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MATHEMATICAL MODELLING FOR THE TREATMENT OF TYPHOID FEVER

(A Case Study of General Sani Abacha Specialist Hospital Damaturu, Yobe State)

Umar Yusuf Madaki*, Mahdi Audu Janda and Saudatu Baba Sambo

Department of Mathematics and Statistics, Yobe State University, Damaturu, Nigeria

ABSTRACT

Typhoid fever is a global disease which is endemic in some African countries (including Nigeria) where hygiene practices are not properly put in place. In this research we focused on "Mathematical Modelling for the Treatment of Typhoid Fever". We used modified model in this research with the compartments, S, I_C, I, and T, where the compartment S(t) is used to represent the number of individuals that are prone to the disease at time t or those susceptible to the disease. $I_C(t)$ is used to represent the number of asymptomatic carriers at time t. I(t) is used to represent the number of individuals who have been infected with the disease and are capable of spreading the disease to the other individuals at time t. T(t) is used to represent the number of individuals who have been infected with the disease and are treated. Data are collected from my case of study "the General Sani Abacha Specialist Hospital, Damaturu Yobe state". We have studied the effect of carriers and treatment on the transmission dynamics of typhoid fever. A disease-free equilibrium was obtained and its stability was analysed using linearized method. We computed the basic reproduction number (R_0) in terms of the model parameters. We were solved the equations of the model for all individuals governing this research. We solve the equation for difference time and in difference experiments, we also carried out numerical experiments of solutions of the model using the model parameters of interest and we also drew the graphs that displayed the results for each compartment of the model.

INTRODUCTION

Typhoid fever is a disease caused by a salmonella bacterium (Salmonella typhi) and transmitted by ingestion of water and/or food contaminated with

faeces (stool) (Abboubakar and Racke, 2019). Typhoid fever is prevalent in areas of the world where hygiene is precarious (WHO,2018).The disease is mainly manifested by a fever that gradually rises to 40◦C, headaches, insomnia, fatigue and anorexia. Fever may be accompanied by digestive signs (stomach ache, diarrhoea or constipation, vomiting). The symptoms can last several weeks. In some cases, the infected host is asymptomatic. but participates in the transmission of the disease. In severe forms without treatment, evolution can be fatal in 10% of cases. The treatment of typhoid fever is based on antibiotic medication. There are 11 to 21 million estimated cases of typhoid fever and approximately 128,000 to 161,000deaths annually, compared to an estimated 6 million cases of paratyphoid fever and 54,000 annual deaths (Jacquinet *et al.*, 2018*).*

Although some progress has been made in the fight against typhoid fever, such as antibiotic treatments, vaccination and environmental sanitation as a means of prevention, typhoid fever is still a public health problem in developing countries. There are two available vaccines to prevent typhoid fever. Although their price in the market of vaccine has become affordable, access in some developing countries remains a problem (WHO, 2018).Thus, the authorities of the areas where this disease occurs must choose between treatment and/or prevention means. Asymptomatic carriers are believed to play an essential role in the evolution and global transmission of typhi, and their presence greatly hinders the eradication of typhoid fever using treatment. Treatment is given to all infected individuals, however antibiotics can be prescribed to treat typhoid fever and vaccination should be considered for household members of known carriers and persons travelling to or living in the developing countries where typhoid fever is common. Different models have been developed to analyse the uptransmission dynamics of typhoid fever as well as the effectiveness of some intervention strategies against the spread of typhoid infections. for example, a mathematical model on the transmission dynamics of typhoid fever (Tilahun *et al.*, 2017). A mathematical model to investigate the effect of carriers on the

transmission dynamics of infectious disease (Darja,2015). A mathematical model to study the effect of carrier on the transmission dynamics of typhoid fever (moffat *et al.,* 2014).The model studies the dynamics of typhoid fever by incorporating vaccination rate as a control measure However, none of them considered treatment as a control measure. In this study, i will formulate the work by incorporating treatment in the dynamics of the disease. The basic reproduction number (R_0) is calculated and finally the modified model is solved numerically.

STATEMENT OF THE PROBLEM

Typhoid fever is a global disease which is endemic in some African countries (including Nigeria) where hygiene practices are not properly put in place. The dynamics of the disease is modelled by many authors. None of the studies incorporate treatment as a control measure. However in this study, we will formulate the work to incorporate treatment in the dynamics of the disease. Furthermore, we also study the existence and stability of the equilibrium states of the model. The basic reproduction number (R_0) is determined using the next generation method and the modified model is solved numerically.

AIM AND OBJECTIVES OF THE STUDY

The aim of this Study is to build up a mathematical model for the treatment of typhoid fever, which has the followings objectives

- To model the treatment of typhoid fever
- To determine the stability of the disease-free equilibrium (DFE) state by linearization method
- To compute the basic reproduction number (R_0) using the next generation method.
- To carry out numerical experiments of solutions of the model using the model parameters of interest.

SIGNIFICANCE OF THE STUDY

Treatment is the commonest method of control and eradication of diseases. Modelling the treatment of typhoid fever is very significant and therefore, very effective method to control or eradicate the disease. The study on this model will be of immense benefit to the ministry of health, hospitals, the state government and other researchers that wish to carryout similar research as the study will be able to discuss the treatment of typhoid fever.

SCOPE AND LIMITATION OF THE STUDY

This study is limited to the formulating a mathematical model for treatment of typhoid fever. Although it limited only to formulating a mathematical model for the treatment of typhoid fever but it can be also apply is some areas of researchers if needed

1.1 RESEARCH QUESTIONS

The study came up with research questions so as to be able to ascertain the objectives of the study. Research questions are very importance in research. The research questions are stated below as follows;

- How to model the treatment of typhoid fever?
- How to determine the stability of the disease-free equilibrium (DFE) state by linearization method?
- How to determine the basic reproduction number (R_0) using the next generation?
- How to carryout numerical experiments of solution of the model using the model parameters of interest?

LITERATURE REVIEW

The reviews of previous studies into closely related problems provide the prospective of the proposed study. Many researchers conducted a research on modelling of typhoid fever.

Peter *et al*. (2018), defined typhoid fever as one of the infectious diseases which is endemic in most part of the world. It is systemic infection caused by Salmonella typhi (S typhi). The bacteria is transmitted through food and water contaminated with faces and urine of an infected patient or a carrier. Once the bacteria enters the body they travel in the human intestines, and then to the bloodstream

Mukhopadhyay *et al*.(2018), stated that typhoid or enteric fever is mainly caused by Salmonella enterica serovar Typhi and also to a lesser extent by S. Paratyphi A. Humans are the only reservoir for these organisms. The main sources of infection are the stool and urine of infected persons, with the important vehicles being contaminated water, food and flies.

Amiciza *et al*.(2019), stated that Typhoid fever (TF), also known as enteric fever, is a potentially life-threatening multi-systemic illness. It is mainly caused by Salmonella enterica, subspecies enterica serovar typhi, and to a lesser extent by serovars paratyphi A, B, and C, which are members of the family of Enterobacteriaceae

Milligan, Paul, and Neuberger (2018), they proposed a paper and stated that typhoid fever is a bacterial infection found mainly among children and adolescents in southern and eastern Asia, Africa, Latin America and the Caribbean. They also added that, typhoid fever spreads through contaminated food, drink, or water. It is usually characterized initially by fever, headache, and abdominal symptoms, although other non-specific symptoms may be present. The infection also sometimes causes confusion or psychosis. In late stages of the infection, intestinal perforation or massive intestinal haemorrhage may occur.

Adu-Gymfi *et al*.(2019), in their research on Salmonella Typhi, were described that Typhoid fever, caused by Salmonella enterica, serovar Typhi, is restricted to humans as its host and evades the human immune system with ease. This quality has been one of the many reasons why it is commonly found as an endemic bacterium in emerging economies. Also, due to a remarkably low yield from blood cultures (median of 1 CFU/mL of blood), Salmonella septicemia is uncommon. New evidence gathered together with clinical investigations have provided insight into the mechanisms that underlie the pathogenesis of typhoid, host restriction as well as antibiotic and vaccine susceptibility

Keeling, M.J and Canon, L. (2019), in their paper "Mathematical Modelling of Infectious Diseases" introduced that, Mathematical models allow us to extrapolate from current information about the state and progress of an outbreak, to predict the future and, most importantly, to quantify the uncertainty in these predictions. Here, we illustrate these principles in relation to the current H1N1 epidemic. They also said that, many sources of data are used in mathematical modelling, with some forms of model requiring vastly more data than others. However, a good estimation of the number of cases is vitally important. Mathematical models, and the statistical tools that underpin them, are now a fundamental element in planning control and mitigation measures against any future epidemic of an infectious disease. Well parameterized mathematical models allow us to test a variety of possible control strategies in computer simulations before applying them in reality, they added.

World Health Organization (2018), introduced Ty2la typhoid vaccine, WHO ssid Ty21a is a live oral vaccine derived from an attenuated strain of S. Typhi, approved for use in children aged six years or older. It is ail able as an enteric-coated capsule and is given in three doses (four doses in North America) every other day. The liquid formulation, which was approved in children over two years old, is not currently available Said WHO. It elicits protection that starts10 to 14 days after the third dose.

Milligan, *et al*.(2018),in their work they introduced Vi polysaccharide vaccine(injection one dose). The said a single dose of Vi polysaccharide vaccine prevents around two-thirds of typhoid cases in the first year after vaccination (year 1: 69%, 95% CI 63% to 74%; 3 trials, 99,979 participants; high-certainty evidence).

Peter *et al*.(2018), proposed that Treatment of typhoid is based on antibiotic susceptibility of the patient blood culture. The oral chloramphenicol, amoxicillin may be used if the strain is sensitive. The chronic carrier state may be eradicated using oral therapy, ciprooxacin or noroxacin. Multi-drug resistant strains of S.Typhi are increasingly common worldwide which makes treatment by antibiotics more difficult and costly.

Nasstrom *et al*.(2018), in their paper "Diagnostic metabolite biomarkers of chronic typhoid carriage" state that, Salmonella Typhi and Salmonella Paratyphi A are the agents of enteric (typhoid) fever; both can establish chronic carriage in the gallbladder. Chronic Salmonella carriers are typically asymptomatic, intermittently shedding bacteria in the feces, and contributing to disease transmission. Detecting chronic carriers is of public health relevance in areas where enteric fever is endemic, but there are no routinely used methods for prospectively identifying those carrying Salmonella in their gallbladder

ZoA *et al*.(2019), in the paper "Antibiotic Resistance and Typhoid" state that, S.Typhi can persist in water and food contaminated with human fecal material, but there is no environmentally adapted stage of the bacterial life-cycle such as the formation of spores. The persistence of S. Typhi in human populations is influenced by clinically silent carriage within certain individuals (carriers) that can be infected for months and even years with periodic shedding of S. Typhi into the environment in contaminated feces. Thus, antibiotic usage can influence both acute typhoid disease and the carrier state. In both states the emergence of antibiotic resistance is theoretically possible. Unlike other enteric bacteria, genetic and phenotypic analysis (eg, through the controlled challenge

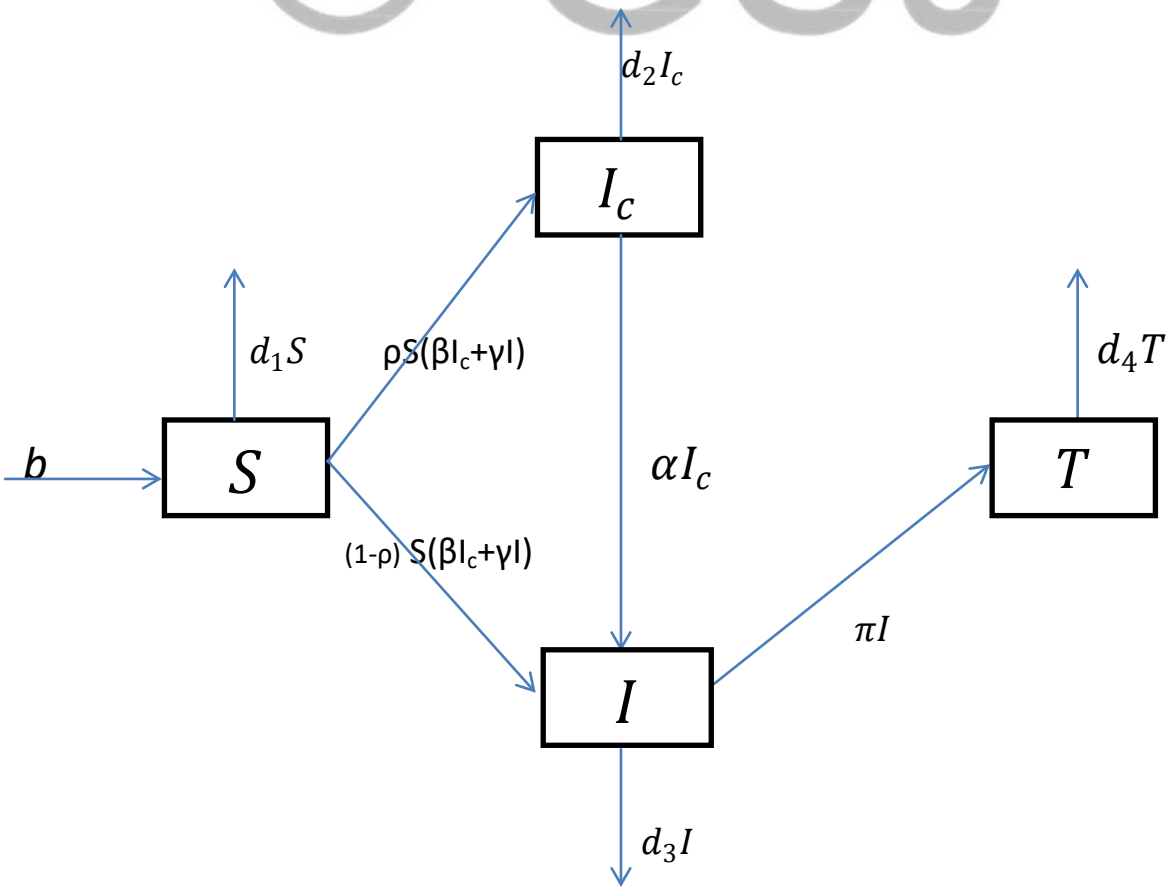
of human volunteers) has indicated that S. Typhi is relatively poorly adapted for growth in the human intestine

MATERIAL AND METHODOLOGY

FORMULATION OF THE MODEL

The compartments used in this study consists of four (4) classes: S(t) is used to represent the number of individuals that are prone to the disease at time t or those susceptible to the disease. $I_C(t)$ is used to represent the number of asymptomatic carriers at time t. I(t) is used to represent the number of individuals who have been infected with the disease and are capable of spreading the disease to the other individuals at time t. T(t) is used to represent the number of individuals who have been infected with the disease and are treated. Those in this category are not able to be infected again or transfer to others.

The schematic diagram for the modified model of the typhoid of the above descriptio



A susceptible individual can be infected through direct contact with an infected individual or carrier. Can also become carrier with probability **ρ**, or shows disease symptom with probability (**1-ρ**). We assume that the rate of transmission **β** for the carrier $\mathbf{I_C}$ is higher than the rate of transmission **γ** for the symptomatically infected individual **I**, due to the fact that, they are more likely to be unaware of their condition, and therefore continue with their life regular behaviors. Carrier may become symptomatic at a rate α. For typhoid disease carriage can remain life-long. We assume **b** influx in to susceptible populations. Let's also consider $\mathbf{d_1}$,$\mathbf{d_2}$,$\mathbf{d_3}$, and $\mathbf{d_4}$ to denote the death rates of those in the susceptible, asymptomatic carrier, infectious and recovered/ treated classes respectively. Here $\mathbf{d_1}$ and $\mathbf{d_4}$ can be considered as natural death rate of the susceptible and treated individuals respectively, while d_2 and d_3 are death rate of the infected and chronic individuals respectively. Symptomatically infected individuals recover with rate **π**, and we assume that the recovered individuals are sometimes immune.

The model has the following systems of differential equations:

$$\frac{dS}{dt} = b - d_1 S - S(\beta I_C + \gamma I) \quad (3.1)$$

$$\frac{dI_C}{dt} = \rho S(\beta I_C + \gamma I) - (d_2 + \alpha) I_C \quad (3.2)$$

$$\frac{dI}{dt} = (1-\rho) S(\beta I_C + \gamma I) - (d_3 + \pi) I + \alpha I_C \quad (3.3)$$

$$\frac{dT}{dt} = \pi I - d_4 T \quad (3.4)$$

Table 1: Description of Variables for model

Variables	Description
S(t)	susceptible individuals at time t
$I_C(t)$	carrier infectious individuals at time t
I(t)	infectious individuals at time t

T(t)	Treated individuals at time t

Table 2 Description of Parameters for model

Parameters	Description
B	rate of influx in to the susceptible populations
d_1,d_4,	natural death rate of the susceptible and treated individuals
d_2,d_3	death rates of the infected and chronic individuals respectively
β	transmission coefficient for the carrier compartment I_C
γ	transmission coefficient for the symptomatically infected I
α	rate of which carriers develop symptoms.
π	rate of recovery
ρ	Probability that newly infected individual is asymptomatic

EXISTENCE OF THE DISEASE-FREE EQUILIBRIUM (DFE) STATE OF THE MODIFIED MODEL

The disease-free equilibrium is the point at which no typhoid disease is present in the population. Now we can recall our four (4) equations above. Those are (3.1) to(3.4)

$$\frac{dS}{dt} = b - d_1 S - S(\beta I_C + \gamma I) \quad (3.1)$$

$$\frac{dI_C}{dt} = \rho S(\beta I_C + \gamma I) - (d_2 + \alpha) I_C \quad (3.2)$$

$$\frac{dI}{dt} = (1-\rho) S(\beta I_C + \gamma I) - (d_3 + \pi) I + \alpha I_C \quad (3.3)$$

$$\frac{dT}{dt} = \pi I - d_4 T \quad (3.4)$$

At equilibrium state, the rate of change of variables represent the individuals are equal to zero, i.e.

$$\frac{dS}{dt} = \frac{dI_C}{dt} = \frac{dI}{dt} = \frac{dT}{dt} = 0$$

Therefore, equating the left hand sides (LHS) of the above equations (3.1) to(3.4) to zero, we have

$$0 = b - d_1 S - S(\beta I_C + \gamma I) \quad (3.5)$$

$$0 = \rho S(\beta I_C + \gamma I) - (d_2 + \alpha) I_C \quad (3.6)$$

$$0 = (1 - \rho) S(\beta I_C + \gamma I) - (d_3 + \pi) I + \alpha I_C \quad (3.7)$$

$$0 = \pi I - d_4 T \quad (3.8$$

Now let $(S, I_C, I, T) = (S_0, I_{C0}, I_0, T_0)$, then equations (3.5) to (3.8) become;

$$0 = b - d_1 S_0 - S_0\left(\beta I_{c_0} + \gamma I_0\right) \quad (3.9)$$

$$0 = \rho S_0\left(\beta I_{c_0} + \gamma I_0\right) - (d_2 + \alpha) I_{c_0} \quad (3.10)$$

$$0 = (1 - \rho) S_0\left(\beta I_{c_0} + \gamma I_0\right) - (d_3 + \pi) I_{c_0} + \alpha I_{c_0} \quad (3.11)$$

$$0 = \pi I - d_4 T_0 \quad (3.12)$$

Assume that $(S_0, 0, 0, T_0)$ is an equilibrium state, then equations (3.9) to (3.12) we have.

From (3.9), we have

$$0 = b - d_1 S_0 \quad (3.13)$$

Also from (3.12), we have

$$0 = -d_4 T_0 \quad (3.14)$$

While the remaining equations are zero, we just ignore them!

From (3.13), we have

$$0 = b - d_1 S_0$$

Or

$$d_1 S_0 = b$$

Dividing both side by d_1, we have

$$S_0 = \frac{b}{d_1}$$

From (3.14), we have

$$0 = -d_4 T_0$$

Or

$$-d_4 T_0 = 0$$

Dividing both side by $-d_4$*, we have*

$$T_0 = -\frac{0}{d_4}$$

Therefore

$$T_0 = 0$$

Therefore at the diseases free equilibrium, the population is free of the disease

$P_o = (S_{0,} I_{C0,} I_{0,} T_0) = (\frac{b}{d_1}, 0, 0, 0)$ (3.15)

$$\begin{pmatrix} S_0 \\ I_{C0} \\ I_0 \\ T_0 \end{pmatrix} = \begin{pmatrix} \frac{b}{d_1} \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

BASIC REPRODUCTION NUMBER ($\mathbf{R_0}$)

The basic reproductive number (R_0) is used to measure the transmission potential of a disease. It is the average number of secondary infections produced by a typical case of an infection in a population where everyone is susceptible (Rothman *et al.*, 2013). If $R_0<1$, each existing infection causes less than one new infection. In this case, the disease will decline and eventually die out. And if $R_0= 1$, each existing infection causes one new infection. The disease will stay alive and stable, but there won't be an outbreak or an epidemic. If $R_0>1$, each existing infection causes more than one new infection. The disease will be transmitted between people, and there may be an outbreak or epidemic.

Table 3: **Illustrates the growth of infection of few different R_0 values**

Now, the basic reproductive number (R_0) of the model re-arranged in (3.16) to (3.19) was calculated using next generation matrix (NGM) as applied in Van den,.D, and watmought, (2005).

$$\frac{dI_C}{dt} = \rho S(\beta I_C + \gamma I) - (d_2 + \alpha)I_C \quad (3.16)$$

$$\frac{dI}{dt} = (1-\rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C \quad (3.17)$$

$$\frac{dS}{dt} = b - d_1 S - S(\beta I_C + \gamma I) \quad (3.18)$$

$$\frac{dR}{dt} = \pi I + \theta S - d_4 R \quad (3.19)$$

From above equations, we notice that our disease classes are as follows;

$$\frac{dI_C}{dt} = \rho S(\beta I_C + \gamma I) - (d_2 + \alpha)I_C \quad (3.20)$$

$$\frac{dI}{dt} = (1-\rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C \quad (3.21)$$

Let

$F_i = \left[\frac{df_i}{dx_j}\right]$ and $V_i = \left[\frac{dv_i}{dx_j}\right]$

Let $(I_C, I) = (x_1, x_2)$

Then, $F = \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} \end{bmatrix}$ and $V = \begin{bmatrix} \frac{\partial v_1}{\partial x_1} & \frac{\partial v_1}{\partial x_2} \\ \frac{\partial v_2}{\partial x_1} & \frac{\partial v_2}{\partial x_2} \end{bmatrix}$ (3.22)

From equation (3.20) and (3.21) we generate

$$Fi = \begin{bmatrix} \rho S(\beta x_1 + \gamma x_2) \\ (1-\rho)S(\beta x_1 + \gamma x_2) \end{bmatrix} \text{ and, } Vi = \begin{bmatrix} (d_2 + \alpha)x_1 \\ -\alpha x_1 + (d_3 + \pi)x_2 \end{bmatrix}$$

Hence we obtain

$\frac{\partial f_1}{\partial x_1} = \rho\beta S,$ $\frac{\partial f_2}{\partial x_1} = (1-\rho)\beta S,$

$\frac{\partial f_1}{\partial x_2} = \rho\gamma S,$ $\frac{\partial f_2}{\partial x_2} = (1-\rho)\gamma S,$

Also,

$\frac{\partial v_1}{\partial x_1} = (d_2+\alpha),$ $\frac{\partial v_2}{\partial x_1} = -\alpha,$

$\frac{\partial v_1}{\partial x_2} = 0,$ $\frac{\partial v_2}{\partial x_2} = (d_3+\pi),$

Now at disease free equilibrium $S = S_0 = \frac{b}{d_1}$ and by substituting the partial derivatives above in equation (3.22) we have,

$$F=\begin{bmatrix} \rho\beta S_0 & \rho\gamma S_0 \\ (1-\rho)\beta S_0 & (1-\rho)\gamma S_0 \end{bmatrix} \quad \text{and} \quad V=\begin{bmatrix} (d_2+\alpha) & 0 \\ -\alpha & (d_3+\pi) \end{bmatrix},$$

Taking the inverse of V, i.e. V^{-1}

$$V^{-1} = \frac{1}{(d_2+\alpha)(d_3+\pi)}\begin{bmatrix} (d_3+\pi) & 0 \\ \alpha & (d_2+\alpha) \end{bmatrix} = \begin{bmatrix} \frac{1}{(d_2+\alpha)} & 0 \\ \frac{\alpha}{(d_2+\alpha)(d_3+\pi)} & \frac{1}{(d_3+\pi)} \end{bmatrix},$$

Therefore

$$(FV^{-1})=\begin{bmatrix} \rho\beta S_0 & \rho\gamma S_0 \\ (1-\rho)\beta S_0 & (1-\rho)\gamma S_0 \end{bmatrix}\begin{bmatrix} \frac{1}{(d_2+\alpha)} & 0 \\ \frac{\alpha}{(d_2+\alpha)(d_3+\pi)} & \frac{1}{(d_3+\pi)} \end{bmatrix},$$

$$= \begin{bmatrix} \frac{\rho\beta S_0}{(d_2+\alpha)} + \frac{\alpha\rho\gamma S_0}{(d_2+\alpha)(d_3+\pi)} & \frac{\rho\gamma S_0}{(d_3+\pi)} \\ \frac{(1-\rho)\beta S_0}{(d_2+\alpha)} + \frac{\alpha(1-\rho)\gamma S_0}{(d_2+\alpha)(d_3+\pi)} & \frac{(1-\rho)\gamma S_0}{(d_3+\pi)} \end{bmatrix}$$

Using the diagonal of the matrix. From which we obtained

$$(\mathrm{FV}^{-1}) = \frac{b}{d_1}\left[\frac{\rho\beta}{(d_2+\alpha)} + \frac{\rho\alpha\gamma}{(d_2+\alpha)(d_3+\pi)} + \frac{(1-\rho)\gamma}{(d_3+\pi)}\right],$$

$$\mathrm{R}_0 = p(\mathrm{FV}^{-1}) = \frac{b}{d_1}\left[\frac{\rho\beta}{(d_2+\alpha)} + \frac{\rho\alpha\gamma}{(d_2+\alpha)(d_3+\pi)} + \frac{(1-\rho)\gamma}{(d_3+\pi)}\right], \quad (3.23)$$

Where p is the spectral radius

STABILITY ANALYSIS OF DISEASE-FREE EQUILIBRUIM (DFE) STATE

We shall examine the local stability of the disease-free equilibrium P_o(3.15)

Using the method of linearized stability,

Now, let

$$f_1 = b - d_1 S - S(\beta I_C + \gamma I) \quad (3.24)$$

$$f_2 = \rho S(\beta I_C + \gamma I) - (d_2 + \alpha) I_C \quad (3.25)$$

$$f_3 = (1-\rho) S(\beta I_C + \gamma I) - (d_3 + \pi) I + \alpha I_C \quad (3.26)$$

$$f_4 = \pi I - d_4 T \quad (3.27)$$

Then the jacobian matrix associated with (3.1) to (3.4) at the disease-free equilibrium state is given by

$$\mathrm{J}_0 = \begin{bmatrix} -d_1 & -\beta\frac{b}{d_1} & -\gamma\frac{b}{d_1} & 0 \\ 0 & \rho\beta\frac{b}{d_1} - (d_2+\alpha) & \rho\gamma\frac{b}{d_1} & 0 \\ 0 & (1-\rho)\beta\frac{b}{d_1} + \alpha & (1-\rho)\gamma\frac{b}{d_1} - (d_3+\pi) & 0 \\ 0 & 0 & 0 & -d_4 \end{bmatrix} \quad (3.28)$$

Now from the matrix (3.28), using the characteristics equation det(J-λI)=0, we notice that $-d_1$, $-d_2$ are the roots and the remaining eigenvalues are found from the quadratic equation below

$$\lambda^2 + A\lambda + B = 0 \quad (3.29)$$

Where

$$A = -\left[\rho\beta\frac{b}{d_1} - (d_2+\alpha) + (1-\rho)\gamma\frac{b}{d_1} - (d_3+\pi)\right]$$

And

$$B = \left[\left(\rho\beta\frac{b}{d_1} - (d_2+\alpha)\right)\left((1-\rho)\gamma\frac{b}{d_1} - (d_3+\pi)\right)\right] - \rho\gamma\frac{b}{d_1}\left((1-\rho)\beta\frac{b}{d_1} + \alpha\right)$$

From Routh Hurwitz criterion above equation have negative real roots provided

$A > 0 \; and \; B > 0$

Therefore

$A > 0 \; implies \; that$

$$-\left[\rho\beta\frac{b}{d_1} - (d_2+\alpha) + (1-\rho)\gamma\frac{b}{d_1} - (d_3+\pi)\right] > 0$$

Or

$$\frac{b}{d_1}(\rho\beta + (1-\rho)\gamma) - [(d_2+\alpha) + (d_3+\pi)] < 0$$

From which we get

$$\frac{b}{d_1}[(d_2+\alpha) + (d_3+\pi)]\left[\frac{(\rho\beta+(1-\rho)\gamma)}{(d_2+\alpha)+(d_3+\pi)} - 1\right] < 0$$

Or

$$\frac{b}{d_1}[(d_2+\alpha) + (d_3+\pi)](R-1) < 0 \text{ , provided } R < 1$$

Where

$$R = \frac{(\rho\beta+(1-\rho)\gamma)}{(d_2+\alpha)+(d_3+\pi)}$$

Similarly for, $B > 0$, implies $R < 1$.

RESULT AND DISCUSSION

VALUES OF VARIABLES AND PARAMETER

The results of this research will be obtained by using defined values of variables and parameters presented in the table 4 and table 3 respectively, some of these data were collected from my case of study “the General Sani Abacha Specialist Hospital, Damaturu Yobe state”. We will also use these values of variables and parameters to draw a graph of four (4) difference experiments.

Table 4: Parameter value for numerical experiments

Experiments / Parameters	1	2	3	4	Source
b	70	85	100	115	Guo *et al* (2006)
d_1	0	0.15	0.15	0.15	Moffat *et al* (2014)
d_3	0	0.1503	0.1503	0.1503	Moffat *et al* (2014)
β	0	0.01	0.009	0.008	Assumed
π	0	0.5	1.8	3.25	Assumed
ρ	0	0.4	0.4	0.4	Assumed
α	0	0.0123	0.0123	0.0123	Moffat *et al* (2014)
γ	0	0.0113	0.0113	0.0123	Moffat *et al* (2014)
d_2	0	0.25	0.20	0.15	Assumed
d_4	0	0.001	0.02	0.1	Assumed

Where,

b = is a rate of influx in to the susceptible populations
d_1,d_4, =natural death rate of the susceptible and treated individuals
d_2,d_3= death rates of the infected and chronic individuals respectively
β = transmission coefficient for the carrier compartment I
γ =transmission coefficient for the symptomatically infected I
α =rate of which carriers develop symptoms.
π = rate of recovery
ρ = Probability that newly infected individual is asymptomatic

Table 5: Variables value for numerical experiments

T	**0**	**1**	**2**	**3**
S	0	100	200	300
I_C	60	50	40	30
I	90	70	50	30

T	0	100	120	140

Where,
T= Time in Years
S= susceptible individuals
I_C= carrier infectious individuals
I= infectious individuals
T= Treated individuals

Solution of the equation of the model

Now, let us use our model equations to solve for each variable of the model to know the relationship andchanges in the population of the individuals for three years in four difference experiments,

From equation (3.1)

$$\frac{dS}{dt} = b - d_1 S - S(\beta I_C + \gamma I)$$

by separation of variable

$$dS = [b - d_1 S - S(\beta I_C + \gamma I)]\, dt$$

Integrating both side, we have

$$\int dS = \int [b - d_1 S - S(\beta I_C + \gamma I)]\, dt$$

Implies

$$S(t) = [b - d_1 S - S(\beta I_C + \gamma I)]t \qquad (4.1)$$

By using the value of parameters and variable of table 4 and table 5, and considering experiments

$$S(t) = [b - d_1 S - S(\beta I_C + \gamma I)]t$$

When t=0

$$S(0) = [70 - 0 \times 0 - 0(0 \times 0 + 0 \times 0)]0$$
$$= 0$$

Next

$$S(t) = [b - d_1 S - S(\beta I_C + \gamma I)]t$$

When t=1

$$S(1) = [85 - 0.4 \times 100 - 100(0.01 \times 50 + 0.0113 \times 70)]1$$
$$= [85 - 15 - 100(0.5 + 0.791)]1$$
$$= [70 - 129.1]1$$
$$= -59.1 \quad \approx= -59$$

Next

$$S(t) = [b - d_1 S - S(\beta I_C + \gamma I)]t$$

When t=2

$$S(2) = [100 - 0.15 \times 200 - 200(0.009 \times 40 + 0.0113 \times 50)]2$$
$$= [100 - 30 - 200(0.36 + 0.565)]2$$
$$= [100 - 30 - 138]2$$
$$= -230$$

Next

$$S(t) = [b - d_1 S - S(\beta I_C + \gamma I)]t$$

When t=3

$$S(3) = [115 - 0.15 \times 300 - 300(0.008 \times 30 + 0.0113 \times 30)]3$$
$$= [115 - 45 - 300(0.24 + 0.339)]3$$
$$= [115 - 45 - 173.7]3$$
$$= -311.1 \approx= -311$$

We see that base on the above solution susceptible individuals decreases every day anytime, we can also see that at the initial years of treatment the value of susceptible is 0 this showing us that there is no treatment at that time, and also after one years it start decreasing the values, this also showing us that the susceptible individuals are responding to treatment

From (3.2)

$$\frac{dI_C}{dt} = \rho S(\beta I_C + \gamma I) - (d_2 + \alpha)I_C$$

by separation of variable

$$dI_C = [\rho S(\beta I_C + \gamma I) - (d_2 + \alpha)I_C]dt$$

Integrating both side, we have

$$\int dI_C = \int [\rho S(\beta I_C + \gamma I) - (d_2 + \alpha) I_C] dt$$

Implies

$$I_C(t) = [\rho S(\beta I_C + \gamma I) - (d_2 + \alpha) I_C] t \quad (4.2)$$

By using the value of parameters and variable of table 4 and table 5, and considering experiments

When t=0

$$I_C(0) = [0 \times 0(0 \times 60 + 0 \times 90) - (0 + 0)0]0$$
$$= 0$$

Next

$$I_C(t) = [\rho S(\beta I_C + \gamma I) - (d_2 + \alpha) I_C] t$$

When t=1

$$I_C(1) = [0.4 \times 100(0.01 \times 50 + 0.0113 \times 70) - (0.25 + 0.0123)50]1$$
$$= [40(0.5 + 0.791) - (0.2623)50]1$$
$$= [51.65 - 13.115]1$$
$$= 38.115 \approx= 38$$

Next

$$I_C(t) = [\rho S(\beta I_C + \gamma I) - (d_2 + \alpha) I_C] t$$

When t=2

$$I_C(2) = [0.4 \times 200(0.009 \times 40 + 0.0113 \times 50) - (0.20 + 0.0123)40]2$$
$$= [80(0.36 + 0.565) - (0.2123)40]2$$
$$= [(74) - (8.492)]2$$
$$= 131.016 \approx= 131$$

Next

$$I_C(t) = [\rho S(\beta I_C + \gamma I) - (d_2 + \alpha) I_C] t$$

When t=3

$$I_C(3) = [0.4 \times 300(0.008 \times 30 + 0.0113 \times 30) - (0.15 + 0.0123)30]3$$
$$= [120(0.25 + 0.339) - (0.1623)30]3$$

$$= [(70.68) - (4.869)]3$$
$$= [(70.68) - (4.869)]3$$
$$= 197.433 \approx= 197$$

We see that base on the above solution asymptomatic carrier individuals increases, that means individuals are responding treatment since there is decreasing in susceptible individuals and increasing in carrier individuals

From equation (3.3)

$$\frac{dI}{dt} = (1-\rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C$$

by separation of variable

$$dI = [(1-\rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C]\, dt$$

Integrating both side, we have

$$\int dI = \int [(1-\rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C]\, dt$$

Implies

$$I(t) = [(1-\rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C]\, t \qquad (4.3)$$

By using the value of parameters and variable of table 4 and table 5, and considering experiments

$$I(t) = [(1-\rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C]\, t$$

When t=0

$$I(0) = [(1-\rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C]\, 0$$
$$= 0$$

Next

$$I(t) = [(1-\rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C]\, t$$

When t=1

$$I(1) = [(0.6)100(0.5 + 0.791) - (0.1503 + 0.5)70 + 0.0123 \times 50]\ 1$$
$$= [(77.46) - (45.521) + 0.615]\ 1$$
$$= 32.554 \approx= 33$$

Next

$$I(t) = [(1 - \rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C]\ t$$

When t=2

$$I(2) = [(0.6)200(0.36 + 0.565) - (0.1503 + 1.8)50 + 0.0123 \times 40]\ 2$$
$$= [(111) - (97.515) + 0.492]\ 2$$
$$= 27.954 \approx 28$$

Next

$$I(t) = [(1 - \rho)S(\beta I_C + \gamma I) - (d_3 + \pi)I + \alpha I_C]\ t$$

When t=3

$$I(3) = [(0.6)300(0.24 + 0.339) - (0.1503 + 3.25)30 + 0.0123 \times 30]\ 3$$
$$= [(104.22) - (102.009) + 0.369]\ 3$$
$$= 7.74 \approx 8$$

From the above solution we see that the population of infected individuals decreases very fast, that means there is a very high rate of treatment.

From (3.4)

$$\frac{dT}{dt} = \pi I - d_4 T$$

by separation of variable

$$dT = (\pi I - d_4 T)dt$$

Integrating both side we have

$$\int dT = \int (\pi I - d_4 T)dt$$

Implies

$$T(t) = (\pi I - d_4 T)t \qquad (4.4)$$

By using the value of parameters and variable of table 4 and table 5, and considering experiments

$T(t) = (\pi I - d_4 T)t$

When t=0

$T(0) = (0 \times 90 - 0 \times 0)0$

$= 0$

Next

$T(t) = (\pi I - d_4 T)t$

When t=1

$T(1) = (0.5 \times 70 - 0.001 \times 100)1$

$= (35 - 0.1)1$

$= 34.9 \approx = 35$

Next

$T(t) = (\pi I - d_4 T)t$

When t=2

$T(2) = (1.8 \times 50 - 0.02 \times 120)2$

$= (90 - 2.4)2$

$= 175.2 \approx = 175$

Next

$T(t) = (\pi I - d_4 T)t$

When t=3

$T(3) = (3.25 \times 30 - 0.1 \times 140)3$

$= (97.5 - 14)3$

$= 250.5 \approx = 250$

From the above solution we see that the population of treated individuals increases very fast it definitely against the population of infected individuals

This is showing us that infected individuals are transferring to treated

Graphs of the model

By using the value in table 4 we can represent our results graphically for each population as follow;

Remembering our table 5

Table of variables value for numerical experiments

T	**0**	**1**	**2**	**3**
S	0	100	200	300
I_C	60	50	40	30
I	90	70	50	30
T	0	100	120	140

Now

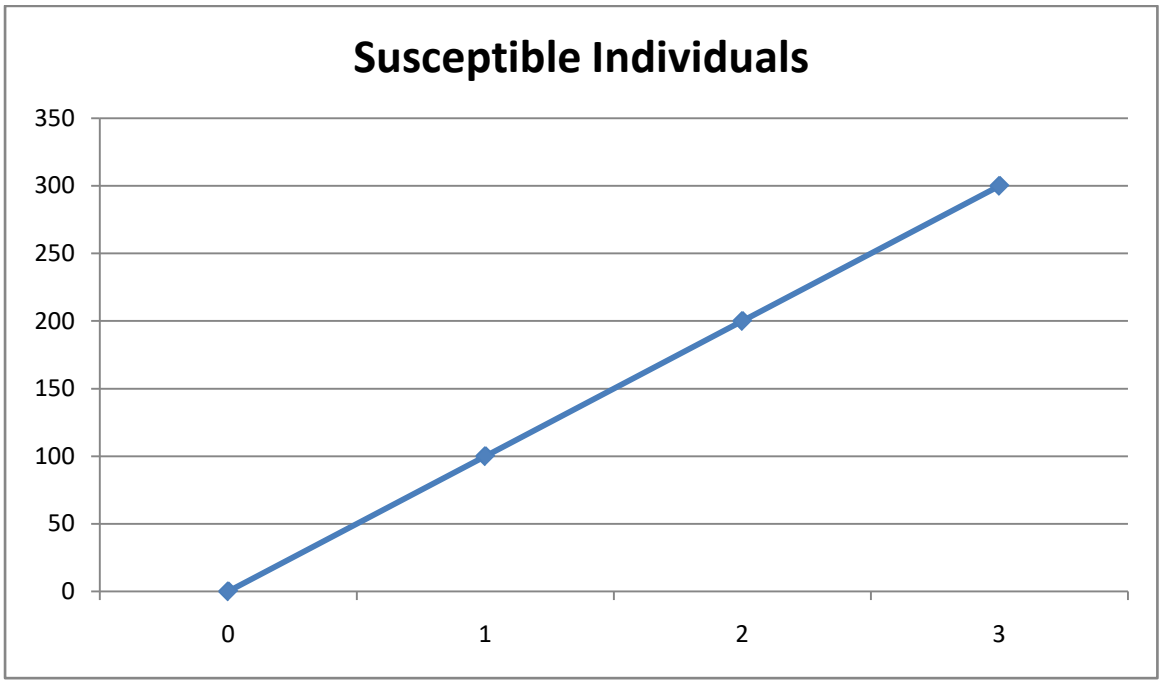
Table 6: showing the value of susceptible individuals at time (T)

T	**0**	**1**	**2**	**3**
S	0	100	200	300

Where,

***S*= Susceptible individuals**
T=Time (Years)

Fig 1.2



Time (Years)

Fig 1.2 shows the graph of susceptible individuals against time, it also means that the susceptible population increases with time.

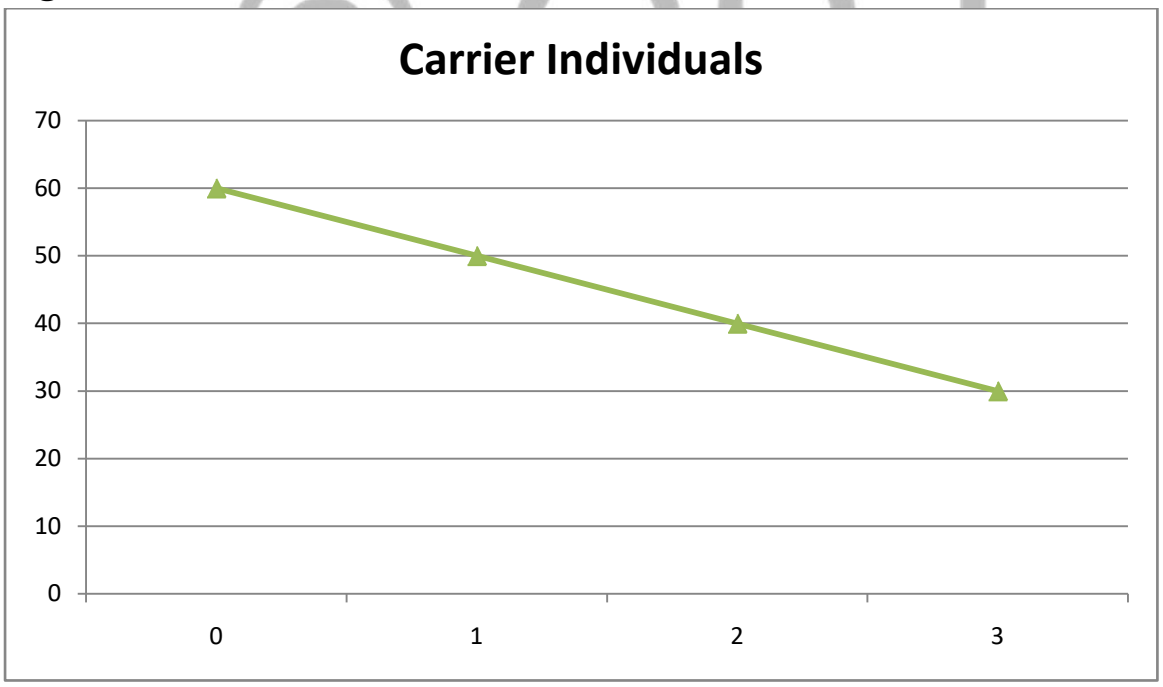
Table 7: shows the value of carrier individuals at time (T)

T	**0**	**1**	**2**	**3**
$\mathbf{I_C}$	60	50	40	30

Where,

$\boldsymbol{I_C}$ **=Carrier individuals**
T=Time (Years)

Fig 1.3



Time (Years)

Fig 1.3 shows the graph of carrier population against time, it also shows that the population of carrier individuals decreases due to the fact that some transferring to treated

Table 8: shows the value of infected individuals at time (T)

T	0	1	2	3
I	90	70	50	30

Where,

***I* =Infected individuals**
T=Time (Years)

Fig 1.4

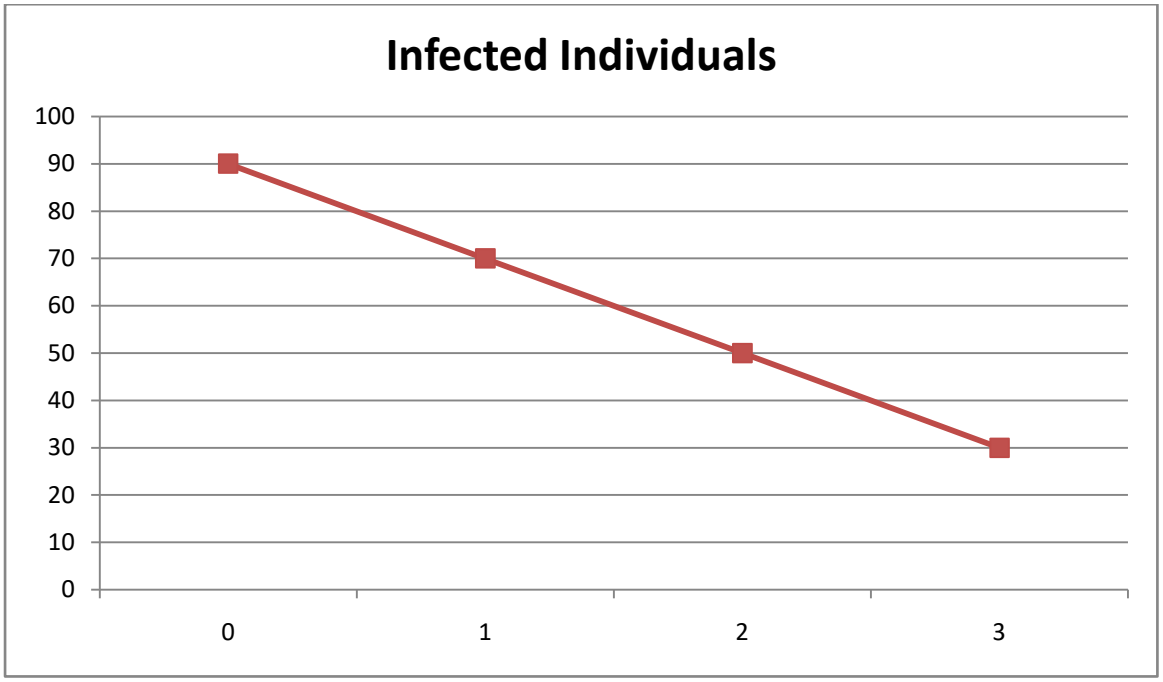


Fig 1.4 shows the graph of infected population against time, it also shows that infected populations decrease, are getting treatment and transferring to treated individuals.

Table 9: shows the value of treated individuals at time (T)

T	**0**	**1**	**2**	**3**
T	0	100	120	140

where,

T=Treated individuals
T=Time (Years)

Fig 1.5

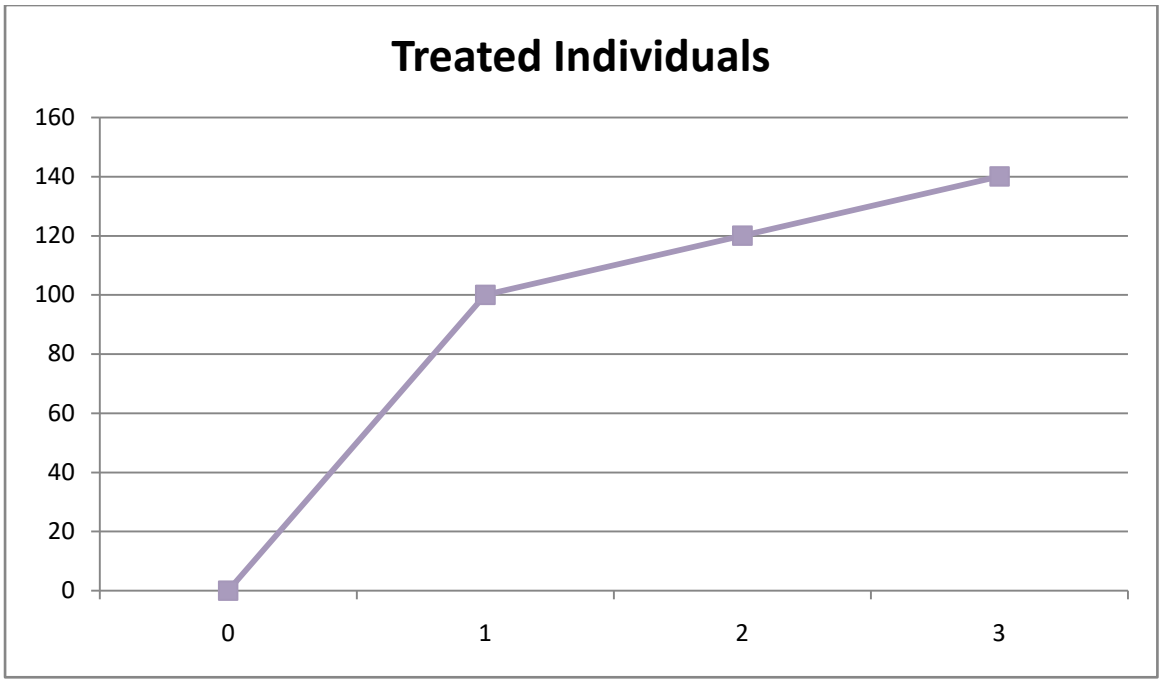


Fig 1.5 shows the graph of treated population against time, it also shows that treated population increases very high all those individuals i.e. infected and carrier are gradually becoming very safe by accepting treatments. That means treatment is the better way to eradicate typhoid fever

SUMMARY, CONCLUSION AND RECOMMENDATION

SUMMARY

In this research, we have studied the effect of carriers and treatment on the transmission dynamics of typhoid fever. A disease-free equilibrium was obtained and its stability was analyzed using linearized method. We computed the basic reproduction number (R_0) in terms of the model parameters.

It was also shown that for the threshold parameter, $R_0 < 1$, the disease-free equilibrium state is locally asymptotically stable and the disease eventually disappears from the population (i.e. dies out). If $R_0 > 1$, the disease-free equilibrium state is unstable, that means the disease can spread in the population (endemic). In order to maintain R_0 below 1, sensitivity analysis suggested that an increase of carriers through p will lead to high prevalence in the community. The infectious population is responsive in both changes in treatment, increasing the level of treatment through π causes the infectious population to drop. However, this decrease in the infectious group becomes much less significant as we move from low to high levels of carriers. In other words, treatment can be effective in reducing the infected population if the number of carriers is small.

- In our model, the following results were obtained;
  - Given $p, b, \beta, \alpha, \gamma, \pi, d_1, d_2, d_3 > 0$ there exists a disease free state of the model given by

$$P_0 = \left(\frac{b}{d_1}, 0,0,0\right)$$

  - R_0 was found using the next generation method

$R_0 < 1$.

  - Solution of the equation of the model, we were solved the equations of the model for all individual governing this research. We solved the equation for difference time and in difference experiments
  - We carried out numerical experiments of solutions of the model using the model parameters of interest and we also drew the graphs that displayed the results for each compartment of the model

CONCLUSION

In this research work, we formulate a model to incorporate treatment in this dynamics of the disease. we studied the modified model to investigate the

effect of treatment on the dynamics of the infection. The existence and stability of a disease-free equilibrium state of modified model was also established and was found to be locally asymptomatically stable. The basic reproduction number R_O that governs the disease transmission was computed by the next generation operator method.

Numerical experiments using published data and the data collected from General Sani Abacha Specialist hospital damaturu, show that treatment can be effective in reducing the number of infected people as well as the number of carriers. The sensitivity analysis of the model parameters, using R_o also indicates that the number of carriers have high impact on the dynamics of the disease.

RECOMMENDATION

The analytical and numerical studies revealed that there is a possibility of controlling/eradication of typhoid fever, provided that the basic reproduction number R_o is less than one. It was also found that, $and\ \pi$ are very most important parameters in the transmission of the disease. I therefore recommend as follows:-

1. There should be proper disposal of the faeces and urine especially the people using bushes hill as toilets and rivers in town as urinals to prevent the spread of the disease.
2. Domestic water should be boiled or chlorinated before drinking to kill the bacteria.
3. Fruits should be washed with clean water before being eaten.
4. Food handlers should be clean, and should be subjected to regular medical check-ups.
5. More research be carried out to identify carriers and find appropriate ways of handling them so as to reduce their role in the dynamics of the infection.

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