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Modelling the Impact of Carrier and Vaccination in Understanding Typhoid Fever Dynamics

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Abstract: **The model consists of five compartments; the susceptible humans, vaccinated humans, infectious humans, carriers humans and the recovered humans. We conducted an analysis on the existence of all the equilibrium points; the disease- free equilibrium and endemic equilibrium. The reproduction number was computed by using the next generation matrix approach. Disease -free equilibrium was found to be locally asymptotically stable and globally asymptotically stable if the reproduction number was less than one. The most sensitive parameter to the basic reproduction number was determined by using various sensitivity objectives that the researchers analyzed. Numerical simulations of the system of differential equations of the epidemic model were carried out for interpretations. It is this view that this research highlighted various objectives. The findings showed that the existence of a large number of carriers who are infectious but show no symptoms. Therefore, carriers do not show symptoms; they will not be part of any treatment program, or prevention program in the system.**

Keywords: **Modelling, Carrier, Vaccine, Typhoid, Dynamic, Infectious, Analysis.**

1. INTRODUCTION

Salmonella typhi is a group of the Salmonella genus which belongs to the family of gram-negative bacteria. Typhoid fever is an acute systemic illness caused by the bacteria salmonella enterica serovar. The disease is mostly acquired by ingestion of food or water contaminated by the faeces of patients and carriers. The transmission related to contamination with infected urine or vomitus can occasionally occur. Direct person-to-person transmission is also possible. The disease is only reservoir of human being. They enter the body and they travel into human intestines, and then to the blood system. Once they enter to the blood system through either one or more of the following that is the lymph node. The abdominal pain, fever, and general ill feeling are the symptoms of the disease. The incubation period is on average 10-14days;however ,three days short is enough to show the signs or the longest is 21 days. There are individuals called carriers and they play an important role in the transmission of the disease. We developed an epidemic model for the dynamics of typhoid fever infections.

There are two widely licensed vaccines against typhoid, the Ty21 a is a multi-dose live oral vaccine, inducing both cellular and antibody-mediated immune responses [1]. At the same time, Vi- polysaccharide (ViPS) which is single-dose injectable vaccine that induces an antibody response to the capsular Vi antigen [2]. Both vaccines demonstrated some moderate efficacy in field trials [3]. Notably, neither is licensed for use in children who are less than two years old. There are several Vi conjugate vaccines (ViCV) in advanced stages of development. Existing data predicts that ViCV can be effectively be administered to infants and elicit a stronger and longer-lasting immune response than ViPS [4]

The modelling techniques can be applied on the spread of typhoid fever and necessary control measures put in place. Managing the typhoid fever epidemic is a challenge in developing countries. Having improvement in sanitation and hygiene and dehydration therapy may reduce the magnitude of the problem but may not be a conclusive answer since there other parameters that should be taken into consideration. Some predictive measures are vital as an anticipation of an epidemic, and planning for other interventions is very important. Mathematical modelling is perceived as a tool to synchronize our understanding of typhoid dynamics into quantitative and perceptible phenomena. The modelling has been used several years to analyse the dynamics of the outbreak as a result of predicting necessary and essential interventions and setting strategies for effectiveness of vaccination applications [5].

According to Nishout et al (1974), mathematical models help in investigating large number of question metabolism and that models also give voice to assumption on how things work [6]. Developed a Mathematical model of infectious disease dynamics to inform prevention and response effort on disease. The model was to enhance understanding and predictive power over population-level and the disease trends. They captured both fundamental aspects of transmission and also the effect of medical and behavioural interactions.

Another mathematical model by Kgosimore et al (2016), studied the developed a deterministic model of typhoid that accounts for relapse of treatment. The Mathematical analysis and numerical simulations are carried out to determine the transmission dynamics of typhoid in a community. The study aims to obtain insight on typhoid transmission dynamics and the role of carriers to the spread of the disease in a community. According to the results they indicate that treatment sustain the carrier infectives who in turn sustains the epidemic in the population in the long run [7].

Another study was undertaken by Chamuchi et al (2016). It studied the impact of control strategies of the effect of carriers on the typhoid fever in Kisii town was investigated. The mathematical model studies the dynamics of typhoid fever by formulating and analysing the impact of carriers, diagnosis and health education on typhoid carriers control in Kenya. The model was in the form of SII_CR. *The* findings of the study discovered that increasing treatment yields a smaller decrease of infectious individuals [8].

2. MODEL DESCRIPTION AND FORMULATION

The model divides the total human population at any time(t)into five sub-populations, (compartments) with respect to their disease status in the system. The total population, represented by N(t), is divided into sub-populations of the Susceptible humans(S), Vaccinated humans(V), Infectious humans (I), Carrier humans ($I_{c)}$ and Recovered vector(R). The total population becomes:

$$N(t) = S(t) + V(t) + I(t) + I_c + R(t),$$

The numbers of susceptible individuals increase by recruitment through births and immigration at a rate **Ω**. The assumption is that proportion f of $S(t)$ progress to carrier class, which is the compliment 1 f progress to symptomatic infectious compartment. According to Carriers can become symptomatic at some rate κ and receive treatment and recover at the rate τ. The Infectious individuals can receive treatment and recover at the rate θ. The susceptible individuals receive vaccination to protect them against infections at the rate of ζ Since vaccine wanes with time, then after its expiry the vaccines can return back to susceptible class at the rate Ψ. The individual vaccinated becomes symptomatic at rate of σ. The study presumes that an individual in each compartment may undergo a natural death at rate μ. this disease induced death rate η. Let β be transmission rates for infectious and carrier individuals.

A description of the model parameters and variables is shown in Table 2.1

TABLE: 2.1

Variable	**Description**
S(t)	Number of susceptible humans
V(t)	Number of vaccinated humans
Ic(t)	Number of infectious humans without clinical signs (carriers) Number of
I(t)	infectious humans with clinical signs
R(t)	Number of recovered humans with partial immunity
parameters	**Description**
Ω	Growth rate population
Ψ	Waning rate of vaccination effect
ζ	Vaccination rate
η	Disease mortality rate
β	Rate of contact with infected individual
κ	Rate of flow from class Ic to class I
σ	Rate of flow from class V to class I
μ	Natural death rate for entire human compartments
θ	Rate of flow from class I to class R
τ	Rate of flow from class I_c to class R
f	fraction of carriers

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2.1 The Model

The model comprises of ordinary Differential Equations (ODEs) as indicated below;

$$\frac{dS}{dt} = \Omega + \zeta V - \beta SI - S(\mu + \Psi)$$

$$\frac{dV}{dt} = \Psi S - \sigma\beta VVI - V(\mu + \zeta)$$

$$\frac{dI}{dt} = (1-f)\beta SI + \sigma\beta VI + \kappa Ic - I(\theta + \mu + \eta)$$

$$\frac{dIc}{dt} = f\beta SI - Ic(\kappa + \tau + \mu)$$

$$\frac{dR}{dt} = \theta I + \tau Ic - \mu R$$

The model is illustrated as shown in the Fig 2.1 below

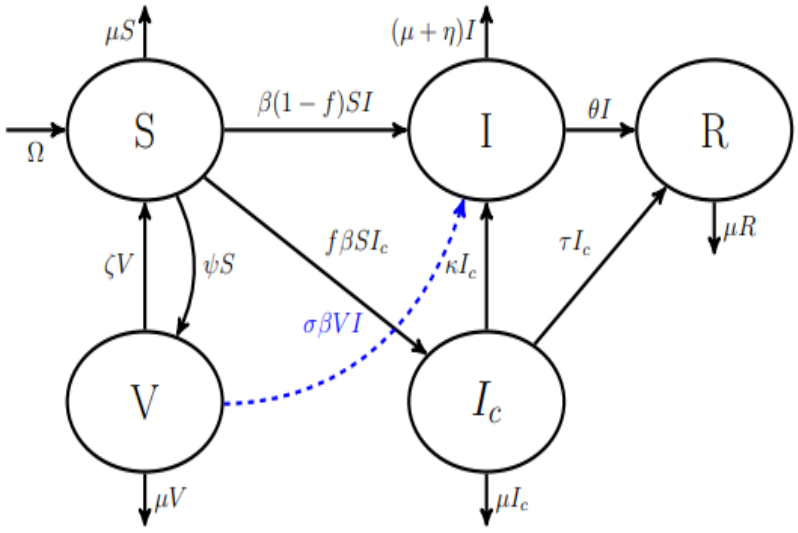

Fig 2.1: The Model Flow

The Assumptions

i. Vaccinated individuals do not become the carriers
ii. Recovered individuals acquire permanent immunity.
iii. Vaccinated individuals are infected at a lower rate than susceptible.
iv. σ is a scaling factor as $0 < \sigma < 1$
v. I_c (Carriers) do not transmit disease.
vi. I_c (Carriers) do not die with disease.

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3. DISEASE_FREE EQUILIBRIUM

The disease-free equilibrium of model system can be obtained using the set;

$\frac{dS}{dt} = \frac{dV}{dt} = \frac{dI}{dt} = \frac{dIc}{dt} = \frac{dR}{dt} = 0$, and in the absence of the disease the formulae will be

I=Ic=R=0, so that:

$S^* = \frac{\Omega(\mu+\zeta)}{\mu(\mu+\Psi+\zeta)}$

$V^* = \frac{\Psi\Omega}{\mu(\mu+\Psi+\zeta)}$

Therefore, DFE will be represented as;

(S*, V*, I*, Ic*, R*) = $(\frac{\Omega(\mu+\zeta)}{\mu(\mu+\Psi+\zeta)}, \frac{\Psi\Omega}{\mu(\mu+\Psi+\zeta)}, 0,0,0)$

4. BASIC REPRODUCTIVE NUMBER

The determination of R_0 is done using the next generation matrix approach [10]. The following method is used to determine the reproduction number: by Letting $x = (x_1, x_2, ..., x_n)^t$, with each x_i 0, be the number of individuals in each compartment, It can be denoted that n to be the number of compartments corresponding to infected individuals where the epidemiological interpretation of the model determines between infected and uninfected compartments. More than one interpretation is possible for some models which will be demonstrated. Following the definition that X_s to be the set of all disease-free states, it can be given by: $X_s = x$ 0 $x_i = 0$, $i = 1, 2, ..., n$. Let f_i be the rate of appearance of new infections in compartment i, $V^+_i(x)$ be the rate of transfer of individuals into compartment i by all other means and $V^-_i(x)$ be the rate of transfer of individuals out of compartment i. It is assumed that each function is continuously differentiable at least twice in each variable. In considering the disease transmission model with non-negative initial conditions given by

$\frac{dxi}{dt} = fi(x) = Fi(x) - Vi(x), 1 \le i \le n$ where $V_i = V^-_i(x)$ $V^+_i(x)$.

If x_0 is a disease free equilibrium of and "$f_i(x)$ satisfies assumptions (A1)–(A5), then the reproduction number is the spectral radius of the next generation matrix $FV^{-1\ -1}$

$F = \left[\frac{\partial f_i(x_0)}{\partial x_j}\right]$ and $V = \left[\frac{\partial v_i(x_0)}{\partial x_j}\right]$ with $1 \le i \le n$ where F is non-negative and is non-singular M-Matrix.

Therefore, we have

$$f = \begin{bmatrix}(1-f)\beta SI + \sigma\beta VI \\ f\beta SI\end{bmatrix}$$

Jacobian matrix at DFE is given by

$$\boldsymbol{F} = \begin{bmatrix}(1-f)\dfrac{\beta\Omega(\mu+\zeta)}{\mu(\mu+\Psi+\zeta)} + \dfrac{\sigma\beta\Psi\Omega}{\mu(\mu+\Psi+\zeta)} & \mathbf{0} \\ \dfrac{\boldsymbol{f\beta\Omega(\mu+\zeta)}}{\mu(\mu+\Psi+\zeta)} & \mathbf{0}\end{bmatrix}$$

$$\boldsymbol{V} = \begin{bmatrix}(\sigma+\mu+\eta) & -\boldsymbol{\kappa} \\ \mathbf{0} & (\boldsymbol{\kappa}+\boldsymbol{\tau}+\boldsymbol{\mu})\end{bmatrix}$$

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Taking $k_1 = (\theta + \mu + \eta)$

$K_2 = (\kappa + \tau + \mu)$

$$\boldsymbol{FV^{-1}} = \begin{bmatrix} (1-f)\dfrac{\beta\Omega(\mu+\zeta)}{\mu(\mu+\Psi+\zeta)k_1} + \dfrac{\sigma\beta\Psi\Omega}{\mu(\mu+\Psi+\zeta)k_1} & \mathbf{0}(1-f)\dfrac{\beta\Omega(\mu+\zeta)\kappa}{\mu(\mu+\Psi+\zeta)k_1k_2} + \dfrac{\sigma\beta\Psi\Omega\kappa}{\mu(\mu+\Psi+\zeta)k_1k_2} \\ \dfrac{\boldsymbol{f\beta\Omega(\mu+\zeta)}}{\mu(\mu+\Psi+\zeta)k_1} & \dfrac{\boldsymbol{f\beta\Omega(\mu+\zeta)}}{\mu(\mu+\Psi+\zeta)k_1k_2} \end{bmatrix}$$

Therefore,

$$R_0 = \frac{(1-f)\beta\Omega\big(\mu+\zeta(\tau+\mu)\big) + \sigma\beta\Psi\Omega(\boldsymbol{\kappa}+\boldsymbol{\tau}+\boldsymbol{\mu})}{\mu(\theta+\mu+\eta)(\kappa+\tau+\mu)(\mu+\Psi+\zeta)}$$

5. GLOBAL STABILITY OF DISEASE - FREE QUILIBRIUM

Considering the approach by Castillo-Chavez theorem, the system is expressed as

$\frac{dX}{dt} = F(X,Z)$

$\frac{dZ}{dt} = G(X,Z), G(X,0)$ where, X ∈ R^{3} = (S, V, R), is the number of non- infected individuals and Z ∈ R^2 are the infected. The following conditions are for global stability of disease-free equilibrium point

E^0= (S*, V*, 0, 0, 0) = $(\frac{\Omega(\mu+\zeta)}{\mu(\mu+\Psi+\zeta)}, \frac{\Psi\Omega}{\mu(\mu+\Psi+\zeta)}, 0,0,0)$ = (X*,0), for X*=$(\frac{\Omega(\mu+\zeta)}{\mu(\mu+\Psi+\zeta)}, \frac{\Psi\Omega}{\mu(\mu+\Psi+\zeta)})$

1. $\frac{dX}{dt} = F(\boldsymbol{X}, 0), X^{'}$ is globally asymptotically stable

2. $G(X,Z) = AZ - \tilde{G}(X,Z), \tilde{G}(X,Z) \geq 0 \; for \; (X,Z) \in \Omega \; where \; A = D_z G(X^*, 0),$

is an M-matrix (in that the off diagonal elements of A are positive) and Γ is the region where the equations of the model make epidemiological sense. If conditions 1 and 2 are satisfied by system then the following theorem holds;

Theorem 5.1 ***Provided that $R_0 < 1$ and the conditions 1 and 2 are satisfied the disease disease-free equilibrium point $E^0 = X^*, 0$ of the system is" globally asymptotically stable".***

$E^0 = (S^{'}, V^{'}, 0, 0, 0)$ is globally stable hence condition 1 satisfied

G (X, Z) can be written as $AZ - \tilde{G}(X,Z), \tilde{G}(X,Z)$ where

G(X,Z) = $\begin{pmatrix} \beta SI \\ 0 \end{pmatrix}$ and A=$\begin{pmatrix} (-a-\lambda)I & + & I\beta S \\ f\beta SI & + & (-b-\lambda)I_c \end{pmatrix}$

AZ - $\tilde{G}(X,Z) = \begin{pmatrix} -a-\lambda & \beta S^* \\ f\beta S & -b-\lambda \end{pmatrix}$

Replacing a and b, the equation become

$\begin{pmatrix} (1-f)\beta SI + \sigma\beta VI + \kappa I_c & - & \beta SI \\ f\beta S & 0 & 0 & -(\kappa+\tau+\mu) \end{pmatrix}$

This also gives *G* (*X, Z*)

Hence *G* (*X, Z*) is satisfied and proofed to be globally asymptotically stable.

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6. STABILITY OF ENDEMIC EQUILIBRIBRIUM

Theorem 4.7.2 *The model (3.1) at the endemic equilibriumE^1 is the stable locally asymptotically if $R_0 > 1$ conditions of Routh-Hurwitz criteria issatisfied.*

Proof: At the endemic equilibrium we obtain the following Jacobian matrix

$$J(E^1) = \begin{pmatrix} -k1 & \zeta & \beta S^* & 0 & 0 \\ \Psi & -k2 & -\sigma\beta V^* & 0 & 0 \\ (1-f)\beta I^* & \sigma\beta I^* & -k3 & \kappa & 0 \\ f\beta I^* & 0 & f\beta S^* & -k4 & 0 \\ 0 & 0 & \theta & \tau & -(\mu+\lambda) \end{pmatrix}$$

$k1 = -\beta I^* - (\mu + \Psi), k2 = \sigma\beta I^* - (\mu + \zeta), k3 = (1-f)\beta S^* + \sigma\beta V^* - (\mu - \zeta)$

$k4 = -(\kappa + \tau + \mu)$

$$\begin{pmatrix} -(k1+\lambda) & \zeta & -\beta S^* & 0 \\ \Psi & -(k2+\lambda) & -\sigma\beta V^* & 0 \\ (1-f)\beta I^* & \sigma\beta I^* & -(k3+\lambda) & \kappa \\ f\beta I^* & 0 & f\beta S^* & -(K4+\lambda) \end{pmatrix} = 0$$

Therefore, the characteristic polynomial is given b y

$$(\lambda+\mu)\big(-\lambda - \beta I^* + (\mu+\zeta)\big)[(\lambda^3 + C1\lambda^2 + c2\lambda + c3)]$$

Therefore, it implies that

$\lambda_1 = -\mu$

$\lambda_2 = -\beta I^* - (\mu + \zeta)$

$\lambda_3 = -(C1\lambda^2 + C2\lambda + C3)$

Where

$C1 = (\mu+\zeta)(1-f)\beta S^* + \sigma\beta V^* + (\theta+\mu+\eta)(\kappa+\tau+\mu)$

$C2 = (\mu+\zeta)(1-f)\beta S^* + \sigma\beta V^* + (\theta+\mu+\eta) + (\kappa+\tau+\mu)(1-f)\beta S^* + \sigma\beta V^* + (\theta+\mu+\eta)$

$+(\kappa+\tau+\mu)(\mu+\zeta) + 2\sigma\beta I^*(\kappa+\tau+\mu) + \Psi[(1-f)\beta S^* + \sigma\beta V^* + (\theta+\mu+\eta)] + \zeta(\mu+\zeta)$

$+2\sigma\beta V^*(\kappa+\tau+\mu) + f\kappa\beta S^*(1-f)\beta S^* + \sigma\beta V^* + (\theta+\mu+\eta) + 2f\kappa\beta I^*(\mu+\zeta) + \beta S^*(\kappa+\tau+\mu)$

$C3 = (\mu+\zeta)(1-f)\beta S^* + \sigma\beta V^* + (\theta+\mu+\eta)(\kappa+\tau+\mu) + [-2\sigma\beta V^*(1-f)\beta S^* + \sigma\beta V^* + (\theta+\mu+\eta)(\kappa+\tau+\mu)] + [-2\sigma\beta V^*(1-f)\beta I^*](\kappa+\tau+\mu) + \zeta\Psi(\mu+\zeta) + \beta S^*(\kappa+\tau+\mu)\Psi$

Hence by the Routh-Hurwitz criteria the system is locally stable if $a_1, a_3 > 0$ and $a_1a_2 > a_3$.

7. NUMERICAL SOLUTIONS

The Numerical simulation was carried out to identify the impact of the model parameters through the employing fourth order Range-Kutta scheme on the system of differential equations using a MATLAB 8.3. The systems of differential equations were resolved over as specific period of time period using Range-Kutta fourth order scheme. The Parameters Used are shown in Table 7.1 below based on the existing literature.

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Table 7.1: Parameter Estimations

Symbol	Description	Value	Source
Ψ	Waning rate of vaccination effect	0.25	[5]
σ	Rate of flow from class V to class I		Estimate
κ	Rate flow from class Ic to class I	0.005	[5]
θ	Rate of flow from class I to R		Estimate
Ω	Population growth rate	10	[9]
τ	Rate of flow from class Ic to R	0.5	[5]
β	Rate of contact with infected individuals	0.0001	[5]
ζ	Vaccination rate	0.1	[5]
η	Disease mortality	0.25	[5]
μ	Natural death rate	0.017	[9]

He generated tables and their parameters are shown below;

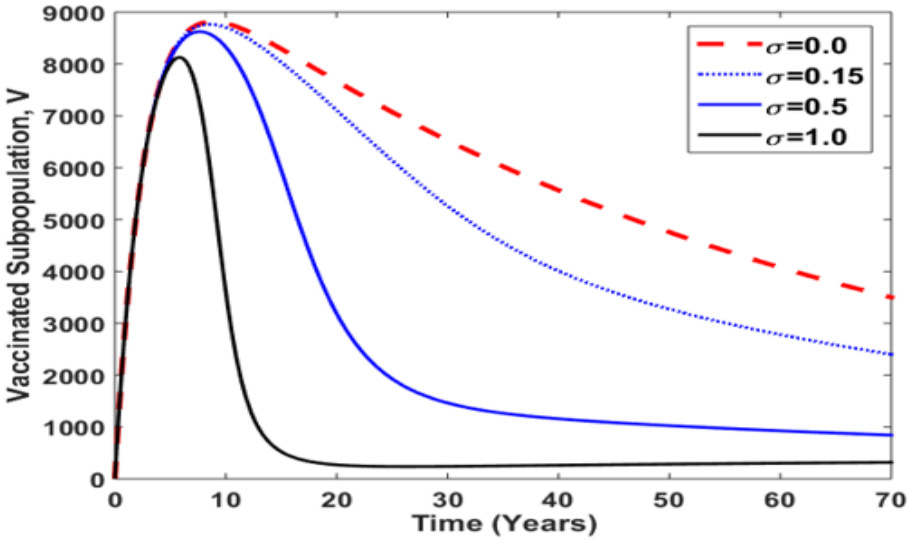

Figure 7.1: Vaccinated Sub Population graph

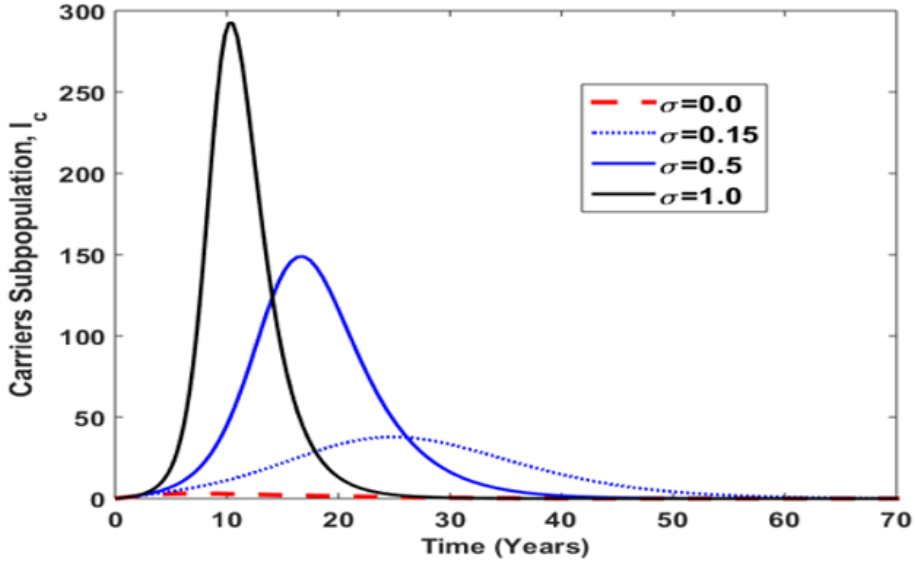

Figure 7.2: Carriers Sub-population graph

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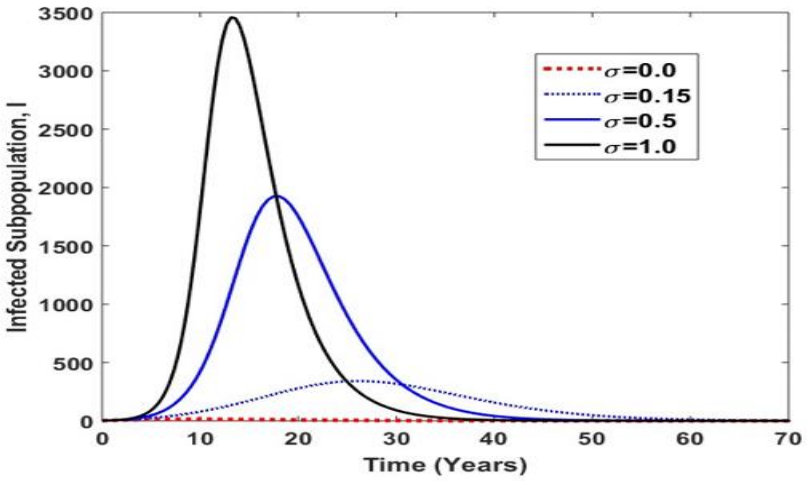

Figure 7.3: Infected Sub-Population graph

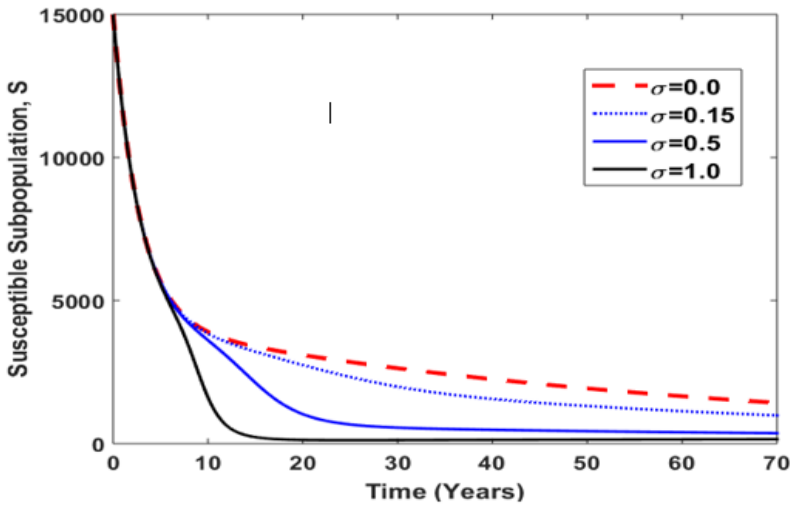

Figure 7.4: Susceptible Sub population graph

Fig. 7.1 shows the analysis of contact rate of the human population with regards to typhoid fever transmission in the system. According to Contact rate it was varied to see that its effects on the typhoid fever dynamics. An elevation in the contact rate grows in the number of the infectious population leads to inflates in effective reproduction number for infectious population and vice versa.

The rate of contact between the susceptible human populations and carriers human population was conducted to identify whether or not the contact rate contributes significantly to the epidemics of the typhoid fever. Figure 7.2 demonstrated a positive effect of the contact rate in disease transmission. An escalation in human interactions contributes significantly to the spread of the typhoid fever infections in the system. This leads to augmentation in effective reproduction number for Carriers population.

Fig.7.3 demonstrates how Susceptible individuals respond to the typhoid fever upon infection. In this figure, the variation of the graphs of susceptible population it was to analyse the typhoid fever dynamics in the system. According to the figure the reduction after about 14 days which is the incubation period of the disease, after which fever and rush develop and the infected stage. After about 40th day the graph remains constant since most of those infected becomes carriers.

Figure 7.4 indicate that, the increasing of vaccination rate has a significant impact on controlling the transmission dynamics of typhoid fever, which leads to reduction in effectively reproduction number, when $R_0 < 1$ then typhoid is effectively controlled or eliminated in the population.

8. CONCLUSION

This research has shown that typhoid fever mainly affecting children and young adults. A simple deterministic of modelling the impact of carrier and vaccination in understanding typhoid fever dynamics. The reproductive number has been computed and Qualitative analysis of the model reveals that; The disease- free equilibrium is both locally and globally-asymptotically stable whenever the reproductive number is less than the unity. With the aid of robust mathematical techniques, it has been demonstrated that the model has a unique endemic equilibrium point which exists if the reproductive number is greater than that unity. According to Routh-Hurwitz criterion method a theory has been used to show that the endemic equilibria is locally asymptotically stable when the reproduction number is greater than unity. in the same way, the sensitivity or parameter contribution analysis was performed on the threshold value for typhoid fever spread. It has been observed that, if carriers individuals become aware of their disease, the number of symptomatically infected individuals declines significantly. In addition, the study revealed that further through simulations that the epidemic is sustained in the population. Implications of these results demonstrate the challenges of carriers infection, the existence of a large number of carriers who are infectious but show no symptoms. However, because carriers do not show symptoms, they will not be part of any treatment program or prevention program. In the high typhoid fever prevalence countries, testing and increasing awareness of carriers will have greater impact on the disease burden than increasing vaccination rates.

9. DATA AVAILABILITY

The data used in the analysis of the alcoholism model were obtained from previously published articles and which have been cited accordingly. Some of the parameter values are assumed and others are taken from published articles. These articles are cited at relevant places within the text as references.

10. CONFLICT OF INTEREST

The authors of this publication declare that there is no conflict of interest regarding the publication of this manuscript.

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