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RESEARCH ARTICLE

PARAMETER ESTIMATION OF ECO-EPIDEMIOLOGICAL MODEL FOR NEWCASTLE DISEASE IN TANZANIA

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ABSTRACT

A deterministic compartmental eco-epidemiological model of Newcastle disease (ND) in Tanzania is proposed and analyzed by using the stability theory of differential equations. The main objective of paper is to estimate the model parameters using maximum likelihood estimation (MLE) and Markov chain Monte Carlo (MCMC) methods. The model is fitted using data for five districts in Dodoma and Singida regions in Tanzania. The sample 10,000 numbers of simulations were used in MCMC in parameters distribution to study the behavior of each parameter in the model. Many parameters show good convergence and we recommend to be used for numerical simulations in similar cases rather than using literature values.

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INTRODUCTION

Newcastle disease (ND) is an economically important disease of poultry for which vaccination is applied as a major preventive measure in many countries (Jibril *et al*., 2014). It is endemic in Africa, Asia, Central America, and some part of South America while sporadic in Europe (Ashraf and Shah, 2014). Tanzania is one of the severely affected by ND with poor surveillance and control measures. ND can cause $90-100\%$ mortality in susceptible chickens. The disease affects mostly chickens and other domestic species such as turkeys, ducks, geese, parrots, pigeons and wild cormorants. The severe impact of ND is mostly notable in domestic poultry particularly to unvaccinated areas, for example in Tanzania the national sample census of agriculture 2012 shows that 52% of chicken households have never applied any vaccination against ND (Chuwa, 2012). Moreover, chickens play a vital role by providing an important source of high-quality nutrition and income at very little costs (Knueppel *et al*., 2009). Based on National Sample of Agriculture 2012, Tanzania had about $43.8m$ chickens kept in urban and rural areas and most of the poultry industries are dominated by private sectors. Figure 1 shows the number of house hold reported ND outbreak.

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Controlling properly ND in Tanzania may help to improve the life standard of the families that rely on poultry (most of people in rural areas depend on poultry keeping activities) otherwise may represent a bigger drain on the economy than any other animal viral disease (Leonardo, 2015). Protecting chickens from ND in Tanzania is still a problematic particularly in rural and remote areas where vaccines are challengeable in terms of application and safety savings. However, more efforts are required in order to out-scale subsidized vaccination programmes against ND. Mathematical models are now used to link the biological process of disease transmission and the epidemics of infectious diseases among humans and other animals resulting from the transmission of a pathogen either through hosts or environment (Grassly and Fraser, 2008). These models are important tool for understanding mechanisms responsible for persistence or extinction of species in natural systems and for decision making regarding intervention programs (Okosun, *et al*., Modelling infectious diseases in species provides an important insight into disease behavior and control measures. Therefore, the role of this paper is to estimate and fit eco-epidemiological model parameters using the methods of Maximum Likelihood Estimator (MLE) and Markov Chain Monte Carlo (MCMC) to determine suitable value for each parameter that will reduce ND in Tanzania. The goodness of fit of the model is determined by how well it fits the observed data (Myung, 2003).

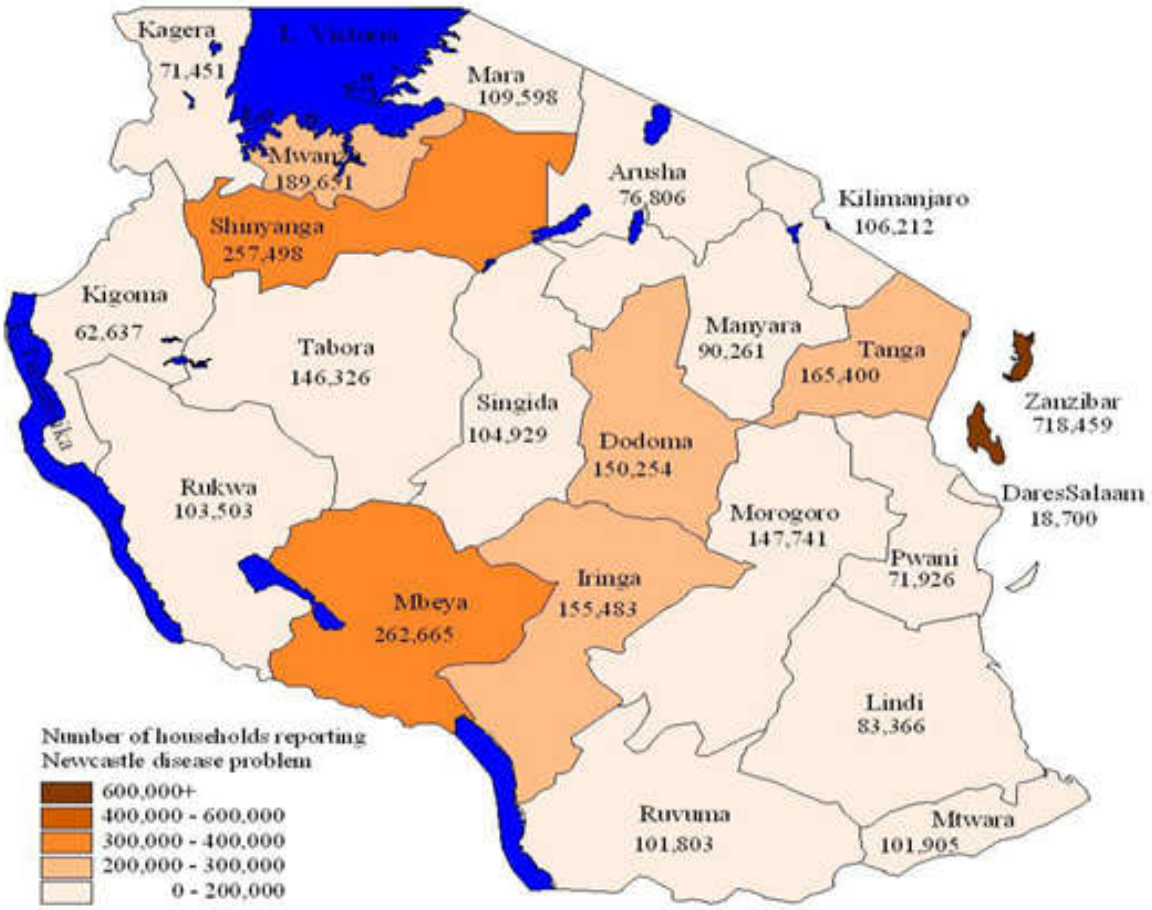

Figure 1. Tanzania map showing number of households reported Newcastle Disease
Source: National sample census of Agriculture (Chuwa, 2012)

Model formulation and Analysis

In this paper we formulate and analyze a mathematical model of ND in Tanzania. The modeled populations include chickens as prey and human being as predator. The epidemiological model comprises of five subclasses namely susceptible prey $S_1(t)$, infected prey $I_1(t)$, susceptible predator $S_2(t)$, infected predator $I_2(t)$ and predator recovery class $R_2(t)$. The model presented under the following assumptions:

(i) The growth rate of prey population follows a logistic function with intrinsic growth rate r and carrying capacity k .

(ii) The prey population gets infection when it comes into contact with other infected prey and this contact process is assumed to follow the simple mass action kinetics with β_1 as the force of infection while human get infection by the rate β_2.

(iii) Natural death rate of prey μ_1 and induced death rate due to disease m reduces the prey population.

(iv) The predator population suffers loss due to the natural death rate μ_2 and increases due to recovery rate θ and through treatment rate γ .

(v) The predation functional response of the predator towards susceptible as well as infected prey is assumed to follow Michaelis-Menten kinetics and is modeled using a Holling type -II functional response with predation coefficients b_1, c_1 b_2, c_2 and half saturation constant a_1, a_2, n_1 and n_2 .

(vi) Consumed susceptible and infected prey are converted into predator with efficiency α_1, α_2, α_3 and α_4. These assumptions lead into the following schematic flow

Mathematical Equations

Considering the assumptions, we formulate the model equations as follows

$$\left.\begin{aligned}
\frac{dS_1}{dt} &= r\left(1-\frac{S_1}{k}\right)S_1 - \beta_1 S_1 I_1 - \frac{b_1 S_1 S_2}{a_1+S_1} - \frac{b_2 S_1 I_2}{a_2+S_1} \\
\frac{dI_1}{dt} &= \beta_1 S_1 I_1 - mI_1 - \mu_1 I_1 - \frac{c_1 I_1 S_2}{n_1+I_1} - \frac{c_2 I_1 I_2}{n_2+I_1} \\
\frac{dS_2}{dt} &= \frac{\alpha_1 b_1 S_1 S_2}{a_1+S_1} + \frac{\alpha_2 c_1 I_1 S_2}{n_1+I_1} - \beta_2 S_2 I_1 - \mu_2 S_2 + \theta R_2 \\
\frac{dI_2}{dt} &= \beta_2 S_2 I_1 - \gamma I_2 - \mu_2 I_2 + \frac{\alpha_3 b_2 S_1 I_2}{a_2+S_1} + \frac{\alpha_4 c_2 I_1 I_2}{n_2+I_1} \\
\frac{dR_2}{dt} &= \gamma I_2 - \theta R_2 - \mu_2 R_2
\end{aligned}\right\} \quad (1)$$

System (1) has to be analyzed with the following initial conditions:

$S_1 > 0,\ I_1 > 0,\ S_2 > 0,\ I_2 > 0,\ R_2 > 0.$

Model Analysis

Lemma 1: *All solutions of the system (1) which start in* R_+^5 *are uniformly bounded.*

Proof: Let $W(t) = S_1(t) + I_1(t) + S_2(t) + I_2(t) + R_2(t)$ (2)

Differentiating and solving (2) we get

$$0 \le W(t) \le \frac{u}{v}(r+1)\left(1-e^{-vt}\right) + W\left(S_1(0), I_1(0), S_2(0), I_2(0), R_2(0)\right)e^{-vt}. \quad (3)$$

Consequently, as $t \to \infty$, we observe $0 \le W(t) \le \frac{u}{v}(r+1)$

where $u = \max\{S_1(0), k\}$, $v = \min\{1, m+\mu_1, \mu_2\}$.

Implying that all solutions of the system (1) are uniformly bounded in the interior of R_+^5 then,

$\Gamma = \left\{(S_1, I_1, S_2, I_2, R_2) \in R_+^5 : W \le \frac{u}{v}(r+1) + \varepsilon\right\}$ for any $\varepsilon > 0$ is bounded.

MATERIALS AND METHODS

The maximum likelihood estimator (MLE) and Markov Chain Monte Carlo (MCMC) methods for parameter estimation and model fitting are considered. We fit the model with the data for 2014 distributed monthly (see Table 1).

The maximum likelihood estimator (MLE)

The idea of maximum likelihood method is to maximize the likelihood function and in this paper, we minimize the sum of squares of residual (SSR) defined as

$$L(\theta) = \sum_{i=1}^{N}\left(y_i - y_i^{est}\right)^2, \quad (4)$$

where $\{y_i\}^N{}_{i=1}$ is the real data and $\left\{y_i^{est}\right\}^N{}_{i=1}$ is the solution of model equations (1) at a given parameter value.

Markov Chain Monte Carlo

Markov chain Monte Carlo (MCMC) methods as presented by Gilks *et al* (Gilks *et al*., 1996) are numerical methods for computing complex multidimensional integrals. The idea is to draw N samples $\theta^{(1)}, \theta^{(2)}, \ldots, \theta^{(N)}$ from the posterior distribution and approximate the expectation as the sample average

$$E\left[g(\theta) \mid y_1, \ldots, y_M\right] \approx \frac{1}{N}\sum_{i=1}^{N} g\left(\theta^{(i)}\right). \quad (5)$$

One difficulty in drawing samples from the posterior distribution is that even for the evaluation of the posterior probability density; we would need to be able to evaluate the normalization constant integral. MCMC methods are a class of Monte Carlo methods, which can draw the samples without the knowledge of the normalization constant. These methods are based on simulating a multidimensional Markov chain, which has been constructed such that it has the posterior distribution as its stationary distribution. In the simulation of the Markov chain we only need to evaluate the ratios of posterior probability densities and thus the evaluation of the normalization constant is not required. The most well-known MCMC methods are the Metropolis, Metropolis-Hastings and Gibbs sampler algorithms (Gilks *et al*., 1996). The Metropolis–Hastings MH algorithm works by sampling a candidate point θ_* from a proposal distribution $q\left(\theta^* \mid \theta\right)$ and then accepting the point with acceptance probability (Gilks *et al*., 1996). The following is the Metropolis–Hastings (MH) algorithm

(i) Draw the starting point, $\theta^{(0)}$, from an initial distribution $p_0(\theta)$

(ii) For $n = 0, 1, 2\ldots$

- Sample a candidate point θ^* from the asymmetric proposal distribution $q\left(\theta^* \mid \theta^{(n)}\right)$.
- Accept the candidate point and set $\theta^{(n+1)} = \theta^*$ with the probability

$$A\left(\theta^{(n)}, \theta^*\right) = \min\left\{1, \frac{q\left(\theta^{(n)} \mid \theta^*\right)}{q\left(\theta^* \mid \theta^{(n)}\right)}\exp\left(\varphi\left(\theta^{(n)}\right) - \varphi(\theta*)\right)\right\} \quad (6)$$

- Generate $u \sim U(1,0)$ from uniform distribution
- Accept θ^* if $|u| \le A\left(\theta^{(n)}, \theta^*\right)$.

In general, the proposal distributions used in MCMC algorithms should result in well mixing of chains and in a suitable acceptance rate. Determining which proposal distribution is the best one for a particular target distribution is a very important, but also a difficult task, because it involves much trial–and–error. The most used proposal distribution is the Gaussian distribution; however, we do not know how to obtain a suitable covariance matrix. One way to overcome this problem is to use adaptive MCMC where the proposal distribution is automatically adapted during the MCMC run

(Haario *et al*., 2006; Haario, 2001; Liang *et al*., 2010)). We present below the adaptive MCMC developed by Haario *et al* (Haario *et al*., 2001):

(i) Initialization; start with initial values θ_0 and Σ_0 then select λ, ε and an initial non–adapting period n_0. For $n_0 = 0$ means the adaptation start as the algorithm start. If the target density is Gaussian then $\lambda = \frac{2.4^2}{d}$.

(ii) At each step, propose a new θ_* from a Gaussian distribution (θ_{n-1}, Σ_0).

(iii) Accept/reject θ_* according to the MCMC accepting probability.

(iv) For $n \geq n_0$ adapt the proposal covariance matrix using:
$\Sigma_n = \lambda\left(\mathrm{cov}(\theta_0, \theta_1, ..., \theta_{n-1}) + \varepsilon \mathbf{I}_d\right)$,
where $\mathbf{I}_d$ is the $d \times d$ identity matrix, ε is a small positive value whose role is to make sure that Σn is not singular, and λ is a covariance scaling factor which optimizes the mixing property of the Metropolis algorithm.

(v) Iterate from (ii) above until you get enough samples.

Numerical analysis

To explore the behavior of ND model parameters, we use numerous numerical simulations and analysis to justify it is biological implications.

Data analysis

In this subsection, we present the data for ND death cases per district as shown in Table 1, and we fit the model and predicting the possible outbreak in Tanzania. The goodness of fit is the criterion to determine the parameter values for the particular model system from which the data were obtained (Jost and Arditi, 2000). From the data we observe that many death cases occur in month of September to December (see Table 1).

Table 1. Chicken death cases due to ND data per district for 2014

Month	Kongwa	Chamwino	Mkalama	Singida	Ikungi	Total
Jan	214	195	189	233	129	960
Feb	123	157	158	237	124	799
March	164	178	168	141	136	787
April	176	219	218	147	195	955
May	138	136	180	139	182	775
June	248	186	299	162	245	1140
July	204	125	86	97	197	709
Aug	234	145	186	102	182	849
Sept	308	271	278	257	243	1357
Oct	354	201	345	762	362	2024
Nov	362	234	456	750	395	2197
Dec	398	365	481	654	308	2206
Total	2923	2412	3044	3681	2698	14758

The goodness of fit is determined through many variations of data been captured by the model and minimize the sum of the square error so as to measure the validity of the formulated model. The accuracy of the model is judged based on explanatory capacity, that is coefficient of determination and sum of residue square (Massawe. Laurencia. Ndalemo, Massawe. Estomih, 2015).

Parameter Estimation

In this subsection we present numerical simulations of model (1) using Matlab 2013b software using the data in Table 1. The model fitting and parameter estimation of the proposed model are carried out using maximum likelihood estimation (MLE) and delayed rejection adaptive Markov chain Monte Carlo (DRAM) method. Randomly samples were generated using normal distribution and the data were fitted using least squares estimate (see Table 2) for the literature values of convectional rate of prey to predator α_1 (Hugo, Massawe, and Makinde, 2012), force of infection among prey population β_1 (Sharma and Samanta, 2015), carrying capacity k (Mukhopadhyay and Bhattacharyya, 2009), prey growth rate (Bornaa, Makinde, and Seini, 2015), predation rate of susceptible prey b_1 (Mukhopadhyay and Bhattacharyya, 2009), and other were estimated.

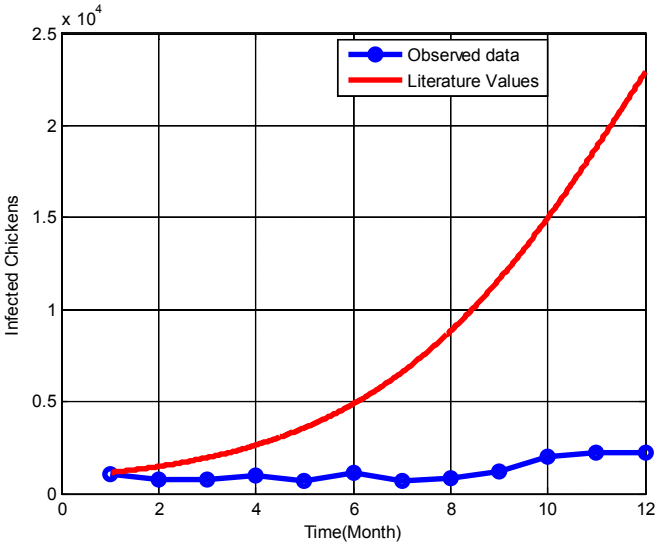

Figure 3. Comparison of the solution of model (1) with literature values and data

(Figure 3) shows the plot of the solution of the model using literature values and data against time, which show bad behavior as the solution deviates from data. Now solving this problem, we need to estimate the model parameter and fit the data as shown in (Figure 4).

The (Figure 4) show at least a good fit behavior as the solution of the model tends close to the trend of the data. However, the model seems to have fit the data well, but we are not sure to what extent these model parameters are correct (Tchuenche, Khamis, Agusto, and Mpeshe, 2011). Therefore, we employ

Markov Chain Monte Carlo (MCMC) methods with 1,000 initial runs using the model parameter values and the results are used as prior distribution to re-run the model with 10,000 simulations in connection with convergence criteria of 10^{-8}. The estimated parameter values are presented in Table 2.

MCMC results

The MCMC plot shows the convergence of the chain and we use this results for parameter estimation (see Table 2) as well as for predictive of the outbreak of ND in Tanzania.

Table 2. MCMC statistics for 10,000 numbers of simulations

Symbol	θ_L	θ_{LSQ}	θ_{mean}	θ_{median}	θ_{std}	Convergence	Kurtosis	Skewness
β_1	0.25	0.2495	0.2236	0.2389	0.0601	0.8112	5.8197	0.1055
b_1	0.01	0.0085	0.0088	0.0087	0.0016	0.9545	3.4141	0.1278
m	0.6	0.5968	0.6475	0.6224	0.111	0.8984	3.3033	0.1952
θ	0.4	0.4048	0.5296	0.4757	0.1873	0.5145	2.6048	0.475
α_2	0.6	0.6078	0.6494	0.615	0.1196	0.8613	2.9523	0.3991
b_2	0.4	0.4019	0.4606	0.4569	0.0648	0.7495	2.7918	0.0711
α_3	0.8	0.8939	0.8291	0.8097	0.0686	0.9168	3.3007	0.1118
a_2	0.8	0.8048	0.7345	0.7379	0.0542	0.8343	2.0085	-0.3429
β_2	0.012	0.0119	0.0361	0.0135	0.0591	0.1741	7.7933	3.5091
γ	0.6	0.612	0.7114	0.6984	0.0966	0.6872	2.8955	3.5091
α_4	0.6	0.6008	0.3986	0.425	0.1971	0.3407	2.1327	-0.2043
α_1	0.6	0.6093	0.7164	0.689	0.1164	0.6856	2.2785	0.6272
n_2	0.05	0.0503	0.1576	0.1282	0.1128	0.0749	2.6142	0.7447
c_2	0.5	0.4974	0.4118	0.4696	0.2072	0.5728	3.0905	0.0748
μ_1	0.25	0.2488	0.3895	0.3146	0.2191	0.3152	2.7367	0.6718
μ_2	0.8	0.8015	0.6295	0.6491	0.164	0.4863	3.8669	-1.0228
a_1	0.25	0.2481	0.2103	0.2229	0.0507	0.6871	2.8838	-0.3324
c_1	0.02	0.0202	0.0858	0.0636	0.0698	0.0615	2.9949	0.9196
n_1	0.03	0.0304	0.1235	0.0814	0.1203	0.0789	7.0481	1.8694

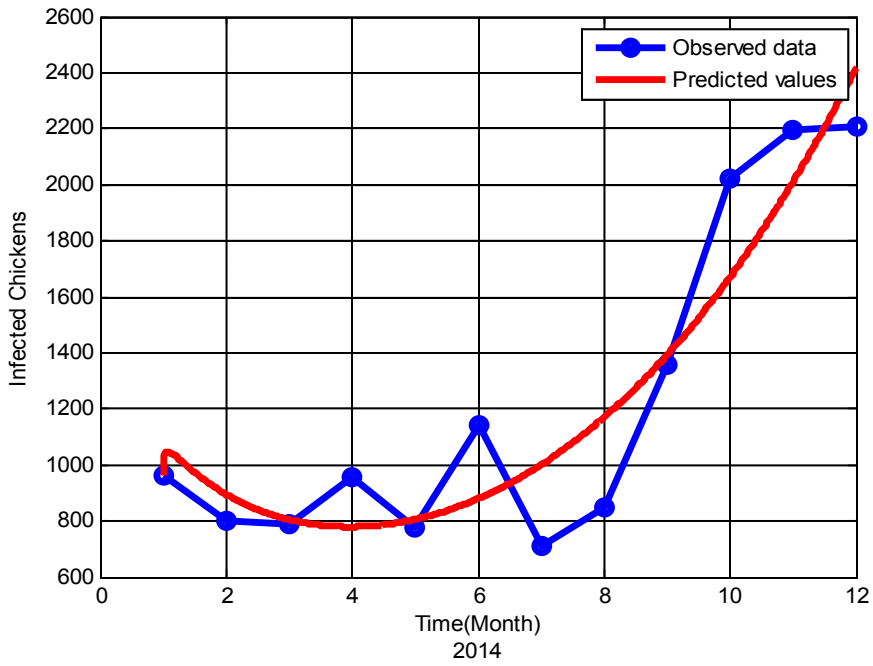

Figure 4. The dynamic behaviour of predicted and observed data for ND model system (1)

Table 2 shows the prior distribution for each parameter; original parameter or literature value (θ_L), least square estimated $_{(\theta_{LSQ})}$, mean (θ_{mean}), median (θ_{median}), standard deviation (θ_{std}) of the model and the convergence of each parameter for 10,000 numbers of simulations. Convergence of MCMC samples can be studied graphically by plotting autocorrelation Figure as showing in the (Figure 5).

The parameter convergence oscillates within the confidence interval and stabilizes around zero with 220 lags as per Figure 5 indicates. The Figure 6 represents the marginal distribution of samples that depict the Gaussian distribution. The results for Figure 7 show the chain of some parameter β_1, b_1 and b_2 at least shows good mixing. The plots in Figure 8 show the chain parameters in pair for some parameters, some pair shows a positive correlation like the mixing between θ and α_2 (4, 5) and m and α_2 (3, 5). The kurtosis and skewness of parameters are computed and results are summarized in Table 2.

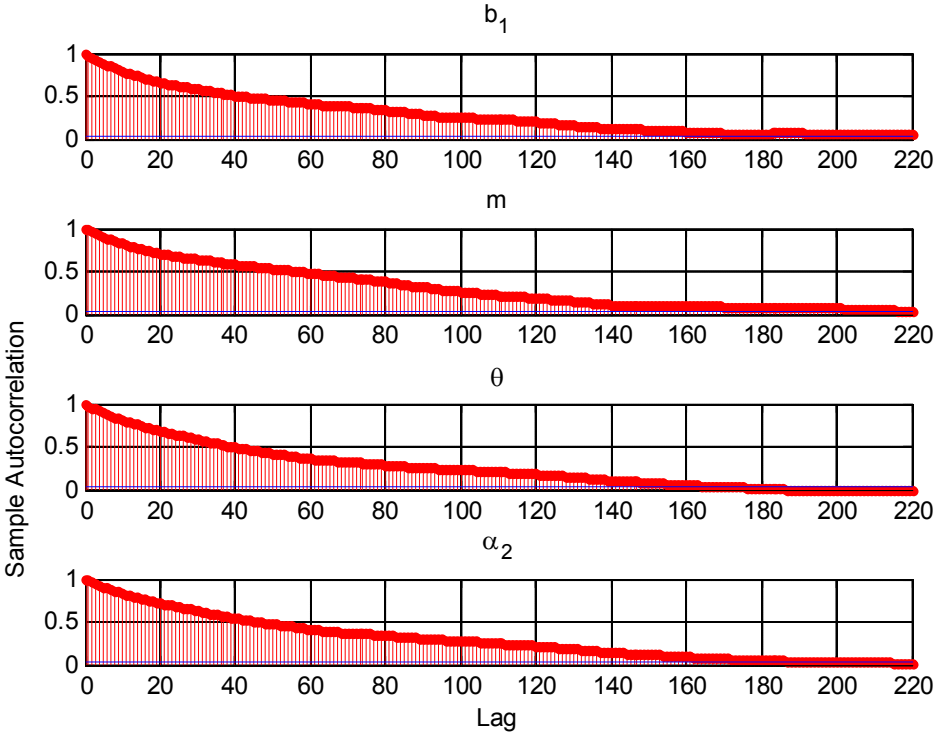

Figure 5. MCMC trace plots. The vertical axis represents samples and the horizontal axis represents number of iterations

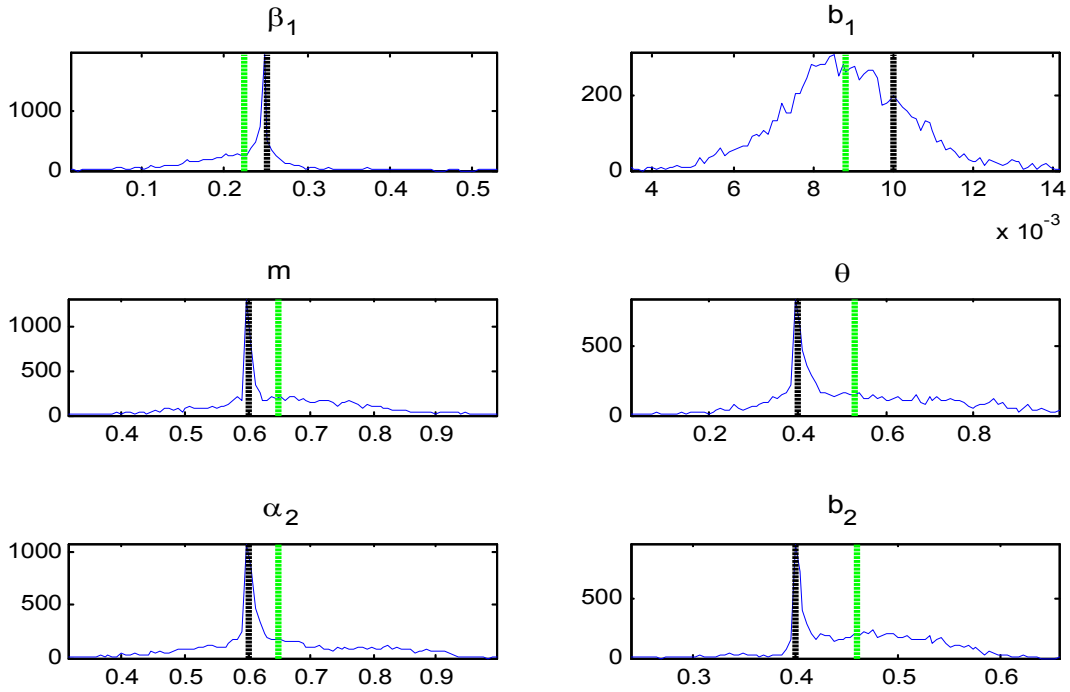

Figure 6. Marginal distribution plot together with mean of MCMC samples (green) and the original parameter values (black)

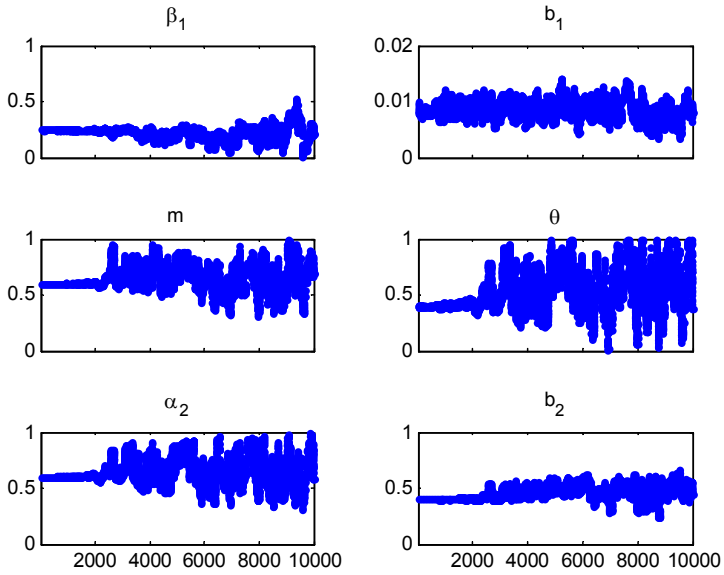

Figure 7. Markov chain Monte Carlo (MCMC) scatter plots

The vertical axis represents samples and the horizontal axis represents number of iterations

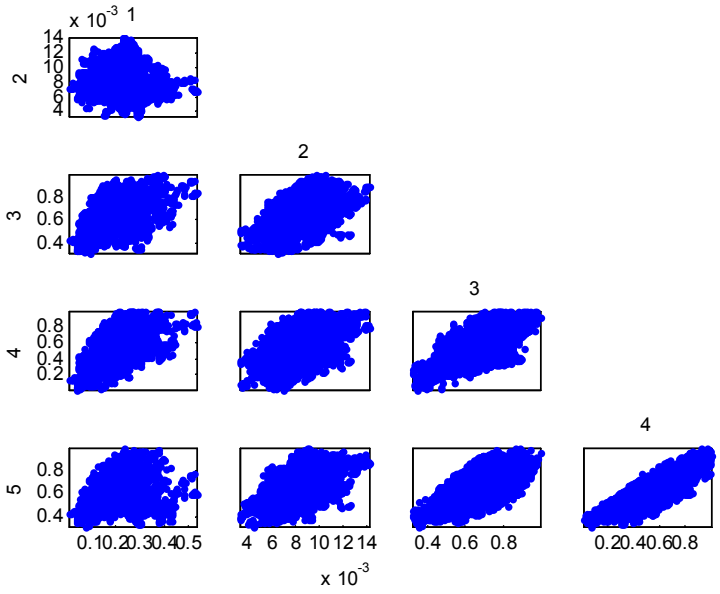

Figure 8. Correlation of pair parameters

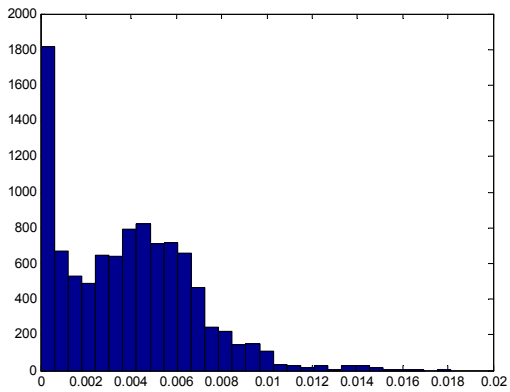

Figure 9. Histogram plot for R_0 distribution plot, x-axis represents R_0 while y-axis represents populations. The trend shows an increase in R_0 tends to decrease chickens population and vice versa

Kurtosis and skewness

Skewness characterizes the asymmetry property of a data distribution around it is mean and is approximately to normal distributions whenever it is values is about zero while kurtosis describes the peakedness or flatness behavior of a distribution in relation with normal distribution. From the Table 3 it is observed that most of the parameters produce the kurtosis of about three which is approximately to normal distribution while others have high values such as β_1, β_2, and n_1. Some parameters have high skewness values as shown in Table 2, which indicates that are not normally distributed.

Conclusion

The parameters for compartmental model of chicken and human system have been rigorously analyzed. The model was well fitted using MLE and MCMC methods for 2014 data obtained from five districts in Tanzania. The Figure 3 used as motivation of fitting and estimating the Model parameters and its' result illustrated in Figure 4. From the MCMC numerical results, shows that many parameter values agree closely to actual data of ND death cases and their kurtosis and skewness values have shown good results compared to normal distributions. The high deviation of some parameter may be caused by random distributions. Therefore, the numerical results for this study recommend that for any developed mathematical model validation and parameter estimation are important aspects before numerical simulations. Hence, result to reflect its phenomena.

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REFERENCES

Ashraf, A. and Shah, M. S. 2014. Newcastle Disease: Present status and future challenges for developing countries. *African Journal of Microbiology Research*, *8*(5), 411–416. http://doi.org/10.5897/AJMR2013.6540

Bornaa, C. S., Makinde, O. D., and Seini, I. Y. 2015. Eco-epidemiology model and Optimal Control of disease transmission between humans and animals. *Commun. Math. Biol. Neurosci.*, (ISSN:2052-2541), 1–28.

Chuwa, A. 2012. *United Republic of Tanzania National sample census of agriculture*. *National bureau of statistics* (Vol. III). Ministry of Livestock Development and Fisheries, Dar es Salaam. Retrieved from www.nbs.org

Gilks, W. R., Richardson, S., and Spiegelhalter, D. J. 1996. Markov Chain Monte Carlo in Practice. *Technometrics*. http://doi.org/10.2307/1271145

Grassly, N. C., and Fraser, C. 2008. Mathematical models of infectious disease transmission. *Nature Reviews. Microbiology*, *6*(3), 234–244. http://doi.org/10.1038/nrmicro1845

Haario, H. 2001. An adaptive Metropolis algorithm. *Bernoulli*, *7*(2), 223–242. http://doi.org/10.2307/3318737

Haario, H., Laine, M., Mira, A., and Saksman, E. 2006. DRAM: Efficient adaptive MCMC. *Statistics and Computing*, *16*(4), 339–354. http://doi.org/10.1007/s11222-006-9438-0

Hugo, A., Massawe, E. S., and Makinde, O. D. 2012. An eco-epidemiological mathematical model with treatment and disease infection in both prey and predator population. *Journal of Ecology and Natural Enviroment*, *4*, 266–279. http://doi.org/10.5897/JENE12.013

Jibril, A. H., Umoh, J. U., Kabir, J., Saidu, L., Magaji, A. A., Bello, M. B., and Raji, A. A. 2014. Newcastle disease in Local Chickens of Live Bird Markets and Households in Zamfara State , Nigeria. *Hindawi Publishing Corporation*, 1–5.

Jost, C., and Arditi, R. 2000. Identifying predator-prey processes from time-series. *Theoretical Population Biology*, *57*(4), 325–337. http://doi.org/10.1006/tpbi.2000.1463

Knueppel, D., Coppolillo, P., Msago, A. O., Msoffe, P., Mutekanga, D., and Cardona, C. 2009. Improving Poultry Production for Sustainability in the Ruaha Landscape, Tanzania. *WildLife Conservation Society*, 24.

Leonardo, S. 2015. *Newcastle disease, Factsheet*. *Poultry Health Research Network*. Retrieved from www.uoguelph.ca/phrn

Liang, F., Chuanhai, L., and Carroll, R. J. 2010. Advancedd Markov Chain Monte Carlo Methods, Learning from past samples. *John Wiley and Sons, Ltd, Chichester, UK.*

Massawe. Laurencia. Ndalemo, Massawe. Estomih. S, M. O. D. 2015. On Parameter Estimation and Validation of Dengue Epidemic in Tanzania. *International Journal of Current Research*, *Vol.7* (Issue, 10), pp.21720–21724.

Mukhopadhyay, B., and Bhattacharyya, R. 2009. Role of predator switching in an eco-epidemiological model with disease in the prey. *Ecological Modelling*, *220*(7), 931–939. http://doi.org/10.1016/j.ecolmodel.2009.01.016

Myung, I. J. 2003. Tutorial on maximum likelihood estimation. *Journal of Mathematical Psychology*, *47*(1), 90–100. http://doi.org/10.1016/S0022-2496(02)00028-7

Okosun, K. O., Ouifki, R., and Marcus, N. 2011. Optimal control analysis of a malaria disease transmission model that includes treatment and vaccination with waning immunity. *Bio Systems*, *106*(2-3), 136–145. http://doi.org/10.1016/j.biosystems.2011.07.006

Sharma, S., and Samanta, G. P. 2015. Stability analysis and optimal control of an epidemic model with vaccination. *International Journal of Biomathematics*, *8*(3). http://doi.org/10.1142/S1793524515500308

Tchuenche, J. M., Khamis, S. A., Agusto, F. B., and Mpeshe, S. C. 2011. Optimal Control and Sensitivity Analysis of an Influenza Model with Treatment and Vaccination. *Acta Biotheoretica*, *59*(1), 1–28. http://doi.org/10.1007/s10441-010-9095-8

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