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Mathematical Model for Transmission Dynamics of Typhoid Fever

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Abstract: *An epidemic model with protection and treatment is investigated for typhoid disease that can be transmitted through infected individuals. In this study, we used a deterministic compartmental model for assessing the effect of protection and treatment on controlling the transmission dynamics of typhoid fever in the community. Stability theory of differential equations is used to study the qualitative behavior of the system. The basic reproduction number that represents the epidemic indicator is obtained by using the next generation matrix. Both the local stability and global stability conditions for disease free equilibrium is established. The endemic equilibrium was determined and the model exhibits a forward trans-critical bifurcation. Numerical simulation of the model showed that an increase in protection and treatment leads to low disease prevalence in a population.*

Keywords*: Mathematical model, Typhoid fever, Basic reproduction number, Protection.*

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I. Introduction

Typhoid fever is a contagious disease, found only in human and occurs due to systemic infection mainly by Salmonella typhi organism [1]. The disease is a major problem in most developing countries where there is lack of proper sanitation and occurs due to contaminated water. The most common type of Salmonella that cause typhoid fever are *Salmonella paratyphi A, B, and C* and *Salmonella paratyphi D,* WHO [2]. The bacteria is transmitted through food and water contaminated with faeces and urine of an infected patient or a carrier [3]. During acute infection, the bacterium multiplies in mononuclear phagocytic cells before being released into the bloodstream [4]. Typhoid fever attack 21 million people and kills 200,000 worldwide every year.

Different models have been developed to analyze the transmission dynamics of typhoid fever as well as the effectiveness of some intervention strategies against the spread of typhoid infections. For instance, Mathematical model for transmission dynamics of typhoid is developed in order to evaluate the potential direct and indirect effects of vaccination [5]. The model is validated against randomized vaccine trials. It is tested on school based vaccination strategies, and it is discovered that typhoid vaccination is expected to lead a short term indirect protection and decrease in typhoid incidences, but vaccination alone is unlikely to lead to elimination of typhoid.

In [6], a simple mathematical model is developed on direct and indirect protection by vaccine and benefits of generic vaccination program. The population is split into vaccinated and the unvaccinated subgroups and its effectiveness redefined. It is found that vaccination reduces the number of susceptible to infection and fewer infected individuals spread the disease among both vaccinated and unvaccinated persons.

A model is developed in [7]. In the model, the number of newly infected persons is expressed as a function of the infectious and susceptible people in a community within a given time. The age structures of the population are established, which enables more detailed simulation of the effect of various interventions and strategies to control the disease in different age groups. The study indicates that once the incidence of the infection has fallen below the threshold, it cannot be maintained in a community due to the loss of the main source of infection chronic carriers as they die out naturally.

Mathematical model for transmission dynamics of typhoid is developed in order to evaluate the potential direct and indirect effects of vaccination [8]. The model is validated against randomized vaccine trials. It is evaluated on school based vaccination strategies, and it is discovered that typhoid vaccination is expected to lead a short term indirect protection and decrease in typhoid incidences, but vaccination alone is unlikely to lead to elimination of typhoid. Both short- and long term carriers contribute to transmission, but not necessarily at the same rate as primary infections.

In [9] a deterministic mathematical model was used to investigate the dynamics of typhoid fever with optimal control strategies and also investigated the cost-effectiveness of the implemented control strategies. The model considered human population N as well as bacteria population B_c. The human population N is divided

into four subclasses: *Susceptible* S, *Infected* I , *Carrier* C, and Recovered R. It was found that effective treatment only without prevention is not the best option in controlling the spread of typhoid fever. Therefore, the study concluded that adequate control measures which adhered to these control strategies viz., preventive and treatment would be a very effective way for fighting the disease and also for cost-effectiveness.

For the past few years different scholars have studied typhoid fever transmission dynamics, for instance see Atunde [10], A. Omame, R. A. Umana, N. O. Iheonu, and S. Chioma [11], M. A. Khan, M. Parvez, S. Islam, I. Khan, S. Shafie, and T. Gul [12], O. C. Akinyi, J. Y. T. Mugisha, A. Manyonge, and C. Ouma [13] and Moffat N C [14]) by using different models and come up with different valuable result.

The dynamics of the disease with compartments PSIT viz., Protected, Susceptible, Infected and Protected, was modeled by the author J. K. Nthiiri (2016). On the study which was done by Nthiiri populations were recruited into the protected compartment P at a rate α by birth or immigration and the remaining $(1-\alpha$ are interring the susceptible compartment $\mathcal{S}$. The susceptible individuals become infected at a rate λ which is the force of infection. In his assumption those individuals in the infected subclass can get treatment and join treated subclass with a rate of β. The treated subclass also increases with individuals who come from infected class by getting treatment with a rate of β. In all the subclasses is the natural death rate of individuals. The details of the existing model that we used as a baseline for our study can be found in the appendix A.

In this study we proposed an improvement of the model [15] that is to show the effect of re-susceptibility of peoples after treatment of typhoid disease. Particularly population groups which are protected against the disease were considered and those who get treatment also may get re-infection once they are cured from typhoid disease.

II. Description and Formulation of Model

The compartments used in this model consist of four classes: $P(t)$ is the compartment used for those which are protected against the disease over a period of time, $S(t)$ is used to represent the number of individuals that are prone to the disease at time *t,* $I(t)$ denotes the number of individuals who have been infected with the disease and are capable of spreading the disease to those in the susceptible categories, and $T(t)$ denotes the number of individuals who have been infected with the disease and are treated. Protected individuals are recruited into the population at per capita rate $\alpha\Lambda$. Susceptible individuals are recruited into the population at per capita rate $(1-\alpha)\Lambda$. Susceptible individuals acquire typhoid infection at per capita rate λ. The susceptible class is increased by birth or emigration at a rate of $(1-\alpha)\Lambda$ and also from treated class by losing temporary immunity with δ rate and from protected class by losing protection with γ rate. Also, λ is the effective force of infection which is given by $\lambda = [\pi\theta(1-\vartheta)/N]$ .Here π is transmission probability rate of typhoid, θ is contact rate of infection and ϑ effective rate of protection against infection. The natural mortality rate is , d is the disease induced mortality rate, and β is the rate of treatment.

The infected subclass is increased from susceptible subclass by λ screening rate. Those individuals in the infected subclass can get treatment and join treated subclass with a rate of β. The treated subclass also increases with individuals who come from infected class by getting treatment with a rate of β. In all the subclasses, μ is the natural death rate of individuals, but in the infective class d is the disease induced death rate. The assumption of this model is that there is re-infection once an individual is treated.

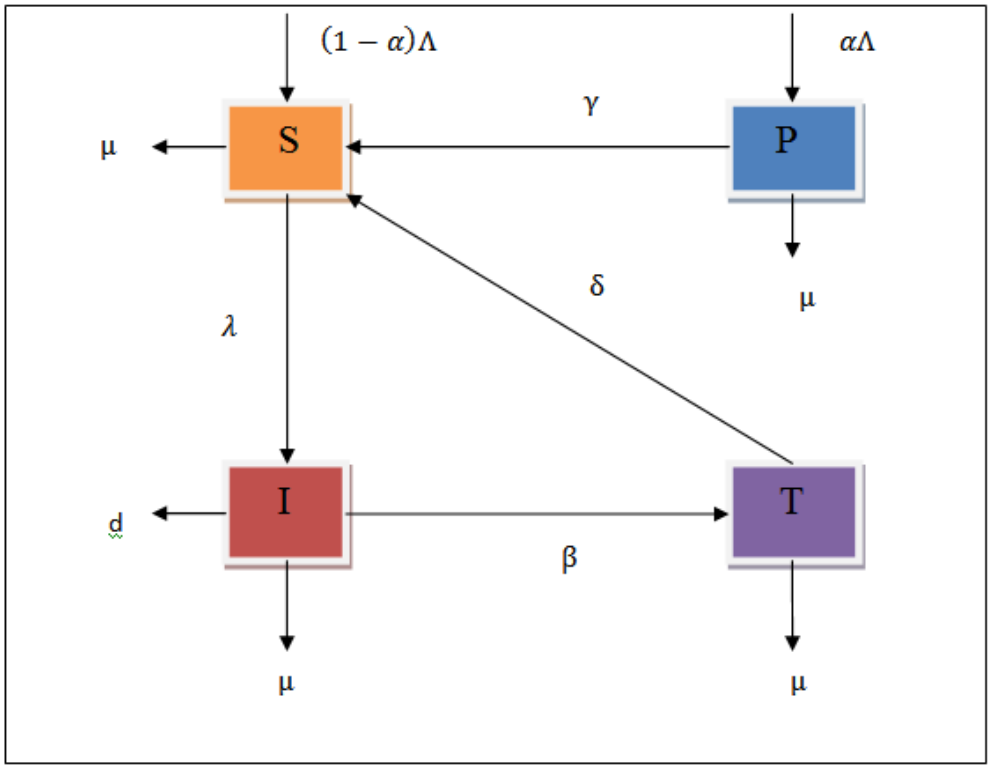

Figure1. Flow diagram of the model

The above model description can be written in four system of differential equation below.

$$dP/dt = \alpha\Lambda - (\gamma + \mu)P \quad (1)$$

$$dS/dt = (1-\alpha)\Lambda + \gamma P + \delta T - (\lambda + \mu)S \quad (2)$$

$$dI/dt = \lambda S - (\mu + \beta + d)I \quad (3)$$

$$dT/dt = \beta I - (\mu + \delta)T \quad (4)$$

Here $\lambda = [\pi\theta(1-\vartheta)I/N]$ is effective force of infection, π is transmission probability rate of typhoid, θ is contact rate of infection and ϑ is effective rate of protection against infection. $N = P + S + I + T$ With initial conditions $P(0) = P_0$, $S(0) = S_0$, $I(0) = I_0$, and $T(0) = T_0$.

III. The Model Analysis

3.1. Theorem 1 (Invariant Region): The positive solutions of the system of model equations (1) – (4) are bounded. Or equivalently, the model variables $P(t)$, $S(t)$, $I(t)$, and $T(t)$ are bounded for all t. We obtained the invariant region in which the model solution is bounded.

Proof: In the given model the total population N is given by $N = P + S + I + T$. Based on the techniques used in [16] we differentiating N both sides with respect to t leading to

$$\frac{dN}{dt} = \frac{dP}{dt} + \frac{dS}{dt} + \frac{dI}{dt} + \frac{dT}{dt} \quad (5)$$

By substituting (1-4) into (5), we can get

$$\frac{dN}{dt} = \Lambda - \mu N - dI \quad (6)$$

In the absence of mortality due to typhoid disease i.e., d = 0, equation (6) becomes

$$\frac{dN}{dt} \leq \Lambda - \mu N \quad (7)$$

Rearranging and integrating both sides of (7), we get $\int [1/\Lambda - \mu N]\, dN \leq \int dt$ or equivalently $-(1/\mu)\ln(\Lambda - \mu N) \leq t + c_1$ where c_1 is integration constant. By applying antilogarithms and introducing arbitrary constants $c_2 = -\mu c_1$ and $A = e^{c_2}$ the general solution can be expressed as

$$\Lambda - \mu N \geq Ae^{-\mu t} \quad (8)$$

By applying initial condition $N(0) = N_0$ in (8), we get

$$A = \Lambda - \mu N_0 \quad (9)$$

By substituting (9) in (8), we get

$$\Lambda - \mu N \geq (\Lambda - \mu N_0)e^{-\mu t} \quad (10)$$

By rearranging (10), we get

$$N \leq (\Lambda/\mu) - [(\Lambda - \mu N_0)/\mu]\ e^{-\mu t} \quad (11)$$

As t→ ∞ in (11), the population size $N \to (\Lambda/\mu)$ which implies that $0 \leq N \leq (\Lambda/\mu)$.

Thus, the feasible solution set of the model enters and remain in the region:

$$\Omega = \{(P,S,I,T)\ \epsilon\ R_+^4 : N \leq (\Lambda/\mu)\} \quad (12)$$

Therefore, the basic model is well posed epidemiologically and mathematically. Hence, it is sufficient to study the dynamics of the basic model in Ω.

3.2 Positivity of Solution

We assumed that the initial condition of the model is non-negative, and we show that the solution of the model is also positive.

Theorem2. **(Positivity)** Solutions of the model equations (1) – (4) together with the non-negative initial conditions $P(0) = P_0$, $S(0) = S_0$, $I(0) = I_0$, and $T(0) = T_0$ are always positive OR the model variables $P(t)$, $S(t)$, $I(t)$, and $T(t)$ are positive for all t and will remain in $\mathbb{R}_+^4$.

Proof: The technique used in [17] is applied on the system of differential equations (1-4) to verify positivity of the solutions.

Positivity of $P(t)$: Consider the equation (1) given by $dP/dt = \alpha\Lambda - (\gamma + \mu)P$. This equation, after discarding the positive term $\alpha\Lambda$, reduces to an inequality $dP/dt \geq -(\gamma + \mu)P$ and can be expressed in variables separable form as $dP/P \geq -(\gamma + \mu)dt$. Up on integration and application of initial condition $P(0) = P_0$, the solution can be obtained to be $P(t) \geq P_0 e^{-(\gamma+\mu)t}$. Now, since $P_0 > 0$ and $e^{-(\gamma+\mu)t} > 0$ it can be concluded that

$$P(t) \geq 0, \quad \forall t \quad (13)$$

Positivity of $S(t)$: Consider the equation (2) given by $dS/dt = (1-\alpha)\Lambda + \gamma P + \delta T - (\lambda + \mu)S$. This equation, after discarding the positive terms $(1-\alpha)\Lambda + \gamma P + \delta T$, reduces to an inequality $dS/dt \geq -(\lambda + \mu)S$ and can be expressed in variables separable form as $dS/S \geq -(\lambda + \mu)dt$. Up on integration and application of initial condition $S(0) = S_0$, the solution can be obtained to be $S(t) \geq S_0 e^{-(\lambda+\mu)t}$. Now, since $S_0 > 0$ and $e^{-(\lambda+\mu)t} > 0$ it can be concluded that

$$S(t) \geq 0, \quad \forall t \quad (14)$$

Positivity of $I(t)$: On applying the same procedure on (3) it can be obtained that

$$I(t) \geq 0, \quad \forall t \quad (15)$$

Positivity of $T(t)$: On applying the same procedure on (4) it can be obtained that

$$T(t) \geq 0, \quad \forall t \quad (16)$$

This completes proof of the theorem. Therefore, the solution of the model is positive.

Lemma1 (Existence) Solutions of the model equations (1) – (4) together with the initial conditions $P(0) > 0$, $S(0) > 0, I(0) > 0$, $T(0) > 0$ exist in $\mathbb{R}_+^4$ i.e., the solution of the model $P(t)$, $S(t)$, $I(t)$, and $T(t)$ exist for all t and will remain in $\mathbb{R}_+^4$.

Proof The right hand sides of the system of equations (1) – (4) can be expressed as follows:

$$f_1(P, S, I, T) = \alpha\Lambda - (\gamma + \mu)P$$
$$f_2(P, S, I, T) = (1-\alpha)\Lambda + \gamma P + \delta T - (\lambda + \mu)S$$
$$f_3(P, S, I, T) = \lambda S - (\mu + \beta + d)I$$
$$f_4(P, S, I, T) = \beta I - (\mu + \delta)T$$

According to Derrick and Grobsman theorem, let Ω denote the region $\Omega = \{(P,S,I,T) \in \mathbb{R}_+^4 : N \leq (\Lambda/\mu)\}$. Then equations (1) – (4) have a unique solution if $(\partial f_i)/(\partial x_j)$, $i,j = 1,2,3,4$ are continuous and bounded in Ω. Also here, $x_1 = P$, $x_2 = S$, $x_3 = I$, $x_4 = T$. The continuity and the boundedness are verified as here under:

For f_1:

$|(\partial f_1)/(\partial P)| = |-(\gamma + \mu)| < \infty$

$|(\partial f_1)/(\partial S)| = 0 < \infty$

$|(\partial f_1)/(\partial I)| = 0 < \infty$

$|(\partial f_1)/(\partial T)| = 0 < \infty$

For f_2:

$|(\partial f_2)/(\partial P)| = |\gamma| < \infty$

$|(\partial f_2)/(\partial S)| = |-(\lambda + \mu)| < \infty$

$|(\partial f_2)/(\partial I)| = |-(\pi\theta(1-\vartheta)S)/(N)| < \infty$

$|(\partial f_2)/(\partial T)| = |\delta| < \infty$

For f_3:

$|(\partial f_3)/(\partial P)| = 0 < \infty$

$|(\partial f_3)/(\partial S)| = |\lambda| < \infty$

$|(\partial f_3)/(\partial I)| = |-(\mu + \beta + d)| < \infty$
$|(\partial f_3)/(\partial T)| = 0 < \infty$
For f_4:
$|(\partial f_4)/(\partial P)| = 0 < \infty$
$|(\partial f_4)/(\partial S)| = 0 < \infty$
$|(\partial f_4)/(\partial I)| = |\beta| < \infty$
$|(\partial f_4)/(\partial T)| = |-(\delta + \mu)| < \infty$
Thus, all the partial derivatives $(\partial f_i)/(\partial x_j),\ i,j = 1,2,3,4$ exist, and they are continuous and bounded in Ω. Hence, by Derrick and Grobsman theorem, a solution for the model (1) – (4) exists and is unique.

3.3 Disease Free Equilibrium (DFE)
To find the disease free equilibrium we consider the steady state of the system (1-4) which will be

$$\begin{aligned} &\alpha\Lambda - (\gamma + \mu)P = 0 \\ &(1-\alpha)\Lambda + \gamma P + \delta T - (\lambda + \mu)S = 0 \\ &\lambda S - (\mu + \beta + d)I = 0 \\ &\beta I - (\mu + \delta)T = 0 \end{aligned} \qquad (17)$$

Now, let $I = 0,\ T = 0$ be substituted in (17) and on solving the resultant equations for non-infected state variables, they are obtained as follows:

On solving the first equation $\alpha\Lambda - (\gamma + \mu)P = 0$ of (17), for P we get
$P = [\alpha\Lambda/(\gamma + \mu)]$
On solving the second equation $(1-\alpha)\Lambda + \gamma P + \delta T - (\lambda + \mu)S = 0$ of (17), for P we get
$S = [(\mu + \gamma - \alpha\mu)\Lambda/\mu(\mu + \gamma)]$
Therefore, the disease free equilibrium E_0 becomes

$$E_0 = \{[\alpha\Lambda/(\gamma + \mu)],\ [(\mu + \gamma - \alpha\mu)\Lambda/\mu(\mu + \gamma)],\ 0,\ 0\} \qquad (18)$$

3.4 Basic Reproduction Number $\mathfrak{R}_0$
The basic reproduction number is the average number of secondary cases a typical infectious individual will cause in a completely susceptible population. In this section, we obtained the basic reproduction number which is the threshold parameter that governs the spread of the disease. To obtain the basic reproduction number, we use the next generation matrix method which is the spectral radius of the next generation matrix.
Consider the newly infected groups (λS) and secondary infected groups $(\mu + \beta + d)$ I on the third equation of the model (1) given by $dI/dt = \lambda S - (\mu + \beta + d)I$. Then by principle of next generation matrix we obtain the newly infected individuals as

$$f = [\lambda S] = \left[\frac{\pi\theta\,(1-\vartheta)I}{N}S\right] \qquad (19)$$

Now, taking the partial derivative of equation (19) with respect to disease compartment I, we get $F = [\pi\theta(1-\vartheta)/N]S$. But, since at disease free equilibrium DFE) $S = [(\mu + \gamma - \alpha\mu)\Lambda/\mu(\mu + \gamma)]$ the function F takes the form as $F = [\pi\theta(1-\vartheta)/N][(\mu + \gamma - \alpha\mu)\Lambda/\mu(\mu + \gamma)]$. On substituting $N = \Lambda/\mu$ the expression for F reduces to the form as

$$F = \left[\frac{\pi\theta\,(1-\vartheta)\,(\mu+\gamma-\alpha\mu)}{(\mu+\gamma)}\right] \qquad (20)$$

To obtain the matrix V we consider the secondary infected group

$$V = (\mu + \beta + d)I \qquad (21)$$

Taking the partial derivative of equation (21) with respect to the disease compartment I, we get $V = (\mu + \beta + d)$ giving $V^{-1} = [1/(\mu + \beta + d)]$. Thus, the product matrix FV^{-1} is computed to be

$$FV^{-1} = \left[\frac{\pi\theta\,(1-\vartheta)\,(\mu+\gamma-\alpha\mu)}{(\mu+\gamma)\,(\mu+\beta+d)}\right] \qquad (22)$$

The basic reproduction number $\mathfrak{R}_0$, which is the spectral radius of the matrix FV^{-1} is thus given by

$$\rho(FV^{-1}) = \left[\frac{\pi\theta\,(1-\vartheta)\,(\mu+\gamma-\alpha\mu)}{(\mu+\gamma)\,(\mu+\beta+d)}\right]$$

Therefore, $$\mathfrak{R}_0 = \left[\frac{\pi\theta\,(1-\vartheta)\,(\mu+\gamma-\alpha\mu)}{(\mu+\gamma)\,(\mu+\beta+d)}\right] \qquad (23)$$

3.5 Local Stability of Disease-Free Equilibrium
Proposition 1: The disease free equilibrium point is locally asymptotically stable if $\mathfrak{R}_0 < 1$ and unstable if $\mathfrak{R}_0 > 1$.
Proof: To prove the proposition we first construct a Jacobean matrix for the system as

$$J = \begin{bmatrix} -(\gamma+\mu) & 0 & 0 & 0 \\ \gamma & -\left[\mu + \frac{\pi\theta\,(1-\vartheta)I}{N}\right] & -\frac{\pi\theta\,(1-\vartheta)S}{N} & \delta \\ 0 & \frac{\pi\theta\,(1-\vartheta)I}{N} & \frac{\pi\theta\,(1-\vartheta)S}{N} - (\mu+\beta+d) & 0 \\ 0 & 0 & \beta & -(\mu+\delta) \end{bmatrix} \quad (24)$$

Now evaluating the Jacobean matrix at disease free equilibrium point E_0 we get

$$J_{E_0} = \begin{bmatrix} -(\gamma+\mu) & 0 & 0 & 0 \\ \gamma & -\mu & -\frac{\pi\theta\,(1-\vartheta)\;(\mu+\gamma-\alpha\mu)}{\mu+\gamma} & \delta \\ 0 & 0 & \frac{\pi\theta\,(1-\vartheta)(\mu+\gamma-\alpha\mu)}{\mu+\gamma} - (\mu+\beta+d) & 0 \\ 0 & 0 & \beta & -(\mu+\delta) \end{bmatrix} \quad (25)$$

Now we compute the Jacobean matrix at disease free equilibrium and investigate its stability effect due to the reproduction number $\mathfrak{R}_0$.

$Trace\left(J_{E_0}\right) = -(\gamma+\mu) - \mu - (\mu+\delta) + \left[\frac{\pi\theta\,(1-\vartheta)(\mu+\gamma-\alpha\mu)}{\mu+\gamma}\right] - (\mu+\beta+d) = -(\gamma+\mu) - \mu - (\mu+\delta) + \mathfrak{R}_0\,(\mu+\beta+d) - (\mu+\beta+d)$

Equivalently it can be expressed as

$$Trace\left(J_{E_0}\right) = -(\gamma+\mu) - \mu - (\mu+\delta) + (\mu+\beta+d)\,(\mathfrak{R}_0 - 1) \quad (26)$$

Since all the parameters involved in the expression for $Trace\left(J_{E_0}\right)$ are positive it can be concluded that $\text{Trace}\left(J_{E_0}\right) < 0$ if $\mathfrak{R}_0 < 1$.

$$Det\left(J_{E_0}\right) = -(\gamma+\mu)(-\mu)\left[\frac{\pi\theta\,(1-\vartheta)(\mu+\gamma-\alpha\mu)}{\mu+\gamma} - (\mu+\beta+d)\right](-(\mu+\delta))$$

$$= -(\gamma+\mu)\mu(\mu+\delta)\left[\frac{\pi\theta\;(1-\vartheta)\;(\mu+\gamma-\alpha\mu)}{\mu+\gamma} - (\mu+\beta+d)\right]$$

Since $\mathfrak{R}_0 = \frac{\pi\theta\,(1-\vartheta)(\mu+\gamma-\alpha\mu)}{(\mu+\gamma)(\mu+\beta+d)} \Rightarrow \mathfrak{R}_0(\mu+\beta+d) = \frac{\pi\theta\,(1-\vartheta)(\mu+\gamma-\alpha\mu)}{\mu+\gamma}$ so we get

$$\text{Det}\left(J_{E_0}\right) = -(\gamma+\mu)\mu(\mu+\delta)[\,\mathfrak{R}_0\,(\mu+\beta+d) - (\mu+\beta+d)]$$

$$= (\gamma+\mu)\,\mu\,(\mu+\delta)\,(\mu+\beta+d)\;(1-\mathfrak{R}_0) \quad (27)$$

The determinant of the Jacobean matrix (25) remains positive if and only if $\mathfrak{R}_0 < 1$.

Thus, the model has a stable disease free equilibrium when $\mathfrak{R}_0 < 1$.

Hence, the proposition proved.

3.6 Global stability of Disease Free Equilibrium

In this section, the global stability of the disease free equilibrium point is analyzed by applying the technique used in [19]. The model system of four equations (1 - 4) can be written in the form of a system of two equations as below:

$$\frac{dX_s}{dt} = A\left(X_s - X_{DFE,s}\right) + A_1 X_i$$

$$\frac{dX_i}{dt} = A_2 X_i$$

Here X_s is the vector representing the non-transmitting compartment and X_i is the vector representing the transmitting compartments. The disease free equilibrium is globally asymptotically stable if A has negative eigenvalues and A_2 is a Metzler matrix i.e., the off-diagonal elements of A_2 are non-negative.

For the model equation (1-4) we have: $X_s = (P,S)^T$ and $X_i = (I,T)^T$

Where the superscript T refers to a transpose of the matrix

We need to check whether a matrix A for non-transmitting compartments has real negative eigen values and that A_2 is Metzler matrix. From the equation for non-transmitting compartments in the model we have:

$$\text{A} = \begin{bmatrix} -(\gamma+\mu) & 0 \\ \gamma & -(\lambda+\mu) \end{bmatrix}$$

From the matrix A above we can get two eigen values $\lambda_1 = -(\gamma+\mu)$ and $\lambda_2 = -(\lambda+\mu)$ both are real and negative. This implies that the system

$$\frac{dX_s}{dt} = A\left(X_s - X_{DFE,s}\right) + A_1 X_i$$

is locally and globally asymptotically stable at disease free equilibrium.

$$A_2 = \begin{bmatrix} -(\mu+\beta+d) & 0 \\ \beta & -(\mu+\delta) \end{bmatrix}$$

$$A_1 = \begin{bmatrix} 0 & 0 \\ 0 & \delta \end{bmatrix} \quad \text{and} \quad X_s - X_{DFE,s} = \begin{pmatrix} P - \frac{\alpha\Lambda}{\gamma+\mu} \\ S - \frac{(\mu+\gamma-\alpha\mu)\Lambda}{\mu(\mu+\gamma)} \end{pmatrix}$$

Since the off-diagonal elements of A_2 are non-negative so A_2 is a Metzler matrix.

3.7 Local Stability of the Endemic Equilibrium point (EE)

The endemic equilibrium denoted by $E^* = (P^*, S^*, I^*, T^*)$ and it occurs when the disease persists in the community. To obtain it, we equate all the model equation (1-4) to zero then we obtain

$$\alpha\Lambda - (\gamma+\mu)P = 0$$
$$(1-\alpha)\Lambda + \gamma P + \delta T - (\lambda+\mu)S = 0$$
$$\lambda S - (\mu+\beta+d)I = 0$$
$$\beta I - (\mu+\delta)T = 0$$

From $\frac{dP}{dt} = 0$ or $\alpha\Lambda - (\gamma+\mu)P = 0$, we get $P^* = \frac{\alpha\Lambda}{\gamma+\mu}$ (28)

From $\frac{dI}{dt} = 0$ or $\lambda S - (\mu+\beta+d)I = 0$

$$\Rightarrow \lambda S - (\mu+\beta+d)I = 0$$
$$\Rightarrow \left(\frac{\pi\theta(1-\vartheta)I}{N}\right)S - (\mu+\beta+d)I = 0$$
$$\Rightarrow S^* = \frac{N(\mu+\beta+d)}{\pi\theta(1-\vartheta)} \quad (29)$$

From $\frac{dT}{dt} = 0$, or $\beta I - (\mu+\delta)T = 0$ we have

$$T^* = \frac{\beta}{\mu+\delta}I^* \quad (30)$$

Again from $\lambda S - (\mu+\beta+d)I = 0$

$$\Rightarrow (\mu+\beta+d)I = \lambda S$$
$$\Rightarrow (\mu+\beta+d)I = \frac{\pi\theta(1-\vartheta)I}{N}S$$
$$\Rightarrow (\mu+\beta+d) = \frac{\pi\theta(1-\vartheta)}{N}S$$
$$\Rightarrow (\mu+\beta+d) = \frac{\pi\theta(1-\vartheta)}{N}(N-P-I-T)$$
$$\Rightarrow N-P-I-T = \frac{N(\mu+\beta+d)}{\pi\theta(1-\vartheta)}$$
$$\Rightarrow N - \frac{\alpha\Lambda}{\gamma+\mu} - I^* - \frac{\beta}{\mu+\delta}I^* = \frac{N(\mu+\beta+d)}{\pi\theta(1-\vartheta)}$$
$$\Rightarrow N - \frac{\alpha\Lambda}{\gamma+\mu} - \left(1+\frac{\beta}{\mu+\delta}\right)I^* = \frac{N(\mu+\beta+d)}{\pi\theta(1-\vartheta)}$$
$$\Rightarrow I^* = \frac{\mu+\delta}{\mu+\beta+\delta}\left[N - \frac{\alpha\Lambda}{\gamma+\mu} - \frac{N(\mu+\beta+d)}{\pi\theta(1-\vartheta)}\right] \quad (31)$$
$$\Rightarrow T^* = \frac{\beta}{\mu+\beta+\delta}\left[N - \frac{\alpha\Lambda}{\gamma+\mu} - \frac{N(\mu+\beta+d)}{\pi\theta(1-\vartheta)}\right] \quad (32)$$

Therefore, the endemic equilibrium point $E^* = (P^*, S^*, I^*, T^*)$ is

$$E^* = \left(\frac{\alpha\Lambda}{\gamma+\mu}, \frac{N(\mu+\beta+d)}{\pi\theta(1-\vartheta)}, \frac{\mu+\delta}{\mu+\beta+\delta}\left[N - \frac{\alpha\Lambda}{\gamma+\mu} - \frac{N(\mu+\beta+d)}{\pi\theta(1-\vartheta)}\right], \frac{\beta}{\mu+\beta+\delta}\left[N - \frac{\alpha\Lambda}{\gamma+\mu} - \frac{N(\mu+\beta+d)}{\pi\theta(1-\vartheta)}\right]\right) \quad (33)$$

Proposition2. The endemic equilibrium of the model (1-4) is locally asymptotically stable if $\mathfrak{R}_0 > 1$.

Proof: To prove the proposition we used the technique [18]. Accordingly, the stability of the endemic equilibrium is investigated using the trace and determinant of the Jacobean matrix at E^*.

$$J_{E^*}\begin{bmatrix} -(\gamma+\mu) & 0 & 0 & 0 \\ \gamma & d_1-\mu & -(\mu+\beta+d) & \delta \\ 0 & -d_1 & 0 & 0 \\ 0 & 0 & \beta & -(\mu+\delta) \end{bmatrix} \quad (34)$$

Where $d_1 = \frac{\mu+\delta}{\mu+\beta+\delta}\left[-\pi\theta(1-\vartheta) + (\mu+\beta+d) + \frac{\alpha\Lambda\pi\theta(1-\vartheta)}{N(\gamma+\mu)}\right]$

Now $Trace(J_{E^*}) = -(\gamma+\mu) - (\mu+\delta) - \mu + d_1$ $(*)$

$$\Rightarrow Trace(J_{E^*}) = -(\gamma+\mu) - (\mu+\delta) - \mu + \frac{\mu+\delta}{\mu+\beta+\delta}\left[-\pi\theta(1-\vartheta) + (\mu+\beta+d) + \frac{\alpha\Lambda\pi\theta(1-\vartheta)}{N(\gamma+\mu)}\right]$$

Since $\Lambda = \mu N$ substitute $\mu = \frac{\Lambda}{N}$ in the above equation

$$\Rightarrow \text{Trace}(J_{E^*}) = -(\gamma+\mu) - (\mu+\delta) - \mu + \frac{\mu+\delta}{\mu+\beta+\delta}\left[-\pi\theta(1-\vartheta) + (\mu+\beta+d) + \frac{\alpha\mu\pi\theta(1-\vartheta)}{(\gamma+\mu)}\right]$$
$$= -(\gamma+\mu) - (\mu+\delta) - \mu + \frac{\mu+\delta}{\mu+\beta+\delta}\left[-\pi\theta(1-\vartheta) + \frac{\alpha\mu\pi\theta(1-\vartheta)}{(\gamma+\mu)} + (\mu+\beta+d)\right]$$

$$= -(\gamma+\mu) - (\mu+\delta) - \mu + \frac{\mu+\delta}{\mu+\beta+\delta}\left[\pi\theta(1-\vartheta)(-1+\frac{\alpha\mu}{(\gamma+\mu)}) + (\mu+\beta+d)\right]$$

$$= -(\gamma+\mu) - (\mu+\delta) - \mu + \frac{\mu+\delta}{\mu+\beta+\delta}[\frac{-\pi\theta(1-\vartheta)(\mu+\gamma-\alpha\mu)}{\gamma+\mu} + (\mu+\beta+d)] \quad (35)$$

Since $\Re_0 = \frac{\pi\theta(1-\vartheta)(\mu+\gamma-\alpha\mu)}{(\mu+\gamma)(\mu+\beta+d)} \Rightarrow \Re_0(\mu+\beta+d) = \frac{\pi\theta(1-\vartheta)(\mu+\gamma-\alpha\mu)}{\gamma+\mu}$ so (35) becomes

$$= -(\gamma+\mu) - (\mu+\delta) - \mu + \frac{\mu+\delta}{\mu+\beta+\delta}[-\Re_0(\mu+\beta+d) + (\mu+\beta+d)]$$

$$= -(\gamma+\mu) - (\mu+\delta) - \mu + \frac{\mu+\delta}{\mu+\beta+\delta}(\mu+\beta+d)(1-\Re_0) \quad (**)$$

$$Trace\,(J_{E^*}) = -(\gamma+\mu) - (\mu+\delta) - \mu + \frac{\mu+\delta}{\mu+\beta+\delta}(\mu+\beta+d)(1-\Re_0) \quad (36)$$

From (36) we can observe that Trace$(J_{E^*}) < 0$ if $\Re_0 > 1$

$$\text{Det}\,(J_{E^*}) = -(\gamma+\mu)\begin{vmatrix} d_1-\mu & -(\mu+\beta+d) & \delta \\ -d_1 & 0 & 0 \\ 0 & \beta & -(\mu+\delta) \end{vmatrix}$$

$$= -(\gamma+\mu)\left[(d_1-\mu)\begin{vmatrix} 0 & 0 \\ \beta & -(\mu+\delta) \end{vmatrix} + (\mu+\beta+d)\begin{vmatrix} -d_1 & 0 \\ 0 & -(\mu+\delta) \end{vmatrix} + \delta\begin{vmatrix} -d_1 & 0 \\ 0 & \beta \end{vmatrix}\right]$$

$$= -(\gamma+\mu)[(\mu+\beta+d)(\mu+\delta)d_1 - \delta\beta d_1]$$

$$= -(\gamma+\mu)[(\mu+\beta+d)(\mu+\delta) - \delta\beta]\,d_1$$

$$= -(\gamma+\mu)[\mu^2+\mu\delta+\beta\mu+\beta\delta+d\mu+d\delta-\delta\beta]\,d_1$$

$$= -(\gamma+\mu)[\mu^2+\mu\delta+\beta\mu+d\mu+d\delta]\,d_1$$

From $(*) and\ (**)$ we have $d_1 = \frac{\mu+\delta}{\mu+\beta+\delta}(\mu+\beta+d)(1-\Re_0)$

$$Det(J_{E^*}) = -(\gamma+\mu)[\mu^2+\mu\delta+\beta\mu+d\mu+d\delta]\frac{\mu+\delta}{\mu+\beta+\delta}(\mu+\beta+d)(1-\Re_0)$$

$$= (\gamma+\mu)[\mu^2+\mu\delta+\beta\mu+d\mu+d\delta]\frac{\mu+\delta}{\mu+\beta+\delta}(\mu+\beta+d)(\Re_0-1) \quad (37)$$

From (37) we can observe that $Det(J_{E^*}) > 0$ if and only if $\Re_0 > 1$

Therefore, the model has an asymptotic stable endemic equilibrium provided that $\Re_0 > 1$

Hence, the proposition is proved.

Lemma 2: The endemic equilibrium point E^* of the model exists and no endemic equilibrium otherwise.

Proof: For the disease to be endemic $\frac{dI}{dt} > 0$ must hold. That is:

$$\Rightarrow \lambda S - (\mu+\beta+d)I > 0$$

$$\Rightarrow (\mu+\beta+d)I < \lambda S \qquad \text{Where } \lambda = \frac{\pi\theta(1-\vartheta)I}{N}$$

$$\Rightarrow (\mu+\beta+d)I < \frac{\pi\theta(1-\vartheta)I}{N}S$$

Using the fact that $S < S_1$ where S_1 is the number of susceptible individuals at DFE

$$\Rightarrow (\mu+\beta+d)I < \frac{\pi\theta(1-\vartheta)I}{N}S_1 \qquad \Rightarrow (\mu+\beta+d) < \frac{\pi\theta(1-\vartheta)}{N}S_1$$

$$\Rightarrow 1 < \frac{\pi\theta(1-\vartheta)}{N(\mu+\beta+d)}S_1 \qquad \text{since } S_1 = \frac{(\mu+\gamma-\alpha\mu)\Lambda}{\mu(\mu+\gamma)}$$

$$\Rightarrow 1 < \frac{\pi\theta(1-\vartheta)}{(\mu+\beta+d)}\frac{(\mu+\gamma-\alpha\mu)}{(\mu+\gamma)}$$

$$\Rightarrow 1 < \Re_0$$

Thus a unique endemic equilibrium exist when $\Re_0 > 1$.

Bifurcation Diagram

The threshold number (basic reproduction number $\Re_0$) plays a major role in determining the qualitative behavior of epidemic models. We note that at $\Re_0 = 1$ the disease-free equilibrium and endemic equilibrium exchange stability. This phenomenon of change of stability, known as *forward bifurcation*, has been observed in several epidemic models

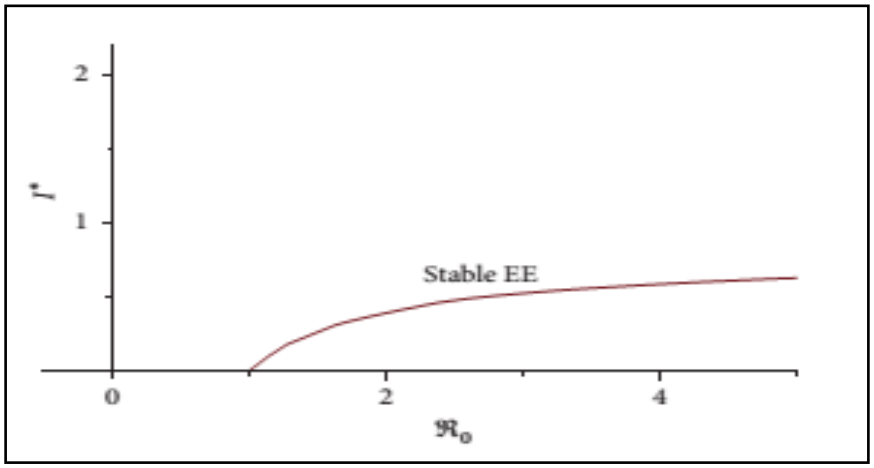

Figure2. Forward bifurcation of typhoid fever model

Table1. Parameter values for typhoid fever model.

Parameter symbol	Parameter description	Value	Source
Λ	Recruitment rate	2.2	Assumed
α	Proportion of protected individuals at birth	0.8	[13]
μ	Natural mortality rate	0.022	Estimated
λ	Effective force of infection	0.0001	Assumed
d	Typhoid induced mortality rate	0.05	Assumed
γ	Rate of loss of protection	0.01	Assumed
β	Rate of treatment	0.9	[13]
δ	Removal rate from treated subclass to susceptible subclass	0.000904	Adutunde,2008
θ	Contact rate of infection	0.003	Assumed
ϑ	Effective rate of protection against infection	0.7	Assumed
π	Transmission probability rate of typhoid	0.015	Assumed

4. Sensitivity Analysis of the model parameters

Sensitivity analysis was carried out to determine the model robustness to parameter values. This will help us in identifying and verifying model parameters that most influence the pathogen fitness threshold for the pathogens. Further, values obtained for sensitivity indexes indicate which parameters should be targeted most for intervention purposes.

Sensitivity analysis of $\Re_0$ with respect to each parameter

The sensitivity analysis of the parameters can be calculated as follows.

$$\theta^{\Re_0} = \frac{\partial \Re_0}{\partial \theta} \times \frac{\theta}{\Re_0} = +1$$

$$\gamma^{\Re_0} = \frac{\partial \Re_0}{\partial \gamma} \times \frac{\gamma}{\Re_0} = +0.38$$

Similarly we can get the sensitivity index of each parameter

Table2. Sensitivity index of the model parameters

Parameter	Sensitivity Index
θ	+1
π	+1
γ	+0.38
δ	0
d	-0.0514
β	-0.93
α	-1.2
ϑ	-2.3

μ	-2.8

Parameters that have positive indices ($\theta,\ \pi\ and\ \gamma$) have great impact on escalating the disease if their number is increasing when other parameters remain constant. Those parameters in which their sensitivity indices are negative (d, $\beta,\ \alpha, \vartheta$ and μ) have an influence of minimizing the burden of the disease in the community as their values increases. The total population mortality and morbidity attributable to typhoid fever can be best reduced by investigating the relative importance of the parameters featuring in the basic reproduction number. To determine how best we can do in order to reduce human mortality and morbidity due to Typhoid fever, it is necessary to know the relative importance of the different factors responsible for its transmission and prevalence.

IV. Numerical Simulations

Numerical simulations were carried based on the parameter values that are listed on Table1. The simulation is carried out using DEDiscover software illustrated that the long term behavior of protection and treatment on the transmission dynamics of typhoid fever. The simulation diagram illustrate that using treatment on typhoid infected population reduces the burden of the disease.

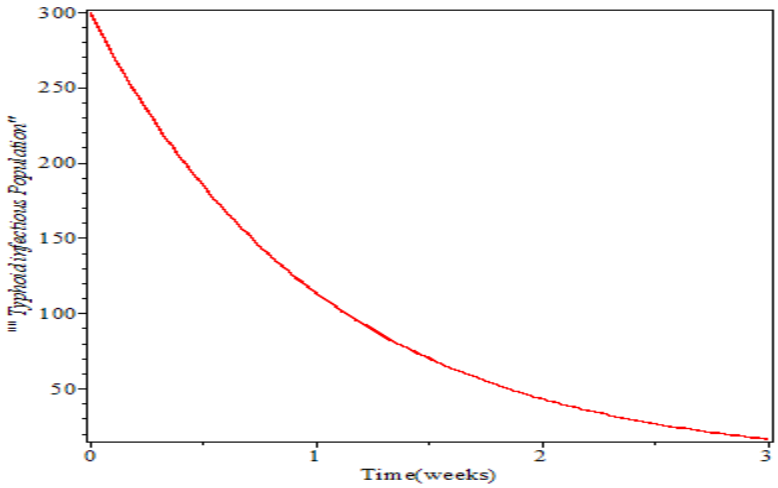

Figure3. Infectivity as a function of time

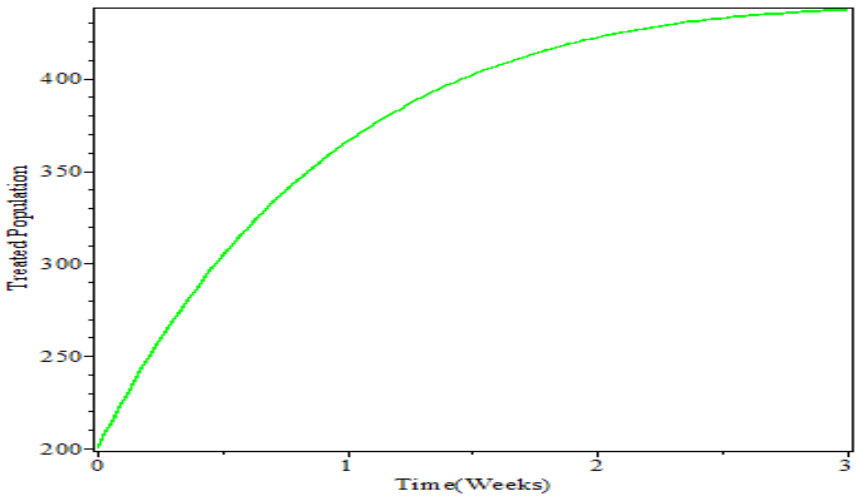

Figure 4. Treatment group as a function of time

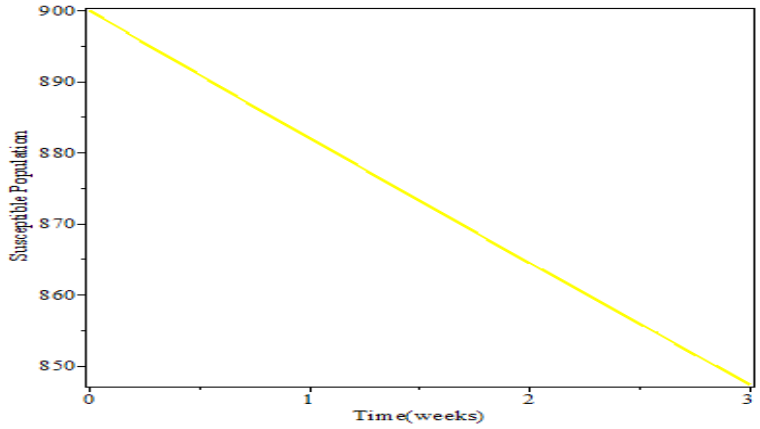

Figure 5. Susceptible population as a function of time

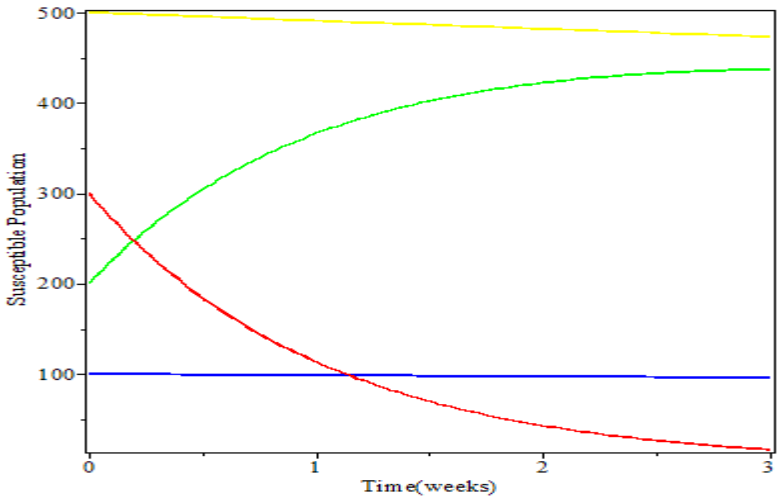

Figure6. Comparison of all variables

V. Conclusion

In this study, a deterministic compartmental model for the transmission dynamics of typhoid fever disease is proposed. The boundedness and positivity of the model is proved. The qualitative analysis of the system shows that the solution of the model is bounded and positive and also the equilibria points of the model are obtained and their local as well as global stability condition is established. The model has a unique disease free equilibrium if $\Re_0<1$ and has endemic equilibrium if $\Re_0>1$. The result that is obtained from the numerical simulation revealed that both protection and treatment are effective to control typhoid disease transmission. Hence an increase in protection and treatment leads to low disease prevalence in a population.

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