British Journal of Mathematics & Computer Science
14(1): 1-10, 2016, Article no.BJMCS.23325
ISSN: 2231-0851

SCIENCEDOMAIN *international*
www.sciencedomain.org

Mathematical Modelling of Typhoid Fever Disease Incorporating Protection against Infection

J. K. Nthiiri[1*], G. O. Lawi[1], C. O. Akinyi[1], D. O. Oganga[1], W. C. Muriuki[1], M. J. Musyoka[1], P. O. Otieno[1] and L. Koech[1]

[1] *Department of Mathematics, Masinde Muliro University of Science and Technology, P.O.Box 190-50100, Kakamega, Kenya.*

Authors' contributions

This work was carried out in collaboration between all authors. Authors JKN and COA designed the study and wrote the first draft of the manuscript. Authors JKN, GOL and WCM performed the Mathematical analysis of the study and the simulations. Authors DOO, MJM, POO and LK managed literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMCS/2016/23325
Editor(s):
(1) Dragos-Patru Covei, Department of Applied Mathematics, The Bucharest University of Economic Studies, Piata Romana, Romania.
(2) Paul Bracken, Department of Mathematics, The University of Texas-Pan American Edinburg, TX 78539, USA.
Reviewers:
(1) Rachana Pathak, University of Lucknow, Lucknow, India.
(2) Sirajo Abdulrahman, Federal University of Technology, Minna, Nigeria.
(3) Nita H. Shah, Gujarat University, Navrangpura, India.
Complete Peer review History: http://sciencedomain.org/review-history/13053

Original Research Article

Received: 25th November 2015
Accepted: 9th January 2016
Published: 23rd January 2016

Abstract

In this study, we have formulated a mathematical model based on a system of ordinary differential equations to study the dynamics of typhoid fever disease incorporating protection against infection. The existence of the steady states of the model are determined and the basic reproduction number is computed using the next generation matrix approach. Stability analysis of the model is carried out to determine the conditions that favour the spread of the disease in a given population. Numerical simulation of the model carried showed that an increase in protection leads to low disease prevalence in a population.

**Corresponding author: E-mail: joycenthiiri@gmail.com;*

Keywords: Reproduction number; protection; typhoid fever.

2016 Mathematics Subject Classification: 68QXX.

1 Introduction

Typhoid fever was so named because its signs and symptoms resembles that of typhus. It is an endemic infectious disease caused by a highly virulent and invasive *Salmonella enterica serovar Typhi (S. Typhi)* that affects human. The bacteria is transmitted through food and water contaminated with faeces and urine of an infected patient or a carrier [1]. Signs and symptoms includes; sustained fever, poor appetite, vomiting , severe headache and fatigue. Incubation period for typhoid fever is about 7-14 days. The intestine is a natural habitat for those enteric bacteria. During acute infection, the bacteria multiplies in mononuclear phagocytic cells before being released into the bloodstream [2].

Treatment 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 using ciprofloxacin or norfloxacin. Multi-drug resistant strains of *S.Typhi* are increasingly common worldwide which makes treatment by antibiotics more difficult and costly [3].

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 [4].

Typhoid fever affects millions of people worldwide each year, where over 20 million cases are reported and kills approximately 200,000 annually. For instance, in Africa it is estimated that 400,000 cases occur annually, an incidence of 50 per 100,000 [5]. It is believed that vaccinating high-risk populations is the best way to control typhoid fever disease. There two types of typhoid fever vaccines namely; oral and injectable vaccines. However they are not 100% effective. If one acquires drug-resistant strain of typhoid fever and is not treated with effective antibiotics, a serious and prolonged illness may result.

A number of mathematical models have been developed and analyzed to explain the dynamics of infectious diseases in humans. Many of these models are described by systems of ordinary differential equations formulated under reasonable assumptions and parameters.

A model is developed in [6]. In the model, the number of newly infected persons is expressed as a function of the infectious and susceptible people in a community within a given time. The age structures of the population are established, which enables more detailed simulation of the effect of various interventions and strategies to control the disease in different age groups. The study indicates that once the incidence of the infection has fallen below the threshold, it cannot be maintained in a community due to the loss of the main source of infection chronic carriers as they die out naturally.

Mathematical model for transmission dynamics of typhoid is developed in order to evaluate the potential direct and indirect effects of vaccination [7]. The model is validated against randomized vaccine trials. It is evaluated on school based vaccination strategies, and it is discovered that typhoid vaccination is expected to lead a short term indirect protection and decrease in typhoid incidences, but vaccination alone is unlikely to lead to elimination of typhoid. Both short- and long-term carriers contribute to transmission, but not necessarily at the same rate as primary infections.

In [8], a simple mathematical model is developed on direct and indirect protection by vaccine and benefits of generic vaccination program. The population is split into vaccinated and the unvaccinated subgroups and its effectiveness redefined. It is found that vaccination reduces the number of susceptible to infection and fewer infected individuals spreads the disease among both vaccinated and unvaccinated persons.

A mathematical model on the impact of control strategies to effectively control the burden of the effect of carriers on the typhoid fever in Kisii town is developed and analyzed. This model studied the dynamics of typhoid fever by formulating and analyzing the impact of carriers, diagnosis and health education on typhoid carriers control in Kenya. The model considers that exposed individuals developed the typhoid fever due to endogenous reactivation and exogenous re-infection. Treatment is ordered to all infected individuals except including those latently infected. A structure for the kind of individual contacts that can result in the infection transmission is then incorporated in the population. This contact structure can be non-homogeneous and it is modeled as a random graph, whose edges describe the contacts between individuals. The research work allows the latent and infectious period to have a distribution other than the exponential. Numerical results show that reducing the typhoid carriers by 9.5% could assist Kisii county government in Kenya to achieve a typhoid free status by 2030 [9].

2 Description and Formulation of the Model

We formulate a model in which the total population is subdivided into the following sub-population classes; S Susceptible class, P Protected class , I Infected class and T Treated class. Susceptible individuals are recruited into the population at per capita rate $(1-\alpha)\Lambda$. Susceptible individuals acquire typhoid infection at per capita rate λ. The general form of this model is given by

$$\begin{aligned}
\frac{dP}{dt} &= \alpha\Lambda - (\gamma+\mu)P \\
\frac{dS}{dt} &= (1-\alpha)\Lambda + \gamma P - (\lambda+\mu)S \\
\frac{dI}{dt} &= \lambda S - (\delta+\beta+\mu)I \\
\frac{dT}{dt} &= \beta I - \mu T
\end{aligned} \tag{2.1}$$

Here, $\alpha\Lambda$ is the recruitment rate into the class of individuals protected against typhoid, $(1-\alpha)\Lambda$ is the recruitment rate into the class of individuals susceptible to typhoid, μ is the natural mortality rate, δ is the disease induced mortality rate, β is the rate of treatment. The assumption of this model is that there is no re-infection once an individual is treated. The total population size at any time t is given by

$$N = P + S + I + T \tag{2.2}$$

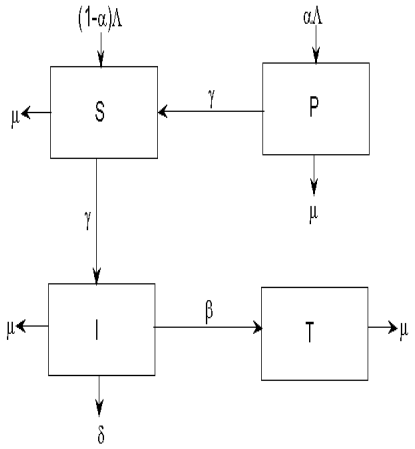

Fig. 1. Flow diagram

3 Analysis of the Model

Since we are dealing with a population, we expect that all population compartments be non negative $\forall t > 0$ in the feasible region Γ where $S(t), P(t), I(t), T(t) \in \Gamma \subset \mathbb{R}^4_+$. It can be shown that all the solutions are bounded in Γ, $\forall t > 0$ such that $0 \leq N \leq \frac{\Lambda}{\mu}$. Thus the model is epidemiologically well posed in the region Γ and can be analysed.

3.1 Existence of equilibrium points

In this section, we shall quantitatively analyse the model to investigate stability of its equilibria both at Disease-free equilibrium(DFE) and at endemic equilibrium(EE). The disease free equilibrium points of the model are its steady state solutions in the absence of infection or disease.

Consider the model(1)

$$\begin{aligned}
\frac{dP}{dt} &= \alpha\Lambda - (\gamma + \mu)P \\
\frac{dS}{dt} &= (1-\alpha)\Lambda + \gamma P - (\lambda + \mu)S \\
\frac{dI}{dt} &= \lambda S - (\delta + \beta + \mu)I \\
\frac{dT}{dt} &= \beta I - \mu T
\end{aligned}$$

To obtain the equilibrium points for the model we set the right hand side to zero.

$$\begin{aligned}
\alpha\Lambda - (\gamma + \mu)P &= 0 \\
(1-\alpha)\Lambda + \gamma P - (\lambda + \mu)S &= 0 \\
\lambda S - (\delta + \beta + \mu)I &= 0 \\
\beta I - \mu T &= 0
\end{aligned} \tag{3.1}$$

where

$$\lambda = \frac{\pi\theta I}{N}. \tag{3.2}$$

Let π be defined as the probability rate of acquiring typhoid fever disease and θ be the contact rate of infection. Let ϑ be the probability of success of protection against typhoid fever disease, thus the effective force of infection λ^p becomes

$$\lambda^p = \frac{\pi\theta(1-\vartheta)I}{N}. \tag{3.3}$$

To calculate the DFE,we set (P, I, T) to be equal to zero. Thus

$$S = \frac{(\mu+\gamma-\alpha\mu)\Lambda}{\mu(\mu+\gamma)}. \tag{3.4}$$

The disease-free equilibrium point E^0 is given by

$$E^0 = (0, \frac{(\mu+\gamma-\alpha\mu)\Lambda}{\mu(\mu+\gamma)}, 0, 0). \tag{3.5}$$

To calculate the EE, we set P, S, I, T not equal to zero.

$$\begin{aligned} P^* &= \frac{\alpha\Lambda}{\mu+\gamma} \\ S^* &= \frac{N(\mu+\delta+\beta)}{\pi\theta(1-\vartheta)} \\ I^* &= \frac{1}{(\mu+\delta+\beta)}(\frac{(\mu+\gamma-\alpha\mu)\Lambda}{(\mu+\gamma)} - \frac{\mu+N(\mu+\delta+\beta)}{\pi\theta(1-\vartheta)}) \\ T^* &= \frac{\beta}{\mu(\mu+\delta+\beta)}(\frac{(\mu+\gamma-\alpha\mu)\Lambda}{(\mu+\gamma)} - \frac{\mu N(\mu+\delta+\beta)}{\pi\theta(1-\vartheta)}) \end{aligned} \tag{3.6}$$

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

$$\begin{aligned} E^* = (\frac{\alpha\Lambda}{\mu+\gamma}, \frac{N(\mu+\delta+\beta)}{\pi\theta(1-\vartheta)}, \frac{1}{(\mu+\delta+\beta)}(\frac{(\mu+\gamma-\alpha\mu)\Lambda}{(\mu+\gamma)} - \frac{\mu+N(\mu+\delta+\beta)}{\pi\theta(1-\vartheta)}), \\ , \frac{\beta}{\mu(\mu+\delta+\beta)}(\frac{(\mu+\gamma-\alpha\mu)\Lambda}{(\mu+\gamma)} - \frac{\mu N(\mu+\delta+\beta)}{\pi\theta(1-\vartheta)}) \end{aligned}$$

3.2 The basic reproduction number

The dynamics of the model are highly dependant on the basic reproduction number. The basic reproduction number commonly denoted R_0 in a given population is the average number of secondary infections caused by a single infectious individual during his her entire life time as an infective when introduced into a totally/ purely susceptible population. The basic reproduction number R_0 , is important in that it is directly related to the effort required to eliminate infection. We determine the R_0 using the next generation matrix approach. Consider a matrix

$$G = FV^{-1} \tag{3.7}$$

where F is the Jacobian of f_j, where f_j is the rate of new infections in compartment j and V is the Jacobian of v_j where v_j is the rate of transfer of infections from one compartment to another.

From the model the associated matrices are

$$F = \begin{pmatrix} \frac{\pi\theta(1-\vartheta)IS}{N} \end{pmatrix}$$

Upon taking the derivative with respect to the disease compartment I, we have

$$F = \begin{pmatrix} \frac{\pi\theta(1-\vartheta)S}{N} \end{pmatrix}$$

At DFE, $S = N$ then

$$F = \begin{pmatrix} \pi\theta(1-\vartheta) \end{pmatrix}$$

and the matrix V is given by

$$\nu = \begin{pmatrix} (\mu+\delta+\beta)I \end{pmatrix}$$

Taking the derivative with respect to I we get

$$V = \begin{pmatrix} \mu+\delta+\beta \end{pmatrix}$$

On computing V^{-1} we have

$$V^{-1} = \begin{pmatrix} \frac{1}{(\mu+\delta+\beta)} \end{pmatrix}$$

thus

$$FV^{-1} = \begin{pmatrix} \frac{\pi\theta(1-\vartheta)}{(\mu+\delta+\beta)} \end{pmatrix}$$

The basic reproduction number R_0, which is the spectral radius of the matrix FV^{-1} is given by

$$\rho(FV^{-1}) = \frac{\pi\theta(1-\vartheta)}{(\mu+\delta+\beta)} \tag{3.8}$$

Therefore

$$R_0 = \frac{\pi\theta(1-\vartheta)}{\mu+\delta+\beta} \tag{3.9}$$

which is the measure of the severity of an epidemic and one of the most important concern parameter for the disease to invade a population.

3.3 Local stability of the Disease-free Equilibrium (DFE)

We now analyse the model to investigate stability of its equilibria(DFE). The disease free equilibrium points of the model are its steady state solutions in the absence of infection or disease.

Theorem 3.1. *The disease-free equilibrium E^0 of the model(1) is locally asymptotically stable whenever $R_0 < 1$.*

Proof. From the model system(1) we have the Jacobian matrix of the linearized system is given by

$$J = \begin{bmatrix} -(\gamma+\mu) & 0 & 0 & 0 \\ \gamma & -(\mu+\frac{\pi\theta(1-\vartheta)I}{N}) & \frac{-\pi\theta(1-\vartheta)S}{N} & 0 \\ 0 & \frac{\pi\theta(1-\vartheta)I}{N} & \frac{\pi\theta(1-\vartheta)S}{N} - (\delta+\mu+\beta) & 0 \\ 0 & 0 & \beta & -\mu \end{bmatrix}$$

We now compute the Jacobian matrix at DFE and investigate its stability effect due to the

reproduction number R_0.

$$J_{E^0} = \begin{bmatrix} -(\gamma+\mu) & 0 & 0 & 0 \\ \gamma & -\mu & -k_1 & 0 \\ 0 & 0 & k_2 & 0 \\ 0 & 0 & \beta & -\mu \end{bmatrix}$$

where $k_1 = \pi\theta(1-\vartheta), k_2 = \pi\theta(1-\vartheta) - (\mu+\delta+\beta)$.

To analyze the stability of the Jacobian at DFE, we compute the trace and the determinant and set the conditions. The Trace(τ) at DFE,E^0 is given by

$$\begin{aligned} \tau(J_{E^0}) &= -(\mu+\gamma) - \mu + k_2 - \mu \\ \tau(J_{E^0}) &= -(\mu+\gamma) - \mu + \pi\theta(1-\vartheta) - (\mu+\delta+\beta) - \mu \end{aligned} \tag{3.10}$$

On substituting the R_0, we have

$$\tau(J_{E^0}) = -(\mu+\gamma) - 2\mu + (R_0-1)(\mu+\delta+\beta) \tag{3.11}$$

which is negative provided that $R_0 < 1$, and the determinant is given by

$$DetJ_{E^0} = \mu^2(\mu+\gamma)(1-R_0) \tag{3.12}$$

The determinant of the Jacobian matrix at DFE remains positive provide that $R_0 < 1$. The model has a stable disease-free equilibrium when $R_0 < 1$. □

3.4 Local stability of the endemic equilibrium of the model (EE)

A disease is endemic in a population if it persists in the population. The stability of endemic equilibrium of the model is studied using the following theorem.

Theorem 3.2. *The endemic equilibrium E^* of the model(1) is locally asymptotically stable whenever $R_0 > 1$.*

Proof. The stability of the endemic equilibrium is investigated using the trace and the determinant. The Jacobian matrix at E^* is given by

$$J_{E^*} = \begin{bmatrix} -(\gamma+\mu) & 0 & 0 & 0 \\ \gamma & -(\mu+\frac{\pi\theta(1-\vartheta)h_3}{N}) & \frac{-\pi\theta(1-\vartheta)h_2}{N} & 0 \\ 0 & \frac{\pi\theta(1-\vartheta)h_3}{N} & \frac{\pi\theta(1-\vartheta)h_2}{N} - (\mu+\delta+\beta) & 0 \\ 0 & 0 & \beta & -\mu \end{bmatrix}$$

where $h_2 = \frac{N(\mu+\delta+\beta)}{\pi\theta(1-\vartheta)}, h_3 = \frac{1}{(\mu+\delta+\beta)}(\frac{(\mu+\gamma-\alpha\mu)\Lambda}{(\mu+\gamma)} - \frac{\mu N(\mu+\delta+\beta)}{\pi\theta(1-\vartheta)})$

The Trace(τ) at E^* is given by

$$\tau(J(E^*)) = -(\mu+\gamma) - (\mu + \frac{\pi\theta(1-\vartheta)h_3}{N} + \frac{\pi\theta(1-\vartheta)h_2}{N} - (\mu+\delta+\beta) - \mu$$

upon substitution we have

$$\tau(J_{E^*}) = -(\mu+\gamma) - \mu R_0 \tag{3.13}$$

which is negative provided that $R_0 > 1$ and

$$\begin{aligned} Determinant &= \mu(\mu+\gamma)(\mu(\mu+\delta+\beta) - \mu\frac{\pi\theta(1-\vartheta)h_2}{N}) + (\mu+\delta+\beta)\frac{\pi\theta(1-\vartheta)h_3}{N}) \\ &= \mu(\mu+\gamma)((\mu(\mu+\delta+\beta)R_0 - \mu(\mu+\delta+\beta)) \end{aligned}$$

Hence

$$DetJ_{E^*} = \mu^2(\mu+\gamma)(\mu+\delta+\beta)(R_0-1) \tag{3.14}$$

Clearly the determinant of the matric is positive provided that $R_0 > 1$. Therefore the model has an asymptotically stable endemic equilibrium provided that $R_0 > 1$. □

3.5 Numerical simulations

Numerical simulations are carried out to graphically illustrate the long term effect of protection on the dynamics of typhoid fever infection.

4 Discussion

Fig. 2 shows the graph of infective against time in days. With high success of protection, there is low contact rate and low prevalence rate hence the infective in the population decreases sharply over time. With low protection there is high contact rate and hence a high disease prevalence in the population.

Table 1. Parameters values of the mode

Parameter description	Symbol	Value	Source
Recruitment rate	Λ	0.0044	[10]
Adjustment parameter	α	0.8	Estimated
Natural mortality rate	μ	0.016	[10]
Disease induced mortality rate	δ	0.005	Estimated
Loss of protection rate	γ	0.001	Estimated
Rate of treatment	β	0.9	Estimated
Transmission probability rate of typhoid	π	0.0011	Estimated
Contact rate of infection	θ	0.0002	[11]
Modification parameter	ϑ	$0 < \vartheta < 1$	Assumed

Fig. 3 shows the graph of susceptible against time in days. With high success of protection there is low contact rate and low prevalence rate hence the susceptible in the population decreases over time. On the contrary, when the protection rate is low, the number of susceptible individuals will be high.

The model shown exhibits that the stable disease-free equilibrium co-exists when the reproduction number is less than unity. Also stable endemic equilibrium co-exists when the reproduction number is greater than unity.

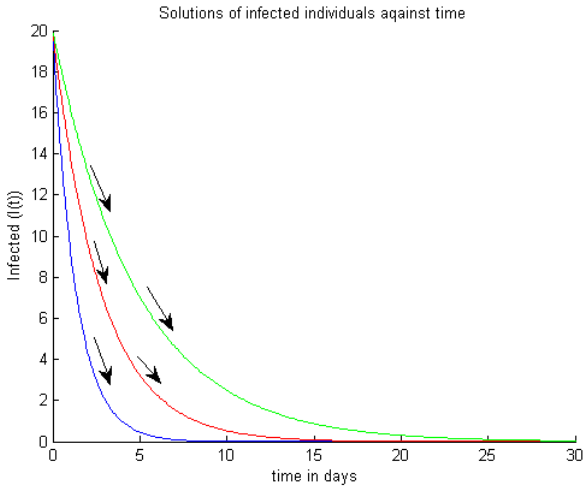

Fig. 2. The graph of I against t

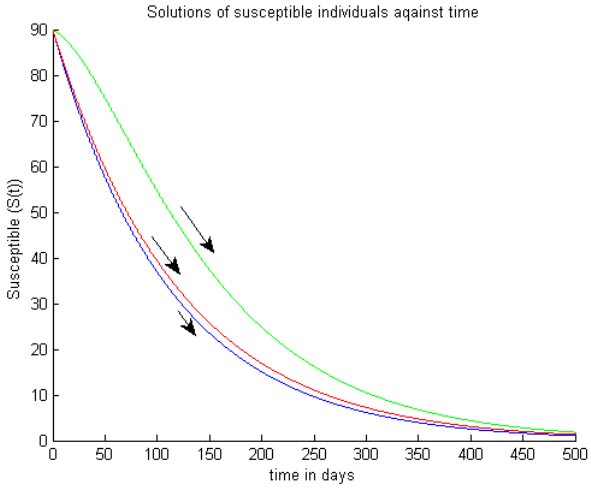

Fig. 3. The graph of S against t

5 Conclusion

We conclude that effective control of typhoid fever prevents rapid progression to infection especially in scarce resource setting where treatment is not readily available. Vaccination is effective to prevent disease induced mortality rate. Moreover improving life standards e.g sanitation and supply of clean water, will reduce the probability of infection hence resulting to less people contacting the infection. Typhoid fever prevention is equally effective in susceptible population. This leads to a very small fraction of individuals in a given population progressing to infective stage.

Acknowledgement

I sincerely acknowledge with thanks the Department of Mathematics staff members, Masinde Muliro University of Science and Technology for their support during this study.

Competing Interests

The authors declare that no competing interests exist.

References

[1] W.H.O. Background paper on vaccination against typhoid fever using New- Generation Vaccines - presented at the SAGE November 2007 meeting, 2007, 11.

[2] Jenkins C, Gillespie SH. Salmonella infection in: G.C. Cook and A.L.Zumla Mansons Tropical Diseases. Elsevier, China. 2009;931-942.

[3] Anwar E, Goldberg E, Fraser A, Acosta CJ, Paul M, Leibovici L. Vaccination for preventing typhoid fever. The Cochrane Database of Systematic Reviews. CD001261;(1)2014.

[4] W.H.O. Background document: The diagnosis, treatment and prevention of typhoid fever, World Health Organization. 2003;1-26.

[5] Kariuki S. Typhoid fever in sub-saharan Africa; Challenges of diagnosis and management of infections. Journal of infection in Developing Countries. 2008;2(6):443-447.

[6] Cvjetanovic B, Grab B, Eumura K. Epidemiological model of typhoid fever and its use in planning and evaluation of antityphoid immunization and sanitation programmes. Bull. W.H.O. 1971;45(1):53-75.

[7] Pitzer VE, Bowles CC, Baker S, Kang G, Balaji V, Farrar J, et al. Predicting the impact of vaccination on the transmission dynamics of typhoid in South Asia: A mathematical modeling study. PLoS Negl Dis. 2014;8(1):1-12.

[8] Cook JH. Are cholera and typhoid vaccines a good investment for slums in Kolkata, India. Pediatr. Infect. Dis. J. 2010;9(5):485-496.

[9] Moffat NC, Johanna K, Jeconiah A, Okwoyo JM. SIIR model and simulation of the effects of carrier on the transmission dynamics of tyhoid fever in Kisii town, Kenya. 2014;2(3):109-116.

[10] Kenya Demographics Profile 2014.

[11] Kariuki S, Ruvathi G, Kiiru J, Mengo DM, Mwituria J, Muyondi J, et al. Typhoid in Kenya is associated with a dominant multidrug resistant *Salmonellaenterica serovar* typhi Haplotype that is also widespread Southeast Asia. J. Clin. Microbiol. 2010;48(6):2171-2176.

Peer-review history:
The peer review history for this paper can be accessed here (Please copy paste the total link in your browser address bar)
http://sciencedomain.org/review-history/13053