Mathematical Analysis and Simulation of Measles Infection Spread with SEIRV+D Model

Maja Kukusheva Paneva[1], Natasha Stojkovikj[2], Cveta Martinovska Bande[2] and Limonka Koceva Lazarova[2]

[1] Faculty of Electrical Engineering, Goce Delcev University, Stip, North Macedonia
[2] Faculty of Computer Science, Goce Delcev University, Stip, North Macedonia
maja.kukuseva@ugd.edu.mk
natasa.stojkovik@ugd.edu.mk
cveta.martinovska@ugd.edu.mk
limonka.lazarova@ugd.edu.mk

Abstract. Measles is a highly contagious infectious disease caused by a virus in the paramyxovirus family. Mathematical models for epidemics are useful tools for understanding and predicting epidemic spread and its dynamics. These mathematical models allow researchers to simulate the spread of measles in the population by presenting the interactions between susceptible, exposed, infected, recovered, and vaccinated individuals. In this paper, an improved SEIRV+D model is developed based on known epidemiology models such as the SIR and SEIR models. The interactions between different compartments are given as a system of six Ordinary Differential Equations (ODEs) that represent the dynamics of the model. Additionally, the natural death rate and natural birth rate are considered. One of the key issues in epidemiology models is the reproduction number, which indicates the average number of secondary infections caused by a single infected individual. Another key issue is the disease-free equilibrium point (steady state) that can help predict disease outbreaks. Both the basic reproduction number and the disease-free equilibrium point have been obtained for the developed model. A case study for North Macedonia is analyzed for two different vaccination rates to demonstrate the impact of vaccination.

Keywords: Epidemic Model, Measles, SEIRV+D Model.

1 Introduction

Measles is considered one of the most contagious infectious diseases within the human population, caused by the measles virus, which can result in a wide spectrum of diseases with significant consequences [1-3]. They are transmitted through respiratory droplets when an infected individual coughs and sneezes, or through direct contact with compromised secretions from the nose or throat of an infected individual.

Over a longer period, dynamic models are considered fundamental for understanding the expansion of contagious diseases within a population [4]. Dynamic models aim to describe the spread and progression of infectious diseases within a population over time. These models aim to capture the complex interactions between individuals and assist in the creation of effective strategies to control the disease, such as vaccination, quarantine, and social distancing.

Modeling measles is based on the SIR (Susceptible-Infected-Recovered) model, as patients who have overcome the disease gain permanent immunity [5-8]. In the past 20 years, multiple variations of the SIR model have been developed by different authors, incorporating factors such as inoculation (vaccination), coinfection, age, and seasonal parameters [9]. All these models strive to improve the accuracy of predictions based on the limited available data on incidents versus mortality.

In this paper, an SEIRV+D model is developed for a case study in North Macedonia under different scenarios. Specifically, the spread of the measles epidemic with a vaccination rate of 74.8%, as in 2018, will be examined. Additionally, the number of infected individuals will be represented for a vaccination rate of 95%, as recommended in [10,11]. A comparison between graphs of infected individuals will be presented for different vaccination rates.

2 Model Description

Mathematical models are used to describe many infectious diseases such as measle, tuberculosis, N1H1, Covid-19 etc. These models study the spread and control of disease and comprehend the dynamics of disease. Mathematical models are derived from SIR model developed by Kermack and McKendrick model, [14].

In this paper, the SEIRV model is modified and adapted for research. The total population at any given time is divided into 6 compartments: susceptible, infected, exposed, recovered, vaccinated, and deceased. The compartments are as follows:

$$N(t) = S(t) + E(t) + I(t) + R(t) + V(t) + D(t) \qquad (1)$$

where time t is in years.

The first compartment, 'susceptible,' includes all individuals who have not yet been infected but are suspected of having the disease and are at risk of infection. The 'exposed' compartment includes individuals who have had contact with an infected person. During the incubation period, exposed individuals are not yet infectious, but they can become infected after this period. 'Infectious' refers to individuals who have developed the disease and can transmit it to others. The 'vaccinated' compartment includes individuals who have received a vaccine. For simplicity in the model used in this research, it is assumed that only one dose of the vaccine is administered.

The 'recovered' compartment includes all individuals who were infectious but have now recovered from measles. Deceased individuals who were infected are part of the 'deceased' compartment. The deployed model is illustrated in Figure 1.

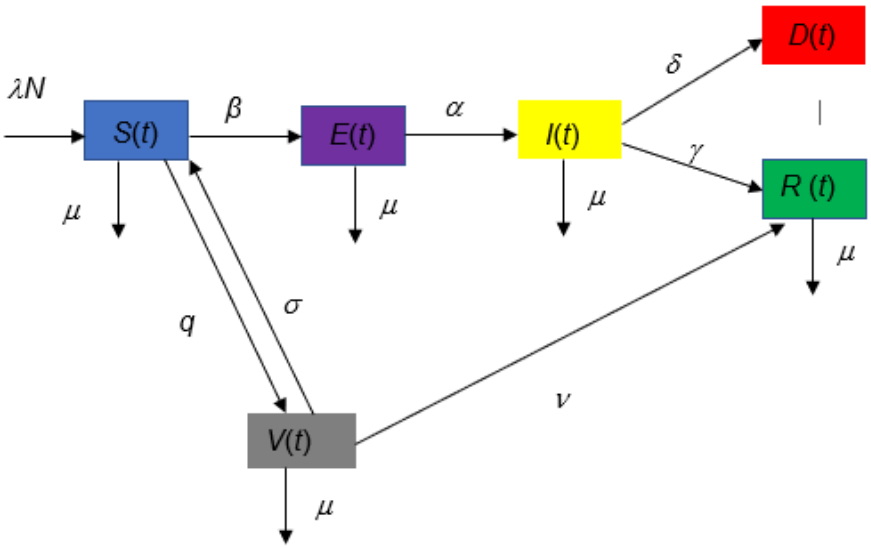

Fig. 1. Flow chart of measles disease

In this model, the 'susceptible' compartment increases due to the birth rate λ in the overall population and the rate of ineffective vaccination σ. Ineffective vaccination occurs when a vaccinated individual does not develop immunity after vaccination and returns to the susceptible compartment. According to [12], the rate of unsuccessful vaccination is 5%. The 'susceptible' compartment decreases due to interactions between the 'susceptible' and 'exposed' compartments. This interaction makes it a potential entry point into the 'exposed' compartment, governed by the transmission rate β and the vaccination rate q. The 'exposed' compartment increases due to interactions between the 'susceptible' and 'infectious' compartments. A susceptible individual has the potential to become exposed through the transmission rate β. This compartment decreases as individuals progress to the 'infectious' state at the incubation rate α. This compartment diminishes by incubation rate α at which the individual becomes infectious. The infected compartment is increased from exposed individuals that have symptoms of measles infection with incubation rate α and diminished by recovery rate γ i.e., recovery time $\tau_{recovery} = \frac{1}{\gamma}$ and death due measles infection with mortality rate δ. The 'recovered' compartment's population increases as individuals heal either through treatment or naturally, driven by the recovery rate γ. Additionally, the population of this

compartment increases through successful vaccination of susceptible individuals, which develops immunity at a rate v. Conversely, the 'death' compartment's population increases due to infected individuals dying from measles infection, influenced by the mortality rate δ. The 'vaccination' compartment's population grows as a result of the vaccination rate q. However, it diminishes due to the combined effects of the mortality rate δ and successful vaccination at a rate v. It's important to note that all compartments, except for the 'death' compartment, experience reduction due to the natural mortality rate μ. This rate signifies deaths resulting from natural causes not related to measles.

Based on the above statements, the modified SEIRV+D model is represented by the following system of stochastic differential equations:

$$\begin{aligned}
\frac{dS(t)}{dt} &= \lambda N - \frac{\beta S(t) I(t)}{N} - qS(t) + \sigma V(t) - \mu S(t) \\
\frac{dE(t)}{dt} &= \frac{\beta S(t) I(t)}{N} - \alpha E(t) - \mu E(t) \\
\frac{dI(t)}{dt} &= \alpha E(t) - \gamma I(t) - \delta I(t) - \mu I(t) \\
\frac{dR(t)}{dt} &= \gamma I(t) + \nu V(t) - \mu R(t) \\
\frac{dD(t)}{dt} &= \delta I(t) \\
\frac{dV(t)}{dt} &= qS(t) - \sigma V(t) - \nu V(t) - \mu V(t)
\end{aligned} \tag{2}$$

The system has nonnegative initial conditions:

$$S(0) = S_0 \geq 0, E(0) = E_0 \geq 0, I(0) = I_0 \geq 0, R(0) = R_0 \geq 0, V(0) = V_0 \geq 0, D(0) = D_0 \geq 0$$

The population is infection- free at disease free equilibrium point (DFEP) known as steady state solution. DFEP is obtained by equating to zero the ride sides of the equations (2).

$$\frac{dS(t)}{dt} = \frac{dE(t)}{dt} = \frac{dI(t)}{dt} = \frac{dR(t)}{dt} = \frac{dV(t)}{dt} = \frac{dD(t)}{dt} = 0 \tag{3}$$

Infection free populations means $I(t) = 0$, thus:

$$\frac{dS(t)}{dt} = \lambda N - qS(t) - \sigma V(t) - \mu S(t) = 0$$

$$\frac{dE(t)}{dt} = \alpha E(t) - \mu E(t) = 0 \qquad (4)$$
$$\frac{dR(t)}{dt} = \upsilon V(t) - \mu R(t) = 0$$
$$\frac{dE(t)}{dt} = qS(t) - \sigma V(t) - \upsilon V(t) - \mu V(t) = 0$$

Solving the system (4) simultaneously it is obtained the disease- free equilibrium point:

$$(S^*, E^*, I^*, R^*, V^*, D^*) = \left(\frac{\lambda N(\sigma + \nu + \mu)}{(q+\mu)(\sigma+\nu+\mu) - \sigma q}, 0, 0, \frac{\nu q \lambda N}{\mu\left[(q+\mu)(\sigma+\nu+\mu) - \sigma q\right]}, \frac{q\lambda N}{(q+\mu)(\sigma+\nu+\mu) - \sigma q}, 0 \right) \qquad (5)$$

The basic reproduction number is a fundamental concept in epidemiology and is defined as the expected number of new infections caused by an infected individual. It is calculated as the largest eigenvalue of the next-generation matrix developed by Van den Driessche and Watmough [13]. The next generation matrix is calculated based on two matrix F and $-V^{-1}$. The matrix F represents the rate of infection transmission between the exposed and infected compartments, while the matrix $-V^{-1}$ encompasses all other transfers across the compartments. For the model (2), the matrix F is given as:

$$F = \begin{pmatrix} 0 & \frac{\beta S}{N} \\ 0 & 0 \end{pmatrix} \qquad (6)$$

The matrix $-V^{-1}$ is given as:

$$-V^{-1} = \begin{pmatrix} \frac{1}{\alpha+\mu} & 0 \\ \frac{\alpha}{(\alpha+\mu)(\gamma+\mu+\delta)} & \frac{1}{\gamma+\mu+\delta} \end{pmatrix} \qquad (7)$$

The next generation matrix is:

$$-FV^{-1} = \begin{pmatrix} 0 & \frac{\beta\lambda(\sigma+\nu+\mu)}{(q+\mu)(\sigma+\nu+\mu) - \sigma q} \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{\gamma+\mu} & 0 \\ \frac{\alpha}{(\alpha+\mu)(\gamma+\mu+\delta)} & \frac{1}{\gamma+\mu+\delta} \end{pmatrix} \qquad (8)$$

Hence, the reproduction number is:

$$\Re_0 = \frac{\beta\lambda(\sigma+\nu+\mu)}{(q+\mu)(\sigma+\nu+\mu)-\sigma q} \cdot \frac{\alpha}{(\alpha+\mu)(\gamma+\mu+\delta)} \tag{9}$$

Theorem 2. *The proposed epidemic model (2) has a unique equilibrium point. If* $\Re_0 > 1$*, the disease-free equilibrium point (5) is unstable, and the disease is spreading in the population. If* $\Re_0 < 1$*, the disease-free equilibrium point (5) is asymptotically stable, and the disease dies off.*

3 Case Study

The parameters of the measles model were estimated using data obtained from the Institute of Public Health of the Republic of North Macedonia [2] over the past five years. The data collected for the period 2018-2022 is presented in Table 1. The base year for this model is 2018, during which 64 new individuals were found to be infected with measles. Subsequently, in 2019, there was an epidemic of measles with 1819 newly detected infected individuals. However, no new cases of measles infection were reported in the years 2020, 2021, and 2022.

Due to the Covid-19 pandemic, the rate of vaccination decreased, which is expected to result in new cases of measles infection.

Table 1. Measles infection in R. N. Macedonia (2018-2022).

Year	Infected individuals
2018	64
2019	1819
2020	0
2021	0
2022	0

In order to describe the measles infection in R. North Macedonia the values in Table 2 are assumed or calculated.

Table 2. Description and estimated values of measles model parameters

Parameters	Description	Value
λ	Birth rate	0.014
β	Transmission rate	0.9
α	Incubation rate	0.125
$\tau_{incubation} = \frac{1}{\alpha}$	Incubation time	8 days

γ	Recovery rate	0.14285
$\tau_{recovery}$	Recovery period	7 days
δ	Mortality rate of measles	0.02
μ	Natural mortality rate	0.0014
σ	Unsuccessful vaccination rate	0.007
v	Successful vaccination rate	0.993
q	Vaccination rate	0.744

Measles vaccine is recommended not only for all newborns and infants but for susceptible adults. In order measles infection to be eliminated, the vaccination rate should achieve ≥0.95 for both doses in every district, [11]. In 2018, the vaccination rate of infants and newborns in R. N. Macedonia is only 74.4%, [10] which led to epidemic in 2019. Thus, in the case study simulations are performed for vaccination rate of 0.95. The model is developed AnyLogic® [15] and simulations are performed to illustrate the impact of vaccination rate on infected and dead individuals over the course of five years. From [16] the population in North Macedonia is 2083127 individuals. In this paper, for simplicity the total population is estimated to $N_0 = 2000000$. The initial number of infected form Table 1 is $I_0 = 64$. The recovery rate is $\gamma = 0.14286$, thus the initially recovered population is $R_0 = 0.14286 I_0 \approx 9$. The initial death population is estimated as $D_0 = 0,02 I_0 = 1,28 \simeq 1$, while the initial exposed population is $E_0 = \frac{I_0}{\alpha} = \frac{I_0}{0.125} = 512.$ If the vaccination rate is 0.744 than the number of initially susceptible individuals is $S_0 = \frac{N_0 - E_0 - I_0 - R_0 - D_0}{1,744} \approx 1146453$ and initial vaccinated population is $V_0 = 0,744 S_0 \approx 852961$.

According to statements given above, the initial conditions from the proposed model are:

$$\left(S_0, E_0, I_0, R_0, D_0, V_0\right) = \left(1146453, 512, 64, 9, 1, 852961\right) \tag{10}$$

If the vaccination rate is 0.95 as recommendation in [10,11], then the initial conditions would be:

$$\left(S_0, E_0, I_0, R_0, D_0, V_0\right) = \left(1025341, 512, 64, 9, 1, 973574\right) \tag{11}$$

The graphs in Figure 2 illustrate the number of infected individuals for both vaccination rates. These graphs clearly show that as a higher percentage of the population becomes vaccinated, the number of infected individuals decreases. These findings emphasize the importance of vaccination and its substantial impact on preventing and controlling the spread of infections.

8

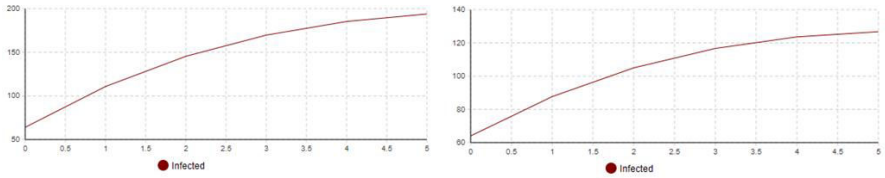

Fig. 2. Infected population for vaccination rate a) 0.744 and b) 0.95.

According to Figure 3, the number of deaths is decreased from 15 individuals to 11 individuals as the vaccination rate is increased. This significant decrease emphases the impact of vaccination.

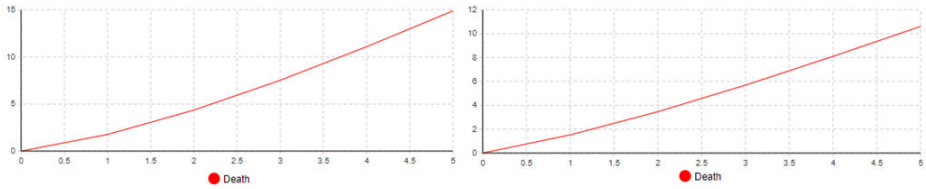

Fig. 3. Death population for vaccination rate a) 0.744 and b) 0.95

4 Conclusion

The transmission dynamics of measles infection depend on various factors, primarily population density, vaccination rates, and the degree of contact among individuals within the population. Mathematical models for infectious diseases have proven to be valuable tools for comprehending the spread of measles, predicting future outcomes and outbreaks, and assessing the effectiveness of vaccination.

In this paper, we have formulated and developed an SEIRV+D model to analyze the dynamics of measles. The disease-free equilibrium point was calculated to determine the reproduction number. Using data from the Public Health Institute of North Macedonia, we conducted simulations to analyze and forecast the course of measles infection from 2018 to 2022. These simulations, performed using AnyLogic® software, underscore the critical role of vaccination in controlling measles and preventing its spread within the population. Notably, the results demonstrate the negative impact of low vaccination rates on disease prevalence, underscoring the need for increased vaccination rates to avert measles outbreaks.

In this study, we simplified the model by assuming only one dose of vaccination is administered. However, the World Health Organization (WHO) recommends a two-dose vaccination schedule. In future research, we intend to enhance the model by incorporating two vaccination compartments and exploring their impact on the dynamics of measles infection.

References

1. CDC: Epidemiology and Prevention of Vaccine- Preventable Diseases, The Pink Book: Courses Textbook, 14th edn. CDC (2021).
2. Institut za javno zdravne na Severna Makedonija: Dvizenje na akutnite zarazani zaboluvanja vo Republika Severna Makedonija vo 2022 (2023).
3. Dairi, A., Harrou, F., Zeroual A., Hittawe, M.M., Sun, Y.: Comparative Study of Machine Learning Methods for COVID-19 Transmission Forecasting. Journal of Biomedical Informatics 118:103791 PMID:33915272 (2021).
4. Bakare, E., Adekunule, Y., Kadiri, K.: **Modelling and Simulation of the Dynamics of the Transmission of Measles**, International Journal of Computer Trends and Technology 3, 174-178 (2012).
5. Lay, M., Becker, A., Madden, W., Metcalf, C., Grenfell, BT.: Comparing and Liking Machine Learning and Semi-Mechanical Models for Predictability of Endemic Measles Dynamics. In PLos Comput Biol: 18(9): e1010251. https://doi.org/10.1371/journal.pcbi.1010251
6. Momoh, A., Ibrahim, M., Uwanta, I., Manga, S.: **Mathematical Model for Control of Measles Epidemiology.** International Journal of Pure and Applied Mathematics 87. 707-717 (2013).
7. Zaman, G., Kang, H., Cho, G., Jung, Optima, J.H.: Strategy of Vaccination & Treatment in an SIR Epidemic Model. In Mathematics and Computer in Simulation 136, 63-77 (2017).
8. Zhou, L., Wang, Y., Li, I.H.: **Global Dynamics of a Discrete Age- structured SIR Epidemic Model with Application to Measles Vaccination Strategies**. Mathematical Bioscience 308, 27-37 (2019).
9. Shinta, R.A, Dipo. A., Bevina, D.H.: Short Review of Mathematical Model of Measles. In AIP Conference Proceedings 2264, 020003 (2020); https://doi.org/10.1063/ 5.0023439 (Published Online: 22 September 2020).
10. Institut za Javno Zdravje homepage, http://iph.mk/wp-content/uploads/2014/09/Imunizacija-izvestaj-2018.pdf last access 2023/05/23.
11. World Health Organization: Weekly epidemiological record, No. 17, 205-228 (2017).
12. Bailey, A., Sapra, A.: **MMR Vaccine.** StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; https://www.ncbi.nlm.nih.gov/books/NBK554450/ (2023).
13. Driessche, P., Waltmough, J.: **Reproduction numbers and sub-threshold endemic equilibra for compartment models of disease transmission**. Mathematical Bioscience, 180 29-48 (2002).
14. Kermack, W.O., McKendrick, A.G.: Contributions to the mathematical theory of epidemics-I, Bull. Math. Biol., 53, No 12 (1991) doi: 10.1007/BF02464423.
15. Anylogic®, https://www.anylogic.com/, last accessed 2023/05/23.
16. Worldometar, North Macedonia Population (2023) - Worldometer (worldometers.info) last accessed 2023/05/26.