JEVNAH
Journal of Evidence-based Nursing and Public Health
JEVNAH 2(2): 138–154
ISSN 3048-2615

Institute for Advanced Science,
Social and Sustainable Future
MORALITY BEFORE KNOWLEDGE

Stability analysis of *Monkeypox* virus transmission dynamics using the SEIVR approach

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Received Date: June 12, 2025 Revised Date: July 10, 2025 Accepted Date: August 31, 2025

ABSTRACT

Backgorund: *Monkeypox* is a zoonotic infection caused by the *monkeypox* virus (*MONKEYPOX*V), which has the potential to be transmitted from animals to humans. This virus can be transmitted through direct contact with infected animals such as monkeys, rats, and squirrels. In 2023, the World Health Organization classified *monkeypox* as a global pandemic, prompting stricter prevention measures worldwide. Given the significant increase in the number of cases and the challenges in controlling the spread of the virus, this study aims to develop a SEIVR (Susceptible, Exposed, Infected, Vaccinated, Recovered) mathematical model that can describe the dynamics of the spread of the *monkeypox* virus in Indonesia. **Methods:** There are two cases of the SEIVR model that will be studied; those are disease-free and endemic cases. From the cases, the stability of the model will be found. The Routh-Hurwitz criterion will also be used to analyze the stability due to the complexity of the eigenvalues. **Findings:** In the study conducted, simulations indicated that the infected population would coexist or remain for a fairly long time. This phenomenon is caused by the stable nature of the model. The dynamics of the model can also be seen by considering the obtained reproductive number. Although the infected population persists for a long time, the numbers are quite low. **Conclusion:** Vaccination does not have a significant impact. Therefore, further research using a treatment compartment or virus transition in rodents needs to be conducted for further study. **Novelty/Originality of this Article:** The novelty of this research lies in the use of the SEIVR model to map the spread of *monkeypox* in Indonesia and analyze its stability using the Routh-Hurwitz criteria and numerical simulations. This approach provides an initial overview of case persistence and vaccination effectiveness.

KEYWORDS: *Monkeypox*; public health; SEIVR model; stability analysis.

1. Introduction

Monkeypox is a disease caused by the *monkeypox* virus (*MONKEYPOX*V), which belongs to the Orthopoxvirus group of the Poxviridae family. This virus is an enveloped virus with a double-stranded DNA genome (Kesuma et al., 2022). Compared to other diseases caused by viruses from the Orthopoxvirus family, *monkeypox* transmission is relatively complex. The transmission makes *monkeypox* a zoonotic disease, meaning it can spread from animals to humans. Transmission can occur through contact with infected animals such as monkeys, rats, and squirrels (Letafati & Sakhavarz, 2023). According to the World Health Organization in the 2024 Mpox article, the primary animal species suspected of carrying this virus has not yet been identified, but rodents are considered potential natural reservoirs. Transmission of the virus from animals to humans can occur through direct

Cite This Article:
Glagah, E. S., Saputro, I. A., Fikri, M. I., Rahmawati, R. N., & Ramdhanu, A. B. (2025). Stability analysis of *Monkeypox* virus transmission dynamics using the SEIVR approach. *Journal of Evidence-based Nursing and Public Health. 2*(2), 138-154. https://doi.org/10.61511/jevnah.v2i02.2025.1837

contact with blood, bodily fluids, or contaminated skin lesions of infected animals (Qelina & Graharti, 2019). Additionally, this disease is also classified as reverse zoonosis or spillback, meaning it can spread from humans back to animals (Noman et al., 2024). According to the FAQ of the Indonesian Ministry of Health in 2022, *monkeypox* can also spread from human to human, with a mortality rate ranging from 1% to 10%. Human-to-human transmission currently occurs more commonly through direct contact with blood, skin lesions, or bodily fluids, as well as items belonging to patients infected with the *monkeypox* virus. The virus can enter through skin wounds, the respiratory tract, or mucous membranes such as the eyes, nose, or mouth (Alakunle et al., 2020). This poses a serious concern for human health and the environment. According to a study conducted by Sari & Hairunisa (2022), some people can have moderate symptoms, while some can be more severe and require health facilities. It can be said that *monkeypox* symptoms vary. The majority of human *monkeypox* cases begin with a series of symptoms such as fever, headache, chills, fatigue, asthenia, swollen lymph nodes, back pain, and muscle pain (Kesuma et al., 2024).

Monkeypox virus was first discovered in a captive monkey species at the State Serum Institute in Copenhagen in 1958 (Patauner et al., 2022). It used to be a colony of macaques under study in Denmark and first infected humans in the Democratic Republic of Congo in 1970. Then in 2003 there was an outbreak in the United States caused by transmission between humans and infected pets. A total of 87 cases were reported by the US Centres for Disease Control and Prevention (CDC) at time. In 2022, the World Health Organization reported the discovery of new cases outside endemic countries, namely the United Kingdom (Farahat et al., 2022). The *monkeypox* virus was first carried by a British citizen who had a history of travelling to Nigeria. From May 2022 to June 2022, there were 3,340 confirmed cases from the Americans and on June 24, 2022, a Taiwanese national was confirmed with *monkeypox* virus with a history of traveling from Germany (World Health Organization, 2022). This proves that *monkeypox* virus has been transmitted in various countries (Thornhill et al., 2022). On May 19, 2022, the World Health Organization declared the shift of *monkeypox* virus infection status to non-endemic and suspected the high potential of *monkeypox* virus to become a wider threat to the world population. Since then, *monkeypox* has often infected humans, especially in endemic areas or countries, the tropical forest region of the Congo Basin and West Africa. Evidently, there have been 1,000 suspected cases actively reported by the Democratic Republic of Congo each year since 2005. Until May 2022, the global community began to pay health attention to this disease due to reports of *monkeypox* cases from 23 non-endemic countries to the World Health Organization (World Health Organization, 2022). At its peak on July 20, 2022, there were 14,000 confirmed cases from more than 70 countries with five deaths, all of which occurred in Africa. Until July 23, the status of *monkeypox* was declared a global health emergency by the World Health Organization (CNBC Indonesia 2022).

Monkeypox is now designated by the World Health Organization as a global pandemic on July 23, 2023, by the Secretary-General of the World Health Organization, Tedros Adhanom Ghebreyesus. Experts included the disease in the global emergency outbreak after concluding that many countries were not adequately prepared to respond. Therefore, every country is required to prevent the spread, such as establishing clean and healthy living socialization and conducting examinations at the nearest health facility. In 2022, several clusters of *monkeypox* were reported in several European and North American countries. The number of cases per week reported increased dramatically, so the World Health Organization finally declared the status of an outbreak and health emergency that requires international attention (Gruber, 2022). Based on data from the Ministry of Health as of August 17, 2024, there were 88 confirmed cases of *monkeypox*. In detail, the cases were spread in DKI Jakarta as many as 59 confirmed cases, West Java 13 confirmed cases, Banten 9 confirmed cases, East Java 3 confirmed cases, Yogyakarta Special Region 3 confirmed cases, and Riau Islands 1 confirmed case (Antara, 2024).

According to research conducted by Qelina & Grahati (2019), the incubation period for *monkeypox* in humans generally lasts 6 to 16 days after an individual is exposed to the virus that causes it. However, in rare cases, the incubation period can be extended to 21 days, indicating variations in the human body's response to this infection. The average incubation period is around 12 days, which is an important benchmark for patient monitoring and contact tracing. In the early stages, typically within the first five days after the virus enters the body, the patient will experience characteristic initial symptoms that tend to be severe. These symptoms include high fever often accompanied by chills, sharp back pain, severe headaches, muscle pain or myalgia, swollen lymph nodes (*lymphadenopathy*), and weakness or asthenia that interferes with daily activities. These symptoms can resemble those of other viral infections, making initial diagnosis challenging without further observation of subsequent symptoms.

One of the more distinctive and helpful symptoms in identifying *monkeypox* is the appearance of a rash on the body. According to Qelina & Grahati (2019), the rash typically appears within 1 to 10 days after the onset of fever. This rash has a characteristic pattern of spread, beginning on the face and gradually spreading to other parts of the body such as the arms, legs, and trunk. The skin lesions initially form as macules, then develop into papules, vesicles, pustules, and eventually harden and form scabs before finally shedding within 2 to 4 weeks. This process represents a fairly lengthy disease course and requires close monitoring, especially in individuals with underlying medical conditions. In addition to causing physical discomfort, the visible rash and lesions also have psychological impacts on patients due to social stigma and feelings of embarrassment resulting from the drastic changes in physical appearance. Therefore, public education about these symptoms is crucial to ensure patients can receive timely treatment and avoid feeling marginalized.

In efforts to reduce the risk of disease transmission, such as *monkeypox*, vaccination has become one of the most effective methods to enhance an individual's immune system against exposure to antigens from viruses, bacteria, or other pathogens. The vaccination process allows the body to recognize and form an immune response to specific pathogens without having to experience infection directly. With the formation of antibodies, the body will be better prepared to fight future infections, so that the disease does not develop or only appears in a very mild form. As explained by Tamara (2021), the main purpose of vaccination is to protect individuals from certain diseases and prevent serious complications that can arise from infection. In the context of diseases such as *monkeypox*, vaccination efforts are crucial, especially when the disease shows a high potential for human-to-human transmission. Vaccination is also a long-term strategy that not only protects individuals but also creates herd immunity when carried out on a massive scale.

While a specific vaccine for *monkeypox* has been in clinical trials in Africa since 2020, as reported by Gumandang (2022), there is another alternative that has been used, namely the conventional smallpox vaccine. This smallpox vaccine is known to have a high potential for protection against *monkeypox* infection, with an efficacy rate of up to 85%, based on laboratory testing and animal trials (CDC, 2022). Although it is not a vaccine specifically developed for *monkeypox*, the success of the smallpox vaccine in stimulating the immune system to fight viruses from the same family offers great hope for controlling the outbreak. Countries like the United States have even taken swift action by stockpiling large quantities of the vaccine and distributing the JYNNEOS vaccine to individuals considered at high risk, such as healthcare workers and those living in endemic areas or with a history of close contact with confirmed cases. This highlights the importance of public health systems being prepared to respond to infectious disease outbreaks with a science-based preventive approach (Saputra et al., 2022).

In addition to vaccination, preventing *monkeypox* also requires public education efforts on various measures that can reduce the risk of transmission. According to Marisah et al. (2022), a comprehensive prevention approach encompasses many aspects, from lifestyle to daily habits. For example, maintaining personal hygiene by regularly washing hands, avoiding contact with wild animals or animals that may serve as virus hosts, and ensuring that consumed meat is thoroughly cooked. Additionally, the public should be advised to avoid physical contact with individuals exhibiting infection symptoms or using personal items that may be contaminated, such as clothing or bedding. For individuals planning to travel to areas with high transmission rates, it is important to understand the risks and strictly follow health protocols, including using personal protective equipment when necessary. Medical personnel treating *monkeypox* patients must also be equipped with full protective gear to prevent cross-infection. Collective awareness and adherence to these preventive measures are key to preventing a wider outbreak and protecting vulnerable groups in the community.

Education and outreach play a crucial role as key factors in efforts to prevent *monkeypox* infections. This strategy can be implemented through a variety of innovative and easily accessible methods for the general public. The use of social media is at the forefront of posting informative, engaging, and easy-to-understand content about the disease, reaching audiences from diverse backgrounds. Additionally, broadcasting news through television plays a vital role in disseminating information quickly and on a large scale, ensuring the public receives the latest updates on *monkeypox* developments. Furthermore, campaigns about the dangers of *monkeypox* can also be conducted online via the internet, utilizing various digital platforms, or through direct interaction with the community. This face-to-face approach, as often done in outreach activities, is a very effective step in building a deeper understanding and directly answering questions or concerns from the community. As a concrete example of the effectiveness of this approach, in 2022, the World Health Organization (WHO) provided support to 21 health organizations. This support aimed to increase public awareness about *monkeypox* through door-to-door campaigns (World Health Organization, 2022), an initiative that directly reaches residents' homes. Research also supports the importance of this education. According to Jairoun et al. (2022), *monkeypox* prevention education has proven effective in reaching diverse segments of the community, with an effectiveness rate of 0.686. This figure underscores that educational efforts have a tangible impact on increasing awareness and prevention practices within communities. Therefore, collaboration and collective efforts are crucial to breaking the chain of *monkeypox* virus transmission and ultimately protecting public health comprehensively. With an educated community, we can build a stronger defense against this disease threat.

Currently, it is important to understand that there is no specific treatment that directly cures *monkeypox*. The primary approach to managing the condition is symptomatic and supportive. This means the main focus is on alleviating the symptoms that arise and providing comprehensive support to aid the patient's recovery process. The objectives of this treatment are clear: to accelerate the healing of skin lesions, which are a characteristic feature of the disease; to prevent or manage high fever, which often accompanies the condition; to reduce fluid loss that may occur due to lesions or fever; to alleviate pain and discomfort experienced by the patient; to minimize the formation of scar tissue post-healing; and, equally important, to prevent secondary infections in open skin lesions. In some countries, such as the United States, Tecovirimat (TPOXX or ST-246) has become an important part of the symptomatic treatment regimen. This antiviral drug is recommended for adult and pediatric patients weighing at least 3 kg, making it the preferred treatment option in cases requiring further intervention. Tecovirimat’s mechanism of action is highly specific: it works by inhibiting the viral envelope protein known as VP37. This mechanism is crucial as it effectively blocks the final stage of viral maturation and its release from infected cells. Thus, Tecovirimat plays a vital role in preventing the virus from spreading further within the host’s body. The safety of Tecovirimat has also been a focus of attention. According to the Centers for Disease Control and Prevention (CDC) in 2022, Tecovirimat is considered safe for human consumption, with only mild side effects reported (CDC, 2022). This data provides further confidence in its use. Additionally, research conducted by O'Laughlin et al. (2022) indicates that Tecovirimat's effectiveness in accelerating the recovery process of patients is estimated to reach 0.726. This figure demonstrates the drug's significant potential in supporting recovery. Although *monkeypox* does not yet have a curative drug, a combination of careful supportive care with antiviral interventions such as Tecovirimat is a key strategy. This approach aims not only to manage the disease but also to improve patient prognosis and quality of life during the infection period. This underscores the importance of research and development of antiviral drugs in addressing the threat of new infectious diseases.

Monkeypox has a significant impact on various aspects of life. From an economic perspective, the threat of travel restrictions from endemic areas or regions experiencing outbreaks to non-endemic areas can affect the tourism and trade sectors. This situation requires significant mitigation efforts, even at a very high cost. For example, Buana (2024) reported in Media Indonesia that the World Health Organization (WHO) has allocated a preparedness and response strategy with a budget of USD 135 million (approximately Rp 2.1 trillion) to launch a preparedness and response strategy to curb the global spread of the *monkeypox* virus. This highlights the significant financial commitment required to address this threat. The social impact is equally concerning. Public fear of emerging infectious diseases can trigger social unrest and erode public trust in government and health authorities. Worse still, misinformation or disinformation about *monkeypox* can exacerbate the situation, creating panic and confusion. In the context of public health, the increase in *monkeypox* cases in various countries has the potential to overwhelm healthcare facilities, especially in developing countries with limited healthcare systems. Therefore, effective preventive measures and global cooperation in monitoring and controlling the spread of this disease are absolutely necessary to prevent more severe impacts. To understand the dynamics of *monkeypox* transmission, one very useful approach is the SEIVR (Susceptible-Exposed-Infected-Vaccinated-Recovered) model. This model considers individuals in various categories: susceptible, exposed, infected, vaccinated, and recovered. By utilizing this mathematical model, researchers can predict disease transmission patterns and evaluate the effectiveness of interventions, enabling the development of more optimal and targeted mitigation strategies.

As science and technology continue to develop, mathematics plays an increasingly significant role in efforts to prevent and control infectious diseases. One of its important contributions is realized through mathematical modeling, which enables the formulation of systematic representations of the phenomenon of disease spread in populations. The application of mathematical modeling, especially in the field of epidemiology, has proven effective in helping researchers and policy makers to understand the dynamics of outbreaks more deeply. Mathematical models are able to simulate various important aspects of an infectious disease, such as the rate of transmission, incubation period, and the impact of interventions such as vaccination, quarantine, and treatment. This field of study is known as mathematical epidemiology, which specifically examines the spread of disease with a quantitative and analytical approach (Nurfadilah et al., 2021).

In the context of *monkeypox*, mathematical modeling is particularly relevant given the disease's characteristics as a zoonosis with the potential for rapid spread both between animals and between humans. By building mathematical models that represent the complex interactions between susceptible, exposed, infected, and recovered individuals, researchers can analyze the dynamics of disease transmission more accurately. In addition, the models can also be used to evaluate the effectiveness of possible control strategies, such as public awareness raising, vector control, selective vaccination and case isolation. Through this approach, mathematical modeling is not only a tool in theoretical research, but also serves as a supporting instrument in evidence-based policy making in the field of public health. Therefore, this study aims to develop a mathematical model of the spread of *monkeypox* to understand the dynamics of its spread and evaluate various control strategy scenarios that can be applied to reduce the rate of infection in the population.

Mathematical modeling is a branch of mathematics that focuses on building models or systems of equations to represent and explain various phenomena in the real world, whether in the natural, social, or health fields (Caldwell & Ram, 1999). In the context of epidemiology, mathematical modeling is an important tool to analyze the spread of infectious diseases and evaluate the effectiveness of control interventions. *Monkeypox*, as a zoonotic disease that has shown an increase in cases in recent years, has been the subject of various studies using mathematical modeling approaches to understand the pattern of spread and the effectiveness of control strategies.

Several recent studies have developed mathematical models to examine the dynamics of *monkeypox* transmission by considering various variables and interventions. Idisi et al. (2023), for example, developed a model that considers the level of awareness of the human population towards *monkeypox* infection. The model showed that increasing public awareness could reduce the number of cases through more preventive behavioral changes, such as the use of personal protective equipment or avoiding contact with virus-carrying animals. This study highlights the importance of social factors in influencing epidemiological parameters.

Meanwhile, Wireko et al. (2023) present a fractional-order-based mathematical model that takes into account quarantined and isolated individuals. The use of fractional-order models aims to capture memory effects and long-term dynamics in disease spread, which cannot be well accommodated by classical integer-order models. This approach is especially important in the case of *monkeypox*, which has a long incubation and infection period. The addition of quarantine and isolation compartments in the model also provides a more realistic picture of the public health policy response.

Another study by Okyere and Ackora-Prah (2023) used a fractional-order Atangana-Baleanu model approach, which emphasizes non-singular kernels to describe memory effects in biological systems. This study demonstrated that fractional-order models can capture short- and long-term fluctuations in contagion more accurately than conventional models. Similarly, Sweilam et al. (2024) developed a fractional-order model that integrates incubation and isolation periods. They showed that incorporating biological aspects such as the incubation period into the model structure provides more realistic estimates of the peak infection and maximum spread time in a population.

Furthermore, Musafir et al. (2024) explored the application of optimal control to a fractional-order model of *monkeypox*. They introduced control variables such as treatment, public education, and quarantine strategies to simultaneously minimize the number of infections and intervention costs. This approach is important because it shows how limited resources can be efficiently allocated for disease control. Optimal control provides a tool for policymakers in choosing the best intervention strategy based on specific objectives, be it minimizing disease burden or optimizing budget use.

Finally, Elsonbaty et al. (2024) discussed a mathematical model that incorporates imperfect vaccination and nonlinear transmission rates. This study shows that the success of the vaccination strategy is highly dependent on the effectiveness of the vaccine and the level of public compliance with the vaccination program. The addition of nonlinear factors in the transmission rate reflects the complexity of disease spread dynamics, especially in situations where interactions between individuals are not homogeneous. As such, the model provides important insights into the real limits of vaccination interventions and the need for other complementary strategies.

Overall, these studies show that mathematical modeling is not only a theoretical tool, but also a strategic tool in designing and evaluating public health policies. These models provide simulations of various scenarios of disease spread and management, which can then be used as the basis for evidence-based decision-making. The diversity of modeling approaches used, ranging from integer-order models to fractional-order models and optimal control, shows the dynamic development of this field in responding to the real challenges of the spread of diseases such as *monkeypox*. By integrating various aspects of biology, behavior, and policy interventions, mathematical modeling serves as a bridge between theory and practice in infectious disease control.

Mathematical modeling in epidemiology not only serves as an academic instrument to understand disease dynamics, but also plays a vital role in public health decision-making. By providing projections and simulations of various disease transmission scenarios, mathematical models allow policy makers to assess the effectiveness of health interventions such as vaccination, isolation, quarantine, or public awareness raising. For example, predictive models can be used to determine when and where a surge in *monkeypox* cases is likely to occur, how much of the population is at risk, and how vaccination or medical resource distribution policies should be structured. Models can also help in identifying critical points in the transmission chain and evaluating the economic or social impact of certain control strategies. In this context, models are part of the evidence-based public health approach, where policies are based on scientific evidence and the results of data analysis, rather than intuition or political pressure. The use of epidemiological models in decision-making also supports the principles of transparency and accountability in the public health system.

Furthermore, various public health frameworks have been designed to support the integration of mathematical modeling into policy practice and crisis management systems. One example is the Integrated Disease Surveillance and Response (IDSR) developed by the World Health Organization (WHO) and adopted by many countries in Sub-Saharan Africa. Through IDSR, disease data is collected and analyzed in real-time to support rapid and accurate evidence-based decision-making-mathematical modeling being an important part of the process. On the other hand, the Health Emergency Preparedness Framework also emphasizes the need to use analytical and predictive tools to plan responses to outbreaks, especially in the context of new infectious diseases or zoonoses. An example of the integration of models into policy was also seen in the response to the *monkeypox* outbreak in Nigeria, where health authorities used local data-based predictive models to direct vaccination interventions and the distribution of medical personnel to areas with the highest risk of transmission. In Indonesia, a One Health framework is being applied to address zoonotic diseases by combining data from the human, animal and environmental health sectors. This approach opens a wide space for the application of comprehensive mathematical models to design multidisciplinary intervention strategies. Thus, mathematical modeling is not only a scientific tool, but also an integral part of modern systems-based and collaborative public health governance. Findings from this study can inform evidence-based decision-making in public health, particularly in optimizing resource allocation and designing targeted interventions. By providing quantitative insights into model outcomes, this study supports policymakers in prioritizing high-risk populations and evaluating the potential impact of preventive strategies. Furthermore, by situating this modeling approach within established public health frameworks, the study facilitates the translation of analytical findings into practical, real-world decision-making tools for health authorities.

2. Methods

This research commenced with an extensive literature review on the *monkeypox* virus and the SEIVR (Susceptible-Exposed-Infected-Vaccinated-Recovered) mathematical model to establish a robust theoretical framework for understanding the transmission dynamics of the virus. This initial phase involved the systematic collection of relevant data and parameter values from credible literature sources to construct a mathematically rigorous model.

Upon identifying the necessary parameters, the SEIVR model specific to the *monkeypox* virus was formulated. The model facilitated the determination of equilibrium points, including the disease-free and the endemic equilibrium. At this stage, a comprehensive stability analysis was conducted for both equilibrium points. The stability of the system was evaluated using the analytical Routh-Hurwitz method (Side, 2020), which provides critical insights into the system's behavior at equilibrium (Mortoja et al., 2018).

Subsequently, parameter-specific calculations were performed based on the collected data. These parameters were analyzed to numerically validate the constructed model. Numerical simulations were employed to visualize the model's solutions, encompassing the dynamics of virus transmission and the effects of vaccination. The analysis of the results was presented through graphical visualizations, demonstrating the population dynamics within each compartment of the SEIVR model over time.

A research flowchart summarizing the entire methodological framework, from the literature review to result analysis, is presented in Figure 1. The flowchart illustrates the systematic progression of the research stages, including model formulation, equilibrium point determination, stability analysis, and simulation result interpretation. This structured approach ensures methodological rigor and transparency, thereby enabling the findings to accurately capture the transmission dynamics of the *monkeypox* virus.

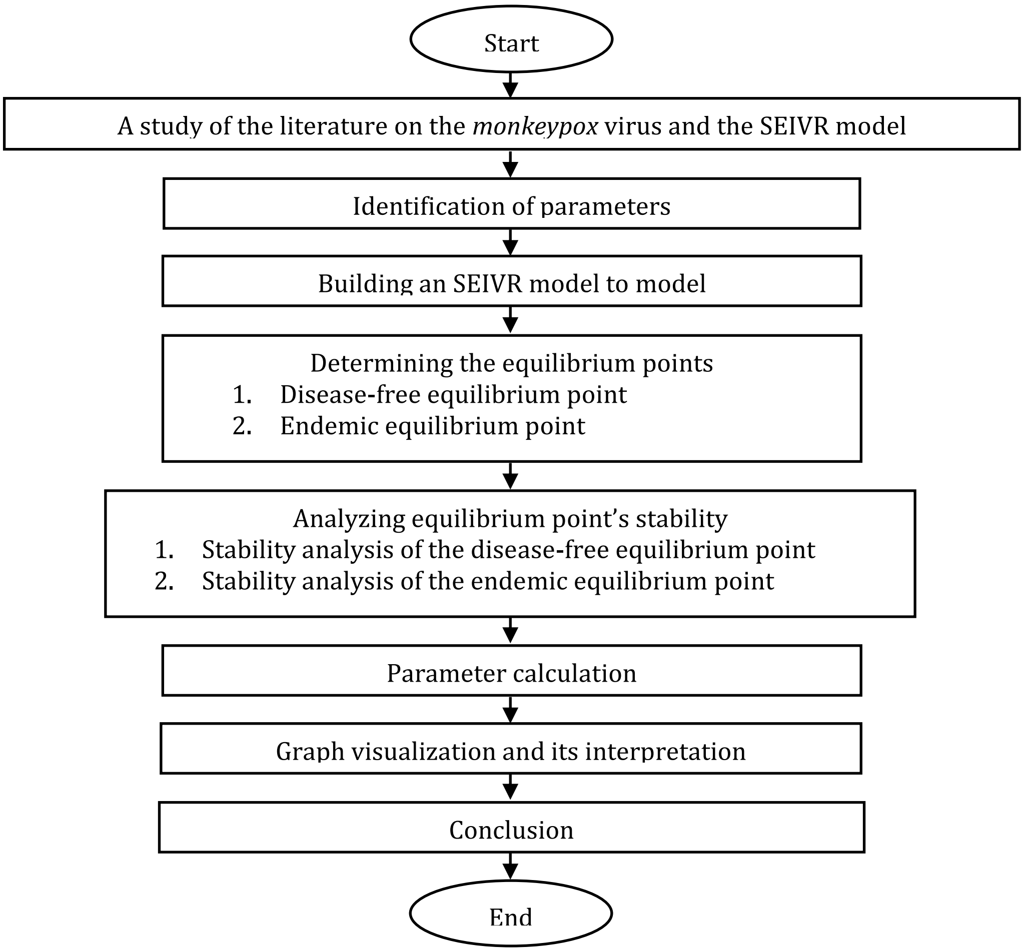

Fig. 1. Research flowchart

3. Results and Discussion

This section presents the findings of the adjusted SEIVR model, emphasizing the transmission dynamics of *monkeypox* and the impact of vaccination and treatment interventions on the spread of the disease. *Monkeypox* is a zoonotic disease that impacts human health and primate species, which act as natural reservoirs for the virus. Transmission takes place from animals to humans and among humans via direct contact with lesions, bodily fluids, or contaminated items. The relatively extended incubation period, spanning from 5 to 21 days, presents a difficulty in managing the disease, as infected persons might spread the virus prior to symptom onset. Grasping this latency phase is essential for creating precise mathematical models that reflect the concealed dynamics of infection and inform prompt interventions.

Recent occurrences of *monkeypox* in areas outside Central and West Africa emphasize the increasing global significance of efficient control measures. Among these, vaccination has become one of the most effective preventive strategies. Research by Lu et al. (2023) and Huang, Mu, & Wang (2022) showed that vaccination before exposure greatly improves immune defense, decreases symptom emergence, and lowers person-to-person transmission. These results highlight that high-risk groups, including healthcare professionals, close contacts, and residents of endemic areas, should be prioritized for vaccination.

In this research, the mathematical framework suggested by Bhunu & Mushayabasa (2011) was enhanced to represent the *monkeypox* epidemiological conditions after 2020. The revised model includes control variables that signify antiviral therapy for infected individuals and immunization for at-risk populations. Moreover, a hidden compartment (E) was added to depict exposed individuals in the incubation stage who have not yet turned infectious. This adjustment offers a more authentic representation of disease dynamics, especially in terms of human movement and the timing of measures taken. The assumptions used follow current epidemiological approaches, as supported by Harris (2022), emphasizing the significance of early detection and rapid response in zoonotic disease management.

The modified SEIVR framework divides the total population into five compartments, such as susceptible population (S), exposed population (E), infected population (I), and recovered population (R). In this section, a mathematical model based on the SEIVR framework applied to the spread of *monkeypox* virus will be discussed, focusing on analyzing the transmission dynamics and formulating solutions to prevent and control the disease. The model used in this study is a modified SEIVR model with the addition of a vaccination compartment (V). Each compartment in the model depends on a time variable (t).

There are several assumptions in the model such as the population that has recovered cannot be infected by the same virus and the vaccinated population cannot be infected by *monkeypox* virus. Another assumption is the transmission of the virus which only occurs between humans. In addition, six parameters will be used which can bee seen in Model (1), those are birth rate (Λ), vaccinated rate (ω), natural death rate (μ), incubation period (σ), infection rate (β), and recovery rate (γ). The system of differential equations describing the transmission of the disease is presented in Model (1).

$$\left.\begin{aligned}\frac{dS}{dt} &= \Lambda - (\beta I + \mu + \omega)S\\ \frac{dE}{dt} &= \beta SI - (\mu + \sigma)E\\ \frac{dI}{dt} &= \sigma E - (\mu + \gamma)I\\ \frac{dV}{dt} &= \omega S - \mu V\\ \frac{dR}{dt} &= \gamma I - \mu R\end{aligned}\right\} \qquad \text{(Eq. 1)}$$

Furthermore, there will two types of discussion cases, which are disease-free case and endemic case. Stability analysis of each equilibrium point will be carried out, and numerical simulation of the model will also be presented to give a clear visualization.

3.1 Equilibrium point and Its stability analysis

The discussion about the equilibrium points of the model will be carried out, which are representing disease-free case and endemic case. Each of the equilibrium point has its own stability condition and the steps to obtain the condition will be given in this section. Furhtermore, an equilibrium point is stable when its value is negative.

3.1.1 Disease-free case

The disease-free equilibrium point $\boldsymbol{E_1} = (S_1, E_1, I_1, V_1, R_1)$ is the condition where there are no individuals infected with *monkeypox* in a population, which occurs when $I = 0$. By satisfying the derivative of each compartment with respect to t, the first equilibrium point is obtained in the form of $\boldsymbol{E_1} = \left(\frac{\Lambda}{\mu+\omega}, 0, 0, \frac{\omega\Lambda}{(\mu+\omega)\mu}, 0\right)$. By doing linearization around the equilibrium point, the Jacobian matrix for $\boldsymbol{E_1}$ is obtained as follows.

$$J_1 = \begin{bmatrix} -(\mu+\omega) & 0 & -\dfrac{\beta\Lambda}{\mu+\omega} & 0 & 0 \\ 0 & -(\mu+\sigma) & \dfrac{\beta\Lambda}{\mu+\omega} & 0 & 0 \\ 0 & \sigma & -(\mu+\gamma) & 0 & 0 \\ \omega & 0 & 0 & -\mu & 0 \\ 0 & 0 & \gamma & 0 & -\mu \end{bmatrix} \qquad \text{(Eq. 2)}$$

Based on the Jacobian matrix of disease-free equilibrium point, there will five negative eigenvalues in λ_1 as follows.

$$\lambda_1 = \left[-(\mu+\omega) \quad -\mu \quad -\mu \quad -\left(\frac{\Theta(\mu+\omega)+\Gamma}{2(\mu+\omega)}\right) \quad -\left(\frac{\Theta(\mu+\omega)-\Gamma}{2(\mu+\omega)}\right)\right] \qquad \text{(Eq. 3)}$$

with $\Theta = (\gamma + 2\mu + \sigma)$ and $\Gamma = \sqrt{(\mu+\omega)[\Theta + 4(\Lambda\beta\sigma - \Omega)]}$. In addition, the fifth eigenvalue will be negative as long as $\Theta(\mu+\omega) > \Gamma$.

3.1.2 Endemic case

The endemic equilibrium point $E_2 = (S_2, E_2, I_2, V_2, R_2)$ is the condition where there are individuals infected with *monkeypox* in the population, which occurs when $I \neq 0$. The second equilibrium point is obtained in the form $E_2 = \left(\frac{\Phi}{\beta\sigma}, \frac{\Lambda\beta\sigma-\Omega}{\sigma(\mu+\sigma)\beta}, \frac{\Lambda\beta\sigma-\Omega}{\beta\Phi}, \frac{\omega\Phi}{\beta\sigma\mu}, \frac{(\Lambda\beta\sigma-\Omega)\gamma}{\beta\Phi\mu}\right)$, with $\Omega = (\gamma+\mu)(\mu(\mu+\omega+\sigma)+\omega\sigma)$ and $\Phi = (\gamma+\mu)(\mu+\sigma)$. By using the same method as free-disease case, the Jacobian matrix for E_2 can be seen in Equation (4).

$$J_2 = \begin{bmatrix} -\dfrac{\Lambda\beta\sigma-\Omega}{\Phi} - (\mu+\omega) & 0 & -\dfrac{\Phi}{\sigma} & 0 & 0 \\ \dfrac{\Lambda\beta\sigma-\Omega}{\Phi} & -(\mu+\sigma) & \dfrac{\Phi}{\sigma} & 0 & 0 \\ 0 & \sigma & -(\mu+\gamma) & 0 & 0 \\ \omega & 0 & 0 & -\mu & 0 \\ 0 & 0 & \gamma & 0 & -\mu \end{bmatrix} \qquad \text{(Eq. 4)}$$

Based on the Jacobian matrix J_2, it is possible to obtain two negative eigenvalues analytically in Equation (5).

$$\lambda_2 = [-\mu \quad -\mu] \qquad \text{(Eq. 5)}$$

while the remaining eigenvalues are written in the form of a characteristic equation as follows.

$$a_3\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0 \qquad \text{(Eq. 6)}$$

With $a_3 = \Phi$, $a_2 = \Phi(\Theta + \mu + \omega) + \Lambda\beta\sigma - \Omega$, $a_1 = \Phi\big(\gamma(2\mu + \omega + \sigma) + \mu(3\mu + 2\omega + 2\sigma) + (\omega\sigma - \Phi)\big) + \Theta(\Lambda\beta\sigma - \Omega)$, and $a_0 = \Phi(\Lambda\beta\sigma - \Omega)$. Furthermore, Routh-Hurwitz criterion is used to find its stability, where the model is stable if $b = a_1a_2 - a_0a_3 > 0$ and $c = a_3b > 0$. From the calculations that have been done, the value of b and c are greater than zero which indicates the stable nature of the model.

3.2 Model simulation

In this subsection, the SEIVR model for the *monkeypox* virus will be analyzed numerically with the help of Python program. It will be done by substituting the parameter values that have already been determined, as shown in Table 1.

Table 1. Parameters of model and their value

Parameters	Value	References
Λ	3	Assumed for simulation purposes
ω	0.0493	Estimated based on data
μ	0.0219	Estimated based on data
σ	0.0329	Estimated based on data
β	0.03	(Al-Shomrani, Musa, & Yusuf, 2023)
γ	0.0575	Estimated based on data

The numerical simulations are conducted based on endemic condition. Therefore, an initial value is certainly needed for each compartment so that the simulation can be carried out. In this study, three simulations were carried out with $S(0)$, $V(0)$, and $R(0)$, values 200, 0, and 0, respectively. Meanwhile, each visualization displayed on Figure 2 represents the condition where $I < E$, $I > E$, and $I = E$. In Figure 2, the first simulation uses the initial values $I(0) = 15$ and $E(0) = 35$, then the second simulation uses the initial values $I(0) = 35$ and $E(0) = 15$, and the last simulation uses the initial values $I(0) = E(0) = 25$.

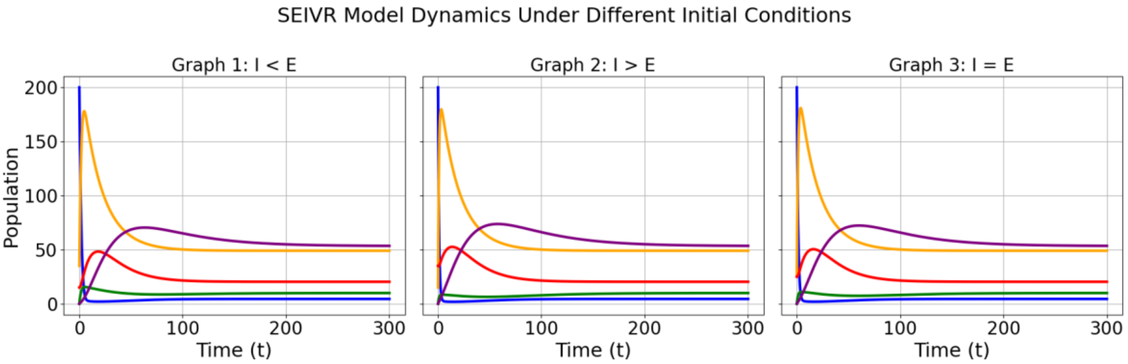

Fig. 2. Population dynamics of susceptible (blue), exposed (yellow), infected (red), vaccinated (green), and recovered (purple) compartments in SEIVR model based on parameter value on Table 1 for time $t \in [0,300]$.

Based on the visualization results in Figure 2, it can be observed that there is not much difference in the spike of the graph for each condition. The number of each population converges to a certain points, which are the endemic equilibrium point E_2 where its value has given in Subsection 3.1.2. Although the model does not include a treatment compartment such as medicine, it can be seen in Figure 2 that the disease will be cured naturally as time goes by. In addition, the infected population is not vanished in the observation domain t with a sufficiently low number, approximate to the equilibrium point.

3.3 Basic reproductive number

In mathematical modelling related to the spread of disease, the basic reproduction number (R_0) can be used to determine the possibility of a disease epidemic in a population in the future. When $R_0 > 1$, each infected individual can transmit the disease to more than one susceptible individual so that the disease can spread quickly in the population (endemic case), while $R_0 < 1$ resulting each infected infected can transmit the disease to less than one susceptible individual so that over time the disease will disappear from the population (disease-free state). In Model (1), the basic reproduction ratio (R_0) can be found using the next generation matrix. In this method, an epidemic model is assumed that can be written in the form of

$$\frac{dX}{dt} = f(X,Y,Z) \tag{Eq. 7}$$
$$\frac{dY}{dt} = g(X,Y,Z) \tag{Eq. 8}$$
$$\frac{dZ}{dt} = h(X,Y,Z) \tag{Eq. 9}$$

where X represents the uninfected subpopulation vector including susceptible, vaccinated, and recovered subpopulations, Y represents the infected but not yet infectious (latent) subpopulation vector, while Z represents the infected and infectious subpopulation vector. From this grouping, it can be written that $X = (S \quad V \quad R)^T$, $Y = E$, and $Z = I$. Furthermore, Equation (7) to (9) can be written in Equation (10) to (12) as follows

$$f(X,Y,Z) = \begin{pmatrix} \Lambda - \beta SI - (\mu + \omega)S \\ \omega S - \mu V \\ \gamma I - \mu R \end{pmatrix} \tag{Eq. 10}$$
$$g(X,Y,Z) = (\beta SI - (\mu + \sigma)E) \tag{Eq. 11}$$
$$h(X,Y,Z) = (\sigma E - (\mu + \gamma)I) \tag{Eq. 12}$$

Note that $(X^*, 0{,}0) = \left(\frac{\Lambda}{\mu+\omega}, 0{,}0, \frac{\omega\Lambda}{(\mu+\omega)\mu}, 0\right)$ is the disease-free equilibrium point of Model (1). When $g(X^*, Y, Z) = 0$, then $E = \frac{\Lambda\beta I}{(\mu+\sigma)(\mu+\omega)}$. Substituting the value of E into the function of $h(X,Y,Z)$ will result in $h(X,Y,Z) = \frac{\Lambda\sigma\beta I}{(\mu+\sigma)(\mu+\omega)} - (\mu + \gamma)I$. Furthermore, it is important to find value of A, which can be obtained by calculating the partial derivative of $h(X^*, \hat{g}(X^*, 0), 0)$ with respect to Z. So it can be obtained $A = \frac{\Lambda\sigma\beta}{(\mu+\sigma)(\mu+\omega)} - (\mu + \gamma)$. The last equation can be written in the form of $A = M - D$ where $M = \frac{\Lambda\sigma\beta}{(\mu+\sigma)(\mu+\omega)}$ and $D = (\mu + \gamma)$. Finally, the value of R_0 can be obtained from $\sup\{MD^1\}$ as follows.

$$R_0 = \frac{\Lambda\sigma\beta}{(\mu + \sigma)(\mu + \omega)(\mu + \gamma)} \tag{Eq. 13}$$

Now, equilibrium points EP_1 and EP_2 can be written respectively by involving the value of R_0 in Equation (13) such as $E_1^*\left(\frac{R_0(\mu+\sigma)(\mu+\gamma)}{\sigma\beta}, 0{,}0, \frac{\omega R_0(\mu+\sigma)(\mu+\gamma)}{\mu\sigma\beta}, 0\right)$ and $\boldsymbol{E}_2^* = \left(\frac{\Lambda}{\mathrm{R}_0(\mu+\omega)}, \frac{(\mu+\gamma)(\mu+\omega)}{\sigma\beta}(R_0 - 1), \frac{\mu+\omega}{\beta}(R_0 - 1), \frac{\Lambda\omega}{\mu\mathrm{R}_0(\mu+\omega)}, \frac{\gamma(\mu+\omega)}{\mu\beta}(R_0 - 1)\right)$. Regarding to the existence of the endemic equilibrium point, the value of R_0 must be greater than one so that the conditions $S > 0$, $E > 0$, $I > 0$, $V > 0$, and $R > 0$ will be met.

Please look back at Figure 2 which is using data from Table 1, the value of the basic reproductive number can be obtained such that $R_0 = 9.55778711 > 1$, and it also can be seen in Figure 2 that the infected population still exists for a long period of time. Of course this is in accordance with the previous discussion that there will be an endemic in the future when $R_0 > 1$.

With this approach, it is expected that the model developed will not only be able to describe the dynamics of the spread mathematically, but can also be used as a tool in the formulation of public health policies. The model is expected to provide strategic information for decision makers regarding the optimal timing for vaccine administration, estimation of quarantine facility requirements, or the spread scenario if no intervention is implemented. The results of this model can also contribute to risk assessment and public health resource planning in the future, particularly in anticipating the potential reemergence of *monkeypox* outbreaks or similar zoonotic diseases.

Moreover, the persistence of low infection rates over a long period of time means the problem is not yet resolved. Therefore, health services must be able to provide an appropriate response, especially with the aim of controlling the spread of the disease and preventing a resurgence. The first thing that can be done is to carry out regular monitoring, especially in terms of early detection so that treatment can be faster. The skills and competencies of health workers also need to be improved because they will be at the forefront when infections occur in the future. But of course, this cannot be done only by a handful of health workers; it requires a concerted effort from the community to ensure better and more comprehensive monitoring. Thus, public education is needed for the general public to increase public awareness of *monkeypox* and how to handle it. Furthermore, preventive measures can also be taken by optimizing vaccinations to ensure that more people are immune to the virus.

To support the measures mentioned above, healthcare facilities must also be improved. This may include providing sufficient and standardized isolation rooms which is crucial for preventing the spread of infection in healthcare facilitiesand. The resources assigned to care for patients must also be adequate so that treatment can be carried out appropriately. Furthermore, healthcare institutions must maintain adequate supplies of medications and personal protective equipment for patient care. Collaboration from various parties will have a positive impact on comprehensive outbreak management.

4. Conclusions

The SEIVR model was employed to analyze the spread of *monkeypox* and revealed the existence of two equilibrium points, namely the disease-free equilibrium and the endemic equilibrium. The disease-free equilibrium represents an ideal state where no infections occur, whereas the endemic equilibrium reflects a condition where the disease persists within the population. Based on simulations, these equilibrium points provide critical insights into the dynamics of the disease under various scenarios.

This research demonstrates that the system stability can be achieved, which indicates the system's ability to maintain equilibrium in the face of disease transmission. Consequently, effectively controlling key parameters is essential in determining whether the disease will be eradicated or become endemic. Simulation results based on assumed *monkeypox* case data highlight two potential scenarios. The first scenario suggests that if public health interventions, such as vaccination and treatment, are implemented effectively, the disease can be controlled and eventually eradicated from the population. In contrast, the second scenario indicates that inadequate control measures could result in *monkeypox* becoming endemic, with a stable but low infection rate within the population.

Moreover, the involvement of basic reproductive number provides additional analysis that is consistent with the stability of the system which has discussed previously. The value of basic reproductive number is affected by the value of each parameter given in Table 1. The obtained value of basic reproductive number indicates the existence of the virus for a long period of time. Therefore, it is necessary to give treatment for the infected subpopulation an also the exposed (latent) ones.

These findings hold significant implications for decision-making in *monkeypox* control efforts in Indonesia. Public health initiatives should focus on managing critical parameters through strategic and sustainable measures to prevent the disease from becoming endemic. The simulations underscore the importance of data-driven approaches in designing effective public health interventions, such as controlling the spread of disease through regular monitoring and early detection, educating the public, optimizing vaccination, improving healthcare facilities, and ensuring the availability of medicines and personal protective equipment. This model can be developed in further reseach in many ways, such as by adding treatment compartment or virus transition in rodents. It can also be developed by implement stochsatic theory or using fractional differential equation in model construction. The discussion about R_0 can also be carried out futher more.

Acknowledgement

The authors would like to thank Fidelis Nofertinus Zai for fruitful discussions at the middle stage of this research, and also Committees of Marscion (Mathematics Profession Seminar and Scientific Writing Competition) 2024 for giving us the opportunity to publish this article.

Author Contribution

The first author contributed in conceptualization and design of the study, mathematical modelling and its analysis, while the other authors contributed in data collection, numerical simulation and its interpretation. The second author contributed in the formulation of reproduction number and its analysis. All authors participated in drafting and revising the manuscipt, approved the final version for publication, and take responsibility for the accuracy and integrity of the work.

Funding

This study received no external funding.

Data Availibility Statement

This study uses the data available in Subsection 3.2.

Conflict of Interest

The authors declare no conflict of interest.

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