	0.32	[2]
Carrying capacity of Listeria	K_L	0.008[0-1]	[2]
Death rate of Listeria	$g_{l3} = (\gamma + \varepsilon)$	0.25	[2]
Meningitis disease death rate	δ_M	[0.05-0.5]0.0009	[6]
Listeriosis disease death rate	δ_L	0.02/365	[2]
Co-infection disease death rate	δ_{LM}	[0.24-0.62]	[20]
Rate of progression from I_M to I_{LM}	ρ_M	0.055	Assumed
Rate of progression from I_L to I_{LM}	ρ_L	0.0655	Assumed
Meningitis rate of lost of immunity	θ_M	[0.04-2] 0.008	[6]
Listeriosis rate of lose of immunity	θ_L	0.2	[2]
Co-infection rate of lose of immunity	θ_{LM}	0.24	Assumed
Meningitis recovery rate	τ_M	0.005	[6]
Listeriosis recovery rate	τ_L	0.034	[2]
Coinfection recovery rate	τ_{LM}	0.062	Assumed
Rate of progression from I_M to R_M	σ_M	[0.1-0.9]0.004	[6]
Rate of progression from I_L to R_L	σ_L	0.034	[2]
Rate of progression from I_{LM} to R_{LM}	σ_{LM}	0.022	Assumed
Rate of progression from C_M to I_M	α_M	[0.1-0.52] 0.52	[6]
Rate of progression from C_M to R_M	ω_M	[0.06-0.2]0.066	[6]

5.2. Sensitivity analysis. Sensitivity analysis is performed to identify the most influential parameters for the expansion as well as for the control of infection in the community. we use the Latin hypercube sampling scheme/Partial Rank Correlation Coefficient (LHS/PRCC) implemented in Matlab to ascertain the major contributors to the model output in relation to other parameters in the model. We capitalise on the coinfection model reproduction number $R_{OH}^{I_{LM}}$. to serve as a predictor of future outbreaks since it is the average number of secondary infections that an infectious individual introduced in a purely susceptible population may give rise to. To implement LHS, we list all the model parameters, hypothetically providing the range in which parameters' values fall. We sample the parameter space without replacement and run the simulations [21]. In order to have a large sample size and more precise results, we perform a thousand simulations at each run. We then evaluate the partial rank correlation coefficients (PRCC) of the relevant parameters. The Tonardo plot in Figure 2 shows the different parameters and their PRCC's.

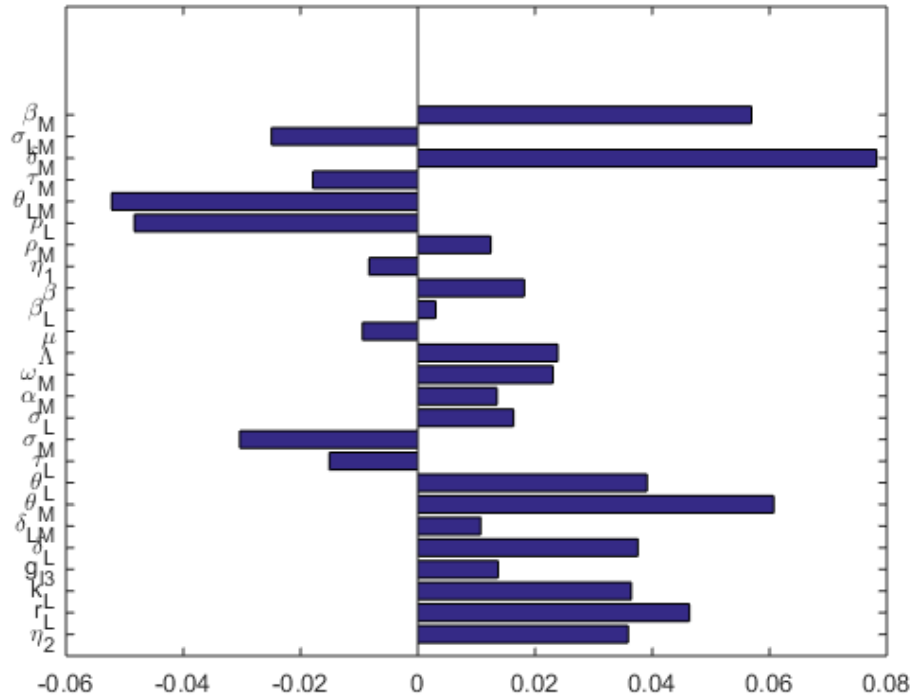
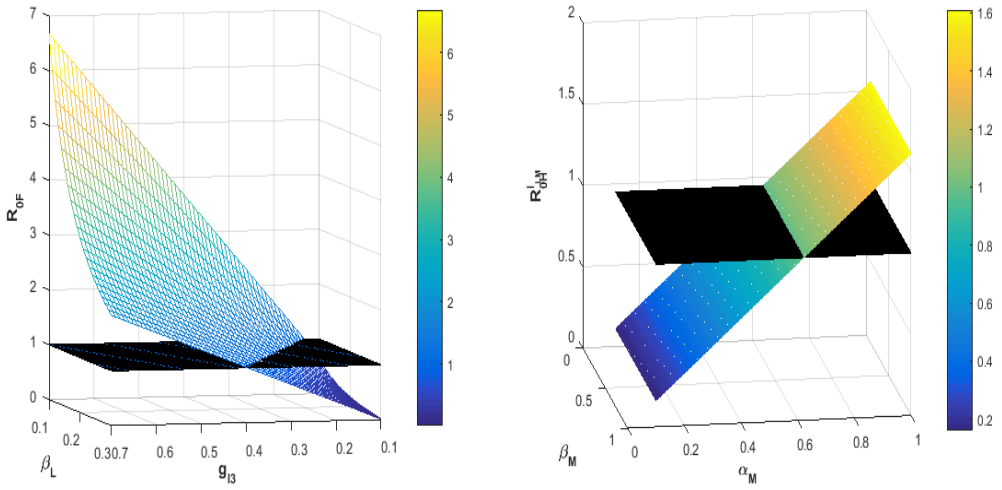


Figure 2. Tornado plot of the model parameters on the co-infection basic reproduction number $(R_{OH}^{I_{LM}})$.

In Figure 2, the parameters that are positively correlated to $R_{OH}^{I_{LM}}$ have great potential in expanding Listeriosis, Meningitis, and their co-infection in the community, because they increase their respective reproduction number, which is the average number of a secondary infection. However, the parameters that are negatively correlated to $R_{OH}^{I_{LM}}$ have a great contribution in controlling the expansion of Listeriosis and Meningitis in the community if their values are increased, keeping other parameters constant.

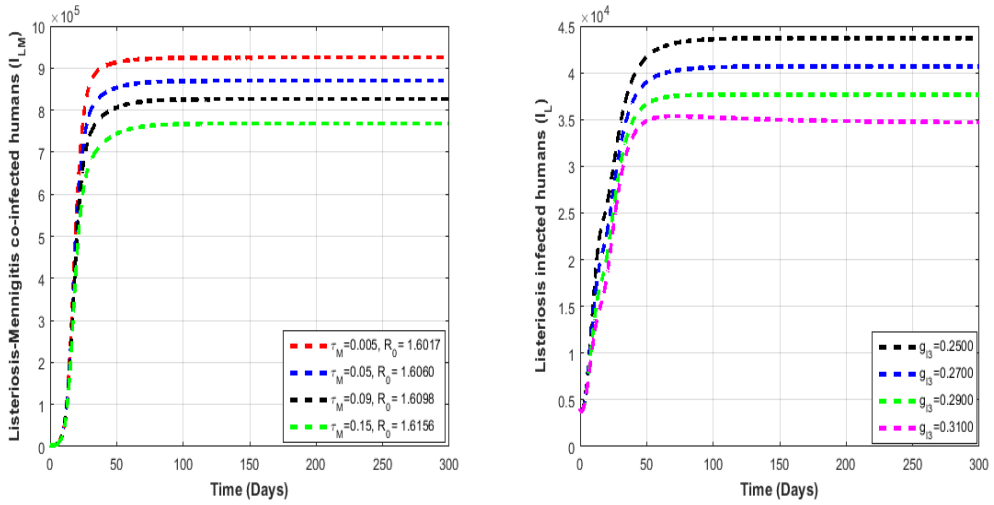
5.3. Simulation results. The values on the R_O^L and $R_{OH}^{I_{LM}}$ axes in Figure 3 are merely arbitrary values that show the relationships between β_l and g_{l3} and between β_M and α_M in Figures 3(a) and 3(b) respectively. Figure 3(a) depicts an increase in the Listeriosis-only reproduction number as more people come in contact with the Listeria pathogens (mainly by consumption of contaminated RTE's). It also shows that an increase in the death rate of listeria (mainly by removal of contaminated food) leads to a decrease in the number of infectious contacts between susceptible humans and the Listeria pathogens, which intend brings down the values of R_O^L, making the disease containment possible in the event of an outbreak.



(a) (b)

Figure 3. 3-D plots of R_O^L as a function of listeria contact rate and death rate of listeria in the environment in (a) and $R_{OH}^{I_{LM}}$ as a function of Meningitis infection rate and (b) the rate of transition from a Meningitis carrier to a Meningitis infectious individuals.

The plot in Figure 4(a) shows that the more Meningitis carriers become infectious, the higher the possibility of both the susceptible individuals and Listeriosis patients becoming infected with Meningitis, thereby increasing in the Meningitis-only, as well as the Meningitis-Listeriosis co-infection reproduction number. Therefore control measures such as early diagnosis and treatment of Meningitis carriers can help to minimise the values of α_M and contain the co-infection.



(a) (b)

Figure 4. (a) The impact of the rate of recovery from Meningitis τ_M on the co-infected population. (b) The impact of the death rate or Listeria, g_{l3} on the infected population.

In Figure 4(a), we observe a steady decrease in the number of Meningitis-Listeriosis co-infected individuals as the rate of recovery from Meningitis τ_M increases. In Figure 4(b), the inverse proportionality between the death rate of Listeria in the environment, g_{l3}, and the Listeriosis infected population shows the importance of the removal of the pathogen from the environment if the disease must be contained. This is justifiable since the main source of the pathogens in this model is RTE foods and food products consumed by humans. Therefore, it is important to implement pathogen removal measures such as proper hygiene in food processing plants, proper cooking of meat and meat products before consumption to facilitate disease control and eradication.

6. CONCLUSIONS

A mathematical model of the co-infection of Listeriosis-Meningitis is presented and analysed. We used mathematical analysis to investigate the boundedness of the model systems and calculate the steady states and the basic reproduction number of each sub-model. Numerical simulations were also carried out to validate some of the analytical findings. We performed a sensitivity analysis of the model equations against the co-infection model reproduction number (threshold) to investigate model parameters that are most significant in driving the infection (see Figure 2). The numerical findings from our simulation enact that the best practices to reduce the co-infection is via practising proper hygiene and increasing the rate of recovery of Meningitis. Thus, to contain the co-infection, policymakers must focus on implementing the control measures that maximise the values of Meningitis recovery rate, τ_M, such as treatment of Meningitis patients and vaccination of susceptible individuals.

We acknowlegede the fact that this work may have shortfalls. The model does not take into account vaccination of Meningitis susceptible individuals. However, vaccination is recommended as a preventive measure for the Meningitis disease. Also, the model was not fitted to any existing data to ascertain how the results presented will be applicable to a real-life scenario. This model can therefore be improved by considering studying and analysing a mathematical model with a combination of hygiene, vaccination and biological control of the pathogens in the environment. Despite these shortfalls, we maintain that the results presented still remains implementable for the control and management of the Listeriosis-Meningitis co-infection disease and infected individuals.

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CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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