MATHEMATICAL ANALYSIS OF A TYPHOID TRANSMISSION MODEL WITH VACCINATION

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Abstract
In this paper, a six compartmental model for typhoid transmission dynamics incorporating vaccination as a controlling measure in human population was formulated. Mathematical analysis was carried out to determine the transmission pattern of typhoid infection in the population. The model was formulated using system of differential equations and we determined the control reproduction number which is a vital threshold parameter for measuring the control and propagation of infectious diseases. The stability analysis was carried out and it was found that typhoid infection undergoes both local and global asymptotic stability. Disease free equilibrium exist, and is locally and globally asymptotically stable if the control reproduction number is less than one and unstable if greater than one. The study shows that typhoid infection is endemic, and locally and globally asymptotically stable if the control reproduction number is greater than one. The model exhibits backward bifurcation which is caused by loss of temporary immunity of recovered human population.

Keywords: *Typhoid, Salmonellae, Model, Bifurcation, Local and Global Stabilities.*

Introduction

Typhoid fever is a systemic infection caused by *Salmonella typhi (S. typhi)* predominantly endemic in under-developing countries of Africa, Asia; and parts of developed countries in South America. Its mode of transmission is through oral route (Crump & Mintz, 2010). Upon entering into the host, the bacteria colonize the small intestine and start replicating rapidly, and thereafter invade the gastrointestinal tract and spread to different vital organs which includes spleen, liver and bone marrow (Raffatellu *et al.,* 2008). The severity of typhoid infection is characterized by initial infective dose, virulence and the host immune depressed response. The Salmonellosis is basically more than 2,000 species causing zoonotic infections, however there are two salmonellae whose only reservoir is the human being: salmonella typhi and paratyphi. Globally, typhoid fever is not a reportable disease in many countries (Getachew *et al*., 2017). The estimated number of cases excluding China is 5-20 million annually, mainly in South East Asia, India and Africa, in countries with poor sanitation and inadequate portable water supply system. Latin America recorded one of the highest number of typhoid fever cases after the cholera epidemic, in 1991 and has significantly reduced the number of cases in the country (Gotuzzo, 2018).

Typhoid fever poses one of the major public health concerns in tropical developing countries, especially in areas where access to clean water and other sanitation measures are limited or inadequate (Stephen, 2017). Typhoid fever has complex pathogenesis and manifests as an acute febrile disease, with relatively long incubation period that involves the transmigration of the microorganism through the Peyer's patch, localizes multiplication in the mesenteric lymph

nodes, and subsequently spread to the liver and spleen prior to showing clinical symptoms. It is a serious life-threatening infection characterized by false diagnosis due to similar signs and symptoms with malaria, which leads to improper controls and management of the disease. Despite extensive work on typhoid, not much is understood on the biology of the human-adapted bacterial pathogen and the complexity of the disease in endemic areas, especially in Africa (Moatlhodi *et al.*, 2016).

Mathematical models have over the years gained wide acceptance as an important tool for studying the dynamics of the transmission of infectious diseases. In the past decades, several authors including Moatlhodi and Gosalamang (2016), Stephen (2017) and Gotuzzo (2018) have adopted mathematical models to study typhoid fever infection and other related diseases. The present study incorporates vaccination as control measure in typhoid model which the above authors did not include and analyzes the model for stability so as to reduce the prevalence of typhoid infection in human population.

Materials and Methods

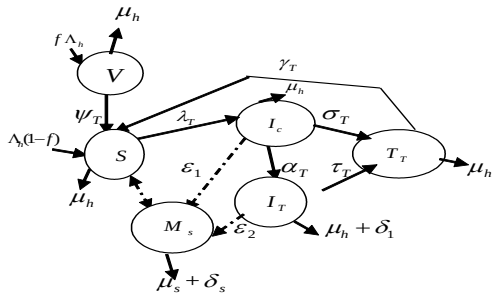
Model formulation: In this study we considered two populations; human population (N_h) and bacteria population (M_s) to describe the dynamic of typhoid infection in a medium, that is, food or water. The human population at time, t is divided into five (5) subclasses depending on the epidemiological status of individual. Susceptible (S): Carrier (I_c): Infected human population (I_T): Treated human (T_T): Vaccinated human (V):

Susceptible humans are recruited at a rate $\Lambda_h(1-f)$. Proportion of human population is vaccinated and loss immunity at a rate (ψ_T). γ_T is the rate at which recovered human population lose temporary immunity and move into susceptible human class. The susceptible human contract typhoid at rate (λ_T), where $\lambda_T = \dfrac{\beta_T M_s(1-\theta)}{K+M_s}$.

The Model equations are:

$$\begin{aligned}
\dot{V} &= f\Lambda_h - k_1 V \\
\dot{S} &= \Lambda_h(1-f) + \gamma_T T_T + \psi_T V - \lambda_T S - \mu_h S \\
\dot{I}_c &= \lambda_T S - k_2 I_c \\
\dot{I}_T &= \alpha_T I_c - \mathrm{k}_3 I_T \\
\dot{T}_T &= \sigma_T I_c + \tau_T I_T - \mathrm{k}_4 T_T \\
\dot{M}_s &= \varepsilon_1 I_c + \varepsilon_2 I_T - \mathrm{k}_5 M_s
\end{aligned} \qquad (1.1)$$

Where $\mathrm{k}_1 = (\psi_T + \mu_h)$, $\mathrm{k}_2 = (\mu_h + \alpha_T + \sigma_T + \varepsilon_1)$, $k_3 = (\mu_h + \tau_T + \varepsilon_1 + \delta_1)$, $k_4 = (\mu_h + \gamma_T)$ and $k_5 = (\mu_s + \delta_s)$



Variables Description

V	Vaccinated human population
S	Susceptible human population
I_C	Carrier human (asymptomatic) with potential typhoid causing bacterium
I_T	Infected human with typhoid fever
T_T	Treated human population of typhoid fever
M_s	Total bacteria (salmonella typhi) in the medium

Fig. 1: Flow Diagram of Typhoid Fever Infection
Table 1: Description of state variables of typhoid model (1.1)

Table 2: Description of parameters of typhoid infection model

Parameters Description	
Λ_h	Birth or emigration rate of human into the susceptible population
ψ_T	Rate at which individual loses immunity and move to susceptible class
μ_h	Natural death rate of all human subclasses
γ_T	Waning rate of temporary immunity of the treated human
τ_T	Treatment rate of infected human with typhoid fever disease
σ_T	Removal rate of carrier human subclass by gaining natural immunity
α_T	Progression rate of carrier human into infective subclass
δ_1	Disease induced death rate of infected human
ε_1	Contribution of carrier human into the medium
ε_2	Contribution of infective human into the medium
μ_s	Natural death rate of the salmonella typhi in the medium
δ_s	Water sanitation leading to death of salmonella typhi
β_T	Exposure/effective contact rate of human to bacteria in the environment.
λ_T	Force of infection for human with typhoid
f	Population of human vaccinated
$1-f$	Proportion of human not vaccinated
θ	Compliance rate of human population to water and food hygiene in the environment

Analysis of the Model

We consider the region $D = \left\{(V, S, I_c, I_T, T_T) \in \mathbb{R}_+^5 : N_h \leq \frac{\Lambda_h}{\mu_h}\right\}$, it can be shown that the set D is positively invariant in the region D and an attractor of all positive solutions of the model (1.1).

Lemma 1: The region D is positively invariant for the model (1.1).

Proof: The derivative of the total human population (N_h) is

$$\dot{N}_h = \dot{V} + \dot{S} + \dot{I}_c + \dot{I}_T + \dot{T}_T = \Lambda_h - \mu_h N_h - \varepsilon_1 I_c - \varepsilon_2 I_T - \delta_1 T_T \quad (1.2)$$

By standard comparison theorem and solving using variable separable method we have

$$N_h \leq \frac{\Lambda_h}{\mu_h} - \left(\frac{\Lambda_h - \mu_h N_0}{\mu_h}\right) e^{-\mu_h t} \quad (1.3)$$

As $t \to \infty$ in (1.3), the human population size $N_h \to \frac{\Lambda_h}{\mu_h}$ which means that $0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}$. Thus, the feasible solution set of the system (1.1) enters and remains in the region D.

$$D = \left\{(S, V, I_c, I_T, T_T) \in \Re_+^5 : N_h \leq \frac{\Lambda_h}{\mu_h}\right\}$$

We therefore conclude that model (1.1) is well posed both epidemiologically and mathematically. Hence, it is sufficient to study the dynamics of the basic model in the region D.

Positivity of the Solutions

We assumed that the initial condition for the model (1.1) is nonnegative. We then show that the solution is also positive.

Lemma 2: Let the initial condition for model (1.1) be $S(t) > 0$, $V(t) > 0$, $I_c(t) > 0$, $I_T(t) > 0$, $T_T(t) > 0$, and $M_s(t) > 0$ then the solutions of $S(t)$, $V(t)$, $I_c(t)$, $I_T(t)$, $T_T(t)$ and $M_s(t)$ will remain positive for all time, $t \geq 0$.

Proof: From the model equation (1.1), we choose the equation for susceptible human $S(t)$ to prove this proposition as follows:

Let $t_1 = \sup\{t > 0 : S(t) > 0, V(t) > 0, I_c(t) > 0, I_T(t) > 0, T_T(t) > 0, M_s(t) > 0\} > 0$

$$\dot{S} = \Lambda_h(1-f) - \lambda_h S - \mu_h S; \dot{S} \geq \Lambda_h(1-f) - (\lambda_h + \mu_h)S$$

$$\dot{S} \geq \Lambda_h(1-f) - (\lambda_h + \mu_h)S \quad (1.4)$$

By integrating factor method

$$\frac{d}{dt}\{S(t)\exp((\mu_h) + \int_0^{t_1} \lambda_T(\omega)d\omega)\} \geq \Lambda_h(1-f)\exp\{(\mu_h) + \int_0^{t_1} \lambda_T(\omega)\,d\omega\} \quad (1.5)$$

$$S(t_1)\exp\{(\mu_h t_1) + \int_0^{t_1} \lambda_T(\omega)d\omega\} - S(0) \geq \int_0^{t_1}[\Lambda_h(1-f)\exp\{(\mu_h y) + \int_0^{y} \lambda_T(\omega)d\omega\}]dy$$

$$S(t_1)\exp\{(\mu_h t_1)+\int_0^{t_1}\lambda_T(\omega)d\omega\}\geq S(0)+\int_0^{t_1}[\Lambda_h(1-f)\exp\{(\mu_h y)+\int_0^{y}\lambda_T(\omega)d\omega\}]dy$$

$$S(t_1)\geq S(0)\exp\{-(\mu_h t_1)-\int_0^{t_1}\lambda_T(\omega)d\omega\}+[\exp\{-(\mu_h t_1)-\int_0^{t_1}\lambda_T(\omega)d\omega\}]$$

$$\int_0^{t_1}\Lambda_h(1-f)[\exp\{(\mu_h y)+\int_0^{y}\lambda_T(\omega)d\omega\}]dy>0 \qquad (1.6)$$

Similarly, the proof holds as all state variables of the model (1.1) remain positive for all time, $t>0$ so that $V(t)>0, I_c(t)>0, I_T(t)>0, M_s(t)>0$

Stability Analysis of Model (1.1)

Local Stability of Disease-Free Equilibrium (DFE) Point ξ_0^*

We determine the disease-free equilibrium (DFE) of model (1.1) by equating the right-hand side of the model equation (1.1) to zero and evaluating its values. Also, we set the force of infection to zero which makes all disease compartments to become zero (i.e. $I_c = I_T = 0$) and solving the equation gives the DFE:

$$\xi_0^* = \left(\frac{f\Lambda_h}{k_1}, \frac{\Lambda_h((1-f)+\psi_T f)}{\mu_h k_1}, 0, 0, 0, 0\right) \qquad (1.7)$$

where $k_1 = (\psi_t + \mu_h)$

Control Reproduction Number, R_T for Model (1.1)

The Stability of ξ_0^* is established using the next generation operator method by using the notation in (Van Den Driessche and Watmough, 2002), so that the matrices F and V are determined as follows from equation (1.1).

At disease free equilibrium F becomes

$$F = \begin{bmatrix} 0 & 0 & \frac{KB_T(1-\theta)S^*}{K^2} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \qquad (1.8)$$

$$V = \begin{bmatrix} k_2 & 0 & 0 \\ -\alpha_T & k_3 & 0 \\ -\varepsilon_1 & -\alpha_2 & k_5 \end{bmatrix} \qquad (1.9)$$

Using Maple software, FV^{-1} is obtained as follows;

$$FV^{-1} = \begin{bmatrix} \frac{B_T(1-\theta)S^*[\alpha_T\varepsilon_2 + k_3\varepsilon_1]}{Kk_2k_3k_5} & \frac{B_T(1-\theta)S^*\varepsilon_2}{Kk_3k_5} & \frac{B_T(1-\theta)S^*}{Kk_5} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

(1.10)

Where $k_1 = (\psi_T + \mu_h)$, $k_2 = (\mu_h + \alpha_T + \sigma_T + \varepsilon_1)$, $k_3 = (\varepsilon_2 + \gamma_T + \delta_T + \mu_h)$, $k_4 = (\mu_h + \gamma_T)$ $k_5 = (\mu_s + \delta_s)$ and K = Concentration of salmonella typhi in the environment.

Therefore, the spectral radius is obtained as:

$$\rho FV^{-1} = \frac{B_T(1-\theta)S^*[\alpha_T\varepsilon_2 + k_3\varepsilon_1]}{Kk_2k_3k_5} \quad (1.11)$$

$$R_T = \frac{B_T(1-\theta)S^*[\alpha_T\varepsilon_2 + k_3\varepsilon_1]}{Kk_2k_3k_5} \quad (1.12)$$

The value R_T is the control reproduction number for typhoid infection

where

$$S^* = \frac{\Lambda_h((1-f) + \psi_T f)}{\mu_h k_1} \quad (1.13)$$

Theorem 1. The disease-free equilibrium point of model (1.1) is locally asymptotically stable if $R_T < 1$ and unstable if $R_T > 1$.

By theorem 1, biologically speaking, typhoid fever would be completely eliminated from human population when $R_T < 1$ if the initial population size of the sub-human populations of the model are in the region of attraction of $\xi^*_{(0)}$. Hence, the disease-free equilibrium (DFE) is locally asymptotically stable (LAS) if $R_T < 1$

Global Stability of Disease-Free Equilibrium (DFE) Point

Theorem 2. The disease-free equilibrium is globally asymptotically stable in the region D if $R_T < 1$.

Proof: We prove this theorem by first developing a Lyapunov function, tactically.

$$V = \frac{\varepsilon_2\alpha_T + k_3\varepsilon_1}{k_2} I_c + \varepsilon_2 I_T + k_3 M_s \quad (1.14)$$

where V = Lyapunov function, I_c, I_T and M_s are infectious compartment extracted from the model (1.1).

Differentiating equation (1.14) and substituting $\dot{I}_c$, $\dot{I}_T$ and $\dot{M}_s$ from (1.1) gives:

$$\dot{V} = \frac{\varepsilon_2\alpha_T + k_3\varepsilon_1}{k_2}\dot{I}_c + \varepsilon_2\dot{I}_T + k_3\dot{M}_s$$

$$\dot{V} = \frac{\varepsilon_2\alpha_T + k_3\varepsilon_1}{k_2}(\lambda_T S - k_2 I_c) + \varepsilon_2(\alpha_T I_c - k_3 I_T) + k_3(\varepsilon_1 I_c + \varepsilon_2 I_T - k_5 M_s)$$

(1.15)

Simplifying gives

$$\dot{V} = \frac{B_T M_s(1-\theta)}{K+M_s}\mathrm{S}\frac{[\alpha_T\varepsilon_2 + k_3\varepsilon_1]}{k_2} - k_3k_5M_s$$

$$= \left[B_T(1-\theta)\mathrm{S}[\alpha_T\varepsilon_2 + k_3\varepsilon_1] - k_2k_3k_5(K+M_s)\right]\frac{M_s}{\mathrm{k}_2(K+M_s)} \qquad (1.16)$$

$$= \left[\frac{B_T(1-\theta)\mathrm{S}[\alpha_T\varepsilon_2 + k_3\varepsilon_1]}{Kk_2k_3k_5} - 1\right]\frac{KM_s}{\mathrm{k}_2(K+M_s)}$$

$$= \left[\frac{KB_T(1-\theta)\mathrm{S}M_s[\alpha_T\varepsilon_2 + k_3\varepsilon_1]}{Kk_2k_3k_5M_s(K+M_s)} - 1\right]k_3k_5M_s$$

$$= \left[\frac{M_sK}{M_s(K+M_s)}.\frac{KB_T(1-\theta)\mathrm{S}[\alpha_T\varepsilon_2 + k_3\varepsilon_1]}{Kk_2k_3k_5} - 1\right]k_3k_5M_s$$

$$\dot{V} = \left[\frac{K}{(K+M_s)}R_T - 1\right]k_3k_5M_s$$

(1.17)

$\dot{V} = 0$, if $M_s = 0$, and $\dot{V} \le 0$, if $R_T < 1$, for all $t > 1$.

Therefore, we conclude that V is a Lyapunov function in D, and it follows from LaSalle's principle in LaSalle (1967) that every solution to the equation (1.1) with initial conditions in D converges to the DFE as $t \to \infty$. This means that $(I_c, I_T, M_s) \to 0$ Substitute $I_c = I_T = M_s = 0$ into model (1.1) gives $S = \frac{\Lambda_h}{\mu_h}$ as $t \to \infty$. Therefore, the DFE is globally asymptotically stable in D.

Existence of Endemic Equilibrium Point (EEP)

We denote endemic equilibrium point (EEP) of model (1.1) by $\xi^{**} = \left(V^{**}, S^{**}, I_c^{**}, I_T^{**}, T_T^{**}, M_s^{**}\right)$ and solving model (1.1) in terms of force of infection setting the rate of change of variables with respect to time at the left-hand sides to zero, we obtain i.e.

$$\left.\begin{aligned} & f\Lambda_h - k_1 V = 0 \\ & \Lambda_h(1-f) + \gamma_T T_T + \psi_T V - \lambda_T S - \mu_h S = 0 \\ & \lambda_T S - k_2 T_c = 0 \\ & \alpha_T I_c - k_3 I_T = 0 \\ & \sigma_T I_c + \tau_T I_T - k_4 T_T = 0 \\ & \varepsilon_1 I_c + \varepsilon_2 T_T - k_5 M_s \end{aligned}\right\} \quad (1.18)$$

Solving the equations individually we obtained the following values:

$$V^{**} = \frac{f\Lambda_h}{k_1}, S^{**} = \frac{\Lambda_h[k_1(1-f)+\psi_T f)}{k_1(\mu_h + \lambda_T^{**})}, I_c^{**} = \frac{\lambda_T S^{**}}{k_2}, I_T^{**} = \frac{\alpha_T \lambda_T S^{**}}{k_3 k_2},$$

$$T_T^{**} = \frac{k_3\sigma_T\lambda_T S^{**} + \sigma_T\alpha_T\lambda_T S^{**}}{k_2 k_3 k_4}, M_s^{**} = \frac{k_3\varepsilon_1\lambda_T S^{**} + \varepsilon_2\alpha_T\lambda_T S^{**}}{k_2 k_3 k_5} \quad (1.19)$$

Therefore, EEP of model (1.1) exist as:

$$\xi_0^{**} = \left(V^{**}, S^{**}, I_c^{**}, I_T^{**}, T_T^{**}, M_s^{**}\right) = \left[\begin{array}{l} \frac{f\Lambda_h}{k_1}, \frac{\Lambda_h[k_1(1-f)+\psi_T f)}{k_1(\mu_h+\lambda_T^{**})}, \frac{\lambda_T S^{**}}{k_2}, \frac{\alpha_T\lambda_T S^{**}}{k_3 k_2}, \\ \frac{k_3\sigma_T\lambda_T S^{**} + \sigma_T\alpha_T\lambda_T S^{**}}{k_2 k_3 k_4}, \frac{k_3\varepsilon_1\lambda_T S^{**} + \varepsilon_2\alpha_T\lambda_T S^{**}}{k_2 k_3 k_5} \end{array}\right] \quad (1.20)$$

Recall that

$$\lambda_T^{**} = \frac{B_T M_s^{**}(1-\theta)}{K + M_s^{**}} \quad (1.21)$$

Substitute the value of M_s^{**} into (1.21)

$$\lambda_T^{**} = \frac{\frac{B_T(1-\theta)\left[(\varepsilon_1 k_3 + \alpha_T\varepsilon_2)\Lambda_h(k_1(1-f)+\psi_T f)\right]\lambda_T^{**}}{k_1 k_2 k_3 k_1(\mu_h + \lambda_T^{**})}}{K + \frac{\left[(\varepsilon_1 k_3 + \alpha_T\varepsilon_2)\Lambda_h(k_1(1-f)+\psi_T f)\right]}{k_1 k_2 k_3 k_1(\mu_h + \lambda_T^{**})}} \quad (1.22)$$

Simplifying (1.22) we obtain

$$B_1\lambda_T^{**2} + B_2\lambda_T^{**} = 0 \Rightarrow \lambda_T^{**}(B_1\lambda_T^{**} + B_2) = 0 \quad (1.23)$$

Either $\lambda_T^{**} = 0$ or $B_1\lambda_T^{**} + B_2 = 0 \Rightarrow \lambda_T^{**} = \frac{-B_2}{B_1} < 0$

(1.24)

Where $B_1 = Kk_1k_2k_3k_5 + (\varepsilon_1 k_3 + \varepsilon_2\alpha_T)\Lambda_h(k_1(1-f) + \psi_T f) > 0$

$$B_2 = K\mu_h k_1k_2k_3k_5 - B_T(1-\theta)\left[(\varepsilon_1k_3 + \alpha_T\varepsilon_2)\Lambda_h(k_1(1-f) + \psi_T f)\right]$$

$$= K\mu_h k_1k_2k_3k_5\left\{1 - \frac{B_T(1-\theta)\left[(\varepsilon_1k_3 + \alpha_T\varepsilon_2)\Lambda_h(k_1(1-f) + \psi_T f)\right]}{K\mu_h k_1k_2k_3k_5}\right\}$$

$$B_2 = K\mu_h k_1k_2k_3k_5\{1 - R_T\}$$

(1.25)

$B_2 < 0$ if $R_T > 1$

Therefore, the model equation (1.1) has a unique (stable) endemic equilibrium if $R_T > 1$ since $\lambda_T^{**} > 0$ for $R_T > 1$

Local stability of Endemic Equilibrium Point (EEP)

Theorem 3. The endemic equilibrium of model (1.1) is locally asymptotically stable if $R_T > 1$ and unstable if $R_T < 1$.

Proof: By theorem 3, biologically speaking, typhoid fever would persist in human population when $R_T > 1$ if the initial population sizes of the sub-human populations of the model are in the region of attraction of $\xi_{(0)}^{**}$

Jacobian expressed in terms of force of infection result thus:

$$\xi_{(0)}^{**} = \begin{bmatrix} -k_1 & 0 & 0 & 0 & 0 & 0 \\ \psi_T & -\left[\lambda_T^{**} + \mu_h\right] & 0 & 0 & \gamma_T & -\lambda_T^{**}S^{**} \\ 0 & \lambda_T^{**}S^{**} & -k_2 & 0 & 0 & \lambda_T^{**}S^{**} \\ 0 & 0 & \alpha_T & -k_3 & 0 & 0 \\ 0 & 0 & \sigma_T & \tau_T & -k_4 & 0 \\ 0 & 0 & \varepsilon_1 & \varepsilon_2 & 0 & -k_5 \end{bmatrix} \quad (1.26)$$

$$\xi_{(0)}^{**} = \begin{bmatrix} -k_1 & 0 & 0 & 0 & 0 & 0 \\ \psi_T & -A & 0 & 0 & \gamma_T & -B \\ 0 & C & -k_2 & 0 & 0 & D \\ 0 & 0 & \alpha_T & -k_3 & 0 & 0 \\ 0 & 0 & \sigma_T & \tau_T & -k_4 & 0 \\ 0 & 0 & \varepsilon_1 & \varepsilon_2 & 0 & -k_5 \end{bmatrix} \quad (1.27)$$

The upper triangular matrices of $\xi_{(0)}^{**}$ is obtained as follow:

$$\xi_{(0)}^{**} = \begin{bmatrix} -k_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & -A & 0 & 0 & \gamma_T & 0 \\ 0 & 0 & -k_2 & 0 & \frac{\lambda_T \gamma_T}{A} & 0 \\ 0 & 0 & 0 & -k_3 & \frac{\alpha_T \lambda_T \gamma_T}{k_2 A} & 0 \\ 0 & 0 & 0 & 0 & -\frac{k_3 k_4 k_2 A - k_3 \sigma_T \lambda_T \gamma_T - \tau_T \alpha_T \lambda_T \gamma_T}{k_2 k_3 A} & 0 \\ 0 & 0 & 0 & 0 & 0 & -k_5 \end{bmatrix} \quad (1.28)$$

Where A = $\left[\frac{B_T M_s^{**}(1-\theta)}{K + M_s^{**}} + \mu_h \right]$

$\lambda_1 = -k_1, \lambda_2 = -A, \lambda_3 = -k_2, \lambda_4 = -k_3, \lambda_6 = -k_5$ and

$$\lambda_5 = -\frac{k_3 k_4 k_2 A - k_3 \sigma_T \lambda_T \gamma_T - \tau_T \alpha_T \lambda_T \gamma_T}{k_3 k_2 A} = -k_4 < 0 \text{ (if } \gamma_T = 0)$$

(This holds for a special case where $\gamma_T = 0$, the cause of backward bifurcation is set to zero)

Hence, the endemic equilibrium point (EEP) is locally asymptotically stable (LAS) if $R_T > 1$ and $\gamma_T = 0$

Global Stability of Endemic Equilibrium Point (EEP)

Theorem 4. The Endemic equilibrium point of model (1.1) is globally asymptotically stable if $R_T > 1$, otherwise unstable if $R_T < 1$

Proof: We shall verify this by setting up a Lyapunov function L defined below
We assume that:

$$\left.\begin{aligned} &\gamma_T = \psi_T = 0, \\ &\text{Let } \Lambda_h(1-f) = \Lambda \\ &\lambda_T = \frac{B_T M_s (1-\theta)}{K + M_s} \Rightarrow \bar{B}_T M_s \end{aligned}\right\} \quad (1.29)$$

$$L = (S - S^{**} - S^{**} \ln \frac{S}{S^{**}}) + (I_c - I_c^{**} - I_c^{**} \ln \frac{I_c}{I_c^{**}}) + A(I_T - I_T^{**} - I_T^{**} \ln \frac{I_T}{I_T^{**}}) + B(M_s - M_s^{**} - M_s^{**} \ln \frac{M_s}{M_s^{**}})$$

(1.30)

Differentiating (1.30) gives:

$$\dot{L} = (\dot{S} - \frac{S^{**}}{S}\dot{S}) + (\dot{I}_c - \frac{I_c^{**}}{I_c}\dot{I}_c) + A(\dot{I}_T - \frac{I_T^{**}}{I_T}\dot{I}_T) + B(\dot{M}_s - \frac{M_s^{**}}{M_s}\dot{M}_s) \quad (1.31)$$

Substitute (1.1) into (1.31) gives

$$\dot{L} = \Lambda - \bar{B}_T M_s S - \mu_h S - \frac{S^{**}}{S}\left[\Lambda - \bar{B}_T M_s S - \mu_h S\right] + (\bar{B}_T M_s S - k_2 I_c - \frac{I_c^{**}}{I_c}[\bar{B}_T M_s S - k_2 I_c] + A((\alpha_T I_c - k_3 I_T) -$$

$$\frac{I_T^{**}}{I_T}(\alpha_T I_c - k_3 I_T)) + B((\varepsilon_1 I_c + \varepsilon_2 I_T - k_5 M_s) - \frac{M_s^{**}}{M_s}(\varepsilon_1 I_c + \varepsilon_2 I_T - k_5 M_s)) \quad (1.32)$$

At steady state from (1.1), $\Lambda = \bar{B}_T S^{**} M_s^{**} + \mu_h S^{**}$

Substitute for Λ in (1.32) gives:

$$\dot{L} = \bar{B}_T M_s^{**} S^{**} + \mu_h S^{**} - \bar{B}_T M_s S - \mu_h S - \frac{S^{**2}}{S}\bar{B}_T M_s - \mu_h \frac{S^{**2}}{S} + \bar{B}_T S^{**} M_s + \mu_h S^{**} + \bar{B}_T M_s S - k_2 I_c - \frac{I_c^{**}}{I_c}\bar{B}_T M_s S + k_2 I_c^{**} + A\alpha_T I_c - Ak_3 I_T$$

$$-A\frac{I_T^{**}}{I_T}\alpha_T I_c + Ak_3 I_T^{**} + B\varepsilon_1 I_c + B\varepsilon_2 I_T - Bk_5 M_s - B\frac{M_s^{**}}{M_s}\varepsilon_1 I_c - B\frac{M_s^{**}}{M_s}\varepsilon_2 I_T + Bk_5 M_s^{**} \quad (1.33)$$

Solving for A and B gives:

$$A = \frac{\bar{B}_T S^{**}\varepsilon_2}{k_3 k_5}, \quad B = \frac{\bar{B}_T S^{**}}{k_5}$$

$$k_2 = \frac{\bar{B}_T S^{**} M_s^{**}}{I_c^{**}}, \alpha_T = \frac{k_3 I_T^{**}}{I_c^{**}}, \varepsilon_1 = \frac{k_5 M_s^{**}}{I_c^{**}} - \frac{\varepsilon_2 I_T^{**}}{I_c^{**}}. \text{ (at steady state)}$$

Substitute for k_2, A and B into (1.33) and simplifying reduces it to

$$\dot{L} = \bar{B}_T M_s^{**} S^{**} + \mu_h S^{**} - \mu_h S - \frac{S^{**2}}{S}\bar{B}_T M_s - \mu_h \frac{S^{**2}}{S} + \mu_h S^{**} - \frac{I_c^{**}}{I_c}\bar{B}_T M_s S + \frac{\bar{B}_T S^{**} M_s^{**} I_c^{**}}{I_c^{**}} - \frac{\bar{B}_T S^{**}\varepsilon_2}{k_3 k_5}\frac{I_T^{**} k_3 I_T^{**} I_c}{I_T I_c^{**}} \quad (1.34)$$

$$+\frac{\bar{B}_T S^{**}\varepsilon_2}{k_3 k_5} k_3 I_T^{**} - \frac{\bar{B}_T S^{**}}{k_5}\frac{M_s^{**}}{M_s}\varepsilon_1 I_c - \frac{\bar{B}_T S^{**}}{k_5}\frac{M_s^{**}}{M_s}\varepsilon_2 I_T + \frac{\bar{B}_T S^{**}}{k_5} k_5 M_s^{**}$$

Further simplifying (1.34) and substituting $\varepsilon_2 = \frac{k_5 M_s^{**} - \varepsilon_1 I_c^{**}}{I_T^{**}}$ into the results:

$$\dot{L} = \bar{B}_T M_s^{**} S^{**} + \mu_h S^{**} - \mu_h S - \frac{S^{**2}}{S}\bar{B}_T M_s - \mu_h \frac{S^{**2}}{S} + \mu_h S^{**} - \frac{I_c^{**}}{I_c}\bar{B}_T M_s S + \bar{B}_T S^{**} M_s^{**} - \frac{\bar{B}_T S^{**} I_T^{**} I_c M_s^{**}}{I_T I_c^{**}} + \frac{\bar{B}_T S^{**} I_T^{**}\varepsilon_1}{k_5 I_T}$$

$$+\bar{B}_T S^{**} M_s^{**2} I_T - \frac{\bar{B}_T S^{**} \varepsilon_1 I_c^{**}}{k_5} - \frac{\bar{B}_T S^{**} M_s^{**} \varepsilon_1 I_c}{M_s k_5} - \frac{\bar{B}_T S^{**} M_s^{**} I_T}{M_s I_T^{**}} + \frac{\bar{B}_T S^{**} M_s^{**2} I_T \varepsilon_1}{k_5 M_s I_T^{**}} + \bar{B}_T S^{**} M_s^{**}$$

(1.35)

$$\dot{L} = \mu_h S^{**}\left[2 - \frac{S}{S^{**}} - \frac{S^{**}}{S}\right] + \bar{B}_T S^{**} M_s^{**}\left[4 - \frac{S^{**}}{S}\frac{M_s}{M_s^{**}} - \frac{I_c^{**}}{I_c}\frac{M_s}{M_s^{**}}\frac{S^{**}}{S} - \frac{I_T^{**}}{I_T}\frac{I_c}{I_c^{**}} - \frac{M_s^{**}}{M_s}\frac{I_T}{I_T^{**}}\right] + \frac{S^{**} I_T^{**} \bar{B}_T \varepsilon_1 I_c}{k_5 I_T}\left[1 - \frac{I_c^{**}}{I_c}\frac{I_T}{I_T^{**}}\right]$$

$$+\frac{S^{**} \bar{B}_T M_s^{**} I_c^{**} \varepsilon_1 I_T}{k_5 M_s I_T^{**}}\left[1 - \frac{I_c}{I_c^{**}}\frac{I_T^{**}}{I_T}\right]$$

(1.36)

We conclude that since the arithmetic mean exceeds the geometric mean, the following inequalities holds:

$$2 - \frac{S}{S^{**}} - \frac{S^{**}}{S} \le 0; \qquad 1 - \frac{I_c^{**}}{I_c}\frac{I_T}{I_T^{**}} \le 0; \; 4 - \frac{S^{**}}{S}\frac{M_s}{M_s^{**}} - \frac{I_c^{**}}{I_c}\frac{M_s}{M_s^{**}}\frac{S^{**}}{S} - \frac{I_T^{**}}{I_T}\frac{I_c}{I_c^{**}} - \frac{M_s^{**}}{M_s}\frac{I_T}{I_T^{**}} \le 0;$$

$$1 - \frac{I_c}{I_c^{**}}\frac{I_T^{**}}{I_T} \le 0$$

Thus $\dot{L} \le 0$ for $R_T > 1$, hence L is a Lyapunov function in D and the EEP is globally asymptotically stable (GAS) (for special case $d = 0$, $\gamma_T = \psi_T = 0,$) based on the LaSalle's Invariance Principle in LaSalle (1969).

Bifurcation Analysis of Model (1)

We investigate the existence of backward bifurcation at $R_T < 1$. We use the Center Manifold theorem as presented by (Augusto, 2017; Castillo-Chavez, 2004; Eguda, *et al.*, 2020).

Theorem 5: Model (1.1) undergoes backward bifurcation when $R_T = 1$ for a special case when $\gamma_T = 0$.

Proof: We prove this theorem based on the Center Manifold theorem as applied in Andrawus *et al.* (2017). From the model (1.1) let $x_1 = V, x_2 = S, x_3 = I_c, x_4 = I_T, x_5 = T_T$ and $x_6 = M_s$. We obtained the following transformation for model (1.1):

$$\begin{aligned}
\dot{\chi}_1 &= f\Lambda_h - k_1 x_1 \\
\dot{\chi}_2 &= \Lambda_h(1-f) + \gamma_T x_5 + \psi_T x_1 - \frac{B_T(1-\theta)x_6 x_2}{K + x_6} - \mu_h x_2 \\
\dot{\chi}_3 &= \frac{B_T x_6(1-\theta)x_2}{K + x_6} - k_2 x_3 \\
\dot{\chi}_4 &= \alpha_T x_3 - k_3 x_4 \\
\dot{\chi}_5 &= \sigma_T x_3 + \tau_T x_4 - k_4 x_5 \\
\dot{\chi}_6 &= \varepsilon_1 x_3 + \varepsilon_2 x_4 - k_5 x_6
\end{aligned} \tag{1.37}$$

The Jacobian of the transform equation is obtained at DFE as:

$$J(\xi^*) = \begin{bmatrix}
-k_1 & 0 & 0 & 0 & 0 & 0 \\
\psi_T & -\mu_h & 0 & 0 & \gamma_T & -\frac{B_T(1-\theta)x_2}{K} \\
0 & 0 & -k_1 & 0 & 0 & \frac{B_T(1-\theta)x_2}{K} \\
0 & 0 & \alpha_T & -k_3 & 0 & 0 \\
0 & 0 & \sigma_T & \tau_T & -k_4 & 0 \\
0 & 0 & \varepsilon_1 & \varepsilon_2 & 0 & -k_5
\end{bmatrix}$$

We consider the case when $B_T = B_T^*$ is chosen as the bifurcation parameter at $R_T = 1$, we obtain that:

$$R_T = \frac{B_T^*(1-\theta)[\alpha_T\varepsilon_2 + k_2\varepsilon_1]S^*}{K\mu_h k_2 k_3 k_5} \Rightarrow B_T^* = \frac{K\mu_h k_2 k_3 k_5}{(1-\theta)[\alpha_T\varepsilon_2 + k_2\varepsilon_1]S^*} \tag{1.38}$$

We determine the right eigenvector of $J(\xi^*)_{B_T = B_T^*}$

$w = (w_1, w_2, w_3, w_4, w_5, w_6)^T$

$$
\begin{aligned}
&w_1 = 0\\
&w_2 = \frac{B_T(1-\theta)x_2[\gamma_T(\sigma_T k_3 + \tau_T \alpha_T) - \mu_h k_2 k_3 k_4]w_6}{K\mu_h k_2 k_3 k_4},\\
&w_3 = \frac{B_T(1-\theta)x_2 w_6}{K k_2},\\
&w_4 = \frac{\alpha_T B_T(1-\theta)x_2 w_6}{K k_2 k_3},\\
&w_5 = \frac{B_T(1-\theta)x_2 w_6[\sigma_T k_3 + \tau_T \alpha_T]}{K k_2 k_3 k_4},\\
&w_6 = w_6 > 0
\end{aligned}
\qquad (1.39)
$$

The above eigenvalues were obtained by solving these equations:

$$
\begin{aligned}
&-k_1 w_1 = 0\\
&\psi_T - \mu_h w_2 + \gamma_T w_5 - \frac{B_T(1-\theta)x_2^* w_6}{K} = 0\\
&-k_2 w_3 + \frac{B_T(1-\theta)x_2^* w_6}{K} = 0\\
&\alpha_T w_3 - k_3 w_4 = 0\\
&\sigma_T w_3 + \tau_T w_4 - k_4 w_5 = 0\\
&\varepsilon_1 w_3 + \varepsilon_2 w_4 - k_5 w_6 = 0
\end{aligned}
\qquad (1.40)
$$

In the same manner we obtained the left eigenvector of $J(\xi^*)_{B_T = B_T*}$ as

$$v = (v_1, v_2, v_3, v_4, v_5, v_6)$$

$$
\begin{aligned}
&-v_1 k_1 + v_2 \psi_T = 0\\
&-v_2 \mu_h = 0\\
&-v_3 k_2 + v_4 \alpha_T + v_5 \sigma_T + v_6 \varepsilon_1 = 0\\
&-v_4 k_3 + v_5 \tau_T + v_6 \varepsilon_2 = 0\\
&v_2 \gamma_T - v_5 k_5 = 0\\
&\frac{-v_2 B_T(1-\theta)x_2}{K} + \frac{v_3 B_T(1-\theta)x_2}{K} - v_6 k_5 = 0
\end{aligned}
\qquad (1.41)
$$

Solving the above gives:

$$
\begin{aligned}
&v_1 = v_2 = v_5 = 0\\
&v_3 = \frac{\alpha_T \varepsilon_2 v_6 + k_3 \varepsilon_1 v_6}{k_2 k_3}, v_4 = \frac{\varepsilon_2 v_6}{k_3}, v_6 = v_6 > 0
\end{aligned}
$$

Formulation of a and b

We compute the associated non-zero partial derivatives at DFE and the bifurcation parameters are presented as follows:

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f}{\partial x_i \partial x_j}(0,0)$$

(1.42))

From the transformed equations (1.37)

$$\frac{\partial^2 f}{\partial x_2 \partial x_6} = \frac{B_T(1-\theta)}{K}$$

$$\frac{\partial^2 f}{\partial x_2 B_T^*} = 0$$

$$\frac{\partial^2 f}{\partial x_6 B_T^*} = \frac{(1-\theta)}{K} x_2$$

$$a = 2v_3 w_2 w_6 \frac{\partial^2 f_3}{\partial x_2 \partial x_6}(0,0)$$

$$a = \left[2\left(\frac{\alpha_T \varepsilon_2 + k_3 \varepsilon_1}{k_2 k_3}\right) \frac{B_T(1-\theta) x_2^* w_6 [\gamma_T(\sigma_T k_3 + \tau_T \alpha_T) - \mu_h K k_2 k_3 k_4}{\mu_h K k_2 k_3 k_4} \right] \frac{B_T(1-\theta)}{K}$$

(1.43)

$$a = G_1 - G_2$$

Where

$$G_1 = \frac{[2(\alpha_T \varepsilon_2 + k_3 \varepsilon_1) \mathrm{B}_T (1-\theta) x_2 w_6 (\gamma_T (\sigma_T k_3 + \tau_T \alpha_T]}{\mu_h K k_2 k_2 k_3 k_3 k_4 K} (1-\theta) \mathrm{B}_T$$

$$G_2 = \frac{(1-\theta) \mathrm{B}_T}{K k_2 k_3 K}$$

and

$$b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial B_T^*}(0,0)$$

(1.44)

$$b = \sum_{k,i=1}^{n} v_3 w_6 \frac{\partial^2 f_3}{\partial x_6 \partial B_T^*}(0,0)$$

$$\frac{k_5 (K + x_6^*) v_6}{B_T(1-\theta) x_2^*} \times \frac{k_3 B_T (1-\theta) x_2^*}{\mathrm{k}_2 \, \alpha_T (K + x_6^*)} \times \frac{(1-\theta) x_2^*}{K}$$

$$b = \frac{k_5 k_3 (1-\theta) x_2^* v_6 w_6}{\mathrm{K} \, k_2 \alpha_T} > 0$$

(1.45)

Since the bifurcation coefficient b is positive, it follows from theorem 2 of Castillo-Chavez and Song (2004) that the transformed model (1.37) will undergo a backward bifurcation if the bifurcation coefficient a is positive.

Results and Discussion

Epidemiologically, typhoid can be eliminated from human population if the initial size of the bacteria population is reduced nearly to zero (small enough) such that the control reproduction number can be brought below unity (i.e. $R_T < 1$). The model (1.1) undergoes the phenomenon of backward bifurcation whenever a stable disease-free equilibrium point coexists with a stable endemic equilibrium point and the associated reproduction number is less than unity. The epidemiological implication of the backward bifurcation of the model (1.1) is that the necessary requirement of the reproduction number being less than unity becomes only a necessity, but not sufficient condition for typhoid fever control, thus the necessity of the use of vaccine. Hence, this research shows that the loss of acquired temporary immunity from treatment of human population of typhoid fever, γ_T is the cause of backward bifurcation in the typhoid transmission model.

Conclusion

In this research, we formulated and analysed compartmental typhoid dynamic transmission model incorporating vaccination as a control measure to eradicate typhoid infection from human population. The quantitative analysis of the models indicates that the solutions of the model are bounded and positive. This study obtained the reproduction number (R_T) for typhoid transmission dynamics and established that the disease-free equilibrium is locally and globally asymptotically stable if $R_T < 1$, and unstable when $R_T > 1$. It was proved that the model will undergo the phenomenon of backward bifurcation for a special case when ($\gamma_T = 0$, $R_T = 1$), i.e. DFE coexists with endemic equilibrium. The study revealed that when adequate environmental sanitation is maintained and portable water are provided with routine proper treatment culture cultivated, then, the medium for breeding salmonellae will be totally checked. To effectively control typhoid fever infection in human population to a very large extent, the study proposed the use of vaccination under strict compliance.

Conflict of Interest

The authors declared that this is an original work, and that this was not published in any electronic media, that all references are dully cited and there are no conflicts of interest regarding the publication of this piece of work

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