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Behavioral Pattern Analysis of the Zika Virus Disease: Its Prevention and Solution

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ABSTRACT

This paper considers a non linear ordinary differential equation model for the risk of microcephaly induced by Zika Virus (ZIKV). A model of mathematical dynamic system is required to develop a non-linear equation based on ZIKV. This research focuses on a group of pregnant women in Armedia (Quindio), Columbia. By solving the non-linear algebraic system, the equilibrium points for each possible cause that induced microcephaly can thus be obtained. The Jacobian method was then used to calculate the eigenvalues for each equilibrium point to estimate the local stability. Following this, the local stability analysis will be used to show the behavior of each equilibrium point acquired. Finally, the results were interpreted and a conclusion was made.

Keywords: *System Dynamic Model, Non-Linear Equation, Jacobian Method, Ordinary Differential Equation.*

1. INTRODUCTION

Zika virus (ZIKV) was first isolated from a Macaque monkey in the forest region in Uganda in the year of 1947. In 1954, the first human case was detected in Nigeria (Rodriguez-Morales et all., 2017). It was caused by arbovirus that is classified under the flavivirus family which also includes the other types of arboviral disease such as Yellow fever, West Nile virus and Dengue virus. It was primarily transmitted by an Aedes Aegypti mosquito. From 1960 to 1983, there were minor outbreaks that occured in regions such as Senegal, Pakistan, Indonesia, Cambodia, Costa Rica and also Malaysia. This happened because of the heavy downpour across the affected countries which led to increase in mosquito breeding. The first colossal outbreak occured in Pacific Island of Yap in the Federated State of Micronesia in 2007 (Duffy et al., 2009).

According to Foy et al., (2011) in 2008, one of the US scientists who conducted a field work in Senegal was infected with ZIKV which then spread to his wife when he returned home from Colorado. This marks the first case of sexual transmission of ZIKV. In 2013 and 2014, the virus had caused an outbreak in Pacific Islands including French Polynesia, Easter Islands, The Cook Island and New Caledonia. The outbreak in French Polynesia had been recorded as 28,000 cases (11% of population) and were intensively investigated.

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Besnard et al., (2014) published an article showing the evidence of perinatal transmission of ZIKV. Clinical and laboratory features of two mothers and their newborns who had ZIKV infection were studied in the article. Based on the result of ZIKV Real-Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) performed on serum collected within four days post delivery date, the infants infection most probably occured by transplacental transmission. This shows that ZIKV can also be transmitted by perinatal transmission.

WHO (2016) released an article stating that ZIKV can be transmitted through blood transfusion. This was based on the outbreak of French Polynesia where a number of 1,505 asymptomatic blood donors were detected to be positive of ZIKV by Polymerase Chain Reaction (PCR).

According to Dana & Branswell (2016), Brazil reported an unusual number of cases of microcephaly among newborn babies. Soon after, Brazil declared a national public health emergency as the number of suspected microcephalic newborn kept on escalating. On 28th November 2015, ZIKV genome was detected in the blood and tissue sample of an affected baby with microcephaly in Brazil. On 5th January 2016, researchers reported the first diagnosis of intrauterine transmissions of ZIKV in two pregnant women in Brazil whose fetuses were diagnosed with microphephaly. Blood sample from both women were tested negative for ZIKV, but it was detected in the amniotic fluid.

The United States Centre for Disease Control and Prevention collaborated with health officials in Brazil to run a research on four microcephaly cases in Brazil[3]. Two out of four newborns died in the first 24 hours of life and the other two were miscarried. ZIKV was found in the brain tissues of the two newborn. Furthermore, placenta of the two fetuses miscarried were tested positive for ZIKV by PCR. All the four women had the presence of fever and rash during their pregnancy[2],[3]. This findings were considered the strongest evidence of an association between ZIKV and microcephaly.

Previously, most of the research done were discussing only the clinical and laboratory features of the mothers and their newborns who had ZIKV infection. Their finding was that most infants were infected via trans placental transmissions or during intrapartum. They had proposed a mathematical dynamics of Susceptible-Infected Pregnant Women-Infected People (SII) model to evaluate the ZIKV transmission which emphasized on the group of susceptible pregnant women that may induced microcephaly. This research will consider four possible routes of perinatal transmissions of ZIKV which are transplacental , intrapartum , during breastfeeding period , as well as close contact between mothers and their newborns.

Therefore, the mathematical model proposed in the previous research will be derived and deduced in order to obtain a set of accepted statements in this research. These will give a better understanding on how the proposed model works. Subsequently, this project is used to verify the non-linear differential equation derived from the Susceptible-Infected Pregnant Women-Infected People (SII) model to predict how ZIKV infection can be recovered in the near future by analyzing the local stability analysis of each equilibrium point.

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2. MATERIALS AND METHOD

2.1 Derived Model

The model used in this research is derived by using a systematic dynamic approach which is also known as Susceptible-Infection-Recover (SIR) Model. The SIR Model is an epidimiological model that compares model which computes the theoretical number of people infected with contagious illness in a closed population over time. In relation to the SIR model, our derivation used in this project will focus on ZIKV infected person and ZIKV infected pregnant women (Munoz, 2016).

2.2 Human Population

In the model of human population, the country's population is initially described as "Susceptible Human Population". When ZIKV carrier mosquitoes transmit their infection to a human, the human will be classified either as "Infected Pregnant Woman" or "Infected Person". It is important to distinguish those two types of infected human because this project studies the relationship between ZIKV infected pregnant women and the risk of microcephaly. Human may leave the dynamic system either through death or recovery where human is considered immune. The epidemic of ZIKV infection follows an exponential shaped graph [9].

2.3 Mosquito Population

The mosquito population will begin as "Mosquito Egg" and "Initial Mosquito Population"[12]. This will only focus on population of mosquito without the virus infection. The mosquitoes will lay eggs and then the eggs will continue to grow without any infection from ZIKV. The eggs and mosquitoes will die off based on their life cycle characteristics. Since climate change has an impact on the mosquitoes' viability, thus it will be taken as a consideration in this case. In this project, only Aedes Aegypti mosquitoes will be used and analysed as ZIKV is primarily transmitted by this species.

2.4 Human & Mosquito Infection Transmission Dynamics

Based on Figure 1**,** the human population used is only the Suspected population group, u_1. Then the suspected population group is further divided into 2 categories; u_2 (infected pregnant women) and u_3 (other infected people). The transmission dynamics of ZIKV between begins when a mosquito from "Susceptible Mosquito Population" which is denoted byv_1 bites on the viremic people. These mosquitoes will then be classified under "Infected Mosquito Population", denoted by v_2 where it will be a threat to further transmit the ZIKV to other humans [9].

When a mosquito from v_2 population bite humans from "Susceptible Human Population", characterized as u_1, it will cause an upsurge in the u_2 and also u_3 population. This cycle of infectivity between infected mosquito to susceptible human, and from infected human to susceptible mosquito will occur repeatedly [9].

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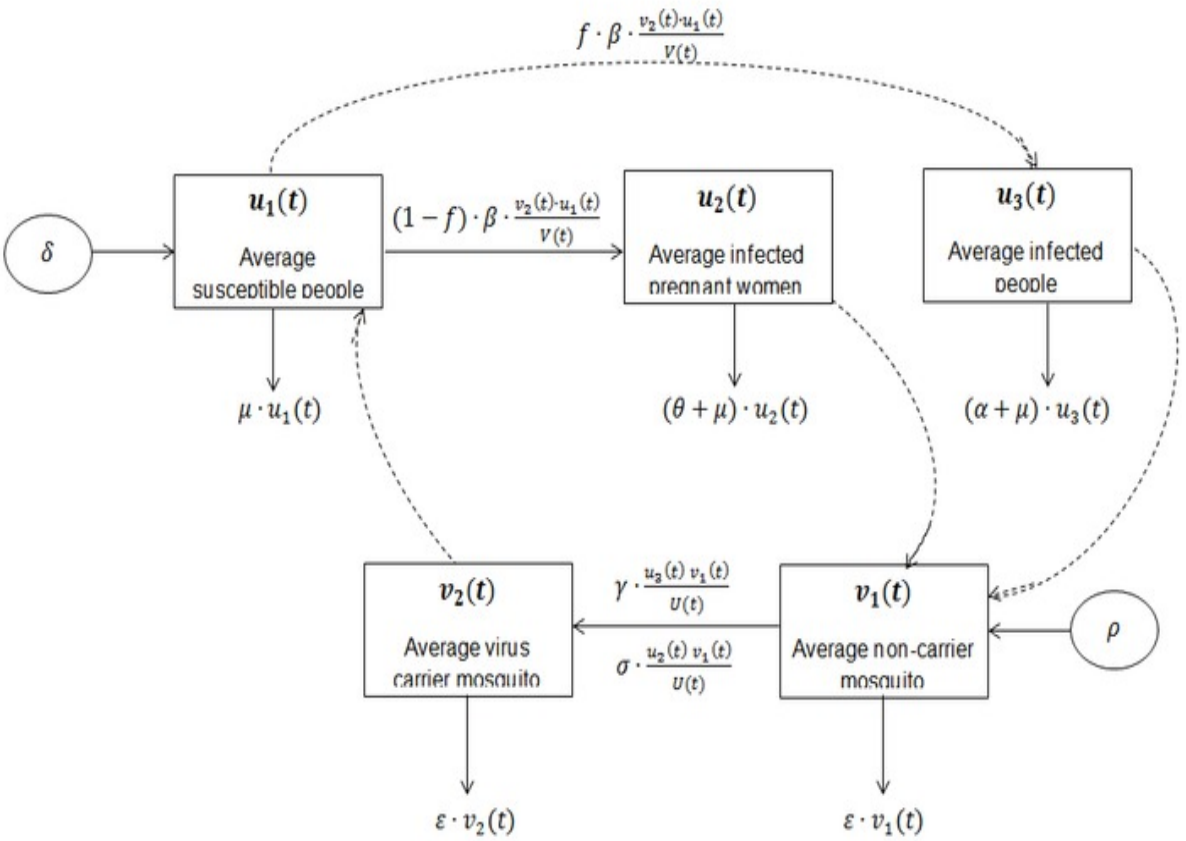

Figure 1 : A system of dynamic approach diagram [9]

2.5 Equation

These are the equations proposed by Muñoz Pizza et al. (2016) where it is obtained through a systematic dynamic approach based on the non-linear ordinary differential equations (ODE). These equations (1-5), are developed based on the main criteria of Zika-Virus transmission

$$\frac{\partial u_1(t)}{\partial t} = \delta - \beta . \frac{v_2(t).u_1(t)}{V(t)} - \mu . u_1(t) \tag{1}$$

$$\frac{\partial u_2(t)}{\partial t} = (1 - f\,) . \beta . \frac{v_2(t).u_1(t)}{V(t)} - (\theta + \mu) . u_2(t) \tag{2}$$

$$\frac{\partial u_3(t)}{\partial t} = f\, . \beta . \frac{v_2(t).u_1(t)}{V(t)} - (\alpha + \mu) . u_3(t) \tag{3}$$

$$\frac{\partial v_1(t)}{\partial t} = \rho - \sigma . \frac{v_2(t).u_1(t)}{V(t)} - \gamma . \left(\frac{u_3(t).\, v_1(t)}{U(t)} \right) - \varepsilon\, . v_1(t) \tag{4}$$

$$\frac{\partial v_2(t)}{\partial t} = \sigma . \frac{u_2(t).v_1(t)}{U(t)} + \gamma . \left(\frac{u_3(t).\, v_1(t)}{U(t)} \right) - \varepsilon\, . v_2(t) \tag{5}$$

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Equation (1)-(5) is non-linear ODE derived from SIIRR model. The rate of change of the average number of susceptible people at time t, refers to the average number of total human population that remains alive without getting infected by the ZIKV-carrier mosquitoes in the population (1).

(2) is about the rate of change of average number of pregnant women infected by ZIKV that may induced microcephaly at time t. It is the fraction of pregnant women among the average number of susceptible people which have been infected by the ZIKV-carrier mosquitoes minus the average number of infected pregnant women's recovery and death rate.

(3) states about the rate of change of the average number of people infected by ZIKV at time t. It is the fraction of people infected by ZIKV among the average number of susceptible people minus the average number of infected people's recovery and death rate.

(4) describes the rate of change of average number of non-carrier mosquitoes in the population at time t. It is the average number of total mosquitoes population that remains alive without getting ZIKV infection from the infected human in the population.

(5) is about the rate of change of the average number of ZIKV carrier mosquitoes at time t. It is the average number of mosquitoes that remains alive and carrying ZIKV infection transmitted by the infected human in the population.

3. LOCAL STABILITY ANALYSIS

This research focuses on finding the local stability analysis based on (1)-(5) for each possible route of perinatal transmission. According to Morgan (2015), a stability analysis is used to show the general behavior of the solution obtained which depends on their initial condition. There are two methods involved in determining the local stability analysis. The first one is solving the non-linear algebraic system to get the equilibrium points. Then by using the Jacobian method, a linearization of the non-linear system is achieved. Hence, a set of eigenvalues is obtained.

For the first method, there are two types of equilibrium points that need to be calculated which include the free of infection and also prevalence equilibrium points. Prevalence refers to a measurement of all individuals affected by the disease at a particular time. Meanwhile, free of infection refers to a condition where there is zero infection of ZIKV among the population in a particular time. All the equilibrium points are obtained by using Maple software. For the second method, equation (1)-(5) are linearized by differentiating the equations with respected variables which are $(u_1(t), u_2(t), u_3(t), v_1(t), v_2(t))$ .Then, the differentiated equations will be arranged in Jacobian matrix to obtain the eigenvalues. These eigenvalues will determine the behavior of each solution.

4. RESULT AND DISCUSSION

Both equilibrium points and eigenvalues are obtained by using Maple software based on infected population probabilities f [9], and the result is tabulated in the table below :

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Table 4.1: Equilibrium point and eigenvalues for f = (0.3, 0.6, 0.85 and 1.0)

f	Equilibrium point $u_1(t), u_2(t), u_3(t), v_1(t), v_2(t)$	Eigenvalues $u_1(t), u_2(t), u_3(t), v_1(t), v_2(t)$	Stability
0.3	(66667,0,0,852,0)	(0.6610,-0.0003,-0.0352,-0.1080, 07788)	Unstable
0.3	(27,278,43,49,803)	(-0.0352,-0.0503,-0.1404,-0.5946,-0.7615)	Stable
0.6	(66667,0,0,852,0)	(0.6759,-0.0003,-0.0352,-0.0808,-0.8209)	Unstable
0.6	(27,159,85,48,805)	(-0.0352,-0.0503,-0.1405,-0.6076,-0.7701)	Stable
0.85	(66667,0,0,852,0)	(0.6885,-0.0003,-0.0352,-0.0611,-0.8532)	Unstable
0.85	(27,60,121,46,807)	(-0.0352,-0.0503,-0.1406,-0.6248,-0.7832)	Stable
1.0	(66667,0,0,857,0)	(-0.0503,0.6961,-0.0003,-.0.0352,-0.8716)	Unstable
1.0	(27,0,142,44,809)	(-0.0503,-0.0352,-0.1406,-0.6400,-0.7971)	Stable

For each value of f taken from Muñoz Pizza et al. (2016), there will be two equilibrium points which are free of infection and prevalence equilibrium points. Prevalence refers to a measurement of all individuals affected by the disease at a particular time where it is unstable. Meanwhile, free of infection refers to a condition where there is zero infection of ZIKV among the population in a particular time. Each equilibrium point will omit the following eigenvalues where it will determine the stability of the equilibrium points. According to Morgan (2015), there are three types of eigenvalues, and each type of eigenvalue leads to a different behaviour of solutions. For positive eigenvalues, it will lead the solution to approach to infinity solution, meanwhile negative eigenvalues cause the solution to approach zero and imaginary eigenvalues cause a solution to have a spiralling behaviour of solutions. From the table above, the eigenvalues obtained are a combination of positive and negative 20 eigenvalues. If the eigenvalues consist of a combination of all negative real parts, then it indicates a negative feedback which is stable. However, if there is one positive real eigenvalue, then the equilibrium points are unstable

5. CONCLUSION

Based on the result obtained, there are two types of equilibrium points for each fraction of infected people, f . For equilibrium points that consist of combination of all negative real parts –this indicates a negative feedback and this is called the free of infection of equilibrium points. At this point, the rate of people infected by ZIKV will tend to be zero. Then, the rate of infected pregnant women will also tend to be zero. Thus, it will reduce the risk of microcephalic babies caused by ZIKV. Meanwhile, for the prevalence equilibrium points, the set of eigenvalues has at least one positive real part which makes it unstable. The rate of pregnant women infected by

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ZIKV at this point will approach infinity since the rate of infected people also approaches infinity. Hence, it will not reduce the risk of microcephaly induced by ZIKV. This project focuses on finding the local stability analysis from the model of microcephaly induced by ZIKV. Therefore, further studies on the derivation of the model are therefore needed to predict the risk of ZIKV in causing microcephaly.

6. REFERENCES

[1] Barlas, Y., & Ya¸sarcan, H. (n.d.). A Method For Finding Equilibrium Points of a Non- Linear Dynamic Model. Besnard, M., Lastère, S., Teissier, A., Cao-Lormeau, V. M., & Musso, D. (2014). Evidence of perinatal transmission of zika virus, French Polynesia, December 2013 and February 2014. Eurosurveillance, 19(13), 1–4.

[2] Cauchemez, S., Besnard, M., Bompard, P., Dub, T., Guillemette-Artur, P., Eyrolle-Guignot, D., Mallet, H.-P. (2016). Association between Zika virus and microcephaly in French Polynesia, 2013âC“15: a retrospective study. www.thelancet.com, 387, 2125–2132. Retrieved from http://www.thelancet.com/pdfs/journals/lancet/PIIS01406736(16)00651-6.pdf

[3] Dana, F., & Branswell, H. (2016). Zika virus likely tied to Brazil's surge in babies born with small heads, CDC saysAP A child born in Brazil late last year with microcephaly. https://www.statnews.com/2016/01/13/zika\discretionary{}{}{}brazil\discretionary{}{}{}cdc \discretionary{-}

[4] Duffy, M. R., Chen, T.-H., Hannock, T. W., Ann, P. M., Jacob, K. L., & Robert, L. S. (2009). Zika Virus Outbreak on Yap Island. ission. The New England Journal of Medicine, 360, 2536–2543.

[5] Enos, J. R., Schott, R., & Schott, E. (n.d.). Modeling the Chikungunya Virus: A System Dynamics Approach. US Military Academy, 1–13.

[6] Foy, B. D., Kobylinski, K. C., Foy, J. L. C., Blitvich, B. J., da Rosa, A. T., Haddow, A. D., Tesh, R. B. (2011). Probable Non-Vector-borne Transmission of Zika Virus, Colorado, USA. Emerging Infectious Diseases, 17(5), 880–882. 23.

[7] Heymann, D. L., Hodgson, A., Alpha Sall, A., Freedman, D. O., Erin Staples, J., Althabe, F., Menon, K. U. (2016). Zika virus and microcephaly: why is this situation a PHEIC? www.thelancet.com, 387, 719–721. http://www.thelancet.com/pdfs/ journals/lancet/PIIS0140-6736(16)00320-2.pdf

[8] Morgan, R. (2015). Rose- Hulman Undergraduate Mathematics Journal Linearization and Stability Analysis of Nonlinear Problems. Rose-Hulman Institute of Technology,16(2),68– 91. http://www.rosehulman.edu/mathjournal

[9] Muñoz Pizza, D. M., Loaiza, A. M., Montoya, J. F. A., Manrique, O. A., Sossa, V. A., Abello Muñoz, C. A., Enríquez, M. A. (2016). A Model for the Risk of Microcephaly Induced by the Zika Virus (ZIKV). Open Journal of Modelling and Simulation, 4, 109–117. Retrieved http://www.scirp.org/journal/ojmsihttp://www.scirp.org/journal/ojmsihttp://www.scirp.org/journal/ojmsi

[10] Rasmussen, S. A., Jamieson, D. J., Honein, M. A., & Petersen, L. R. (2016). Zika Virus and Birth Defects Reviewing the Evidence for Causality. New England Journal of Medicine, 374(20), 1981–1987.

[11] Rodriguez-Morales, A. J., Ruiz, P., Tabares, J., Ossa, C. A., Yepes-Echeverry, M. C., Ramirez Jaramillo, V., Grobusch, M. P. (2017). Mapping the ecoepidemiology of Zika virus infection in urban and rural areas of Pereira, Risaralda, Colombia, 2015e2016: Implications for public health and travel medicine. Elsevier, 1–10. http://www.travelmedicinejournal.com/article/S1477-8939(17)30075-3/pdf

[12] Wang, J.-N., & Ling, F. (2016). Zika Virus Infection and Microcephaly: Evidence for a Causal Link. International Journal of Environmental Research and Public Health, 13(1031), 1–9. 24

p-ISSN 1675-7939; e-ISSN 2289-4934

[13] WHO. (2016). Zika virus and safe blood supply: Questions and answers. Retrieved from http://www.who.int/features/qa/zika\discretionary{-}{}{}safe\ discretionary{-}{}{}blood/e
[14] WHO. (2017). WHO | Zika virus. World Health Organization. Retrieved from http:// www.who.int/mediacentre/factsheets/zika/en/
[15] World Health Organizations. (2015). WHO-Microcephaly. Retrieved from http://www.who .int/mediacentre/factsheets/microcephaly/en

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