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THE EFFECTS OF VACCINATION TO THE DYNAMICS OF RUBELLA VIRUS WITH SEASONALITY

ABADI*, RUDIANTO ARTIONO, BUDI PRIYO PRAWOTO

Department of Mathematics, Universitas Negeri Surabaya, Surabaya 60231, Indonesia

Abstract. This paper studies the transmission model of rubella virus in the population of women of childbearing age who transmit the disease to babies they gave birth to. The analysis is divided for system with seasonality only and system with seasonality and vaccination. Basic reproduction number of the first system is calculated and used to determined the endemic state which corresponds to a stable periodic solution. The information, namely parameter values when endemic state of first system taken place are then used to study the impact of vaccination to control rubella transmission in the second system. The results shows that vaccination program is helpful to eradicate the virus. We also obtained the threshold for the coverage and efficacy of the vaccination program.

Keywords: rubella; seasonality; vaccination; stability.

2010 AMS Subject Classification: 37N25, 92B05.

1. INTRODUCTION

Since the outbreak of congenital cataracts due to maternal rubella infection (German measles) in 1941, rubella has remained an important disease and public health concern worldwide [10]. Congenital Rubella Syndrome (CRS) is the most feared complications resulted from rubella infection to the early-phase fetus.

*Corresponding author

E-mail address: abadi@unesa.ac.id

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In order to control, eliminate, or even eradicate the spread of rubella virus among human population, there are many efforts have been done. The implementation of immunization using rubella-containing vaccine is the most effective effort in controlling the transmission of rubella virus. For example, in the Americas the use of vaccine eliminated rubella in 2009 [10], while in Australia the virus has been reduced by 99% in 2010 compared to the pre-vaccination period (1960–70) [8].

The transmission of infectious disease like rubella is affected by pathogen appearance and disappearance, environmental changes, and host-behavior changes [5]. Those are represented in the form of seasonal patterns. For rubella case, in the absence of vaccination, it has annual seasonal outbreaks which usually occur in the spring and large epidemic every 3-9 years ([5], [11], [10]). In epidemiology, such seasonality is considered as the contact rate of virus and represented by functions that have periodic/cyclic behavior (see [4]). A fundamental concept in the study of disease transmission is the basic reproduction ratio/number [3]. It is used as the threshold parameter to determine the occurrence endemic of the disease or not.

Seasonality in the transmission of rubella virus is implied to the effort for controlling, eliminating or eventually eradicating the disease. Common approach to control infectious diseases worldwide is by implementation of vaccination program. There are many strategies that might be used in the implementation of vaccination program. Grassly and Fraser [9] derived some results from applying routine and pulse vaccination strategies for infectious diseases. They concluded the importance of considering the interaction of control strategies with seasonal dynamics and the importance of considering the timing of immunization days. Gao et. al. [7] studied the effects of mixed vaccination strategy, namely first vaccination and pulse vaccination, in SIRS epidemic model with vertical transmission and periodic infection rate. They found the threshold parameter for a disease to be extinct or persist. They concluded that mixed vaccination strategy works for disease control. Gao, et. al. [8] showed that selective vaccination to schoolgirl applied by Australian government in the period of 1971 – 88 reduced CRS incidence by 90%, but only reduced 1 – 4% in rubella incidence. Wu et. al. [17] studied age-structured transmission model of rubella by comparing seven vaccination strategies for reducing CRS burden in East Java, Indonesia. Based on those comparison results, they recommended that

substituting either 9-month or both 9-month and 6-year-old measles vaccine with a combined measles-rubella vaccine is much more effective and cost-effective. More vaccination strategies implemented in WHO regions are explained in the work by Lambert et. al. [10]. One of their recommendations says that for countries newly introducing rubella-containing vaccine should begin with MR campaign for a wide-range age, then immediately followed by MR or MMR vaccines in one or two doses routine vaccination program. In addition, countries should apply immunization program to women of childbearing age besides adolescent girls.

This paper aims to study the transmission models of rubella virus with seasonality and vaccination. Regarding the recommendation in [10], the study focuses on women of childbearing age population. Because we also want to study the probability of CRS incidence, the study also focuses on newly born infants of rubella infected women of childbearing age, in particular infected infants due to vertical transmission and those who are recovered from rubella. The model follows the one studied by Sun and Hsieh [15], particularly its vaccination modeling. The study starts with the analysis of system with seasonality only in order to determine threshold parameter when outbreaks take place. By knowing threshold parameter for endemic of the first system, we continue the analysis for the second system that combined seasonality with vaccination. The purpose of the analysis of the second system is to study the effects vaccination to the endemic state of the first system.

2. MATERIALS AND METHODS

The mathematical model under study consists of two populations, namely childbearing age women and newly born infants of rubella infected mothers. This model is the refinement of our work in [1] that considered seasonality of rubella incidence in women population. In this model we also consider the implementation of a vaccination strategy which is applied to the childbearing age women. By considering a vertical transmission we also studied the impact of the virus to newly born infants with CRS. In this study we used Susceptibles (S) – Exposed/Latent (E) – Infectives (I) – Recovered (R) model for the women and we only focus on the dynamic of the virus in the infants. The assumptions used in the model are the followings.

i. The women population is assumed to be closed,

ii. The dynamics of susceptible women population is affected by natural birth rate, the natural death rate and contacts between infective women with susceptible individuals,

iii. the infection rate is assumed to be seasonal,

iv. There is an incubation rate before exposed individuals become infective individuals,

v. Less than three months of pregnancy of infected infants due to vertical transmission will be aborted, according to medical consideration,

vi. Vaccination program being implemented for a certain coverage and efficacy level.

Following the idea by Sun and Hsieh [15], the model is formulated as follows.

$$
\begin{aligned}
\frac{dS_m}{dt} &= \alpha N - \frac{\beta(t)(1-p)I_m S_m}{N} - \frac{(1-q)p\beta(t)I_M S_M}{N} - (\mu + qp)S_m \\
\frac{dE_m}{dt} &= \frac{\beta(t)(1-p)I_m S_m}{N} + \frac{(1-q)p\beta(t)I_M S_M}{N} - (\eta + \mu)E_m \\
\frac{dI_m}{dt} &= \eta E_m - (\theta + \mu)I_m \\
\frac{dR_m}{dt} &= \theta I_m - \mu R_m + qpS_M \\
\frac{dI_c}{dt} &= \delta I_m - (\rho + \tau)I_c \\
\frac{dR_c}{dt} &= \rho I_c - \tau R_c.
\end{aligned} \tag{1}
$$

where S_m, E_m, I_m, and R_m are Susceptible-Exposed-Infectives-Recovered childbearing age women, respectively, while $I_c$and R_c are infectives and recovered infants, respectively. α is the birth rate of the women,

$$\beta(t) = \beta_0(1 + \varepsilon\cos(2\pi t)) \tag{2}$$

is the seasonal infection rate of infective women to susceptible women (See Dietz [4] for reference), μ is the natural death rate of the women, η is the constant incubation rate of exposed women to become infective women, θ is the recovery rate of women from being infectives, δ is the proportion birth rate from infective mothers, ρ is the recovery rate of the children from being infectives, τ is the natural death rate of the children, whereas p the number of child bearing women being vaccinated (vaccine coverage rate, $0 \leq p \leq 1$) and q the proportion of susceptible women being recovered (vaccine efficacy rate, $0 \leq q \leq 1$). All parameters of the system are assumed to be non-negative.

Using the following re-scaling

$$\bar{S}_M = \frac{S_M}{N},\ \bar{E}_M = \frac{E_M}{N}, \bar{I}_M = \frac{I_M}{N}, \bar{R}_M = \frac{R_M}{N}, \bar{I}_C = \frac{I_C}{N}, \bar{R}_C = \frac{R_C}{N}$$

and after dropping the bars, we obtained the following system.

$$\begin{aligned}
\frac{dS_m}{dt} &= \alpha - \beta(t)(1-p)I_m S_m - (1-q)p\beta(t)I_M S_M - (\mu + qp)S_m \\
\frac{dE_m}{dt} &= \beta(t)(1-p)I_m S_m + (1-q)p\beta(t)I_M S_M - (\eta + \mu)E_m \\
\frac{dI_m}{dt} &= \eta E_m - (\theta + \mu)I_m \\
\frac{dR_m}{dt} &= \theta I_m - \mu R_m + qpS_M \\
\frac{dI_c}{dt} &= \delta I_m - (\rho + \tau)I_c \\
\frac{dR_c}{dt} &= \rho I_c - \tau R_c.
\end{aligned} \tag{3}$$

with $\beta(t)$ is the same as (2).

The analysis of system (3) was started with finding the equilibria of the system. The equilibria being obtained is then determined their stability as done by Aron and Schwartz [2], Moneim and Greenhalgh [12] or Wang and Zhao [16], or Gao et. al. [7]. Finally, we did numerical simulations to illustrate the analysis and drew the interpretation of the solutions.

3. Results and Discussion

As we wanted to study the effects of vaccination to the transmission of the virus, the analysis of system (3) were divided into two parts. First part is the system without vaccination and the second part is the one with vaccination.

3.1. System without Vaccination.

The purpose of analyzing the following system is to determine the threshold quantities with which the stability of the solutions is concluded. By taking the values of $p = 0$ and $q = 0$ in system (3) that correspond to no vaccination being implemented to women population, resulting in the following system.

$$
\begin{aligned}
\frac{dS_m}{dt} &= \alpha - \beta_0(1+\varepsilon\cos(2\pi t))I_m S_m - \mu S_m \\
\frac{dE_m}{dt} &= \beta_0(1+\varepsilon\cos(2\pi t))I_m S_m - (\eta+\mu)E_m \\
\frac{dI_m}{dt} &= \eta E_m - (\theta+\mu)I_m \\
\frac{dR_m}{dt} &= \theta I_m - \mu R_m \\
\frac{dI_c}{dt} &= \delta I_m - (\rho+\tau)I_c \\
\frac{dR_c}{dt} &= \rho I_c - \tau R_c.
\end{aligned} \tag{4}
$$

The equilibria of system (4) were obtained by taking the right-hand sides of (4) equal zeroes. The *Disease-Free Equilibrium* (*DFE*) was reached by taking $I_m = I_c = 0$, to have

$$DFE := (\frac{\alpha}{\mu}, 0, 0, 0, 0, 0). \tag{5}$$

Meanwhile, the *Endemic Solution* (*ES*) is given by

$$ES := (S_m^*, E_m^*, I_m^*, R_m^*, I_c^*, R_c^*) \tag{6}$$

where

$$
\begin{aligned}
S_m^* &= \frac{\alpha}{\mu R_0(1+\varepsilon\cos(2\pi t))} \\
E_m^* &= \frac{\alpha(R_0(1+\varepsilon\cos(2\pi t))-1)}{(\mu+\eta)(1+\varepsilon\cos(2\pi t))} \\
I_m^* &= \frac{\mu(R_0(1+\varepsilon\cos(2\pi t))-1)}{\beta_0(1+\varepsilon\cos(2\pi t))} \\
R_m^* &= \frac{\theta(R_0(1+\varepsilon\cos(2\pi t))-1)}{\beta_0(1+\varepsilon\cos(2\pi t))} \\
I_c^* &= \frac{\mu\delta(R_0(1+\varepsilon\cos(2\pi t))-1)}{\beta_0(\rho+\tau)(1+\varepsilon\cos(2\pi t))} \\
R_c^* &= \frac{\rho\delta(R_0(1+\varepsilon\cos(2\pi t))-1)}{\beta_0\tau(\rho+\tau)(1+\varepsilon\cos(2\pi t))}
\end{aligned}
$$

and

$$R_0 = \int_0^1 \frac{\eta\beta(t)S_{DFE}}{(\eta+\mu)(\theta+\mu)}dt. \tag{7}$$

(See Moneim and Greenhalgh [12] or Wang and Zhao [16] for references on threshold quantities of non-autonomous/periodic systems). It is obvious that *ES* is a periodic solution.

Taking $\beta(t) = \beta_0(1+\varepsilon\cos(2\pi t))$ (from (2))and $S_{DFE} = \frac{\alpha}{\mu}$ (from (5)) we have

$$R_0 = \frac{\alpha\eta\beta_0}{\mu(\eta+\mu)(\theta+\mu)}, \tag{8}$$

i.e. the basic reproduction ratio for rubella virus transmission with seasonality.

3.1.1. *Simulation I.* Considering the basic reproduction (8), for the purpose of numerical simulation we choose parameter values as presented in Table 1.

TABLE 1. Parameter values.

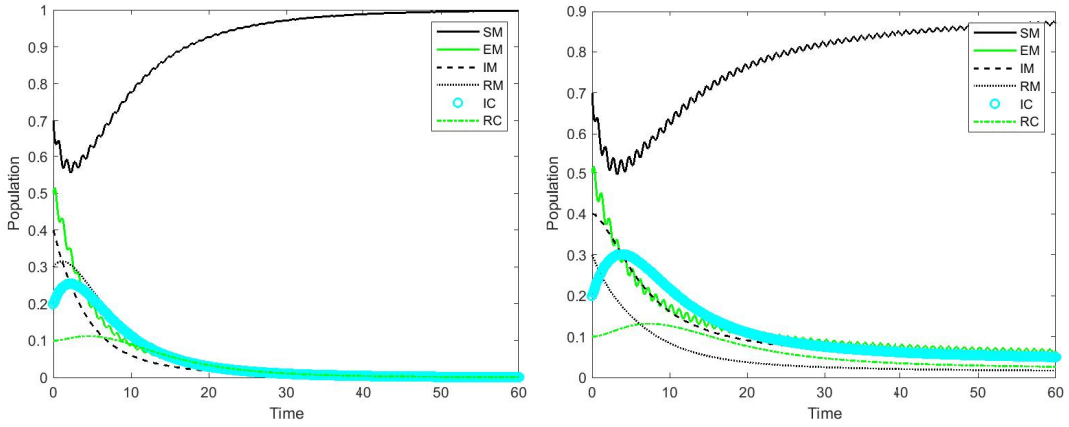
Description	Parameter	Values (Day^{-1})
Contact rate	β_0	0.9
Amplitude of periodicity	ε	0.8
Birth rate of women	α	0.3
Natural death rate of women	μ	0.3
Incubation rate of infective women	η	0.3
proportion birth rate of infective infants	δ	0.3
Recovery rate of infective infants	ρ	0.1
Natural death rate of infants	τ	0.2

From (8) and the parameter values as in Table 1, we obtain the threshold quantity of the recovery rate of infective women

$$\theta = \frac{\beta\eta - \mu\eta - \mu^2}{\mu+\eta} = 0.15,$$

from which we can determine the stability of the *DFE* and the occurrence of endemic solution which is, in this case, a stable periodic orbit. These are confirmed by Fig. 1.

The stability of *DFE* can be proven by following the methods in [6], [12], or [15]. Meanwhile, the stability of *ES* can be proven by using the methods in [2], [16], or [7].



(i) (ii)

FIGURE 1. (i) Stable Disease Free Equilibrium for $\theta = 0.3$ ($R_0 < 1$), and (ii) Stable Endemic (periodic) Solution for $\theta = 0.1$ ($R_0 > 1$).

3.2. System with Vaccination. Having the information about the dynamics of rubella virus transmission with seasonal contact rate, in this subsection we study the impact of vaccination applied to susceptible women population, particularly in the endemic state. Hence, we analyze system (3) where vaccine coverage rate (p) and vaccine efficacy rate (q) are considered.

The disease free state of system (3) is given by

$$DFE_V := (\frac{\alpha}{pq+\mu}, 0, 0, \frac{pq\alpha}{\mu(pq+\mu)}, 0, 0). \tag{9}$$

Meanwhile, the *Endemic Solution* is given by

$$ES_V := (S_m^{**}, E_m^{**}, I_m^{**}, R_m^{**}, I_c^{**}, R_c^{**}) \tag{10}$$

where

$$\begin{aligned}
S_m^{**}(t) &= f_1(v^T, \cos 2\pi t) \\
E_m^{**}(t) &= f_2(v^T, \cos 2\pi t) \\
I_m^{**}(t) &= f_3(v^T, \cos 2\pi t) \\
R_m^{**}(t) &= f_4(v^T, \cos 2\pi t) \\
I_c^{**}(t) &= f_5(v^T, \cos 2\pi t) \\
R_c^{**}(t) &= f_6(v^T, \cos 2\pi t)
\end{aligned}$$

with ν is the vector whose components are the parameters of system (3). This endemic solution, ES_V, is a periodic orbit.

Following similar lines as the analysis of system 4, by employing DFE_V we obtain the averaged basic reproduction ratio

$$R_0 = \frac{\alpha\eta\beta_0}{(pq+\mu)(\eta+\mu)(\theta+\mu)}. \tag{11}$$

3.2.1. *Simulation II.* We now ready to study the dynamics of rubella virus transmission when vaccination program is implemented. Starting from the endemic state which takes place whenever

$$q < \frac{\alpha\eta\beta_0 - \mu^2\eta - \eta\mu\theta - \mu^3 - \mu^2\theta}{p(\eta\mu + \eta\theta + \mu^2 + \mu\theta)}. \tag{12}$$

This corresponds to $R_0 > 1$.

Taking the parameter values are the same as those in the Simulation I, we have

$$q < \frac{0.0375}{p}.$$

As $0 \leq p \leq 1$ we may take $p = 0.8$ such that $q < 0.0468$. So, $q = 0.0468$ is the maximum vaccine efficacy that the endemic of rubella virus transmission occurs. On the other hand, if we take $q > 0.0468$ the condition (12) is violated and hence, we are in the disease free state. Fig. 2 illustrates this situation. In Fig 2 (i), due to small vaccine efficacy ($q = 0.04$) there exist rubella incidence in women population and, as a consequence, in infants population as well. This is a stable periodic orbit. (See [2], [16], or [7] for the methods for determining the stability of periodic solution). Fig. 2 (ii) shows that increasing vaccine efficacy greater than 0.0468 results in eradication of virus transmission and at the same time recovered individuals increase in number. Taking $q = 0.4$ the solution converges to the stable disease free equilibrium. (See [6], [12] or [15] for stability theorem for *DFE*).

4. CONCLUSIONS

The determination of the basic ratio number of both systems with seasonality only (4) and with seasonality combined with vaccination (3) is an important stage of the analysis. From the endemic state of (4) it is easy to understand how is the impact of vaccination to control

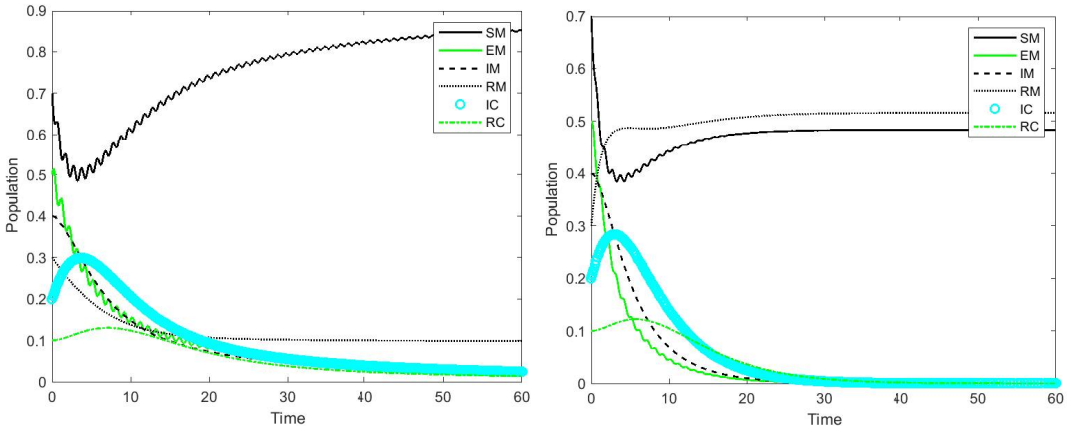


FIGURE 2. (i) Stable Endemic (periodic) solution for $q = 0.04$ ($R_0 > 1$), and (ii) Stable Disease Free Equilibrium for $q = 0.4$ ($R_0 < 1$).

rubella virus transmission. The analysis gives the conditions of vaccination coverage (p) and vaccination efficacy (q) to eliminate or eventually to eradicate the virus. The occurrences of the periodic solution of the endemic state of the systems might be further studied to find possible periodic doubling bifurcations (see [2] and [14]) and other bifurcations.

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CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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