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CHIKUNGUNYA EPIDEMIC MODELLING AND APPLICATION OF MCMC METHODS

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ABSTRACT

We have formulated model for the transmission dynamics of the Chikungunya. We have formulated *a SEIRD model* for Chikungunya. Monte Carlo analysis was performed to determine the sensitivity of infection dynamics to the parameters. We have estimated the posterior mean of the rate of infection from susceptible to infected is 0.1411 (0.1308, 0.1513) per day and the posterior mean rate of the rate of recovery in a community is 0.0245 (0.0249, 0.0257) per day. It shows that, greater rate of infection than rate of recovery for possible intensity of increment in infections. The estimated reproduction number R_0^T is 2.7938 with credible interval (2.0305, 3.5925).

KEYWORDS: Chikungunya, Gibbs Sampling, Markov Chain Monte Carlo, Outbreak and Vector

1. INTRODUCTION

CHIK is caused by the Chikungunya virus which is transmitted to humans by *Aedes aegypti* mosquitoes. Chikungunya (CHIKV) virus has re-emerged as an important pathogen causing epidemics of the disease in several countries. The epidemic resurgence of CHIKV was recorded in 2000 in the Democratic Republic of Congo (DRC), in Indonesia during 2001-03 and in India during 2005-06, after a gap of 39, 20 and 32 years respectively. CHIK is an acute febrile illness that is rarely fatal, although patients can experience debilitating symptoms that persist for months to years. Chikungunya occurs in Africa, Asia and the Indian subcontinent. Starting in February 2005, a major outbreak of Chikungunya occurred on the islands of the Indian Ocean. A large number of imported cases in Europe were associated with this outbreak, probably in 2006 when the Indian Ocean epidemic was at its peak. A large outbreak of Chikungunya in India occurred in 2006 and 2007 (WHO, 2006; Talawar and Pujar, 2010). Several other countries in South-East Asia were also affected. Since 2005, India, Indonesia, Maldives, Myanmar and Thailand have reported over 1.9 million cases. In December 2013, France reported 2 laboratory-confirmed autochthonous cases in the French part of the Caribbean island of St Martin. Since then, local transmission has been confirmed in over 43 countries and territories in the WHO Region of the Americas. As of April 2015, over 1,379,788 suspected cases of Chikungunya have been recorded in the Caribbean islands, Latin American countries, and the United States of America. 191 deaths have also been attributed to this disease during the same period. Canada, Mexico and USA have also recorded imported cases (WHO, 2013).

In the Americas in 2015, 693,489 suspected cases and 37,480 confirmed cases of Chikungunya were reported to the Pan American Health Organization (PAHO) regional office, of which Colombia bore the biggest burden with 356,079 suspected cases. This was less than in 2014 when more than 1 million suspected cases were reported in the same region. The decreasing trend continues in 2016, with about 31,000 cases reported to PAHO as of 18 March 2016, representing a 5-fold decrease compared to the same period in 2015. Despite this trend, Chikungunya remains a threat in the region with Argentina recently reporting its first Chikungunya outbreak (WHO, 2017). See *Figure 1* and *Figure 2* for the distribution of Chikungunya all over the world and Table 1, for the distribution in India.

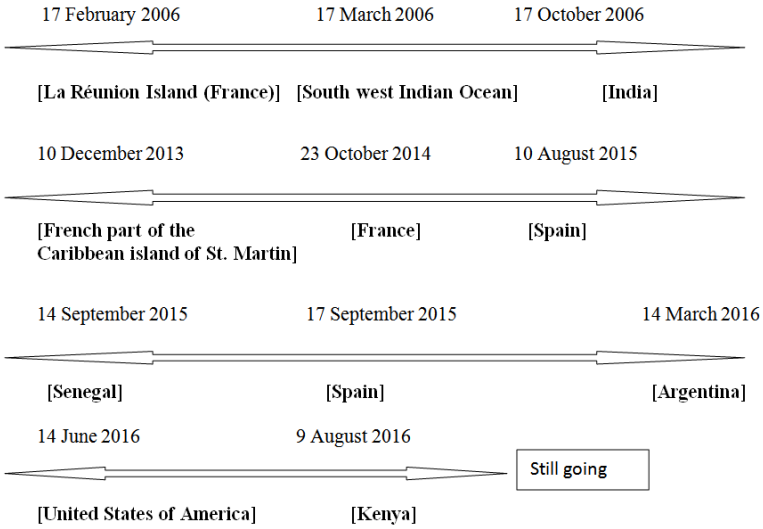

Figure 1: Some Recent Outbreaks

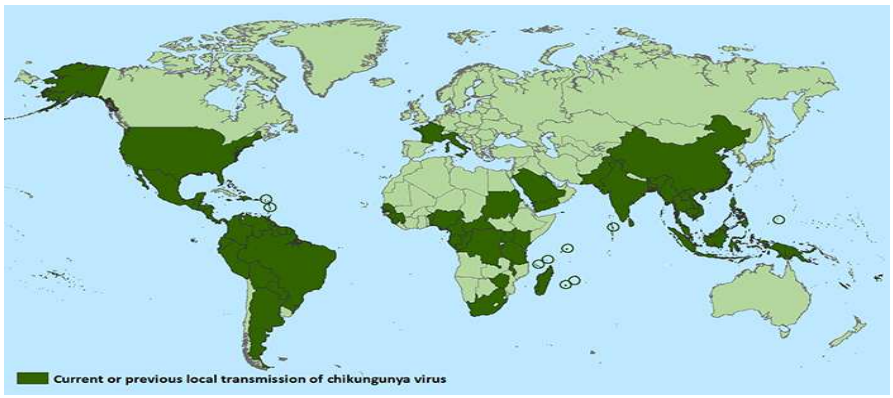

Figure 2: Spread of Chikungunya over more than 50 Countries (CDC, 2017)

Table 1: Clinically Suspected Chikungunya Fever Cases Since 2010

Affected States/UTs	2010	2011	2012	2013	2014	2015	2016	2017
Andhra Pradesh	116	99	2827	4827	1359	817	960	788
Goa	1429	664	571	1049	1205	561	337	237
Gujarat	1709	1042	1317	2890	574	406	3285	1916
Karnataka	8740	1941	2382	5295	6962	20763	15666	7723
Kerala	1708	183	66	273	272	175	129	67
Maharashtra	7431	5113	1544	1578	1572	391	7570	2379
Rajasthan	1326	608	172	76	50	7	2506	333
Tamil Nadu	4319	4194	5018	859	543	329	86	44
West Bengal	20503	4482	1381	646	1032	1013	1071	272
Delhi	120	110	6	18	8	64	12279	183
Puduchery	11	42	45	146	399	245	463	115
India	48176	20402	15977	18840	16049	27553	64057	15432

Source: *http://www.nvbdcp.gov.in/24-07-2017*

2. REVIEW OF LITERATURE

In the present paper, we have discussed stochastic model of the vector borne disease such as Chikungunya and estimated its parameter values using MCMC methods. The modelling of diseases transmitted by vectors has increased in the past years, displaying public health problems around the world. Actually, there exists several mathematical models

applied to the transmission dynamics of the Chikungunya by Aedes aegypti [Patz et al, 1998; Poletti et al, 2011; Moulay et al 2012; Moulay et al, 2011; Ruiz-Moreno et al, 2012; Dommar et al, 2014; Osorio et al. 2015] as well as some papers treating the dynamics of the population growth of the mosquitoes, including different factors. The epidemiological models are generally described with dynamic systems that help us to explain the connection between different epidemiological variables. The main goal of these models is to describe a system as real as possible.

In Moulay et al. (2011), models for the transmission of the Chikungunya virus to human population are discussed. Global analysis of equilibria is given, using Lyapunov functions and results of the theory of competitive systems and stability of periodic orbits. Moulay et al. (2012) formulated an optimal control problem, based on biological observations. Three main efforts are considered in order to limit the virus transmission, looking at time dependent breeding site's destruction, prevention and treatment efforts, for which optimal control theory is applied. Using analytical and numerical techniques, it is shown that there exist cost effective control efforts. In consideration of the risk of Chikungunya introduction to the US, Ruiz-Moreno et al. (2012) developed a model for disease introduction based on virus introduction by one individual and their study combines a climate-based mosquito population dynamics stochastic model with an epidemiological model to identify temporal windows that have epidemic risk. A simple, deterministic mathematical model of the transmission of the virus between humans and mosquitoes was constructed and parameterised with the up-to-date literature on infection biology. The model is fitted to the large Re´union epidemic, resulting in an estimate of 4.1 for the type reproduction number of Chikungunya (Yakob and Clements, 2013). Naowarat and Tang (2013) proposed a dynamical model of Chikungunya fever assuming constant human and mosquito populations and determined the stability of the model using the Routh- Hurwitz criteria. The numerical simulations are given in order to illustrate the transmission behaviors of disease for different values of parameters.

Manore et al. (2014) adapted a mathematical mosquito-borne disease model to Chikungunya and dengue in Aedes aegypti and Aedes albopictus mosquitoes and to understand the differences in transient and endemic behaviour of Chikungunya and dengue. They have derived analytical threshold conditions and important dimensionless parameters for virus transmission; performed sensitivity analyses on quantities of interest such as the basic reproduction number, endemic equilibrium and first epidemic peak; and computed distributions for the quantities of interest across parameter ranges.

3. SEIRD TRANSMISSION MODEL WITH VECTOR

We have formulated *a SEIRD model* for the transmission dynamics of the Chikungunya. Here, susceptible human population not yet infected, but capable of catching the disease is S_h, exposed population who are infected but not infectious isE_h, infectious population who are ready to infect other susceptible is I_h, recovered or removed individual is R_h and D_h Compartment represents the population, which died from the disease. In a system of equations (1), I_v is the proportion of infected mosquito population, V means vector or the mosquito population. Model parameters are; a, the rate of infection from susceptible to infected via infected mosquitoes, k the rate of exposed, γ the rate of recovery, $the\ \mu\ rate$ of death due to disease, p the rate of recruitment of vectors or mosquitoes and m the rare moving or died mosquitoes.

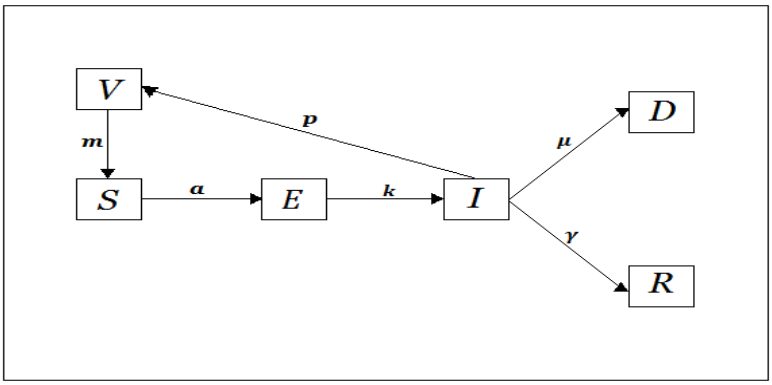

Figure 3: Transmission Diagram of SEIRD Model with Vector

The system of non-linear differential difference equations for continuous time dynamics of SEIRD model become

$$\frac{dS_h}{dt} = -aS_hI_v$$

$$\frac{dE_h}{dt} = aS_hI_v - kE_h$$

$$\frac{dI_h}{dt} = kE_h - (\gamma + \mu)I_h \quad \textbf{(1)}$$

$$\frac{dR_h}{dt} = \gamma I_h$$

$$\frac{dD_h}{dt} = \mu I_h$$

$$\frac{dV}{dt} = pI_v - mV$$

Where I_v=$\frac{V}{V+V_0}$, V is concentration of the infective agent in the reservoir and the transmission rate is modelled by a saturating function of V_0, so that as $V \to \infty$ the transmission rate approaches the constant a at a rate determined by V_0, infective agents die or are removed from the reservoir at rate mV and the per capita rate at which new infected agents are added to the reservoir is p

$$\tilde{E}|s, C \sim Bin(S, Pi(a, V, V_0))$$

Where $Pi(a, V, V_0) = 1 - exp\left(\frac{-aV}{V+V_0}\right)$ **(2)**

$$\hat{I}|i \sim Bin(i, p_I),$$

Where $p_I = 1 - e^{-k}$ **(3)**

$$\hat{R}|i \sim Bin(i, p_r),$$

where $p_r = 1 - e^{-\gamma}$ **(4)**

$$\hat{D}|i, \hat{r} \sim Bin(i - \hat{r}, p_d),$$

where $p_d = 1 - e^{-\mu}$ **(5)**

Vector concentration could be in thousands of individuals. So the evolution of vector becomes

$$V(t+1) - V(t) = [pI(t)] - d_v$$

d_v becomes number of infectious agents which has a distribution

$$d_v \sim Bin(C, p_v)$$

Whereas prior for $\mathrm{p_r}, \mathrm{p_d}, \mathrm{p_e}$ follows beta distribution such as $\mathrm{Beta(a, b)}$; $\mathrm{Beta(c, d)}$ and $\mathrm{Beta(e, f)}$.

Posterior forms of the above model become

$$\begin{aligned}
&\mathrm{p_r} \sim \mathrm{Beta}\left(\mathrm{a} + \textstyle\sum_{t=1}^{T} \hat{r}_t, \mathrm{b} + \sum_{t=1}^{T} \mathrm{I(t)} - \hat{r}_t\right) \\
&\mathrm{p_e} \sim \mathrm{Beta}\left(\mathrm{e} + \textstyle\sum_{t=1}^{T} \hat{r}_t, \mathrm{f} + \sum_{t=1}^{T} \mathrm{I(t)} - \hat{r}_t\right) \\
&\mathrm{p_d} \sim \mathrm{Beta}\left(\mathrm{c} + \textstyle\sum_{t=1}^{T} \hat{d}_t, \mathrm{d} + \sum_{t=1}^{T} \mathrm{I(t)} - \hat{r}_t - \hat{d}_t\right)
\end{aligned} \quad \textbf{(6)}$$

Here posterior form of the parameter is also beta distribution. So, to estimate model parameter we have used Gibbs sampling.

4. MCMC SIMULATION

Monte Carlo analysis was performed to determine the sensitivity of infection dynamics to the parameters. To initialize this process for evaluation of epidemic growth over time, initial values of transition rates are considered as $a = 0.2$, $\gamma = 0.01$, $\mu = 0.05$, $\mathrm{p} = 0.8$, $\mathrm{m} = 0.05$ and $\mathrm{k} = 0.9$. We have performed 25000 iterations for each run of the MCMC algorithm following 5000 burnin. In order to avoid autocorrelation within successive samples, we have allowed every 10th observation to participate in making inference (i.e. Thinning).

The output was recorded to constitute samples from the posterior distribution and the convergence was visually assessed through trace plots. Trace plots provide a useful method for detecting problems with MCMC convergence and mixing.

Table 2: Posterior Summary of the SEIRD Model Parameter for Chikungunya Disease

Model Parameters	Posterior Mean	5th percentile	95th percentile
$\boldsymbol{a}$	0.1411	0.1308	0.1513
$\boldsymbol{\gamma}$	0.0249	0.0245	0.0257
$\boldsymbol{\mu}$	0.0524	0.0447	0.0602
$\boldsymbol{p}$	0.523	0.401	0.652
$\boldsymbol{m}$	0.0401	0.0267	0.0538
$\boldsymbol{k}$	0.8512	0.8229	0.8795

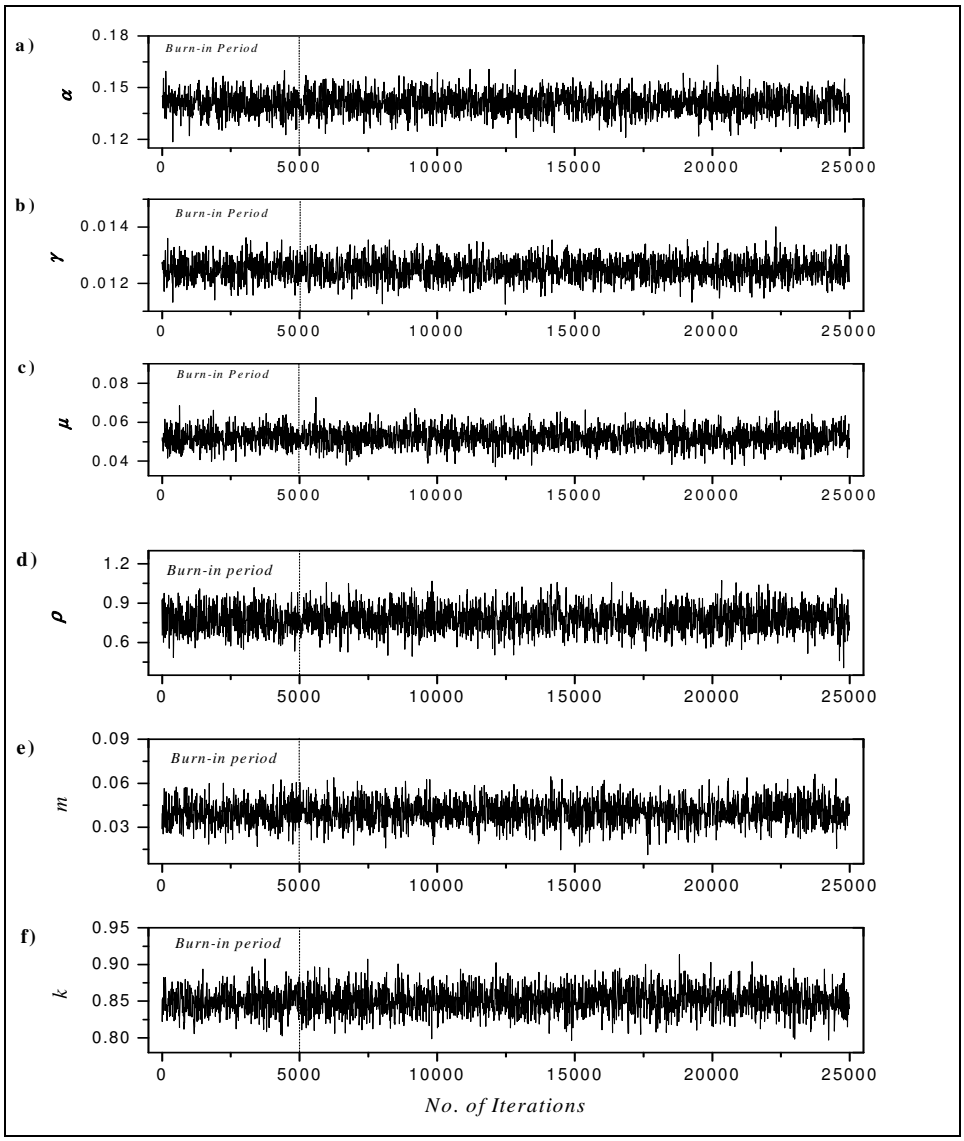

Figure 4: Summary of the Posterior Distribution for the SEIRD Model a) Realizations of Model Parameter a, b) Realizations of Model Parameter γ, c) Realizations of Model Parameter μ, d) Realizations of Model Parameter p, e) Realizations of Model Parameter m and f) Realizations of Model Parameter k

RESULTS AND DISCUSSION

The results from Table 2 shows that, the posterior mean of the rate of infection from susceptible to infected is 0.1411 (0.1308, 0.1513) per day and for the exposed group is 0.8512 (0.8229, 0.8795) per day. The posterior mean of the rate of recovery in a community is 0.0249 (0.0245, 0.0257) per day, whereas the posterior mean of the rate of death due to disease is 0.0524 (0.0447, 0.0602), the posterior mean of death rate of recruitment of vectors or mosquito's is 0.523 (0.401, 0.652) per day and the posterior mean of rate of removing or died mosquito's is 0.0401 (0.0267, 0.0538). Clearly, greater rate of infection than rate of recovery shows possible intensity of increment in infections.

Let us introduce the following reproduction number, which is defined as the average number of secondary infections produced by an infected individual in a completely susceptible population

$$R_0 = \sqrt{\frac{akp}{\gamma(k+\mu)}} \quad \textbf{(7)}$$

Where $R_0^T = R_0^2$ is the type reproduction number

The estimated type reproduction number R_0^T is 2.7938 with credible interval (2.0305, 3.5925).

Sensitivity Analysis of R_0^T

Our estimated R_0^T is found to be 2.79 with a range of (2.03, 3.59) as compared to Bacae¨r (2007) who produced the first ordinary differential equation model and calculated the R_0^T to be 3.4 after fitting it to the Re´union outbreak data. Dumont and Chiroleu (2010) estimated R_0^T between 1.46 and 1.78 for the same epidemic. Massad et al. (2008) parameterised their model based on the risk of an outbreak in Singapore and calculated an RT of 1.22. Our estimates are also comparable with Boelle et al. (2008) who derived a value of 3.7 for the R_0^T. Yakob and Clements (2013) estimated R_0^T falls in the middle of their estimated range of between 1.8 and 6 after fitting it to the Re´union epidemic outbreak data. Manore et al. (2014) estimated R_0^T as 1.10. However, making the distinction becomes important when assessing control because R_0^T Will always underestimate the level of control required for elimination of a vector-borne disease (Yakob and Clements, 2013). If we use the parameter values of Yakob and Clements (2012) for us R_0^T which gives 5.054, where we considered $a = \beta_1$= 014, $p = \lambda_2$=0.5, γ=0.25, $k = \lambda_1\phi$=0.485, μ=0.0524 and m=0.05.

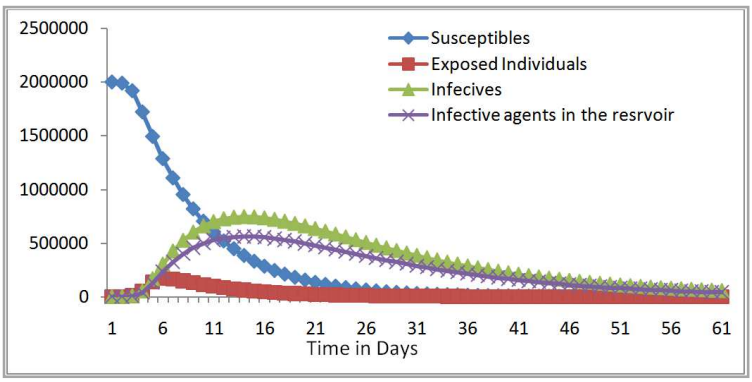

Figure 5: Effect of State Variables of SEIRD Model

Figure 5 indicate the trajectories of state variables of SEIRD model. In order to find effect of state variables in SEIRD model, we used parameter values given in Table 2.

CONCLUSIONS

Our estimated value 2.79 with a range of (2.03, 3.59) for R_0^T is comparable with Boelle et al. (2008) and Yakob and Clements (2013). The estimated model parameter values are also reasonable and Figure 5 gives the possible nature of trajectories for susceptible, exposed, infective human and infected mosquitoes in the reservoir.

Limitations of the Model

In the model formulation we have considered disease induced rate, but Chikungunya is rarely fatal and deaths due to disease are also very less.

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