Journal of Modern Mathematics and Statistics 5 (2): 54-59, 2011
ISSN: 1994-5388

Impact of Vaccines on Controlling Typhoid Fever in Kassena-Nankana District of Upper East Region of Ghana: Insights from a Mathematical Model

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Abstract: Vaccination is an important prevention and control measure for the spread of typhoid fever. In this study, we develop a simple mathematical model to explore the impact of vaccination on the transmission dynamics of typhoid fever in Kassena-Nankana district of Upper East region of Ghana. Analytical results of the model show that the quantities R_v and R_0 which represent the vaccine-induced reproduction number and the no vaccine induced reproduction number, respectively provide threshold conditions that determine the prevalence of typhoid fever in a community. These threshold conditions can be used to gain important insights into the impact of vaccination on controlling typhoid fever. Numerical results have been provided to illustrate the analytical findings.

Key words: Salmonella paratyphi, typhoid fever, vaccines, reproductive number, stability, Zimbabwe

INTRODUCTION

Typhoid is endemic in many developing countries and remains a substantial public health problem despite recent progress in water and sanitation coverage (Lauria *et al*., 2009). Globally, it is estimated that typhoid causes >16 million cases of illness each year, resulting in >600,000 deaths (Kariuki *et al*., 2004). Typhoid fever is a communicable disease found only in man and occurs due to systemic infection mainly by Salmonella typhi organism. It is an acute generalized infection of the reticuloendothelial system, intestinal lymphoid tissue and the gall bladder. Incubation period, usually 10-14 days but it may be as short as 3 days or as long as 21 days depending upon the dose of the inoculums. The epidemic is transmitted by feco-oral route or urine-oral route either directly through hands soiled with feces or urine of cases or carriers or indirectly by ingestion of contaminated water, milk, food or through flies (Singh, 2001). The new-generation Vi polysaccharide vaccine is a safe and effective public health intervention against typhoid (Lauria *et al*., 2009; Acosta *et al*., 2004) report an efficacy of 55-70% for 2-3 years. Mathematical models have become invaluable management tools for epidemiologists both shedding light on the mechanisms underlying the observed dynamics as well as making quantitative predictions on the effectiveness of different control measures. The literature and development of mathematical epidemiology is well documented and can be found (Anderson, 1991; Bailey, 1975; Brauer and Castillo-Chavez, 2000). In light of the pervious literature, we wish to use a mathematical model to assess the impact of vaccines on the long term dynamics of typhoid fever in Kassena-Nankana district of upper East region of Ghana.

MODEL FORMULATION

An SIR type of the epidemic model is proposed to study, the dynamics of typhoid fever in Kassena-Nankana district of Upper East region of Ghana (Adetunde, 2008). Vital dynamics and impact of tyhoid vaccines are not considered in this study. The model presented in this study adopts a similar structure as described by Adetunde (2008). We introduce a vaccinated class and include the vital dynamics. Based on the epidemiological status, the host population is subdivided into five classes namely: Susceptibles S(t); Vaccinated V(t); Infectives I(t); Carriers C(t) and Recoveries R(t). Thus, the total population is given by N = S+V+I+C+R. Assume that there is a constant recruitment rate A (into the susceptible class) and a per capita natural death rate μ, the model takes the form:

$$\left.\begin{aligned} S' &= \Lambda - \alpha SI - (\phi + \mu)S + \omega V \\ V' &= \phi S - (\omega + \mu)V \\ I' &= \alpha SI - (\beta + b + \sigma + \mu)I \\ C' &= \beta I - (\gamma + \mu + d)C \\ R' &= \gamma C + bI - \mu R \end{aligned}\right\} \quad (1)$$

A transition diagram between these epidemic classes is shown in Fig. 1. Susceptible individuals are vaccinated at percapita rate ϕ and the immunity wanes at per capita rate ω: assuming homogeneous mixing of the population

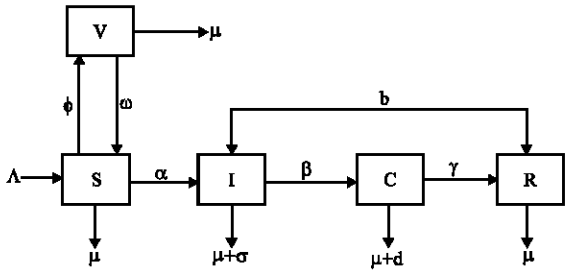

Fig. 1: Model flow diagram

Table 1: Model parameters and their interpretations

Parameters	Symbols	Values	Refrences
Recruitment rate	A	1000,000	Lauria *et al.* (2009)
Natural mortality rate	μ	0.018 year^{-1}	Adetunde (2008)
Per capita infection rate	α	0.0072 year^{-1}	Adetunde (2008)
Rate of recovery for carriers	γ	0.115 year^{-1}	Adetunde (2008)
Rate for infectious individuals	b	0.096 year^{-1}	Adetunde (2008)
Per capita disease-induced mortality rate	σ	0.9 year^{-1}	Adetunde (2008)
Per capita carrier-induced mortality rate	d	0.013 year^{-1}	Adetunde (2008)
Rate at which susceptible individuals are vaccinated	ϕ	0.9 year^{-1}	Lauria *et al.* (2009)
Rate at which the vaccine wanes	ω	0.33 year^{-1}	Lauria *et al.* (2009), Acosta *et al.* (2004)
Rate of progression from infective to carrier	β	0.03-0.05	Adetunde (2008)

susceptible individuals acquire typhoid fever at a constant rate α after ingestion of solid or liquid food which contains the Salmonella paratyph bacteria.

The main source of typhoid is asymptomatic carriers. An individual can asymptomatically carry the typhoid germ for days to years without showing any of the symptoms of typhoid fever. In such carriers, the typhoid bacillus continues to multiply in the gall bladder. It reaches the intestine through the bile duct. The silent carriers are the source of typhoid germs for the continued episodes of infections (Senthil-Kumar and Prabakaran, 2005). Hence, β denotes the rate of progression from infective to carrier stage, γ and b are the per capita rates of recovery from carrier and infectious stage, respectively. Individuals infected with typhoid fever suffer an additional disease induced mortality denoted by σ and d for infectious and carriers, respectively. Model parameters and their dimensions are shown in Table 1.

Basic properties of the model: We study the basic results of solutions for model system 1 which are essential in the proofs of stability.

Lemma 1: The equations preserve positivity of solutions.

Proof: The vector field given by the right hand side of system 1 points inward on the boundary of $\mathbb{R}^5_+ \setminus \{0\}$: For example if $V = 0$ then $V' = \phi S \geq 0$. All the other components are similar.

Lemma 2: Each strictly positive is bounded in L^1 norm by max $\{N(0), \Lambda/\mu\}$.

Proof: The L^1 norm of each strictly positive solution is N and it satisfies the inequality $N' \leq \Lambda - \mu N$. Solutions to the arbitrary equation $M' = \Lambda - \mu M$ are monotone increasing and bounded by Λ/μ if $M(0) < \Lambda/\mu$. They are monotone decreasing and bounded above if $M(0) \geq \Lambda/\mu$. Since, $N' \leq M'$, the claim follows:

Corollary 1: The region;

$$\Phi = \left\{(S, V, C, I, R) \in \mathbb{R}^5_+ : N \leq \frac{\Lambda}{\mu}\right\} \quad (2)$$

is invariant and attracting for system 1.

Theorem 1: For every non-zero, non-negative initial value, solutions of model system 1 exist $\forall t \geq 0$.

Proof: Local existence of solutions follows from standard arguments since, the right-hand side of system 1 is locally Lipschitz. Global existence follows from the a priori bounds.

ANALYTICAL AND NUMERICAL RESULTS

Disease-Free (DFE): Model system 1 has an evident DFE given by:

$$v^0 = \left(S^0, V^0, I^0, C^0, R^0\right) = \left(\frac{\Lambda(\mu+\omega)}{\mu(\mu+\phi+\omega)}, \frac{\Lambda\phi}{\mu(\mu+\phi+\omega)}, 0, 0, 0\right)$$

Reproductive number: The linear stability of v^0 is obtained using the next generation matrix (Van Den Driessche and Watmough, 2002) for system 1. Using the notation in Van Den Driessche and Watmough (2002), the positive matrix F and the non-singular matrix V for the new infection terms and the remaining transfer terms are respectively given (at the disease-free equilibrium) by:

$$F = \begin{bmatrix} \frac{\alpha\Lambda(\mu+\omega)}{\mu(\mu+\phi+\omega)} & 0 \\ 0 & 0 \end{bmatrix} \quad (3)$$

And:

$$V = \begin{bmatrix} \beta+\sigma+b+\mu & 0 \\ \beta & d+\gamma+\mu \end{bmatrix}$$

Thus, the reproductive number for system 1 denoted by R_v is given by:

$$R_v = \frac{(\mu+\omega)\alpha\Lambda}{\mu(\mu+\phi+\omega)(\beta+\sigma+b+\mu)} = \left[\frac{(\mu+\omega)}{(\mu+\phi+\omega)}\right]\left[\frac{\alpha\Lambda}{\mu(\beta+\sigma+b+\mu)}\right] \quad (4)$$

We note that in the absence of typhoid vaccination ($\phi = \omega = 0$), R_v reduces to:

$$R_v = R_0 = \frac{\alpha\Lambda}{\mu(\beta+\sigma+b+\mu)}$$

The biological interpretations of these quantities R_v and R_0 are as follows. The quantity R_v represent the number of secondary cases produced by typhoid fever infective in the presence of vaccination in Kassena-Nankana district of Upper East region of Ghana, R_0 measures the average number of new infections produced by a typhoid fever infective in the absence of any intervention strategies in Kassena-Nankana district of Upper East region of Ghana. Using Theorem 2 in Van Den Driessche and Watmough (2002), the following result is established.

Lemma 3: The disease-free equilibrium v^0 of system 1 is Locally-asymptotically Stable (LAS) if $R_v \leq 1$ and unstable if $R_v > 1$.

Sensitivity analysis of the reproductive rates: In many epidemiological models, the magnitude of the reproductive number is associated with the level of infection. The same is true in model 1. We evaluate the impact of vaccination on controlling the dynamics of typhoid fever. The normalised forward sensitivity index with respect to ϕ (vaccination rate) one gets (Arriola and Hyman, 2005):

$$U_\phi = \frac{\phi}{R_v}\frac{\partial R_v}{\partial \phi} = -\frac{\phi}{\mu+\phi+\omega} \quad (5)$$

Results in Eq. 5 shows that increasing ϕ will lead to a decrease in R_v, biologically this suggests that an increase in vaccination rate of susceptible individuals will have a positive impact on controlling typhoid fever in Kassena-Nankana district of Upper East region of Ghana. Furthermore, we note that Eq. 4 can be rewritten as:

$$R_v = \frac{(\mu+\omega)\alpha\Lambda}{\mu(\beta+\sigma+b+\mu)(\mu+\phi+\omega)} = \left[\frac{(\mu+\omega)}{(\mu+\phi+\omega)}\right]\left[\frac{\alpha\Lambda}{\mu(\beta+\sigma+b+\mu)}\right] = \frac{(\mu+\omega)}{(\mu+\phi+\omega)}R_0 \quad (6)$$

Since;

$$\frac{(\mu+\omega)}{(\mu+\phi+\omega)} < 1$$

this implies that $R_v < R_0$. Biologically, this suggests that whenever there is vaccination in Kassena-Nankana district of Upper East region of Ghana then the number of new typhoid cases is reduced compared to a scenario when there is no vaccination. Further, taking the partial derivative of Eq. 6 with respect to R_0, one gets:

$$\frac{\partial R_v}{\partial R_0} = \frac{(\mu+\omega)}{(\mu+\phi+\omega)} > 0 \quad (7)$$

Equation 7 confirms the above suggestion that vaccination of susceptible individuals in Kassena-Nankana district of Upper East region of Ghana will essential on controlling transmission dynamics of typhoid fever. We now graphically examine the relationship between R_v and R_0, ϕ. Figure 2 shows that vaccination of susceptible individuals is an important typhoid fever intervention strategy in Kassena-Nankana district of Upper East region of Ghana. Using a theorem (Castillo-Chavez *et al*. (2002), we now show the global stability of the DFE in the case that the basic reproduction number is less than unity ($R_v < 1$).

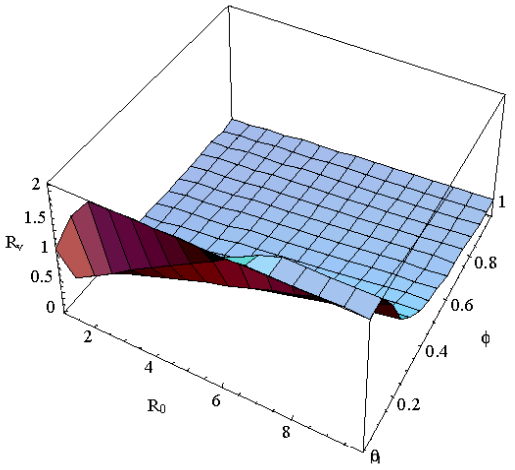

Fig. 2: Model flow diagram

Theorem 2: The DFE ν^0 of the model system 1 is globally asymptotically stable provided $R_\nu<1$ and unstable if $R_\nu>1$.

Proof: Researchers write system 1 in the form (Castillo-Chavez *et al.*, 2002):

$$\begin{aligned} X'(t) &= F(X, Y), \\ Y'(t) &= G(X, Y),\ G(X, 0) = 0 \end{aligned} \tag{8}$$

Where, X = (S, V, R) and Y = (I, C). Here, $X \in \mathbb{R}^3_+$ denotes (its components) the number of uninfected individuals and $Y \in \mathbb{R}^2_+$ denoting (its components) the number of infected individuals. The disease-free equilibrium is denoted by $\nu^0 = (X_0, 0)$ where;

$$X_0 = \left(\frac{\Lambda(\mu+\omega)}{\mu(\mu+\phi+\omega)}, \frac{\Lambda\phi}{\mu(\mu+\phi+\omega)}, 0 \right)$$

We have to prove the following two conditions:

$$\begin{aligned} &(H1)\ \text{For}\ X'(t) = F(X,0), (H2) G(X, Y) = UY - \\ &\hat{G}(X, Y),\ \hat{G}(X, Y) \geq 0\ \text{for}\ (X, Y) \in \Phi \end{aligned} \tag{9}$$

X is a globally asymptotically stable are satisfied where Φ is a positively invariant attracting domain. Consider:

$$F(X, 0) = \begin{bmatrix} \Lambda + \omega V - (\phi+\mu)S \\ \phi S - (\omega+\mu)V \end{bmatrix}$$

and;

$$U = \begin{bmatrix} \frac{\Lambda\alpha(\mu+\omega)}{\mu(\mu+\phi+\omega)} - (\beta+b+\sigma+\mu) & 0 \\ \beta & -(\gamma+d+\mu) \end{bmatrix}$$

Thus;

$$\hat{G}(X, Y) = \begin{bmatrix} \hat{G}_1(X, Y) \\ \hat{G}_2(X, Y) \end{bmatrix} = \begin{bmatrix} \alpha I S \left(\frac{S^0}{S} - 1 \right) \\ 0 \end{bmatrix} \tag{10}$$

Thus, $\hat{G}(X, Y) = 0$ holds only when $R_\nu = 1$ for $S = S^0$. It is easy to verify that the disease-free equilibrium state is the only fixed point of the system 1 in the sub space $S \leq S^0$ hence, b $\hat{G}(X, Y) \geq 0$ thus the equilibrium state ν^0 is globally asymptotically stable.

Endemic equilibrium: Model system 1 has an EE given by:

$$\nu^* = (S^*, V^*, I^*, C^*, R^*)$$

$$\nu^* \begin{cases} S^* = \frac{\Lambda}{\mu R_0}, V^* = \frac{\phi}{\mu(\mu+\omega)R_0} \\ I^* = \frac{\mu R_0}{R_\nu}(R_\nu - 1) \\ C^* = \frac{\beta\alpha R_\nu(\gamma+d+\mu)}{\mu R_0}(R_\nu - 1) \\ R^* = \frac{(b\mu^2 R_0^2 + \beta\alpha\gamma(d+\gamma+\mu)(R_\nu^2)(R_\nu - 1)}{\mu_2 R_0 R_\nu} \end{cases} \tag{11}$$

Thus, system 1 has an endemic equilibrium ν^* which makes biological sense only whenever $R_\nu>1$: This leads to Theorem 3.

Theorem 3: There endemic equilibrium ν^* exists whenever $R_\nu>1$. The local stability of ν^* is given by the Jacobian evaluated in this point considering infected classes I and C is given by:

$$J(\nu^*) = \begin{bmatrix} \alpha S - (\beta+b+\sigma+\mu) & 0 \\ \beta & -(\gamma+d+\mu) \end{bmatrix} \tag{12}$$

Equation 12, we note that the eigeinvalues are:

$$\begin{aligned} \lambda_1 &= -(\gamma+d+\mu) \\ \lambda_2 &= \alpha S - (\beta+b+\sigma+\mu) = (\beta+b+\sigma+\mu)\left(\frac{S}{S^*} - 1 \right) \end{aligned} \tag{13}$$

Since $S<S^*$ whenever $R_\nu>1$, thus $\lambda_2<0$. We summarize the result in Theorem 4.

Theorem 4: There endemic equilibrium ν^* exists and is locally asymptotically-stable whenever $R_\nu>1$. We carried out numerical simulations to demonstrate the impact of vaccination on controlling new in-fectious and carrier typhoid cases in Kassena-Nankana district of Upper East region of Ghana.

The parameter values are showed in Table 1. The 4th order Runge-Kutta numerical scheme coded in C++ programming language is used for the numerical simulations of model system 1.

The final set of simulations (Fig. 3a, b) presents a) the dynamics of the cumulative new infectious cases and b) cumulative new carrier cases. It confirms the observations from the sensitivity analysis of the reproductive number R_ν that vaccination is essential on controlling the dynamics of typhoid fever in in Kassena-Nankana district of Upper East region of Ghana.

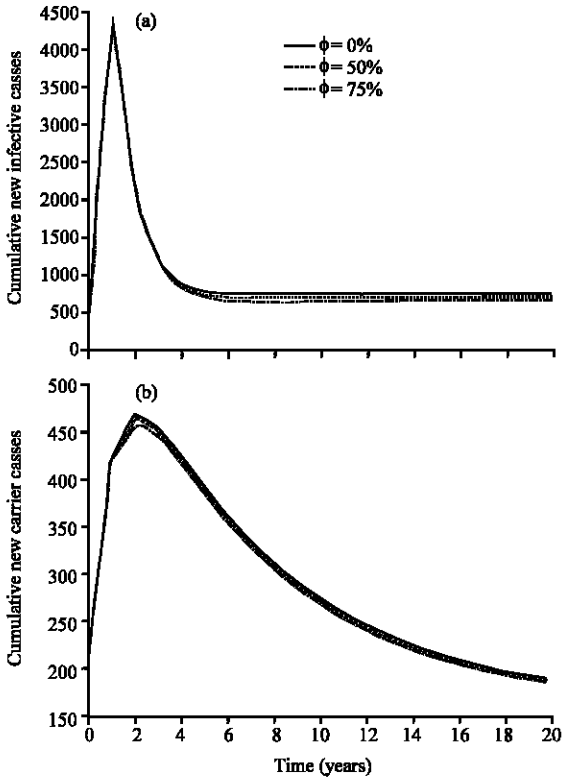

Fig. 3: The impact of vaccination on controlling typhoid fever is described over 20 years. The rest of the parameters are fixed on their baseline values and the following assumed initial conditions have been used for illustration purpose; S = 10000, V = 200, I = 200, C = 200 and R = 20

CONCLUSION

Typhoid fever, caused by Salmonella enterica serovar. Typhi is endemic in most parts of Central America (Fica *et al*., 1996; Olarte and Galindo, 1973), Southeast (Ling *et al*., 2000; Mirza *et al*., 1996, 2000) and the Indian subcontinent (Rahman *et al*., 2002; Shanahan *et al*., 1998) and recently increasing numbers of cases have been reported in Africa (Kariuki *et al*., 2000; Mills-Robertson *et al*., 2002). The impact of vaccination on controlling the long term dynamics of typhoid fever in Kassena-Nankana district of Upper East region of Ghana has been comprehensively investigated using a deterministic mathematical model. Results from the study, demonstrates that vaccination is an essential typhoid intervention strategy so as to reduce cumulative new typhoid cases in Kassena-Nankana district of Upper East region of Ghana. Hence, there is need for the government and health sector to encourage vaccination of susceptible individuals so as to reduce typhoid-induced mortality and prevalence.

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