Maternal Antibody Susceptible Vaccinated Infected Recovered (MSVIR) Model for Tetanus Disease and Its Applications in Indonesia

Purnami Widyaningsih, Primadita Candrawati, Sutanto, Dewi Retno Sari Saputro

Mathematics Department of Mathematics and Natural Sciences Faculty Sebelas Maret University, Surakarta, Indonesia
E-mail: purnami.w@staff.uns.ac.id, primaditacandrawati12@gmail.com, sutantomipa@gmail.com, dewiretnoss@staff.uns.ac.id

Abstract. Tetanus is caused by Clostridium tetani bacteria that infect open wounds. Tetanus infection can cause death if not treated promptly. SIR models are constructed to explain the spread of infectious diseases. Tetanus is not an infectious disease, but SIR models still can be used. Infected persons can not transmit the disease through contact. Tetanus infection is affected by the environment and first aid when injured. Lack of environment and awareness in first aid will increase the case of tetanus. Prevention efforts are done by vaccination in children, women of childbearing age, and pregnant women as protection for mother and baby (maternal antibody). The purposes of this research are to formulate SIR model with vaccination and maternal antibody (MSVIR) for tetanus disease and to apply the model in Indonesia. The MSVIR model is a first order linear differential equation system with five dependent variables, there are M, S, V, I, and R, and an independent variable t (time). The parameter’s values were estimated based on data in 2009-2014. The accuracy of this model was measured based on data in 2015-2016 years. The relative error rates on 2015-2016 were -0.0567 and 0.0825. The model is considered good enough. Based on the predictions during 2011-2030, the incidence of tetanus will increase 6.62% by 1.2% average increase per year.

1. Introduction
Tetanus disease is caused by Clostridium tetani bacteria which can infect all ages. Bacteria infect humans through open wounds exposed to dirt, punctured by rusty, or exposed to burns. Tetanus is not an infectious disease so that healthy individuals can not be infected by interacting with infected individuals. Clostridium tetani can not survive with oxygen so that this bacteria can not spread through the air. However, tetanus infection can be fatal or can cause death.

Tetanus still infects many adults. There was a rapid increase in incidence of tetanus, from 225 people in 2013 to 1032 people in 2014. In 2016, Indonesia ranked 7th in the world with the most cases of tetanus infection according to the WHO version [20].

Vaccination is commonly used for controlling diseases such as measles, diphtheria, polio, pertussis, tuberculosis, tetanus, etc. Now, the vaccination program is provided in all developing countries against these diseases. Usually there are different schedules for different vaccines and diseases. As an effort to control tetanus infection, for example, vaccination is carried out on toddlers, children aged 6-9 years, women of childbearing age, and pregnant women. Immunity
from the mother’s body will be distributed to the baby through the placenta, so that the baby gets passive immune from the mother.

Mathematical modeling can be used to study the spread of diseases. Historically, researchers have used mathematical models to identify the spread of infectious diseases such as measles [19, 14, 15], rubella [6], HIV [12, 9], tuberculosis [21], to what just happened such as ebola [2] and Zika virus [4].

In 1989, Hethcote [7] constructs the susceptible infected recovered (SIR) model to determine the spread of infectious diseases. In 2011, Liu et al. [13] developed the SIR model with vaccination. In this model vaccinated compartment is added, which is a group of individuals who have received the vaccine. SIR model with vaccination is written as susceptible vaccinated infected recovered (SVIR) model. Alexander et al. [1] and Shim [16] used SVIR models to study the transmission dynamics of influenza with vaccination. In 2000, Hethcote [8] developed the SIR model by adding a maternal antibody compartment, which is a group individuals who have received passive immune from the mother and an exposed compartment, which is a group individuals who have been infected but the people still in the incubation period. SIR model with passive immune and exposed is written as maternal antibody susceptible exposed infected recovered (MSEIR). At the models, Hethcote [8] considered the MSEIR models with the total population is not constant.

Along with the development of science, mathematical modeling is not only used to study the spread of infectious diseases, but also non-communicable diseases such as diabetes. Boutayeb et al. [5] introduced the diabetes complication (DC) model to find out how many changes of diabetics without complications (D) and diabetics with complications (C). In the DC model the number of new patients (incidence) of diabetes is assumed to be constant. The susceptible diabetes complication (SDC) model was developed by Widyaningsih et al. [22] with the number of incidences is not constant and is determined by considering lifestyle factors and genetic factors. Even public illnes as such as drugs can also be modeled. Sutanto et al. [17] have used the analogy of ebola model with isolation treatment [2] in drug abuse with rehabilitation. This can be done because there are similarities characteristic of its spread, that is through social interaction as media spread.

Tetanus is not an infectious disease so it is assumed that infected individuals can not transmit the disease through contact. Tetanus infects susceptible individuals when the wound is exposed to Clostridium tetani.

By combining of Liu et al. [13] model and Hethcote [8] model, maternal antibody susceptible vaccinated infected recovered (MSVIR) model will be constructed for infectious diseases. Motivated by the fact that the DC model and SDC model can be used to study the spread of non-communicable diseases, the MSVIR model will be established for tetanus. Here the total population is assumed to be changing in size. Then, the model is applied to tetanus disease in Indonesia.

2. The SIR Model

The SIR model was introduced by Kermack and McKendrick [10] in 1927. The SIR model was developed by Hethcote [7] to explain the spread of measles, chickenpox, diphteria, polio, and pertussis. Population is divided into three compartments which are susceptible (S), infected (I), and recovered (R). Susceptible compartment which include all individuals that stands the risk of being infected. Infected compartment which include all individuals that are infected and actively infectious. Recovered compartment which include all individuals that have experienced recovery.

The model is assumed to be constant or there is no change in the population at any time, all of new births are assumed healthy and belong to susceptible compartment, and there is only one disease in the population. Birth rate and death rate are assumed to be equal ($\mu$), so that the
susceptible compartment increases by $\mu N$ individuals as the number of births. All individuals in the population mix homogeneously so that transmission can occur to susceptible individuals when in direct contact with infected individuals. On the other word, Hethcote [7] SIR model was constructed for infectious diseases. If $\beta$ is the transmission rate, then the number of individuals $S$ who are infected as much as $\beta SI_N$. The complete SIR model by Hethcote [7] is

$$\begin{align*}
\frac{dS}{dt} &= \mu N - \beta SI_N - \mu S \\
\frac{dI}{dt} &= \beta SI_N - \gamma I - \mu I \\
\frac{dR}{dt} &= \gamma I - \mu R,
\end{align*}$$

where $S(0) > 0, I(0) > 0, R(0) \geq 0$ and $\mu, \beta, \gamma > 0$. The three parameters consecutively state birth rate or natural mortality rate, the transmission rate, and recovery rate. Model (1) is a first order nonlinear differential equation system.

3. The MSVIR model

An increase in tetanus sufferers is influenced by the number of incidences. Incidence is the proportion of the number of new cases to the number of people at risk in an area. Tetanus-prone areas tend to have dirty environments or unhealthy lifestyles. According to WHO [20], the developing countries watch out for tetanus because their awareness of a healthy environment is still low. In addition, in developing countries there are still remote areas with limited medical devices so that during childbirth there are still many non-sterile assistive device.

Regarding to “spread” of tetanus disease the population is divided into three compartments. Susceptible (S) compartment which include all individuals that stands the risk of being infected by tetanus. Infected (I) compartment which include all individuals that are infected by tetanus. Recovered (R) compartment which include all individuals that have experienced recovery from tetanus. Different from model (1), tetanus is not an infectious disease so tetanus infection is not through contact with infected individuals. S individuals are infected through wounds exposed to dirt and contain tetanus bacteria. According to Baldy et al. [3], vaccination is a program to actively increase a person’s immunity against a disease. Prevention of tetanus is done by vaccinating susceptible individuals. DPT vaccine for toddlers, DT vaccine for children 6-9 years, and TT vaccine for women of childbearing age and pregnant women. Vaccinated individuals are grouped into vaccinated (V) compartment. Pregnant women who are vaccinated will transfer passive immunity to the conceived baby, so that when the baby is born will be grouped into maternal antibody (M) compartment.

It is assumed that the population is not constant, so the birth rate is not the same as the death rate. If the birth rate $\theta$, the number of birth is $\theta N$ individuals. In this study, births are classified into two, ie birth with passive immunity and birth without passive immunity. If $p$ is the proportion of individuals who born with passive immunity, the compartment of M increases by $p\theta N$, and the compartment of S increases by $(1-p)\theta N$.

In this model, there are two types of death, ie natural death and death caused of tetanus. If death caused of tetanus rate is $\sigma$, then the compartment of I decreases by $\sigma I$. If the natural death rate is denoted by $\mu$, then each compartment of $M, S, V, I$, and $R$ will decrease by $\mu M, \mu S, \mu V, \mu I$, and $\mu R$.

Babies who have passive immunity will turn into susceptible individuals after 6 months. If the effectiveness of passive immune rate is $\delta$, then the compartment of $S$ will increase by $\delta M$. If vaccination rate is $\alpha$, then the compartment of $S$ will decrease by $\alpha S$ and the compartment of $V$ will increases by $\alpha S$. Tetanus vaccine does not last a lifetime, so vaccinated individuals
can still be possible to become susceptible individuals again. If effectiveness of vaccine rate is $\omega$, then the compartment of $V$ decrease by $\omega V$ and the compartment of $S$ increases by $\omega V$.

Tetanus infected individuals not only from susceptible compartment. There are vaccinated individuals who are infected with tetanus because of their weak immune system and dirty environment. If the infection rate is $\beta$ and vaccine failure rate is $\beta_1$ then the compartment of $I$ increases by $\beta S$ and $\beta_1 V$. The compartment of $R$ increases because of infected individuals who recover after getting treatment and Anti Tetanus Serum (ATS). If the recovery rate is $\gamma$ then the compartment of $R$ increases by $\gamma I$. Therefore, the complete maternal antibody susceptible vaccinated infected recovered (MSVIR) model for tetanus disease is

$$\begin{align*}
\frac{dM}{dt} &= p\theta N - (\mu + \delta)M \\
\frac{dS}{dt} &= (1 - p)\theta N + \delta M + \omega V - (\beta + \alpha + \mu)S \\
\frac{dV}{dt} &= \alpha S - (\beta_1 + \omega + \mu)V \\
\frac{dI}{dt} &= \beta S + \beta_1 V - (\gamma + \mu + \sigma)I \\
\frac{dR}{dt} &= \gamma I - \mu R.
\end{align*}$$

(2)

where $M(0) \geq 0$, $S(0) \geq 0$, $V(0) \geq 0$, $I(0) \geq 0$, $R(0) \geq 0$ and $\theta, \alpha, \beta, \beta_1, \gamma, \delta, \omega, \sigma, \mu > 0$. The nine parameters consecutively state birth rate, vaccination rate, infection rate, vaccine failure rate, recovery rate, effectiveness of passive immune rate, effectiveness of vaccine rate, death caused of tetanus rate, and natural death rate. Model (2) is a first order linear differential equation system.

4. Application

The MSVIR model is applied to determine population growth of tetanus in Indonesia. Data are obtained from Profil Kesehatan Indonesia Kemenkes RI [18], World bank [23], and World Health Organization (WHO) [20]. The data used are the number of population in Indonesia, the number of individual who get tetanus vaccine, crude birth rate (CBR), crude death rate (CDR), the number of tetanus incidence, and the number of death due to tetanus in 2009-2016.

The data used in estimate the parameters are annual data in 2009-2014. The result of parameters estimation are the proportion of birth with passive immune ($p$) is 0.650516, birth rate ($\theta$) is 0.0181, natural death rate ($\mu$) is 0.00708910, death caused of tetanus rate ($\sigma$) is 0.31179, effectiveness of passive immune rate ($\delta$) is 0.992911, vaccination rate ($\alpha$) is 0.165045, effectiveness of vaccine rate ($\omega$) (based on Lestari [11] effectiveness of vaccine tetanus is 10 years) is 1/10 = 0.1, infection rate ($\beta$) is 0.00000145498, vaccine failure rate ($\beta_1$) is 0.00000156397, and recovery rate ($\gamma$) is 0.651732. Based on the values of these parameters, maternal antibody susceptible vaccinated infected recovered (MSVIR) model for tetanus disease in Indonesia is

$$\begin{align*}
\frac{dM}{dt} &= 0.0117743N - M, \\
\frac{dS}{dt} &= 0.00632566N + 0.992911M + 0.1V - 0.172136S, \\
\frac{dV}{dt} &= 0.165045S - 0.107091V, \\
\frac{dI}{dt} &= 0.00000145498S + 0.00000156397V - I, \\
\frac{dR}{dt} &= 0.651732I - 0.00708910R.
\end{align*}$$

(3)
The system (3) is first order linear differential equation system. The initial value are used refers to the number of individuals M, S, V, I, and R in 2009 \((t=0)\). Based on the data obtained initial value ie

\[
(M(0), S(0), V(0), I(0), R(0)) = (3841909, 208603432, 25110638, 231, 153).
\]

The solution of system (3) with initial value (4) for the first 15 years (2009-2024) is determined using the fourth-order Runge-Kutta algorithm. The solution of the system approach (3) shows the growth pattern of tetanus disease in Indonesia and it is seen in Figure 1. The number of individuals S has decrease considerably who initially (2009) 208603432 people to 116038000 in the 12th year, then the following year slowly rises. The number of individuals V has increase considerably who initially (2009) 25110638 people to 124322000 in the 6th year, then the following year slowly rises. The number of individuals I has a rapid increase who initially 231 people to 361 in the 4th year, then the following year slowly rises until 416 people in the 15th year. Incidence data for the last two years will be compared with the estimation result (model completion). The relative error values of incidence for 2015-2016 are shown in Table 1.

![Figure 1. The number of individual S (yellow), V (purple), and I (green) for the first 15 years.](image)

**Table 1.** Exact value, estimation value, dan relative error of tetanus incidence

| Year | Data | Estimation | Relative error |
|------|------|------------|----------------|
| Incidence | 2015 | 353 | 373 | -0.0567 |
| | 2016 | 412 | 378 | 0.0825 |

Based on Tabel 1, the relative error of tetanus incidence in 2015 was -0.0567, it means that the incidence of tetanus was only 5.67% higher than the actual data. The relative error of tetanus incidence in 2016 was 0.0825 it means that the incidence of tetanus was only 8.25% lower than the actual data. Thus, the MSVIR (3) is accurate enough. The model then is used to predict the incidence of tetanus. The prediction of tetanus incidence based on model (3) for 2017-2024 is shown in Table 2.

**Table 2.** Tetanus incidence in 2017-2024

| Year | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 |
|------|------|------|------|------|------|------|------|------|
| Incidence | 383 | 388 | 393 | 397 | 402 | 406 | 411 | 416 |

The predictions of tetanus incidence will increase by 8.6% between 2017-2024 with an average increase of 1.2% each year. Although the increase is not large, it needs to be watched out and the target of the vaccine also needs to be reviewed.
5. Conclusion

Based on the discussion, it is obtained three conclusions.

(i) The MSVIR model for tetanus disease is

\[
\begin{align*}
\frac{dM}{dt} &= pθN - (μ + δ)M \\
\frac{dS}{dt} &= (1 - p)θN + δM + ωV - (β + α + μ)S \\
\frac{dV}{dt} &= αS - (β_1 + ω + μ)V \\
\frac{dI}{dt} &= βS + β_1V - (γ + μ + σ)I \\
\frac{dR}{dt} &= γI - μR.
\end{align*}
\]

where \( M(0) \geq 0, S(0) \geq 0, V(0) \geq 0, I(0) \geq 0, R(0) \geq 0 \) and \( θ, α, β, β_1, γ, δ, ω, σ, μ > 0 \).

The nine parameters consecutively state birth rate, vaccination rate, infection rate, vaccine failure rate, recovery rate, effectiveness of passive immune rate, effectiveness of vaccine rate, death caused of tetanus rate, and natural death rate.

(ii) The MSVIR model is applied to determine population growth of tetanus in Indonesia. Incidence data for 2015-2016 were compared with the estimation result (model completion). The relative errors of them were no more than 9%. By these measurements the accuracy of the model is classified to be accurate enough.

(iii) In the 2017-2024 time frame, the incidence of tetanus is predicted will increase to 8.6% with an average increase of 1.2% each year.

References

[1] Alexander M E, Bowman C, Moghadas S M, Summers R, Gumel AB, and Sahai B M 2004 A vaccination model for transmission dynamics of influenza SIAM J. Appl. Dyn. Syst. 3 503-524

[2] Azizah A, Widyaningsih P, and Saputro D R S 2017 J.Phys: Conf. Series 855 012008 1-6

[3] Baldy, L. M., S. W. Roush, and L.McIntyre, 2013. Manual for the Surveillance of Vaccine Preventable Diseases, sixth ed., Creat Space Independent Publishing Platform, USA.

[4] Bonyah E and Okosun K O 2016 Mathematical modeling of Zika virus Asian Pacific J. of Tropical Disease 6 673-679

[5] Boutayeb A, Twizell E H, Achouayb K, and Chetouani A 2004 A mathematical model for the burden of diabetes and its complication BioMedical Engineering Online 3 20

[6] Hethcote H W 1983 Measles and rubella in the United States Am. J. Epidemiol. 117 2-13

[7] Hethcote H W 1989 Three basic epidemiological models Ap. Math. Ecology 18 119-144

[8] Hethcote, H. W., 2000. The Mathematics of Infectious Diseases, Society for Industrial and Applied Mathematics 42, 599-653.

[9] Jacquez J A, Simon C P, Koopman J S, Sattenspiel L, and Perry T 1988 Modeling and analyzing HIV transmission: The effect of contact patterns Math. Biosci. 92 119-199

[10] Kermack W O and McKendrick A G 1927 A contribution to the mathematical theory of epidemics Proc. of the Royal Society of London 115 700-721

[11] Lestari N 2011 Epidemologi Penyakit Menular Universitas Sriwijaya

[12] Lin X, Hethcote H W, and van den Driessche P 1993 An epidemiological model for HIV/AIDS with proportional recruitment Math. Biosci. 118 181-195

[13] Liu X, Takeuchi Y, and Iwami S 2008 SVIR epidemic models with vaccination strategies J. of The. Biology 253 1-11

[14] London W P, Yorke J A 1973 Recurrent outbreaks of measles, chickenpox and mumps I: Seasonal variation in contact rates Am. J. Epidemiology 98 453-468

[15] Schenzle D 1984 An age-structured model of pre- and post-vaccination measles transmission IMA J. Math. Appl. Med. Biology 1 169-191
[16] Shim E 2006 A note on epidemic models with infective immigrants and vaccination Math. Biosci. Eng. 3 557-566
[17] Sutanto, Azizah A, Widyaningsih P, and Saputro DRS 2017 AIP Conf. Proc. 1847 020018 (2017) doi: 10.1063/1.4983873
[18] Tim Sekretariat Jenderal Kementerian Kesehatan RI 2010-2017 Profil Kesehatan Indonesia Tahun 2009-2016 (Jakarta: Kementerian Kesehatan Republik Indonesia)
[19] Tudor D W 1985 An age-dependent epidemic model with application to measles Math. Bioscience 73 131-147
[20] WHO (World Health Organization) 2016 Tetanus total reported cases
[21] Widyaningsih P, Nugroho A A, and Saputro DRS 2018 AIP Conf. Proc. 2014 020121-1-020121-6
[22] Widyaningsih P, Affan R C, and Saputro D R S 2018 J. Phys.: Conf. Series 1028 012110, 1-5
[23] World Bank 2016 Birth and Death Rate, Crude