Dynamical analysis of diphtheria epidemic model with natural immunity rate on exposed individuals

N Izzati1,* and A Andriani2

1 Department of Electrical Engineering, Faculty of Engineering, Hasyim Asy’ari University, Tebuireng - Jombang, 61471 Indonesia
2 Department of Informatics Management, Faculty of Information Technology, Hasyim Asy’ari University, Tebuireng - Jombang, 61471 Indonesia

* nailulizzati@unhasy.ac.id

Abstract. Diphtheria disease remains endemic in some countries due to the lack of immunization coverage, such as Indonesia, where healthcare are something need to be pursued and optimized. In the last three years, there are still some areas in Indonesia that its complete basic immunization coverage are less than 50%. Apart from being caused by low immunization coverage, other factors as nutritional adequacy, environmental hygiene and virulence levels of the disease also influence the occurrence of diphtheria outbreaks. In this study, we propose a mathematical model that considers natural immunity rate of the exposed individuals in the spread of diphtheria. This study aims to understand the dynamics of the proposed model. The behavior of the system is known by analysing the stability of its equilibrium points. Numerical simulations using Maple are also carried out to illustrate the dynamics of the system. The stability analysis and numerical simulations show that the disease-free equilibrium point is stable if \( R_0 < 1 \), whereas the endemic equilibrium point is only feasible and stable if \( R_0 > 1 \). The results shown that complete basic immunization coverage and natural immunity rate of the population affect the basic reproduction number.

1. Introduction

Diphtheria is one of the infectious diseases that still looms over Indonesia. During 2017-2019, there were 2870 diphtheria cases and 96 deaths reported [1,2]. Diphtheria is a disease caused by bacteria *Corynebacterium diphteriae*. Diphtheria is characterized by inflammation at the site of infection, especially in the mucous membranes of the pharynx, larynx, tonsils, nose and skin. 94% of diphtheria cases attack the tonsils and pharynx, some of the symptoms are pain in the throat and high fever. The death due to diphtheria occurs if the infected one does not get a proper treatment and has weak immunity. The mortality rate is about 5-20%. The cause of death is mostly due to airway obstruction, damage of the heart muscle, and abnormalities of the central nervous system and kidneys [3].

Regardless of the mortality rate of diphtheria, the disease could be prevented by carrying out complete and routine immunizations according to the child's age. Complete basic immunization is one of the programs of Indonesian government to provide diphtheria vaccine. However, the program still needs to be improved, as there were provinces where the complete basic immunization coverage is less than 50%, such as Papua (29.6%) [1] and Aceh (49.6%) [2]. Aside from having a complete basic immunization, the natural immunity level of an individual also plays important role in preventing diphtheria. A strong natural immunity could be obtained from adequate nutrition, healthy lifestyle, and
good personal and environmental hygiene. The physical environment of the house, such as the type of floor and ventilation, also affects the spread of diphtheria [4].

Many studies discussed mathematical model of the spread of diphtheria. Some of study examined the effect of vaccination program on the spread. For example, Puspita et al considered SIQR model to study the effect of vaccination and quarantine program on the outbreak [5]. Ilahi and Widiana considered SEIR model to study the effectiveness of vaccine in the outbreak [6]. On the other hand, a study discussed SIR model by considering the ability of infected humans to recover naturally, and exclude the effect of medication and vaccine as treatment and prevention [7]. While other studies mentioned the important role of immunization coverage and a proper treatment to minimize the spread [8]. Matsuyama et al indicated that a certain percentage of vaccination coverage has to be satisfied to prevent the epidemic [9]. Djafaraa et al found that high primary vaccination coverage and booster vaccinations for preschool and school-age children are vital to prevent future outbreaks of diphtheria [10]. A study about regression model stated that the increase of percentage of diphtheria immunization coverage and the number of community health centers be able to decrease the number of diphtheria cases [11]. Here, we study SEIQR model that considers natural immunity rate of the exposed individuals in the spread of diphtheria. The model also considers the coverage of complete basic immunization program as prevention, and quarantine program as the treatment. The aim of this study is to understand the dynamics occur in the proposed model.

2. Methods
In the first stage of this study, a library research was carried out to collect information and data about diphtheria, such as the causes, transmission, prevention, treatment, and mortality rate. The information is also derived from interviewing a clinic doctor. The informations and data obtained from the first stage are processed to construct a compartment diagrams and mathematical model of the spread of diphtheria. In the second stage, the dynamics of the constructed model is analyzed by discovering the equilibrium points on its steady states. Stability analysis of the equilibrium points is figured out from the eigenvalues of the characteristic equation. While the basic reproduction number ($R_0$) is obtained from the next-generation matrix. In the third stage, numerical simulations are executed by Maple and elaborated to illustrate the effect of parameter values on $R_0$ and the dynamics occur in the model. Numerical simulations also meant to verified the stability analysis.

3. Results and discussions
This section discusses the process of constructing a mathematical model that describes the spread of diphtheria with the influence of natural immunity rate on exposed individuals. Stability analysis, basic reproduction number and numerical simulations of the model are also discussed.

3.1. Proposed mathematical model
In the spread of diphtheria, let an area with a total population of $N$ is divided into five groups, i.e. susceptible, exposed, infected, quarantine, and recovered. Individuals who do not get vaccinated are included in the susceptible group ($S$), while those who get vaccinated are assumed to be immune and included in the recovered group ($R$). The existence of interaction rate of the susceptible and the infected allows the transmission of diphtheria disease. A susceptible individual who interacts with an infected individual is called an exposed individual ($E$). Exposed individuals who have strong natural immunity are likely not to be infected by diphtheria and are assumed to be included in the susceptible group. While the exposed individuals who have weak natural immunity could be infected by a certain period of time. The infected individual ($I$) will receive treatment and be quarantined. The infected individual in quarantine ($Q$) may recover or die due to diphtheria disease. We assume that individuals who recovered ($R$) cannot be infected by diphtheria anymore, or have become immune to diphtheria. This model also assumes that the population number is affected by natural mortality rate. Based on the assumptions built, we obtain a compartment diagram presented in Figure 1. The proposed model is mathematically expressed by equations (1)-(5).
Figure 1. Compartment diagram of diphtheria epidemic model with natural immunity rate on exposed individuals.

\[
\begin{align*}
\frac{dS}{dt} &= (1 - p)\mu N - \frac{\alpha SI}{N} - \delta S + \phi E \\
\frac{dE}{dt} &= \frac{\alpha SI}{N} - \beta E - \phi E - \delta E \\
\frac{dI}{dt} &= \beta E - \gamma I - \delta I - \theta I \\
\frac{dQ}{dt} &= \gamma I - \epsilon Q - \delta Q \\
\frac{dR}{dt} &= p\mu N + \epsilon Q - \delta R
\end{align*}
\]

Parameters of the system are defined as follows: \( p \) is proportion of vaccinated people within population, \( \mu \) is birth rate, \( \delta \) is natural mortality rate, \( \alpha \) is the rate of interaction of the susceptible and infected, \( \beta \) is transmission rate, \( \phi \) is proportion of the number of exposed individuals with good natural immune, \( \gamma \) is the handling or treatment rate (the rate of infected individuals get quarantined each time unit), \( \epsilon \) is recovery rate, \( \theta \) is mortality rate due to diphtheria. All variables and parameters are positive.

3.2. Steady state
Dynamics of the model, i.e. system (1)-(5), could be studied from the stability of its equilibrium points. The system has two steady states, disease-free equilibrium state \( E_0 = \left(\frac{(1-p)\mu N}{\delta}, 0, 0, 0, \frac{p\mu N}{\delta}\right) \) and endemic equilibrium state \( E_1 = (\hat{s}, \hat{e}, \hat{i}, \hat{q}, \hat{r}) \). State \( E_0 \) is always feasible because all the parameters are positive, whereas \( E_1 \) is conditionally feasible. State \( E_1 \) is lengthy algebraic expressions regarding system parameters. Thus, further analysis of state \( E_1 \) is carried out numerically.

3.3. Basic reproduction number
The value of \( R_0 \) indicates the transmission potential of a disease. To study the basic reproduction number \( R_0 \), we take the derivative of effected classes given in equation (2) and (3) of the model. Let \( x = (E, I) \) and \( \frac{dx}{dt} = F - V \), where 
\[
F = \begin{pmatrix}
\alpha (1-p) \mu \\
\delta & 0 & 0 & 0 & 0 \\
\delta & \beta & 0 & 0 & 0 \\
\delta & 0 & \gamma + \delta & 0 & 0 \\
\delta & 0 & 0 & \gamma + \delta & 0
\end{pmatrix}
\]
and 
\[
V = \begin{pmatrix}
0 & 0 & 0 & 0 & 0 \\
0 & -\beta & 0 & 0 & 0 \\
0 & 0 & -\gamma - \delta & 0 & 0 \\
0 & 0 & 0 & -\gamma - \delta & 0 \\
0 & 0 & 0 & 0 & -\gamma - \delta
\end{pmatrix}
\]
Then, we obtain 
\[
FV^{-1} = \begin{pmatrix}
(\beta + \phi + \delta)E \\
(\alpha \beta)N & 0 & 0 & 0 & 0 \\
0 & -\beta & 0 & 0 & 0 \\
0 & 0 & -\gamma - \delta & 0 & 0 \\
0 & 0 & 0 & -\gamma - \delta & 0
\end{pmatrix}
\]
This matrix is the Jacobian of \( F \) and \( V \) at disease-free equilibrium \( (E_0) \), respectively. \( F \) is the matrix of rates of secondary effected individuals, and \( V \) is the matrix of transmission rates.

The value of \( R_0 \) is defined as the dominant eigen value of \( FV^{-1} \), where
\[
\mathbf{FV}^{-1} = \begin{pmatrix}
\frac{a\beta(1-p)\mu}{\delta(\beta+\phi+\delta)(y+\delta+\theta)} & \frac{a(1-p)\mu}{\delta(y+\delta+\theta)} \\
0 & 0
\end{pmatrix}.
\]

The eigen values of \(\mathbf{FV}^{-1}\) are \(\lambda = 0\) and \(\lambda = \frac{a\beta(1-p)\mu}{\delta(\beta+\phi+\delta)(y+\delta+\theta)}\) therefore the basic reproduction number of the model is \(R_0 = \frac{a\beta(1-p)\mu}{\delta(\beta+\phi+\delta)(y+\delta+\theta)}\).

### 3.4. Local asymptotic stability

In this subsection, the local stability of disease-free and endemic equilibrium are discussed. Jacobian matrix of the system at disease-free state is given by matrix \(J_{E_0}\):

\[
J_{E_0} = \begin{pmatrix}
-\delta & \phi & -\frac{a(1-p)\mu}{\delta} & 0 & 0 \\
0 & -\beta - \phi - \delta & \frac{a(1-p)\mu}{\delta} & 0 & 0 \\
\beta & -\gamma - \delta - \theta & 0 & 0 \\
0 & 0 & \gamma & -\epsilon - \delta & 0 \\
0 & 0 & 0 & \epsilon & -\delta
\end{pmatrix}.
\]

Solving \(|J_{E_0} - \lambda I| = 0\), led us to equation (6), which gives the eigen values of \(J_{E_0}\):

\[
(\delta + \lambda)(\epsilon + \delta + \lambda)(\delta + \lambda) \left[-\lambda^2 - \lambda(y + 2\delta + \theta + \beta + \phi) - (\beta + \phi + \delta)(y + \delta + \theta) + \frac{a\beta(1-p)\mu}{\delta}\right] = 0.
\]

From equation (6), we know that three of the eigen values are negative, i.e. \(\lambda_{1,2} = -\delta, \lambda_3 = -\epsilon - \delta\), and the other two, \(\lambda_4\) and \(\lambda_5\), are defined by polynomial (7).

\[
\frac{1}{(\beta + \phi + \delta)(y + \delta + \theta)} \lambda^2 + \frac{(y + 2\delta + \theta + \beta + \phi)}{(\beta + \phi + \delta)(y + \delta + \theta)} \lambda + 1 - R_0 = 0.
\]

It is clear that \(\lambda_4\) and \(\lambda_5\) are negative if \(1 - R_0 > 0\). In other words, disease-free equilibrium \(E_0\) is asymptotic stable if \(R_0 < 1\) and unstable if \(R_0 > 1\).

As mentioned in subsection 3.2, endemic equilibrium \(E_1\) is not always feasible. \(E_1\) is only feasible and stable under particular condition, i.e \(R_0 > 1\). The existence of \(E_1\) is shown by some scenarios discussed in subsection 3.5.

### 3.5. Numerical simulation

Here, numerical simulations of the system are presented. The initial condition of the simulations is 95% of the total population is susceptible and 5% remained is infected, i.e. \(S(0) = 0.95, E(0) = 0, I(0) = 0.05, Q(0) = 0, R(0) = 0\). Some of parameter values are taken from former researches (i.e. \(\alpha = 0.57\) [5], \(\beta = 0.23\) [12], \(\epsilon = 0.5\) [5]), or processed from various data sources (i.e. \(\mu = 0.019\) and \(\delta = 0.006\) [13], \(\theta = 0.05\) [3]), and some are chosen hypothetically (See Table 1). Here, we elaborate some scenarios to describe the dynamics of the system.

Table 1 shows the results of the scenarios considered in numerical simulations. Scenario A1-A2 illustrate the system in the absence of vaccination program and natural immunity rate of the exposed individuals. From scenario A1, it is known that if there are no prevention nor treatment against diphtheria outbreaks, in this case the complete basic immunization coverage and natural immunity rate are 0, and there is no quarantine for infected individuals, then over time the total population decreases by 50% with \(R_0 = 31,413\). Whereas in scenario A2, even without natural immunity or vaccination, with the treatment in quarantine, the \(R_0 = 4,941\) is lower than scenario A1. Scenarios B1-B2 show the role of immunization coverage in the absence of natural immunity rate. It shown that in scenario B2, with a higher immunization coverage, the \(R_0\) is lower than scenario B1. The same goes in scenario C1-C2 and D1-D2, with a proportion of population who have strong natural immunity, the higher immunization...
coverage, the lower $R_0$. And scenario E shows the result if the coverage of basic immunization program and natural immunity rate were 100%.

**Table 1.** Values of the parameters and numerical simulation results.

| Parameter | A1 | A2 | B1 | B2 | C1 | C2 | D1 | D2 | E  |
|-----------|----|----|----|----|----|----|----|----|----|
| $\gamma$  | 0  | 0.3| 0.3| 0.3| 0.3| 0.3| 0.3| 0.3| 0.3|
| $\phi$    | 0  | 0  | 0  | 0  | 0.3| 0.3| 0.9| 0  | 0  |
| $p$       | 0  | 0  | 0  | 0.9| 0.3| 0.9| 0.3| 0.9| 0  |
| $R_0$     | 31,413| 4,941| 3,459| 0.494| 1.523| 0.218| 0.719| 0.103| 0  |

**Feasible steady states**

- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$

**Stable steady states**

- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$

**$S_f$, $E_1$**

- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$
- $E_0$, $E_1$

**$R_0$**

- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$
- $S_f$, $E_1$

**Total population**

| 0.499 | 2.822 | 2.951 | 3.167 | 3.063 | 3.167 | 3.167 | 3.167 | 3.167 |

Figure 2. (a) Population densities with respect to number of days for $\phi = p = \gamma = 0$, (b) $\phi = 0$, $p = \gamma = 0.3$, (c) $\phi = p = \gamma = 0.3$, (d) $\phi = \gamma = 0.3$, $p = 0.9$, (e) $\phi = 0.9$, $p = \gamma = 0.3$, (f) $\phi = p = 1$, $\gamma = 0.3$. 

Susceptible: green 
Exposed: black 
Infected: red 
Quarantine: yellow 
Recovered: blue
From Table 1, it is also known that the scenario with a higher natural immunity rate has a lower $R_0$. Scenarios with a higher $R_0$ have a higher number of exposed and infected individuals. Meanwhile, scenarios with lower $R_0$ tended to have a higher number of recovered individuals. The dynamics of the system for some scenarios are plotted in Figure 2. The results obtained are in accordance with the concept of basic reproduction number, i.e. if $R_0 > 1$, then each existing infection causes more than one new infection. The disease will be transmitted between people, and there may be an outbreak or epidemic. And if $R_0 < 1$, then each existing infection causes less than one new infection, and the disease will decline and eventually die out [14,15].

4. Conclusion
Based on the results and discussion, it is known that the higher the complete basic immunization coverage, the lower $R_0$. And the more people with strong natural immunity, the lower $R_0$. At the same time, an increase in these two factors causes the exposed, infected, and quarantine decrease, while the recovered increase. The system would be disease free if $R_0 < 1$, and there might be an outbreak if $R_0 > 1$. The results shown that the complete basic immunization coverage and the natural immunity rate of the exposed population influence the dynamics of the model. This leads to bifurcation in the system. However, the existence of bifurcation is not discussed in this article.

Acknowledgement
This study is supported and fully funded by Directorate of Research and Community Service, Ministry of Research and Technology of Republic of Indonesia. Authors would like to thank all colleagues for their contributions to this study, especially to LPPM Hasyim Asy’ari University and Rosydina Robi’aqolbi as Head of Al-Ishlah Health Clinic and staffs.

References
[1] Budijanto D et al 2019 Profil Kesehatan Indonesia 2018 (Jakarta: Ministry of Health of Republic Indonesia) pp 210, 136
[2] Budijanto D et al 2020 Data dan Informasi Profil Kesehatan Indonesia 2019 (Jakarta: Ministry of Health of Republic Indonesia) pp 155, 118
[3] Anggraeni N D et al 2017 Pedoman Pencegahan dan Pengendalian Difteri (Jakarta: Ministry of Health of Republic Indonesia) p 6
[4] Prabowo J and Iriani D U 2020 Journal of Routine Population Health and Public Health (JRPH) 1(1) 20-25
[5] Puspita G, Kharis M, and Supriyono 2017 UNNES J. Math. 6 25-35
[6] Ilahi F and Widiana A 2018 IOP Conf. Ser.: Mater. Sci. Eng. 434 012006
[7] Husain H S 2019 J. Phys.: Conf. Ser. 1280 022051
[8] Izzati N et al 2020 J. Phys.: Conf. Ser. 1663 012042
[9] Matsuyama R et al 2018 PeerJ 6:e4583 https://doi.org/10.7717/peerj.4583
[10] Djaafara B et al 2020 Transmission Dynamics and Control Strategies During the 2017 Diphtheria Outbreak in Jakarta, Indonesia: A Modelling Study https://ssrn.com/abstract=3516127 or http://dx.doi.org/10.2139/ssrn.3516127
[11] Ohyver M and Pudjiastuti H 2018 Procedia Computer Science 135 643–647
[12] Fathoni M I, Mardlijah, and Hariyanto 2015 Pros. Sem. Nas. Mat. dan Pend. Mat. 2015 (Surabaya: Universitas Negeri Surabaya) pp 229-38
[13] Ministry of National Development Planning, Central Bureau of Statistics Indonesia and United Nations Population Find (UNPFPA) Indonesia 2013 Indonesia Population Projection 2010-2035 (Jakarta: BPS-Statistic Indonesia) pp 34, 84-468
[14] Diekmann O et al 1990 J. Math. Biol. 28 pp 365–382 https://doi.org/10.1007/BF00178324
[15] Delamater P L et al 2019 Emerging Infectious Diseases 25(1) https://doi.org/10.3201/eid2501.171901