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Modelling and Stability Analysis of Typhoid Fever Transmission Dynamics with control Strategies

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Abstract

Typhoid, an acute gastro-intestinal infection and a waterborne disease continues to emerge in developing countries and remains an important global health challenge. In this paper, we develop a deterministic compartmental mathematical model for assessing the effects of education campaigns, vaccination and treatment on controlling the transmission dynamics of typhoid fever in the community. We have shown that the disease free equilibrium state of the model is locally asymptotically stable if the basic reproduction number is less than unity otherwise if the basic reproduction number is greater than unity then the disease persists and the unique endemic equilibrium is globally asymptotically stable in the interior of the feasible region under some conditions. Numerical simulation reveals that when each of the controls increased it tends to decrease the disease outbreak, this is in support with analytical results which yielded the same results. We performed sensitivity analysis on the key parameters that drive the disease dynamics in order to determine their relative importance to disease transmission and prevalence.

Keywords: typhoid; reproductive number; treatment; vaccination; stability; gastro-intestinal infection.

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1. Introduction

Typhoid is a major public health concern in tropical developing countries, especially in areas where access to clean water and other sanitation measures are limited [1, 2, 3].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, localized multiplication in the mesenteric lymph nodes, and subsequent spread to the liver and spleen prior to showing clinical symptoms [4]. 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 [5].

The disease is endemic in many developing countries and despite recent progress in water and sanitation coverage, it remains a substantial public health problem. Globally, it is estimated that typhoid causes over 16 million cases of illness each year, resulting in over 600,000 deaths [6]. Typhoid has a long storied history as a public health scourge. *Salmonella enterica serovar Typhi (S. Typhi)* is a human restricted bacterial pathogen transmitted via faecal contamination of food and water [7]. While improvements in water and sanitation led to the elimination of typhoid from most developed countries during the twentieth century, the global burden of typhoid fever has recently been estimated to be between 13.5 and 26.9 million episodes and 190,000 to 216,000 deaths annually [8].

In many developing nations, the public health goals that can help prevent and control the spread of typhoid fever disease through safe drinking water, improved sanitation and adequate medical care may be difficult to achieve. Health education is paramount to raise public awareness and induce behavior change [9].

Several mathematical models have been developed to explain the dynamics of the disease [6, 10,11,12,13, 22] but none has incorporated a combination of public health education campaigns, vaccination and treatment as control strategies. This study is at hand to fill the gap by developing an $SVII_cR$ (susceptible, vaccinated, symptomatic infectious, asymptomatic infectious and recovered) model of typhoid fever with the mentioned control strategies. We assume that all susceptible individuals are equally likely to be infected by infectious individuals in case of contact, we also assume direct transmission of typhoid from infected individuals to susceptible individuals and that there is a constant recruitment rate to the susceptible population. Furthermore, we assume that the rate of transmission for carriers is greater than that of symptomatic infectious individuals.

2. Model Formulation

In this paper, we develop a deterministic compartmental typhoid transmission model that captures vaccination, education campaign and treatment as control as strategies. In order to study the impact of these control strategies on the dynamics of typhoid fever, this model considers the human population, $N(t)$ divided into five sub-populations namely; susceptible, $S(t)$, vaccinated, $V(t)$, infectious, $I(t)$, Typhoid carriers, $I_c(t)$, and recovered individuals, $R(t)$. Individuals are recruited into the susceptible population by either immigration or birth at the

rate a constant rate Λ. We assume that proportion p of $S(t)$ progress to carrier class, while the compliment $1-p$ progress to symptomatic infectious compartment. Carriers can become symptomatic at some rate α or die due to typhoid at the rate d_1.

Infectious individuals can receive treatment and recover at the rate η. Recovered individuals may become susceptible again at the rate ω_2, this is due to the fact that typhoid does not confer permanent immunity on recovery. Susceptible individuals receive vaccination to protect them against infection at the rate θ.

Since vaccine wanes with time, then after its expiry the vaccinees can return back to susceptible class at the rate ω_1. We assume that an individual in each compartment may undergo a natural death at rate μ. Let β and γ be transmission rates for infectious and carrier individuals respectively then the susceptible population $S(t)$, is exposed to force of infection denoted by λ, where $\lambda = \beta I + \gamma I_c$.

It must be clear in mind that $1-\psi_e$ is an educational parameter that caters for limiting both carriers and symptomatic individuals from spreading typhoid. In fact this parameter lies in an interval $0 < \psi_e < 1$. When $\psi_e = 0$ it means that no education campaigns are in place so susceptible population are ignorant of typhoid fever and when $\psi_e = 1$ then it means that the all susceptible individuals are fully aware of typhoid fever, that is to say they know what causes the diseases, how it is spread and how to avoid contracting the disease.

Detailed description of parameters is shown in Table 1 while the compartmental flow diagram of the model is shown by Figure 1.

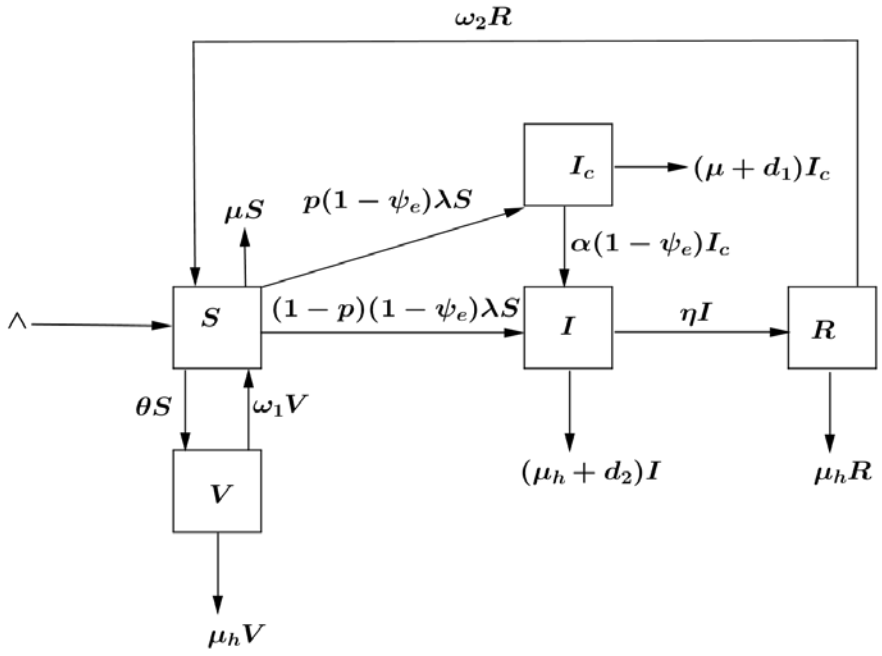

Figure 1: A compartmental diagram for the Typhoid transmission dynamics model that incorporates public Health Education Campaigns, Vaccination and Treatment.

Table 1: Parameters and their description

Parameter	Value	Description	Source
Λ	10^6/year	Recruitment rate	[16,17]
ω_1	0.1/year	Rate at which the vaccine wanes	Estimated
ω_2	0.3/year	Rate at which recovered individuals lose immunity	Estimated
η	0.15/year	Recovery rate for symptomatic infectious individuals	[6]
θ	0.6/year	Rate at which susceptible individuals are vaccinated	Estimated
β	0.02/year	Transmission rate for symptomatic infectious individuals	Estimated
γ	0.01/year	Transmission rate for carrier individuals	[16]
p	0.5/year	Proportion of newly infected individuals who become carrier	[8]
ψ_e	0.4/year	Education parameter	Estimated
α	0.04/year	Rate at which carriers develop symptoms	[16]
μ	0.142/year	Natural mortality rate of individuals	[16]
d_2	0.012/year	Disease-induced mortality rate of symptomatic individuals	[16]
d_1	0.01/year	Disease-induced mortality rate of carriers	[16]

2.1 Model Equations

From the description of the dynamics of typhoid and with the aid of the compartmental diagram in Figure 1, the following set of non-linear ordinary differential equations can be derived:

$$\frac{dS}{dt} = \Lambda + \omega_1 V + \omega_2 R - (\theta + \mu + (1-\psi_e)(\beta I + \gamma I_c))S \quad (1)$$

$$\frac{dV}{dt} = \theta S - (\omega_1 + \mu)V \quad (2)$$

$$\frac{dI}{dt} = (1-p)(1-\psi_e)(\beta I + \gamma I_c)S - (\eta + d_2 + \mu)I + \alpha(1-\psi_e)I_c \quad (3)$$

$$\frac{dI_c}{dt} = p(1-\psi_e)(\beta I + \gamma I_c)S - (\mu + d_1 + \alpha(1-\psi_e))I_c \quad (4)$$

$$\frac{dR}{dt} = \eta I - (\omega_2 + \mu)R \quad (5)$$

2.2 Feasibility Region

From system (1-5) we have:

$$\frac{dN}{dt} = \Lambda - \mu N - d_1 I_c - d_2 I \leq \Lambda - \mu N \quad (6)$$

Thus,

$$N(t) \leq \frac{\Lambda}{\mu}(1 - \mathrm{e}^{-\mu t}) + N(0)\mathrm{e}^{-\mu t} \tag{7}$$

as $t \to \infty$, $\mathrm{e}^{-\mu t} \to 0$ and hence $N(t) \leq \frac{\Lambda}{\mu}$. Therefore, the model can be studied in the feasible region

$$D = \left\{(S, V, I, I_c, R) \in \mathbb{R}_+^5 : S + V + I + I_c \leq \frac{\Lambda}{\mu}\right\} \tag{8}$$

which is bounded and positively invariant.

3. Model analysis

The model system (1-5) is analyzed qualitatively to get insights into its dynamical features which give better understanding of the impact control strategies on the transmission dynamics of typhoid fever.

3.1 Equilibria

Setting the left hand side of system (1-5) equal to zero, we have:

$$0 = \Lambda + \omega_1 V + \omega_2 R - (\theta + \mu + (1 - \psi_e)(\beta I + \gamma I_c))S \tag{9}$$

$$0 = \theta S - (\omega_1 + \mu)V \tag{10}$$

$$0 = (1 - p)(1 - \psi_e)(\beta I + \gamma I_c)S - (\eta + d_2 + \mu)I + \alpha(1 - \psi_e)I_c \tag{11}$$

$$0 = p(1 - \psi_e)(\beta I + \gamma I_c)S - (\mu + d_1 + \alpha(1 - \psi_e))I_c \tag{12}$$

$$0 = \eta I - (\omega_2 + \mu)R \tag{13}$$

Model system (1-5) has a disease-free equilibrium

$$E_0 = \left(S^0, V^0, I^0, {I_c}^0, R^0\right) = \left(\frac{\Lambda(\omega_1 + \mu)}{\mu(\theta + \omega_1 + \mu)}, \frac{\Lambda\theta}{\mu(\theta + \omega_1 + \mu)}, 0, 0, 0\right). \tag{14}$$

An endemic equilibrium $E^* = (S^*, V^*, I^*, {I_c}^*, R^*)$ satisfies $S^*, V^*, I^*, {I_c}^*, R^* > 0$.

From the equilibrium equations we can show that E^* exists with

$$S^* = \frac{(\mu + d_2 + \eta)(\mu + d_1 + \alpha(1 - \psi_e))}{(1 - \psi_e)\{(1 - p)\beta\left(\mu + d_1 + \alpha(1 - \psi_e)\right) + p\gamma(\mu + d_2 + \eta) + p\beta\alpha(1 - \psi_e)\}}$$

For E^* to exist in the feasible region D, the necessary and sufficient condition is that:

$$0 < S^* < \frac{\Lambda(\omega_1+\mu)}{\mu(\theta+\omega_1+\mu)} \quad \text{or equivalently,} \quad \frac{\Lambda(\omega_1+\mu)}{\mu(\theta+\omega_1+\mu)S^*} \geq 1 \tag{15}$$

Define

$$R_e = \frac{1}{S^*}\frac{\Lambda(\omega_1+\mu)}{\mu(\theta+\omega_1+\mu)}$$

$$\mathcal{R}_e = \frac{(1-\psi_e)\Lambda(\omega_1+\mu)}{\mu(\theta+w_1+\mu)}\left[\frac{(1-p)\beta}{(\mu+d_2+\eta)} + \frac{p\gamma}{(\mu+d_1+\alpha(1-\psi_e))} + \frac{p\alpha\beta(1-\psi_e)}{(\mu+d_2+\eta)(\mu+d_1+\alpha(1-\psi_e))}\right]$$

Then R_e is a threshold parameter that determines the number of equilibria. We will show in Section (3.2) that R_e is the basic reproduction number.

Proposition . If $R_e < 1$ then E_0 is the only equilibrium in system (1-5); if $R_e > 1$, then there are two equilibria, disease free equilibrium, E_0 and a unique endemic equilibrium, E^*.

3.2 The Reproduction Number, R_0

The basic reproduction number denoted by R_0 is the average number of secondary infections caused by an infectious individual during his or her entire period of infectiousness [14].The basic reproduction number is an important non-dimensional quantity in epidemiology as it sets the threshold in the study of a disease both for predicting its outbreak and for evaluating its control strategies. Thus, whether a disease becomes persistent or dies out in a community depends on the value of the reproduction number, R_0. Furthermore, stability of equilibria can be analyzed using R_0; if $R_0 < 1$ it means that every infectious individual will cause less than one secondary infection and hence the disease will die out and when $R_0 > 1$, every infectious individual will cause more than one secondary infection and hence the disease will invade the population. A large number of R_0 may indicate the possibility of a major epidemic. For the case of a model with a single infected class, R_0 is simply the product of the infection rate and the mean duration of the infection.

In this paper, the reproductive number accounts for the average number of new typhoid cases generated by a single typhoid infected individual (either from symptomatic class or from chronic enteric carriers) introduced into a wholly susceptible population.

Due to complicated epidemics in our model, we compute the reproduction number, R_e using the next generation operator approach by [15].The reproduction number for the model in system eqn. (1-5) is:

$$\mathcal{R}_e = \frac{(1-\psi_e)\Lambda(\omega_1+\mu)}{\mu(\theta+w_1+\mu)}\left[\frac{(1-p)\beta}{(\mu+d_2+\eta)} + p\left(\frac{\gamma}{(\mu+d_1+\alpha(1-\psi_e))} + \frac{\alpha\beta(1-\psi_e)}{(\mu+d_2+\eta)(\mu+d_1+\alpha(1-\psi_e))}\right)\right] \tag{16}$$

Considering equation (16) above, we can give the interpretations of the effective reproduction, $\mathcal{R}_e$ of our model as follows:

When a single infective is introduced into the population, with probability $1-p$ it is a non-carrier, hence makes β effective contacts per unit time. This is multiplied by the average infectious period $\frac{1}{\mu+d_2+\eta}$ for non-carriers; with probability p the infective is a carrier, and hence makes γ effective contacts per unit time during the average period $\frac{1}{\mu+d_1+\alpha(1-\psi_e)}$ it remains a carrier. This number should be augmented by the number of infections $\frac{\beta(1-\psi_e)}{\mu+d_2+\eta}$ caused by this infective after it becomes a non-carrier, with probability $\frac{\alpha}{\mu+d_1+\alpha(1-\psi_e)}$ to survive the carrier stage. Therefore, the expression in the big square brackets in (16) is the per capita average number of secondary infections. This number multiplied by the number of susceptibles at the disease-free equilibrium, $\frac{\Lambda(\omega_1+\mu)}{\mu(\theta+\omega_1+\mu)}$ and educational parameter $1-\psi_e$ gives R_e.

3.3 Local Stability of Disease-Free Equilibrium point (DFE)

We show that, the variation matrix, $\mathbf{J}(E_0)$ of model system (1-5) has negative trace and positive determinant. The partial differentiation of (1-5) with respect to (S, V, I, I_c, R) at the disease free equilibrium gives:

$$J(E_0) = \begin{bmatrix} -(\theta+\mu) & \omega_1 & -(1-\psi_e)\beta S^0 & -(1-\psi_e)\gamma S^0 \\ \theta & -(\omega_1+\mu) & 0 & 0 \\ 0 & 0 & (1-p)(1-\psi_e)\beta S^0 - (\eta+d_2+\mu) & p(1-\psi_e)\gamma S^0 + \alpha(1-\psi_e) \\ 0 & 0 & p(1-\psi_e)\beta S^0 & p(1-\psi_e)\gamma S^0 - (\mu+d_1+\alpha(1-\psi_e)) \end{bmatrix}$$

We have the following stability result that shows R_e is a sharp threshold.

Proposition 2.

E_0 is locally asymptotically stable if $R_e < 1$ and is unstable if $R_e > 1$.

Proof

We want to show, when $R_e < 1$, that the Routh-Hurwitz conditions hold, namely,

$tr(J(E_0)) < 0$ and $det(J(E_0)) > 0$

$$tr\big(J(E_0)\big) = (1-p)(1-\psi_e)\beta S^0 + p(1-\psi_e)\gamma S^0 - \big(\mu+d_1+\alpha(1-\psi_e)\big) - (\eta+d_2+\mu) - (\theta+\mu) - (\omega_1+\mu)$$

$$= (1-p)(1-\psi_e)\beta S^0 + p(1-\psi_e)\gamma S^0 - \big(4\mu+\theta+\omega_1+\eta+d_1+d_2+\alpha(1-\psi_e)\big)$$

If $(1-p)(1-\psi_e)\beta S^0 + p(1-\psi_e)\gamma S^0 < \big(4\mu+\theta+\omega_1+\eta+d_1+d_2+\alpha(1-\psi_e)\big)$ then $tr(J(E_0)) < 0$

also,

$$\det\big(\mathrm{J}(E_0)\big) = \mu(\theta + \omega_1 + \mu)(ad - bc) = \mu(\theta + \omega_1 + \mu)ad(1 - \mathcal{R}_e)$$

where $\mathcal{R}_e = \frac{bc}{ad}$

$$a = (1-p)(1-\psi_e)\beta S^0 + p(1-\psi_e)\gamma S^0$$

$$b = (1-p)(1-\psi_e)\gamma S^0 + \alpha(1-\psi_e)$$

$$c = p(1-\psi_e)\beta S^0$$

$$d = p(1-\psi_e)\gamma S^0 - (\mu + d_1 + \alpha(1-\psi_e))$$

Therefore, $\det\big(\mathbf{J}(E_0)\big) > 0$ if and only if $\mathcal{R}_e < 1$. This proves the proposition.

3.4 Global Stability of Disease-Free Equilibrium point (DFE)

Theorem 1. *E_0 is globally asymptotically stable in the feasible region D if $R_e \leq 1$.*

Proof. To prove the global asymptotic stability of E_0 we use the method of Lyapunov functions.

Define $L = XI + YI_c$

where $X = \frac{\beta}{(\mu+d_2+\eta)}$, $Y = \left(\frac{\gamma}{(\mu+d_1+\alpha(1-\psi_e))} + \frac{\alpha\beta(1-\psi_e)}{(\mu+d_2+\eta)(\mu+d_1+\alpha(1-\psi_e))}\right)$

then we have

$$\frac{dL}{dt} = X\,\frac{dI}{dt} + Y\frac{dI_c}{dt} \tag{17}$$

$$= X\big((1-p)(1-\psi_e)(\beta I + \gamma I_c)S - (\eta + d_2 + \mu)I + \alpha(1-\psi_e)I_c\big)$$

$$+Y[p(1-\psi_e)(\beta I + \gamma I_c)S - (\mu + d_1 + \alpha(1-\psi_e))I_c]$$

If we substitute the values of X and Y in equation (17) above and simplifying we shall get

$$\frac{dL}{dt} = (R_e s - 1)(\beta I + \gamma I_c) - \frac{2\beta\alpha(1-\psi_e)}{(\mu + d_2 + \eta)}\, I_c$$

Using the condition that $0 < S^* < \frac{\Lambda(\omega_1+\mu)}{\mu(\theta+\omega_1+\mu)}$ we have:

$$\frac{dL}{dt} \leq (R_e \frac{\Lambda(\omega_1 + \mu)}{\mu(\theta + \omega_1 + \mu)} - 1)(\beta I + \gamma I_c) - \frac{2\beta\alpha(1-\psi_e)}{(\mu + d_2 + \eta)}\, I_c \leq 0$$

So $\frac{dL}{dt} \leq 0$ if $R_e \leq 1$. Furthermore, $\frac{dL}{dt} = 0$ if $I = I_c = 0$ or $R_e = 1$ and $S^* = \frac{\Lambda(\omega_1+\mu)}{\mu(\theta+\omega_1+\mu)}$.

Therefore the largest invariant set in the closure of D where $\frac{dL}{dt} = 0$ is the singleton $\{E_0\}$. LaSalle's Invariance Principle [19], E_0 is globally asymptotically stable in D, completing the proof.

3.5 Global Stability of Endemic Equilibrium Point

Global stability of the EE is explored via the construction of a suitable Lyapunov function. Since the DFE is locally stable this will suggest local stability of the EE for the reverse condition as in condition [11], we only investigate the global stability of the endemic equilibrium.

Theorem 2

If $R_e > 1$, then the system has a unique EE point $P*$ which is GAS in D.

Proof

Consider the following function:

$$Z = A_1(S - S^* lnS) + A_2(V - V^* lnV) + A_3(I - I^* lnI) + A_4(I_c - I_c{}^* lnI_c) + A_5(R - R^* lnR)$$

Differentiating each state variable with respect to time we get:

$$Z' = A_1\left(1 - \frac{S^*}{S}\right)s' + A_2\left(1 - \frac{V^*}{V}\right)V' + A_3\left(1 - \frac{I^*}{I}\right)I' + A_4\left(1 - \frac{I^*c}{I_c}\right)I_c' + A_5\left(1 - \frac{R^*}{R}\right)R'$$

If we substitute the expressions for S', V', I', I'_c, R' from equations (3-5) we get:

$$\frac{dZ}{dt} = A_1(1 - \frac{S^*}{S})[\Lambda + \omega_1 V + \omega_2 R - (\theta + \mu + (1 - \psi_e)(\beta I + \gamma I_c))S]$$

$$+A_2\left(1 - \frac{V^*}{V}\right)[\theta S - (\omega_1 + \mu)V]$$

$$+A_3\left(1 - \frac{I^*}{I}\right)[(1 - p)(1 - \psi_e)(\beta I + \gamma I_c)S - (\eta + d_2 + \mu)I + \alpha(1 - \psi_e)I_c]$$

$$+A_4\left(1 - \frac{I^*c}{I_c}\right)[p(1 - \psi_e)(\beta I + \gamma I_c)S - (\mu + d_1 + \alpha(1 - \psi_e))I_c]$$

$$+A_5\left(1 - \frac{R^*}{R}\right)[\eta I - (\omega_2 + \mu)R]$$

further simplification yields

$$\frac{dZ}{dt} = A_1\left(1-\frac{S^*}{S}\right)\omega_1 V\left(1-\frac{V^*}{V}\right) + A_1\left(1-\frac{S^*}{S}\right)\omega_2 R\left(1-\frac{R^*}{R}\right) - A_1\left(1-\frac{S^*}{S}\right)^2(\theta+\mu)SV(1-\frac{V^*}{V})$$

$$-A_1\left(1-\frac{S^*}{S}\right)(1-\psi_e)\beta I\left(1-\frac{I^*}{I}.\frac{S^*}{S}\right) - A_1\left(1-\frac{S^*}{S}\right)(1-\psi_e)\gamma SI_c\left(1-\frac{I_c^*}{I_c}.\frac{S^*}{S}\right)$$

$$+A_2\left(1-\frac{V^*}{V}\right)\theta S(1-\frac{V}{V^*}.\frac{S^*}{S}) + A_3\left(1-\frac{I^*}{I}\right)(1-p)(1-\psi_e)\beta IS\left(1-\frac{S^*}{S}\right)$$

$$+A_3\left(1-\frac{I^*}{I}\right)(1-p)(1-\psi_e)\gamma SI_c\left(1-\frac{I_c^*}{I_c}.\frac{I}{I^*}\right) + A_4\left(1-\frac{I_c^*}{I_c}\right)\beta IS\left(1-\frac{I_c}{I_c^*}.\frac{I^*}{I}.\frac{S^*}{S}\right)$$

$$+A_4\left(1-\frac{I_c^*}{I_c}\right)\gamma SI_c\left(1-\frac{S^*}{S}\right) + A_5\left(1-\frac{R^*}{R}\right)\eta I\left(1-\frac{I^*}{I}.\frac{R}{R^*}\right)$$

which can be further simplified to:

$$\frac{dZ}{dt} = -A_1\left(1-\frac{S^*}{S}\right)^2(\theta+\mu)SV\left(1-\frac{V^*}{V}\right) - A_1\left(1-\frac{S^*}{S}\right)(1-\psi_e)\beta I\left(1-\frac{I^*}{I}.\frac{S^*}{S}\right)$$

$$-A_1\left(1-\frac{S^*}{S}\right)(1-\psi_e)\gamma SI_c\left(1-\frac{I_c^*}{I_c}.\frac{S^*}{S}\right)$$

$$+A_1\left(1-\frac{S^*}{S}\right)\omega_1 V\left(1-\frac{V^*}{V}\right) + A_1\left(1-\frac{S^*}{S}\right)\omega_2 R\left(1-\frac{R^*}{R}\right) + A_2\left(1-\frac{V^*}{V}\right)\theta S(1-\frac{V}{V^*}.\frac{S^*}{S})$$

$$+A_3\left(1-\frac{I^*}{I}\right)(1-p)(1-\psi_e)\beta IS\left(1-\frac{S^*}{S}\right)$$

$$+A_3\left(1-\frac{I^*}{I}\right)(1-p)(1-\psi_e)\gamma SI_c\left(1-\frac{I_c^*}{I_c}.\frac{I}{I^*}\right)$$

$$+A_4\left(1-\frac{I_c^*}{I_c}\right)\beta IS\left(1-\frac{I_c}{I_c^*}.\frac{I^*}{I}.\frac{S^*}{S}\right) + A_4\left(1-\frac{I_c^*}{I_c}\right)\gamma SI_c\left(1-\frac{S^*}{S}\right)$$

$$+A_5\left(1-\frac{R^*}{R}\right)\eta I\left(1-\frac{I^*}{I}.\frac{R}{R^*}\right)$$

this result can in same way be written as:

$$\frac{dZ}{dt} = -A_1\left(1-\frac{S^*}{S}\right)^2(\theta+\mu)SV\left(1-\frac{V^*}{V}\right) - A_1\left(1-\frac{S^*}{S}\right)(1-\psi_e)\beta I\left(1-\frac{I^*}{I}.\frac{S^*}{S}\right)$$

$$-A_1\left(1-\frac{S^*}{S}\right)(1-\psi_e)\gamma SI_c\left(1-\frac{I_c^*}{I_c}.\frac{S^*}{S}\right) + F(S,V,I,I_c,R)$$

where $F(S,V,I,I_c,R) = A_1\left(1-\frac{S^*}{S}\right)\omega_1 V\left(1-\frac{V^*}{V}\right) + A_1\left(1-\frac{S^*}{S}\right)\omega_2 R\left(1-\frac{R^*}{R}\right)$

$$+A_2\left(1-\frac{V^*}{V}\right)\theta S(1-\frac{V}{V^*}.\frac{S^*}{S})$$

$$+A_3\left(1-\frac{I^*}{I}\right)(1-p)(1-\psi_e)\beta IS\ \left(1-\frac{S^*}{S}\right)$$

$$+A_3\left(1-\frac{I^*}{I}\right)(1-p)(1-\psi_e)\gamma SI_c\ \left(1-\frac{I_c^*}{I_c}.\frac{I}{I^*}\right)$$

$$+A_4\left(1-\frac{I_c^*}{I_c}\right)\beta IS\left(1-\frac{I_c}{I_c^*}.\frac{I^*}{I}.\frac{S^*}{S}\right)+A_4\left(1-\frac{I_c^*}{I_c}\right)\gamma SI_c\ \left(1-\frac{S^*}{S}\right)$$

$$+A_5\left(1-\frac{R^*}{R}\right)\eta I\left(1-\frac{I^*}{I}.\frac{R}{R^*}\right)$$

F is non-positive using a modified version of Barbalat's Lemma [20] or by following the approach of Mc Cluskey [21]. Thus, $F \le 0$ for some $S, V, I, I_c, R > 0$.

Hence $\frac{dZ}{dt} \le 0$ for all S, V, I, I_c, R and is zero when $S = S^*, V = V^*, I = I^*, I_c = I^*_c, R = R^*$. Therefore, the largest compact invariant set in D such that $\frac{dZ}{dt} = 0$ is the singleton $\{E^*\}$ which is the endemic equilibrium point. Lassalle's invariant principle [19] guarantee that E^* is globally asymptotically stable (GAS) in $\overset{0}{D}$,the interior of D. Thus we have proved theorem 4.

4. Simulation and discussions

The main objective of this study was to model the effects of public health education campaign, vaccination and treatment on the dynamics of typhoid fever. In order to support the analytical results, Numerical results were presented with the aid of MATLAB programming language, we present graphical representations showing the variations in parameters with respect to effective reproduction number.

Most of the parameters used were obtained from literature survey and the rest were assumed. In order to perform simulations, baseline values of parameters from Table 1 presented were used.

Figure 2 shows that, increase in the transmission rates γ and β leads to increase in effective reproduction number. More importantly, it can be noted that transmission rate for asymptomatic individuals, γ is greater than transmission rate for symptomatic individuals, β since an increase or decrease in R_e due to γ is more rapid than that due to β.This means that the carriers transmit the disease more rapid in the community as compared to symptomatic individuals. This might be attributed to the fact that, symptomatic individuals are quickly treated as they become sick whereas carriers can live with the disease for sometimes long in so doing they keep on transmitting the disease until they show up symptoms and hence treated.

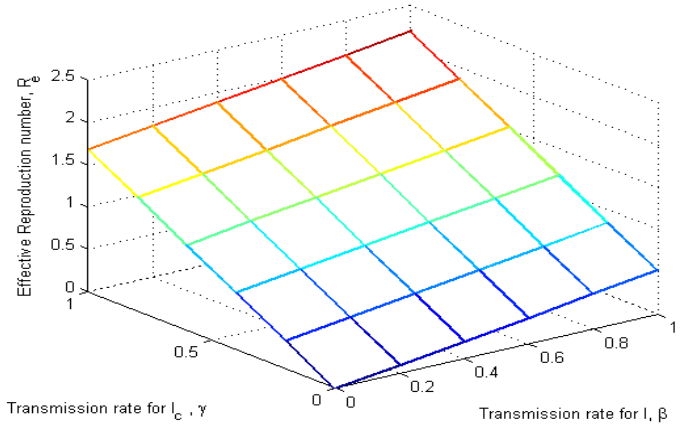

Figure 2: Effects of symptomatic and asymptomatic Infectious transmission rates on $\boldsymbol{R_e}$.

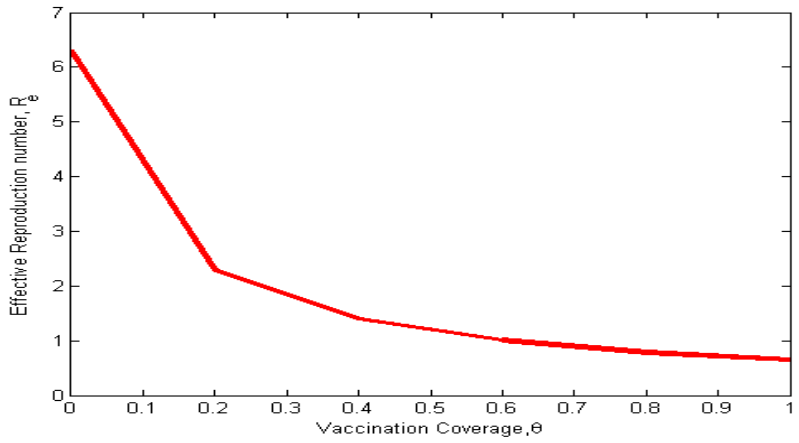

Figure 3: Effects of varying vaccination coverage on R_e.

Figure 3 shows that, high level of vaccination coverage leads to reduction in effective reproduction number, when $R_e < 1$ then typhoid is effectively controlled or eliminated in the population.

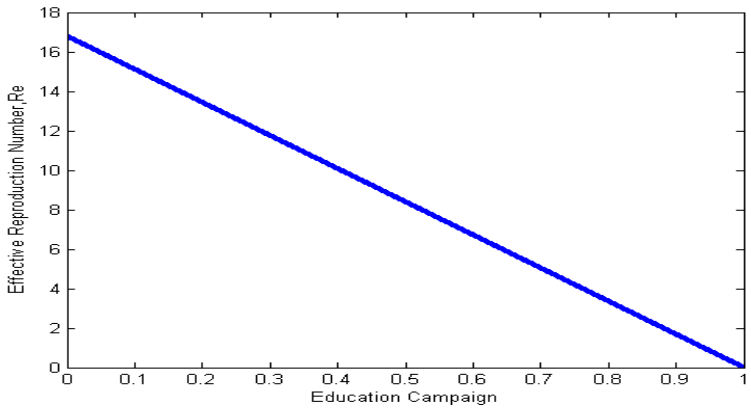

Figure 4: Effects of education campaigns on the transmission dynamics of typhoid fever.

Figure 4 shows that, mass education campaign causes a significant reduction in the effective reproduction number and hence effective control or elimination of typhoid cases.

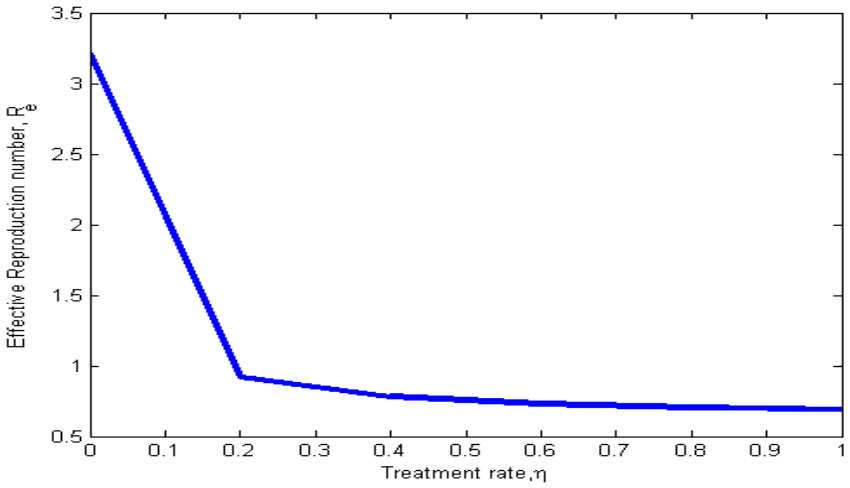

Figure 5: Effects of Treatment on the reproductive number, R_e.

Figure 5 shows that, high treatment rate causes a sharp reduction in the effective reproduction number. It should be emphasized that carefully taken therapeutic treatment to an ill individual tends to kill all *salmonella typhi* bacteria from the host. When all bacteria are killed then an individual recovers from typhoid, in such a situation the disease tends to diminish in the population.

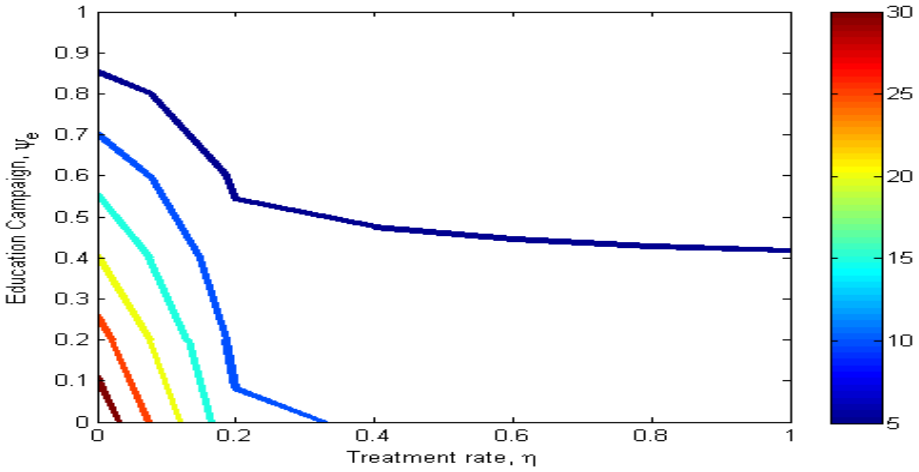

Figure 6: Effects of varying both education campaigns and treatment rates on R_e.

It is obvious from figure 6 that high level of treatment and education campaigns leads reduction in effective reproduction number and hence causes effective control or elimination of typhoid during an outbreak. It can be seen that high effort is needed to educate a large number of people so as to eliminate the outbreak. Treatment on its own side has a dramatic impact on the epidemic only when carefully administered to sick individuals early.

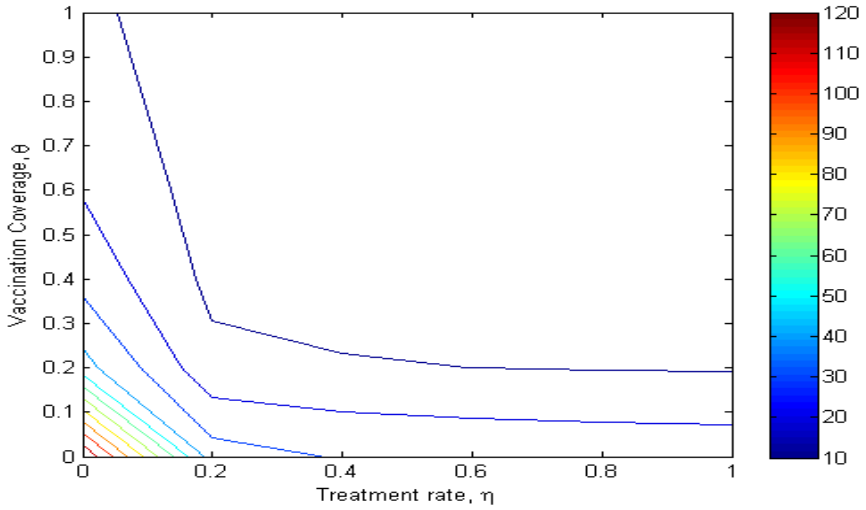

Figure 7: Effects of varying both Treatment and vaccination coverage on R_e.

Contours in Figure 7 shows that a decrease of both treatment and vaccination coverage causes an increase in typhoid fever, whereas an increase of these controls tend decrease the disease.

5. Sensitivity Analysis of R_e

Sensitivity analysis is used to determine how sensitive a model is to changes in the value of the parameters of the model and to changes in the structure of the model. It helps to build confidence in the model by studying the uncertainties that are often associated with parameters in models. Sensitivity indices allow us to measure the relative change in a state variable when a parameter changes. Sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values (since there are usually errors in data collection and presumed parameter values). Thus we use it to discover parameters that have a high impact on R_e and should be targeted by intervention strategies. If the result is negative, then the relationship between the parameters and R_e is inversely proportional. In this case, we will take the modulus of the sensitivity index so that we can deduce the size of the effect of changing that parameter. On the other hand, a positive sensitivity index implies a direct relationship between a given parameter and R_e.

The explicit expression of R_e is given by the equation (5.4). Since R_e depends only on thirteen parameters, we derive an analytical expression for its sensitivity to each parameter using the normalized forward sensitivity index [18] as follows:

$$\Upsilon_{\theta}^{R_e} = \frac{\partial R_e}{\partial \theta} \times \frac{\theta}{R_e} = -0.8401$$

Table 2 illustrates the sensitivity indices of R_e, evaluated at the baseline parameter values given in Table 1. From table 2 it is clear that R_e is most sensitive to η, thus, treating symptomatic infectious individuals is likely to have more impact in eradicating the typhoid fever. Model parameters whose sensitivity indices are near −1 or +1

suggest that a change in their magnitude have a significant impact on either increasing or decreasing the size of R_e. Thus, the remaining most sensitive parameters are recruitment rate, Λ ,vaccination rate, θ , education campaign, $\psi_e$and transmission rate for carrier individuals, γ in that order. The rest of the parameters whose indices are less than 0.5 in magnitude as shown in the table 2 contribute less to typhoid fever dynamics but their contribution is still significant.

Table 2: Parameters and their sensitivity indices

Parameter	Sensitivity Index	Description
$\boldsymbol{\Lambda}$	+1	Recruitment rate
$\boldsymbol{\omega_1}$	+0.33	Rate at which the vaccine wanes
$\boldsymbol{\omega_2}$	+0.3	Rate at which recovered individuals lose immunity
$\boldsymbol{\eta}$	-2.8570	Recovery rate for symptomatic infectious individuals
$\boldsymbol{\theta}$	-0.8404	Rate at which susceptible individuals are vaccinated
$\boldsymbol{\beta}$	+0.3807	Transmission rate for symptomatic infectious individuals
$\boldsymbol{\gamma}$	+0.6187	Transmission rate for carrier individuals
$\boldsymbol{p}$	+0.2387	Proportion of newly infected individuals who become carrier
$\boldsymbol{\psi_e}$	-0.8284	Education parameter
$\boldsymbol{\alpha}$	-0.0394	Rate at which carriers develop symptoms
$\boldsymbol{\mu}$	-0.2234	Natural mortality rate of individuals
$\boldsymbol{d_2}$	-0.0221	Disease-induced mortality rate of symptomatic individuals
$\boldsymbol{d_1}$	+0.01	Disease-induced mortality rate of asymptomatic individuals

6. Conclusions and recommendations

In this paper we have developed a deterministic mathematical for typhoid that captures education campaigns, vaccination and treatment as control strategies. The disease free equilibrium has been calculated and proved to be locally asymptotically stable when $R_e < 1$ and globally asymptotically stable when $R_e > 1$.

The effective reproduction number, R_e has been calculated and from which different control strategies have been analyzed. The results have shown that controlling typhoid dynamics depends on different factors. Unless integrated effort is put into action, it is quite difficult to eradicate or even to limit typhoid epidemics. We recommend that different sectors like the education sector, sanitation sector and water supply organizations as well as health sector should work together so as to limit typhoid outbreak in the population.

It must be emphasized that, both direct and indirect education is a critical factor in typhoid control, it that has a greater and longer-lasting effect on disease management. Education should therefore target both human-to-

human contact and also the intakes of pathogen material. We thus recommend that any typhoid-control program be developed in collaboration with culturally specific population-level education of susceptible and infected individuals.

We must point out that vaccination, education campaigns and medical therapy and antibiotic treatment are not the only control measures against a typhoid outbreak. Water sanitation is also a possible prevention and intervention strategies. On the other hand, vaccination does not always work out due to the limitations of the medical development level and financial budget, which is also a restriction in our study. Moreover, in this paper, we consider the vaccination as a continuous state, since sometimes the vaccination process is discontinuous or seasonal, it can be modeled by impulsive differential equations, which is one of our future works.

The other limitation, which should be acknowledged, is that the model developed in this study assumes that the disease is transmitted through human contact only, although the disease can be acquired through consumption, mainly of water, but sometimes of food, that has been contaminated by sewage containing the excrement of people suffering from the disease.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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