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RESEARCH ARTICLE

Design and Investigation of Mathematical Model for the Vaccination and Transmission of Monkeypox Virus without Lifelong Immunity

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Abstract

Objective: For the purpose of evaluating the potential for outbreaks of monkeypox (MPX) in a metropolitan region and defining necessary public health measures to restrict the spread of the virus through the use of a model of its dissemination, the preventive interventions have a critical role in the management of infectious diseases. The objective of this study is to assess the feasibility of managing and eliminating MPX through the use of voluntary vaccination and treatment measures. **Methods:** We developed two equilibriums for the model, endemic and disease-free, via standard methods. Using the comparison theorem and the next-generation matrix, it was demonstrated that the DFE is both locally and globally asymptotically stable if $R_0 < 1$. By using linearization approach, the endemic equilibrium point only occurred when $R_0 > 1$. Through the utilization of model and sensitivity analysis techniques, we are able to discern the pivotal public health elements and afterwards show several scenarios based on distinct transmission assumptions. **Findings:** Based on the findings of the study, implementing measures to isolate individuals with diseases from the wider community can effectively mitigate the transmission of diseases. A comprehensive examination of the model parameters using sensitivity analysis indicates that when the treatment and vaccination control parameters are augmented, there is a decrease in the fundamental reproduction numbers of the model. These reproduction numbers serve as a crucial threshold for identifying new infections within host populations. **Novelty:** Our research highlights the importance of treatment, vaccination, and public understanding as the exclusive preventive measures in the context of monkeypox. Furthermore, our analysis led us to the determination that disease can be managed and controlled, but achieving lasting immunity is not yet possible, given the absence

of definitive treatments and vaccination for monkeypox infection.
2010 Mathematics Subject Classification: 81T99, 93A30.

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1 Introduction

The monkeypox virus, which belongs to the Orthopoxvirus genus and family of Poxviridae, is the infectious disease that causes monkeypox [(1)]. It mostly affects animals, especially rodents, squirrels, and monkeys. Direct contact with wild animals, especially rodents and primates, is the primary route of monkeypox viral transmission to humans. However, it should be noted that transmission between humans occurs quite regularly as well. Human-to-human transmission is linked to respiratory droplet inhalation, skin-to-skin contact, exposure to contaminated surfaces or objects in the environment of an infected patient, and scratching an infected wound [(2)]. While incidences of infection can be discovered worldwide, the majority of cases are found in isolated communities near tropical rain forests in Central and West Africa, where people frequently come into contact with sick animals [(3)]. Following the successful eradication of smallpox, the monkeypox virus has emerged as the leading orthopoxvirus. In humans, monkeypox virus infection causes symptoms that are similar to but milder than smallpox [(4)]. Some people who may have monkeypox have reported experiencing symptoms like fever, headache, lumbago, muscle aches, lymph nodes, rigours, and exhaustion. Monkeypox, a mild disease with a 7-14 day incubation period, can cause severe symptoms in individuals with weakened immune systems.

In 1958, outbreaks in a group of monkeys used for research led to the discovery of the first human case of monkeypox. There have been a total of 89,581 cases of infection documented worldwide, including 30,767 cases in the United States [(5)]. In May 2022, there was a massive outbreak of mpox [(6)]. There have been 6106 confirmed cases and 51 suspected cases of mpox in over 30 non-endemic countries as of June 6, 2022, and this figure is steadily increasing [(7)]. Nguyen et al. [(8)] estimate that monkeypox infection has a 10% fatality rate, with a greater risk in children under 10. Due to shared clinical features [(9)], smallpox and human monkeypox are closely related. Primate, rodent, and pet bites and sneezes are the most common routes of transmission for monkeypox to people. There is currently no approved and effective treatment for monkeypox virus infection; however, noval antivirals such as Tecovirimat, Brincindofovir, and vaccinia immune globulin can suppress the infection. Due to a decline in smallpox herd immunity, the prevalence of monkeypox has rapidly increased during the past ten years [(10)]. The smallpox vaccine is 85 % effective in preventing monkeypox [(11)]. Most newborns are now at risk for mpox [(12)] because vaccination against smallpox was discontinued in 1980 and there is no medical cure for it. Therefore, it is important to anticipate mpox outbreak trends and implement efficient prevention and control measures.

Due to previous neglect, less is known about the transmission pathways of the disease. However, few studies have utilised mathematical models to investigate the dynamics of the monkeypox virus. A deterministic mathematical model [(13)] was developed for the monkeypox outbreak, suggesting that isolating diseased individuals from other populations may reduce the disease incidence. The authors of [(14)] used nonlinear differential equations to study how monkeypox spreads. They found that a person's immune system has a big effect on how well they get over an orthopoxvirus infection. The game theoretic model case study of the dynamics of the monkeypox virus is used to evaluate vaccination approaches [(15)]. Using a fractional order mathematical model, Olumuyiwa J. P. et al. [(16)] examine the dynamics of monkeypox transmission. Recently, in [(17)], the authors developed a mathematical model with environmental

transmission to examine the dynamics and potential controlling methods of the monkey pox outbreak in 2022. TeWinkel[18], Somma et al.[19], Mesady E.I. et al.[20], and Grant et al.[21] all made significant additions. Having researched the details of monkeypox viral transmission, we intend to analyse the various elements that can slow the disease's spread and how those effects trickle down to the population's basic reproduction rate.

This study developed a multi-group model based on mpox's natural history to understand transmission and prevention in humans, aiding in estimating transmission risk, evaluating treatment and vaccination efficacy.

2 Methodology

2.1 The Model's Description

The model in this research splits the population into two groups: non-human primates, or some wild rodents, and humans. Rodents were further classified into sub-classes, i.e., Susceptible (S_m), Exposed/Latent (E_m), Infected (I_m), and Recovered (R_m). The rodents are added at a constant birth rate (A_m) into the Susceptible class(S_m) and they are exposed to the monkeypox virus at a rate λ_m after entering into contact with an infected rodent with

$\lambda_m = \beta_{m1} \frac{I_m}{N_m}$

where β_{m1} is the product of the effective contact rate and infection probability per contact. The exposed primate travels towards the infected class (I_m) at b_m after incubation. Infected animals can transfer the disease to others, die at a rate of d_m, or recover spontaneously at a rate of ε_m and enter the region of (R_m). All rodents in the model experience a natural mortality rate of μ_m.

Moreover, the overall human host population was subdivided into the sub-populations of Susceptible (S_h), Vaccinated (V_h), Exposed (E_h), Infected (I_h), and Recovered (R_h) humans. By birth and migration at a constant rate A_h, the susceptible population is recruited into S_h. A susceptible person either receives a monkeypox vaccine at a rate α_h and progresses to (V_h) with lifetime immunity, or they are exposed to the virus after coming into contact with an infected person or rodents, i.e., a non-human primate, at a rate λ_h with

$\lambda_h = \beta_{m2} \frac{I_m}{N_m} + \beta_h \frac{I_h}{N_h}$

where β_{m2} is the product of the effective contact rate and the probability that a human will contract the disease after coming into contact with an infectious non-human primate animal, and the product of the effective contact rate and the probability of contracting monkeypox after interaction with an infectious human is β_h. The exposed individual in class (E_h) dies at a constant rate d_h, and this was taken as a novelty of the research work. This death rate was due to the extremely low immunity (which may be due to old age or infection of another disease) of the exposed person. Due to virus infection, it moves at a rate of b_h to the infected class (I_h) after the incubation period. As a result of the virus, people in (I_h) either pass away or recover after getting treatment at a rate of εh into (R_h). There is no permanent immunity, since some of them eventually lose it in (R_h) and start to become susceptible once more at a rate δ_h. The natural mortality rate μ_h is the same for every member of the human subpopulation. All model parameters are non-negative and will be assumed to have the table values during simulations and sensitivity analysis. Below is the model's schematic diagram, used in this description.

2.2 Model Equations

We generated the following model equations from the model's description and the schematic picture shown in Figure 1.

$$S_m^{'} = A_m - (\mu_m + \lambda_m) S_m \tag{1}$$

$$E_m^{'} = \lambda_m S_m - (\mu_m + b_m) E_m \tag{2}$$

$$I_m^{'} = b_m E_m - (\mu_m + d_m + \varepsilon_m) I_m \tag{3}$$

$$R_m^{'} = \varepsilon_m I_m - \mu_m R_m \tag{4}$$

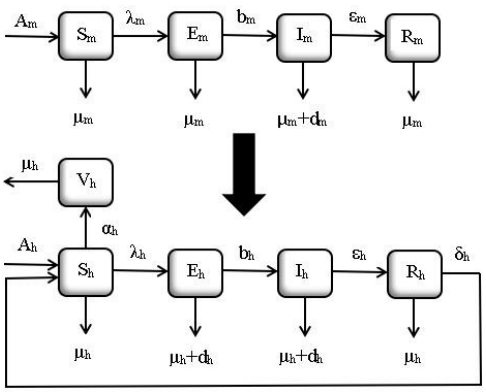

Fig 1. Transmission model of Non-human primates and Human

$$S_h^{'} = A_h - (\mu_h + \lambda_h + \alpha_h) S_h + \delta_h R_h \tag{5}$$

$$V_h^{'} = \alpha_h S_h - \mu_h V_h \tag{6}$$

$$E_h^{'} = \lambda_h S_h - (\mu_h + d_h + b_h) E_h \tag{7}$$

$$I_h^{'} = b_h E_h - (\mu_h + d_h + \varepsilon_h) I_h \tag{8}$$

$$R_h^{'} = \varepsilon_h I_h - \mu_h R_h - \delta_h R_h \tag{9}$$

Additionally, we have the total population of both humans and non-human primates i.e.,

$$N_m(t) = S_m + E_m b + I_m + R_m \tag{10}$$

$$N_h(t) = S_h + V_h + E_h + I_h + R_h \tag{11}$$

With the following non-negative initial conditions:

$$S_m(0) \geq 0, E_m(0) \geq 0, I_m(0) \geq 0, R_m(0) \geq 0 \tag{12}$$

$$S_h(0) \geq 0, V_h(0) \geq 0, E_h(0) \geq 0, I_h(0) \geq 0, R_h(0) \geq 0 \tag{13}$$

$$S_m(0) + E_m(0) + I_m(0) + R_m(0) \leq N_m(0) \tag{14}$$

and

$$S_h(0) + V_h(0) + E_h(0) + I_h(0) + R_h(0) \leq N_h(0) \tag{15}$$

Table 1. Model parameter values

Parameter	Value	Source
A_m	0.2	Assumed
A_h	0.029	(22)
μ_m	0.1	Assumed
μ_h	0.02	(22)
d_m	0.2	Assumed
d_h	0.1	(22)
ε_m	0.3	Assumed
ε_h	0.83	(22)
b_m	0.3	Assumed
b_h	0.095	(13)
α_h	0.1	Assumed
β_{m1}	0.0027	(22)
β_{m2}	0.00252	(22)
β_h	0.000063	(22)

2.3 Model Evaluation

The model analysis starts by demonstrating that all of the model's feasible solutions are uniformly bounded in the proper subset of Ω. Hence, the feasible area

$$\Omega = \begin{cases} (S_m, E_m, I_m, R_m) \in R_+^4; N_m \leq \dfrac{A_m}{\mu_m} \\ (S_h, V_h, E_h, I_h, R_h) \in R_+^5; N_h \leq \dfrac{A_h}{\mu_h} \end{cases} \tag{16}$$

is considered. Therefore, following appropriate substitution and differentiation of Equations (10) and (11), we derived

$$N_m^{'}(t) \leq A_m - \mu_m N_m \tag{17}$$

and

$$N_h^{'}(t) \leq A_h - \mu_h N_h \tag{18}$$

Now that we have applied the values of Equation (10) to the above mentioned differential in- equality, we obtain

$$\begin{cases} N_m \leq N_m\,(0)e^{-\mu_m t} + \dfrac{A_m}{\mu_m}(1 - e^{-\mu_m t}) \\ N_h \leq N_h\,(0)e^{-\mu_h t} + \dfrac{A_h}{\mu_h}(1 - e^{-\mu_h t}) \end{cases} \tag{19}$$

Here, $N_m(0)$ and $N_h(0)$ are the initial populations of the rodents or non-human primates and the humans respectively. Hence, $0 \leq N_m \leq \frac{A_m}{\mu_m}$ *and* $0 \leq N_h \leq \frac{A_h}{\mu_h}$ *as* $t \to \infty$.

As long as $N_m(0) \leq \frac{A_m}{\mu_m}$ and $N_h(0) < \frac{A_h}{\mu_h}$, it follows that $\frac{A_m}{\mu_m}$ and $\frac{A_h}{\mu_h}$ are upper bounds for N_m and N_h, respectively. As a result, the region Ω, a positively invariant set, is where the model equations' feasible solution enters. The system is therefore properly presented both mathematically and epidemiologically.

2.4 Model Equilibrium Points

The model's disease-free (E_0) and endemic (E^*), which only occurred when $R_0 > 1$, was determined using standard approaches, and its equilibrium points are as follows.

DFE points (disease free equilibrium) are steady state solutions to the model equations. Furthermore, at this point, rodents or non-human primates and humans do not have the monkeypox virus. Equilibrium points are obviously the solutions to the model equations that fulfill the conditions, i.e.

$S_m^{'} = E_m^{'} = I_m^{'} = R_m^{'} = S_h^{'} = V_h^{'} = E_h^{'} = I_h^{'} = R_h^{'} = 0$

It may be produced by applying these conditions to the model (Equations (1), (2), (3), (4), (5), (6), (7), (8) and (9)) system of nonlinear differential equations. Furthermore, the presence of no sickness indicates that $I_m = 0$ and $I_h = 0$, as these belong to the afflicted classes of both the human population and non-human primates. These circumstances allow us to get the disease-free equilibrium points.

Therefore, the disease free equilibrium points i.e.

$E_0 = (S_h, V_h, E_h, I_h, R_h, S_m, E_m, I_m, R_m)$

$$= \left[\frac{A_h}{\alpha_h+\mu_h}, \frac{A_h}{\mu_h}.\frac{\alpha_h}{\alpha_h+\mu_h}, 0, 0, 0, \frac{A_m}{\mu_m}, 0, 0, 0\right] \tag{20}$$

Now, for endemic equilibrium points E*, put all the differential equations of the model is equal to zero and then solve, i.e.

$$E^* = \left(S_h^*, V_h^*, E_h^*, I_h^*, R_h^*, S_m^*, E_m^*, I_m^*, R_m^*\right) \tag{21}$$

Where,

$$S_h^* = \frac{A_h+\delta_h R_h^*}{(\mu_h+\lambda_h^*+\alpha_h)},\ V_h^* = \frac{\alpha_h}{\mu_h}.\frac{A_h+\delta_h R_h^*}{(\mu_h+\lambda_h^*+\alpha_h)},$$
$$E_h^* = \frac{\lambda_h}{\mu_h+b_h+d_h}.\frac{A_h+\delta_h R_h^*}{(\mu_h+\lambda_h^*+\alpha_h)}$$
$$I_h^* = \frac{b_h\lambda_h(A_h+\delta_h R_h^*)}{(\mu_h+b_h+d_h)(\mu_h+\lambda_h^*+\alpha_h)(\mu_h+d_h+\varepsilon_h)},$$

$$R_h^* = \frac{\varepsilon_h b_h \lambda_h^* A_h}{(\mu_h+\delta_h)(\mu_h+b_h+d_h)(\mu_h+\lambda_h^*+\alpha_h)(\mu_h+d_h+\varepsilon_h)-\varepsilon_h b_h \lambda_h^* \delta_h},$$
$$S_m^* = \frac{A_m}{(\mu_m+\lambda_m^*)},\ E_m^* = \frac{\lambda_m^* A_m}{(\mu_m+b_m)(\mu_m+\lambda_m^*)},$$
$$I_m^* = \frac{b_m\lambda_m^* A_m}{(\mu_m+b_m)(\mu_m+\lambda_m^*)(\mu_m+d_m+\varepsilon_m)},\ R_m^* = \frac{\varepsilon_m b_m \lambda_m^* A_m}{\mu_m(\mu_m+b_m)(\mu_m+\lambda_m^*)(\mu_m+d_m+\varepsilon_m)}$$

With

$$\lambda_m^* = \beta_{m1}\frac{I_m^*}{N_m^*}, \qquad \lambda_h^* = \beta_{m2}\frac{I_m^*}{N_m^*} + \beta_h\frac{I_h^*}{N_h^*},$$
$$N_m^* = \frac{A_m - d_m I_m^*}{\mu_m} \quad and \quad N_h^* = \frac{A_h - d_h I_h^*}{\mu_h}$$

2.5 Local Stability of the Disease-Free Equilibrium (DFE) Point

Using the next-generation matrix, the model's basic reproduction number was calculated. It is described as the largest eigenvalue or spectral radius of characteristic equation $\left|FV^{-1} - eI\right| = 0$. The corresponding matrices F and V for the new infectious terms and remaining transition terms, assessed at the disease-free equilibrium, are respectively. Therefore,

$$F = \begin{bmatrix} 0 & \frac{\beta_{m1}S_m}{N_m} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\beta_{m2}S_h}{N_m} & 0 & \frac{\beta_h S_h}{N_h} \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{22}$$

$$V = \begin{bmatrix} (\mu_m+b_m) & 0 & 0 & 0 \\ -b_m & (\mu_m+d_m+\varepsilon_m) & 0 & 0 \\ 0 & 0 & (\mu_h+b_h+d_h) & 0 \\ 0 & 0 & -b_h & (\mu_h+d_h+\varepsilon_h) \end{bmatrix} \tag{23}$$

Therefore,

$$FV^{-1} = \begin{bmatrix} \frac{\beta_{m1}b_m}{y_m} & \frac{\beta_{m1}}{(\mu_m+d_m+\varepsilon_m)} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ \frac{A_h\beta_{m2}\mu_m b_m}{A_m y_m(\alpha_h+\mu_h)} & \frac{A_h\beta_{m2}\mu_m}{A_m(\mu_m+d_m+\varepsilon_m)(\alpha_h+\mu_h)} & \frac{\beta_h b_h \mu_h}{y_h(\alpha_h+\mu_h)} & \frac{\beta_h\mu_h}{(\alpha_h+\mu_h)(\mu_h+d_h+\varepsilon_h)} \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{24}$$

where $y_m = (\mu_m + b_m)(\mu_m + d_m + \varepsilon_m)$ and
$y_h = (\mu_h + b_h + d_h)(\mu_h + d_h + \varepsilon_h)$.

Hence, the basic reproduction numbers of the model are $R_0 = \{R_{0,m}, R_{0,h}\}$, where $R_{0,m}$ is the monkeypox induced reproduction number for rodents or non-human primates and $R_{0,h}$ is the reproduction number for human. Hence,

$$R_{0,m} = \frac{\beta_{m1} b_m}{(\mu_m + b_m)(\mu_m + d_m + \varepsilon_m)} \tag{25}$$

$$R_{0,h} = \frac{\beta_h b_h \mu_h}{(\mu_h + b_h + d_h)(\mu_h + d_h + \varepsilon_h)(\alpha_h + \mu_h)} \tag{26}$$

Theorem 2.1 The disease- free equilibrium is locally asymptotically stable if $R_0 < 1$ and is unstable if $R_0 > 1$ with $R_0 = max\{R_{0,m}, R_{0,h}\}$.

2.6 Local Stability of the Endemic Equilibrium (EE) Point

The linearization approach will be used to determine the local stability. As a result, the Jacobian matrix J of model Equations (1), (2), (3), (4), (5), (6), (7), (8) and (9) is

$$J = \begin{pmatrix} -(\mu_m + x) & 0 & -m & 0 & 0 & 0 & 0 & 0 & 0 \\ x & -(\mu_m + b_m) & m & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b_m & -j_m & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \varepsilon_m & -\mu_m & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -n & 0 & -(\mu_h + \alpha_h + w) & 0 & 0 & z & \delta_h \\ 0 & 0 & 0 & 0 & \alpha_h & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & n & 0 & w & 0 & -(\mu_h + b_h + d_h) & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & b_h & -j_h & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \varepsilon_h & -(\mu_h + \delta_h) \end{pmatrix}$$

In J, the matrix elements are partial derivatives denoted by the notations $f_1 S_h = \frac{\partial f_1}{\partial S_h}$ and so on, and we put some replacements i.e.

$x = \frac{\beta_{m1} I_m^*}{N_m^*}, m = \frac{\beta_{m1} S_m^*}{N_m^*}, n = \frac{\beta_{m2} S_h^*}{N_m^*}, w = \frac{\beta_{m2} I_m^*}{N_m^*} + \frac{\beta_h I_h^*}{N_h^*}$

$$z = \frac{\beta_h S_h^*}{N_h^*}, j_h = (\mu_h + d_h + \varepsilon_h), j_m = (\mu_m + d_m + \varepsilon_m)$$

Next, we solve the matrix by row-reducing in an upper triangular matrix using simple row operations, and we get the following eigen values such that

$$e_1 = -(\mu_m + x), \qquad e_2 = -(\mu_m + x)(\mu_m + b_m)$$
$$e_3 = -r_m, \qquad e_4 = -r_m \mu_m$$
$$e_5 = -r_m(\mu_h + \alpha_h + w), \qquad e_6 = -\mu_h r_m(\mu_h + \alpha_h + w)$$
$$e_7 = -r_m^2(\mu_h + \alpha_h + w)(\mu_h + b_h + d_h)$$
$$e_8 = -j_h r_m^2(\mu_h + \alpha_h + w)(\mu_h + b_h + d_h)$$
$$e_9 = -j_h r_m^2(\mu_h + \delta_h)(\mu_h + \alpha_h + w)(\mu_h + b_h + d_h)$$

where $r_m = [j_m(\mu_m + x)(\mu_m + b_m) - m\mu_m b_m]$

Hence, all the eigen values e_i for i = 1,2,…,9 are real and negative. Therefore, endemic equilibrium is locally asymptotically stable from the below theorem:

Theorem 2.2 The endemic equilibrium (E^*) is locally asymptotically stable if $R_0 > 1$ with $R_0 = max\{R_{0,m}, R_{0,h}\}$.

2.7 Global Stability Analysis of Disease Free Equilibrium Point

Theorem 2.3 The disease- free equilibrium is locally asymptotically stable if $R_0 < 1$ and is unstable if $R_0 > 1$.

Proof: The following inequality uses the comparison theorem to compare the rate of change of the model's variables that reflect the infectious classes

$$\begin{bmatrix} E_m' \\ I_m' \\ E_h' \\ I_h' \end{bmatrix} \leq (F-V) \begin{bmatrix} E_m \\ I_m \\ E_h \\ I_h \end{bmatrix} - M_1\theta_1 \begin{bmatrix} E_m \\ I_m \\ E_h \\ I_h \end{bmatrix} - M_2\theta_2 \begin{bmatrix} E_m \\ I_m \\ E_h \\ I_h \end{bmatrix} - \theta_3 \begin{bmatrix} E_m \\ I_m \\ E_h \\ I_h \end{bmatrix} \tag{27}$$

where F and V are defined in Equations (22) and (23) respectively, and $M_1 = 1 - \frac{S_h^0}{N_h^0}, M_2 = 1 - \frac{V_h^0}{N_h^0}$, θ_1, θ_2 and θ_3 are non-negative matrices. And also $S_h^0 \leq N_h^0$ then $V_h^0 \leq N_h^0$. Therefore, from the Equation (27), we have

$$\begin{bmatrix} E_m' \\ I_m' \\ E_h' \\ I_h' \end{bmatrix} \leq (F-V) \begin{bmatrix} E_m \\ I_m \\ E_h \\ I_h \end{bmatrix}$$

Hence, from Equations (22) and (23), the value of matrix $(F-V)$ is

$$(F-V) = \begin{pmatrix} -(\mu_m + b_m) & \beta_{m1} & 0 & 0 \\ b_m & -(\mu_m + d_m + \varepsilon_m) & 0 & 0 \\ 0 & \frac{A_h \beta_{m2} \mu_m}{A_m(\alpha_h + \mu_h)} & -(\mu_h + b_h + d_h) & \frac{\beta_h \mu_h}{(\alpha_h + \mu_h)} \\ 0 & 0 & b_h & -(\mu_h + d_h + \varepsilon_h) \end{pmatrix} \tag{29}$$

The characteristic equation of the matrix inEquation (29) is $|(F-V) - eI| = 0$ and the eigen values e are obtained, such that

$$\beta_{m1} = -\left((\mu_m + d_m + \varepsilon_m)(\mu_m + b_m) - \beta_{m1} b_m\right], \quad e_{11} = -(\mu_m + d_m + \varepsilon_m)$$
$$e_{12} = -\left[(\mu_h + d_h + \varepsilon_h)(\mu_h + b_h + d_h) - \frac{\beta_h \mu_h b_h}{(\alpha_h + \mu_h)}\right], \quad e_{13} = -(\mu_h + d_h + \varepsilon_h)$$

As a result, all four eigenvalues of the matrix $(F-V)$ have a negative real part, implying that the matrix is stable if $R_0 < 1$. Hence, using the system equations in Equations (1), (2), (3), (4), (5), (6), (7), (8), (9), (10) and (11), $(E_m, I_m, E_h, I_h) \to (0,0,0,0)$ as $t \to \infty$. Therefore, by the comparison theorem as used before, $(E_m, I_m, E_h, I_h) \to (0,0,0,0)$ as $t \to \infty$. Now, examining the model system Equations (1), (2), (3), (4), (5), (6), (7), (8), (9), (10) and (11) at $E_m = I_m = E_h = I_h = 0$ gives

$$S_h^0 = \frac{A_h}{(\alpha_h + \mu_h)}, V_h^0 = \frac{A_h}{\mu_h}\frac{\alpha_h}{(\alpha_h + \mu_h)}, S_m^0 = \frac{A_m}{\mu_m} \; and \; (R_m, R_h) \to (0,0) \; as \; t \to \infty$$

for $R_0 < 1$. Therefore, disease free equilibrium is globally asymptotically stable for $R_0 < 1$.

2.8 Numerical Simulations for the Model

Using the parameter values in Table 1, numerical simulations for the model were run in this section. Some of these parameters were taken from existing literature when it was accessible, and when it wasn't, they were assumed for the sake of examples to match the model analysis. To simulate the model system using the parameters, we utilized MATLAB encoded with an ODE45 solver and an initial population of S_m = 250, E_m = 125, I_m = 75, R_m = 50, S_h = 8000, V_h = 5000, E_h = 3000, I_h = 2000 and R_h = 2000.The computed basic reproduction number of the model for both human and non- human primates were

$$R_{0,m} = 3.375 \times 10^{-3} \tag{30}$$

$$R_{0,h} = 4.884 \times 10^{-6} \tag{31}$$

2.9 Sensitivity Analysis of Parameters in the Model

Sensitivity analysis's objective is to determine qualitatively which parameters have the most impact on the model's output. The normalized forward sensitivity analysis index of a variable to a parameter is the ratio of the relative change in the parameter.

Definition: The normalized forward sensitivity index of a variable τ that depends, differentiable, on a parameter p is defined as

$$\Upsilon_p^{\tau} = \frac{\partial_\tau}{\partial_p} \times \frac{p}{\tau}$$

We determine the sensitivity analysis of fundamental reproductive number R_0 to the model's parameters. These indices enable us to determine the significance of each parameter values in Table 1for the spread of illness indices with positive signs demonstrate that the value of R_0 rises as the related parameters are raised, whereas indices with negative signs demonstrate that the value of R_0 falls as the corresponding parameters rise. To find out which factors most strongly influence the findings of our investigation, we do this analysis. As a result, several variables are purposefully left out of the sensitivity analysis because of their comparatively minor role in the process of disease transmission. Examples include the natural births and deaths in both humans and non-human primates. Table 2 displays the findings of the analysis.

Table 2. Numerical values of sensitivity indices for model parameters inR_0 and λ_h^*

Parameter Symbol	Sensitivity Index
d_m	-0.133
d_h	-0.089
ε_m	-0.15
ε_h	-0.105
b_m	0.25
b_h	0.17
α_h	-0.83
βm_1	1
βm_2	0.168
β_h	1

Since the sensitivity indices for the control parameters are negative, it follows from Table 2 that R_0 will decrease when the values of these control parameters α_h *and* ε_h are increased.

3 Results and Discussions

Using[13] as a framework, we examined the transmission patterns of monkeypox viral infection in the context of combined vaccination and treatment interventions. After gaining knowledge on the incubation rates of the monkeypox virus, Olumuyiwa et al.[13] proposed the addition of a novel compartment that accounts for the latent or exposed populations of both non-human primates and humans. This article demonstrates that the latent compartment in the context of vaccination has a greater influence. Figure 2 depicts how the human population that is susceptible to disease is reducing exponentially, but the population that has received vaccinations has been increasing exponentially until reaching equilibrium before beginning to decline. Figure 2 also demonstrates how the effect of vaccination causes the number of exposed and infected people to initially rise up to the threshold point before beginning to decline. This may be explained by the fact that when the vaccination is administered, the number of humans who are susceptible to the disease will continue to decline, resulting in the majority of people in the class receiving the vaccine. The increase in vaccinated class can be explained by the continuous vaccination being carried out on the susceptible humans, while the population decline was caused by the fact that the compartment was only refilled by the low vaccination rate α_h and the class also experiences natural mortality.

The infected class continued to decline as a result of the treatment intervention, as seen in Figure 3, whereas the recovered class grew exponentially up to equilibrium level before beginning to decline. This is because helping the diseased people recharges the recovered person. And because of this, the recovered class dies out exponentially as the infected human approaches to zero.

Figure 4 shows that the recoverable human class rises exponentially up to equilibrium before dying out exponentially owing to a lack of immunity. The susceptible human population declines, although in a very slower manner. This indicates that the affected population first recovered from the illness with the aid of treatment, but because of a lack of immunity, they were susceptible once more and left the recovered compartment. Thus, our hypothesis is validated by the evidence that an individual previously infected with monkeypox does not possess lifetime immunity to the disease.

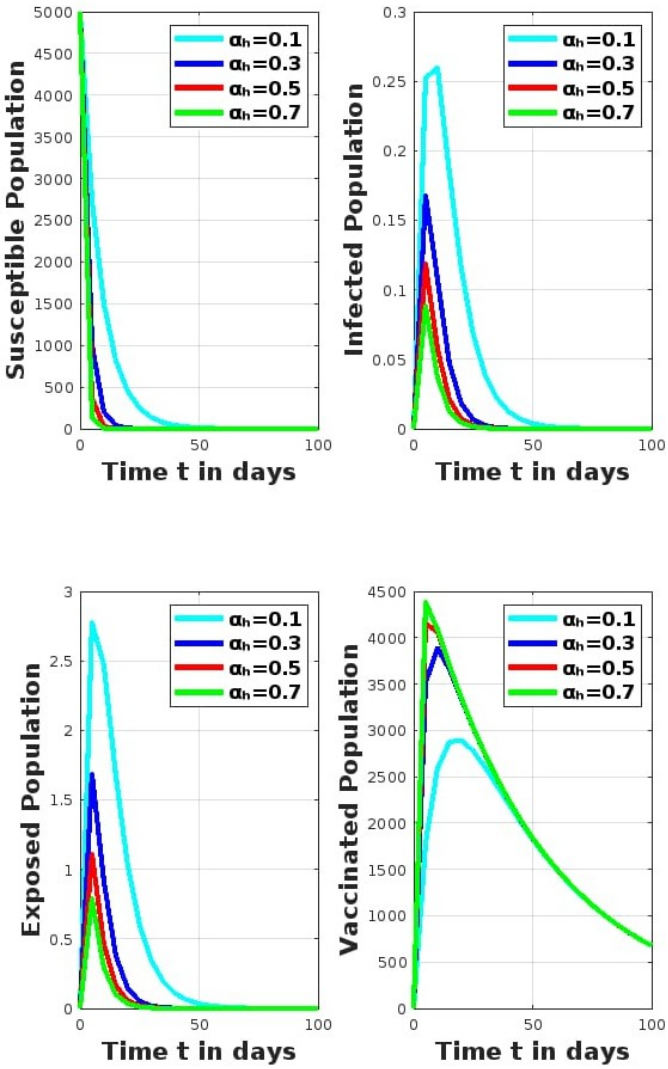

Fig 2. Effect on different classes for the variation in α_h

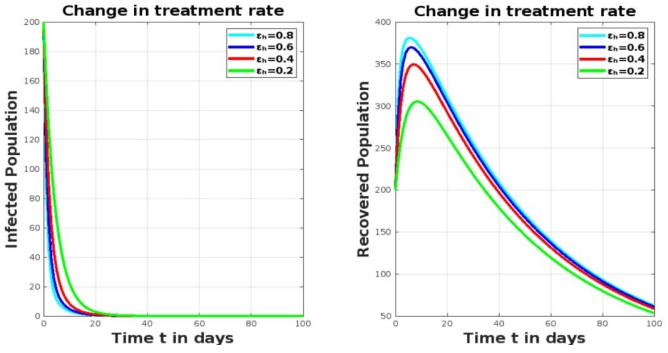

Fig 3. Effect on Infected and Treatment class for the variation in $s\varepsilon_h$

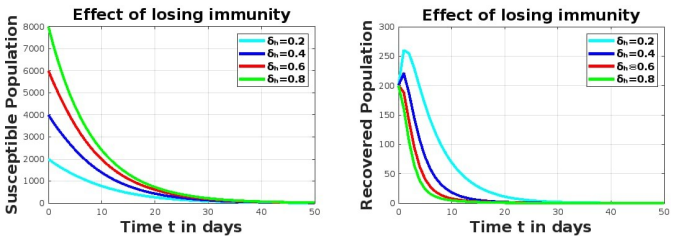

Fig 4. Effect on Susceptible and Recovered class for the variation in δ_h

4 Conclusion

In this study, we created a mathematical model to describe how the monkeypox virus spreads when vaccination and therapy are used in tandem. Basic reproduction number has been estimated using next-generation matrix technique. An analysis was conducted on the developed model. The disease-free equilibrium has been determined to have local and global asymptotic stability when the basic reproduction number, $R_0 < 1$, and instability when $R_0 > 1$. We used parameter values from the available literature to do numerical simulations and sensitivity analysis for the model and its parameters. The results of the exercise showed that if the model's suggested steps are taken, the disease will be eradicated from humans as well as non-human primates in time. Sensitivity analysis showed that with an increase in the control parameter rates of vaccination and treatment, the interventions provide the best protection against the monkeypox virus infection in the human population.

The utilization of this model is proposed for the analysis of the dynamics of the monkey- pox virus epidemic. Current research generally supports the belief that taking measures such as strengthening vaccination efforts, imposing quarantine protocols, establishing appropriate treatment facilities, and minimizing contact with infected rodents may effectively reduce the transmission of the virus.

References

1) National Center for Emerging and Zoonotic Infectious Diseases(NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP), Monkeypox. 2021. Available from: https://www.cdc.gov/poxvirus/monkeypox/index.html.
2) Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox Virus in Nigeria: Infection Biology, Epidemiology, and Evolution. *Viruses*. 2020;12(11):1–29. Available from: https://doi.org/10.3390/v12111257.
3) Of IG. Guidelines for management of monkeypox disease. 2022. Available from: https://main.mohfw.gov.in/?q=diseasealerts-0.
4) What you should know about Monkeypox. 2003. Available from: https://stacks.cdc.gov/view/cdc/26229.
5) National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP), Monkeypox. *Centers for Disease Control and Prevention*. 2022. Available from: https://www.cdc.gov/poxvirus/Mpox/reponse/2022/index.html.
6) Kozlov M. Monkeypox goes global: why scientists are on alert. *Nature*. 2022;606:15–16. Available from: https://doi.org/10.1038/d41586-022-01421-8.
7) Multi-country monkeypox outbreak in non-endemic countries. 2022. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385.
8) Nguyen PY, Ajisegiri WS, Costantino V, Chughtai AA, Macintyre CR. Reemergence of Human Monkeypox and Declining Population Immunity in the Context of Urbanization, Nigeria, 2017–2020. *Emerging Infectious Diseases*. 2021;27(4):1007–1014. Available from: https://wwwnc.cdc.gov/eid/article/27/4/20-3569_article.
9) Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, et al. The changing epidemiology of human monkeypox-A potential threat? A systematic review. *PLoS Neglected Tropical Diseases*. 2022;16(2):1–20. Available from: https://doi.org/10.1371/journal.pntd.0010141.
10) Brand SPC, Cavallaro M, Cumming F, Turner C, Florence I, Blomquist P, et al. The role of vaccination and public awareness in forecasts of Mpox incidence in the United Kingdom. *Nature Communications*. 2023;14:1–12. Available from: https://doi.org/10.1038/s41467-023-38816-8.
11) Meyer H, Ehmann R, Smith GL. Smallpox in the Post-Eradication Era. *Viruses*. 2020;12(2):1–11. Available from: https://doi.org/10.3390/v12020138.
12) Beer EM, Rao VB. A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy. *PLOS Neglected Tropical Diseases*. 2019;13(10):1–20. Available from: https://doi.org/10.1371/journal.pntd.0007791.
13) Olumuyiwa JP, Sumit K, Nitu K, Festus AO, Kayode O, Rabiu M. Transmission dynamics of Monkeypox virus: a mathematical modelling approach. *Modeling Earth Systems and Environment*. 2022;8:3423–3434. Available from: https://doi.org/10.1007/s40808-021-01313-2.
14) Ngungu M, Addai E, Adeniji A, Adam UM, Oshinubi K. Mathematical epidemiological modeling and analysis of monkeypox dynamism with non-pharmaceutical intervention using real data from United Kingdom. *Frontiers in Public Health*. 2023;11:1–16. Available from: https://doi.org/10.3389/fpubh.2023.1101436.
15) Bankuru SV, Kossol S, Hou W, Mahmoudi P, Rychtář J, Taylor D. A game-theoretic model of Monkeypox to assess vaccination strategies. *PeerJ*. 2020;8:1–22. Available from: https://doi.org/10.7717/peerj.9272.
16) Olumuyiwa JP, Oguntolu FA, Ojo MM, Oyeniyi AO, Jan R, Khan I. Fractional order mathematical model of monkeypox transmission dynamics. *Phys Scr*. 2022;97:1–25. Available from: https://iopscience.iop.org/article/10.1088/1402-4896/ac7ebc/pdf.
17) Alshehri A, Ullah S. Optimal control analysis of Monkeypox disease with the impact of environmental transmission. *AIMS Mathematics*. 2023;8(7):16926–16960. Available from: https://www.aimspress.com/article/doi/10.3934/math.2023865.
18) TeWinkel RE. Stability analysis for the equilibria of a monkeypox model. 2019. Available from: https://dc.uwm.edu/etd/2132.

19) Somma SA, Akinwande NI, Chado UD. A mathematical model of monkey pox virus transmission dynamics. *Ife Journal of Science*. 2019;21(1):195–204. Available from: https://doi.org/10.4314/ijs.v21i1.17.
20) El-Mesady A, Elsonbaty A, Adel W. On nonlinear dynamics of a fractional order monkeypox virus model. *Chaos, Solitons & Fractals*. 2022;164:112716. Available from: https://doi.org/10.1016/j.chaos.2022.112716.
21) Grant R, Nguyen LBLL, Breban R. Modelling human-to-human transmission of monkeypox. *Bulletin of the World Health Organization*. 2020;98(9):638–640. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7463189/pdf/BLT.19.242347.pdf/.
22) Risk assessment: Monkeypox multi-country outbreak. 2022. Available from: https://www.ecdc.europa.eu/en/publications-data/risk-assessment-monkeypox-multi-country-outbreak.