A mathematical model of human Metapneumovirus (HMPV) dynamics

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Abstract

Human metapneumovirus is a viral infectious disease of health concern. In this paper, we developed a mathematical model on HMPV spread and showed that the modeled equation was mathematically well posed and epidemiologically meaningful. We adopted the dynamical system analysis technique in the model, particularly obtaining the threshold quantity $\mathcal{R}_0$, the basic reproduction number via the next generation matrix approach and also proved the existence of fixed points (steady states). The study on sensitivity analysis informed that the exposure rates of human population are the most significant in influencing new infections in the system. Lastly, we examined the short and long term dynamics of the disease within the basin of attractions using appropriate tools, and found out that there is possibility of wiping out HMPV from the populace with time provided attention is paid to awareness, exposure, and improved dietary to boost immunity level

Keywords and phrases: Human Metapneumovirus; dynamics; MSC Classification; Epidemiological Mathematical Model

1 Introduction

The first case of the human metapneumovirus (HMPV) was recorded in 2001, from nasopharyngen aspirates (NPAs) obtained from young children in Netherlands [1]. HMPV is a newly described member of the pneumyoviradae family and belongs to the genus metapneumovirus [1]. It is common among young children, elderly persons and immunocompromised individuals. HMPV is the major etiological agent responsible for about 5-10 percent of hospitalization of children suffering from acute respiratory tract infections [2]. The human metapneumovirus (HMPV) is a new member of the paramyoviradae family [1]. It belongs to the order mononigaviraes and the sub family paramyxovirinae [2] Swagatika panda et al. [2] also stated that the subfamily paramyxovirinae can also be grouped into pneumovirinae and pneumorino. The HMPV is similar with the human respiratory system virus (HRSV) but the HRSV falls under the pneumorinae subfamily while the HMPV falls under the metapneumovirus [2]. The HMPV is a viral pathogen affecting the respiratory system and it's genus is the metapneumovirus genus. HMPV is the major etiological agent responsible for about 5 percent to 10 percent of hospitalization of children suffering from acute respiratory tract infections, initial infection with HMPV usually occurs during early childhood but reinfection are common throughout life [2]. Human metapneumovirus (HMPV) exits as 2 genotypes A and B based on the sequence variability of the attachment G and fusion F surface glycoproteins. HMPV is a negative strand RVA virus that replicates in the cytoplasm, it is similar to the AMPV (a. Metapneumovirus), following HMPV exposure, an innate

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cell , B cell and T cell immune response usually developed within days [3]

Guy Bolvin et al. [1] wrote that since the initial report of HMPV by the dutch researchers in 2001, HMPV has been found in most parts of the world, including Europe, north America, Asia and Africa, particularly in countries like the United State of America (USA), Canada, the United Kingdom (UK), Germany, France, Japan, to mention a few. HMPV isolates were initially found to grow on tertiary monkey kidney and LLC - MK2 (rhesus monkey kidney), it is a respiratory pathogen of primates [1]. The virus has also been identified in HIV - infected and immunocompromised children from south Africa, study has shown that HMPV is not a new pathogen, with serological evidence of human infection dating from 1958 [1]. Most case of HMPV is recorded during the winter or early spring month, the role of HMPV as the cause of ARTI has been evaluated in many studies [1]

Guy Bolvin et al [1] presented a diagram of the human metapneumovirus (HMPV) observed under an electron microscope. Pleomorphic, spherical and filamentous particles were observed, the spherical enveloped particles varied in size, with a mean diameter of $< 209nm$. The mueolapsid had a length varying from 200 to $1000nm$, and a diameter of 17mm. The HMPV does not contain non structural genus. Some symptoms of human metapneumovirus (HMPV) includes: Cough, Fever, Runny nose, Wheezing. A few ways to prevent human metapneumovirus (HMPV) includes: frequent hand washing, avoid contact with infected persons; avoid sharing personal items; staying home when symptomatic.

Guy Bolvin et al [1]. In their work examined the human metapneumovirus under an electron microscope, they discovered spherical and filamentous particles, with the spherical enveloped particles varying in size. They also talked about countries (Canada, Japan, Germany) where cases of the virus have been found, and noted that most cases occurred during the winter or early spring month. Although the first case of the virus was in 2001, Guy Bolvin et al.[1] mentioned that they have been cases since 1958 with serological evidence of human infection. They mentioned that the RT- PCR was used to detect cytopathic effect among supernatants due to the various delay before it shows symptoms. Guy Bolvin et al.[1] also noted that no vaccines, chemotherapeutic agents or antibody preparations are currently approved for the prevention or treatment of HMPV, but the combined use of WIG and ribavina could be envisaged for treating severe HMPV infections in immunocompromised patients.

Swagatika panda et al. [2] in their work (human metapneumovirus: a review of an important respiratory pathogen) pointed out some risk factors of HMPV as premature birth, heart or neural disorders, preexisting nosocomial infection. Swagatika panda et al.[2] also wrote that HMPV - infected children were found to be more likely to require supplemental oxygen to have a longer stay in the intensive care unit (ICU) and more likely to have undergone chest radiography. They also noted that recent studies using animal models for HMPV infection and reverse genetics platforms have shed some light on HMPV pathogenetics and have allowed us to evaluate live vaccine candidates.

Charles J. Russel et al.[3]. In their work (human metapneumovirus: a largely unrecognized threat to human health) claimed it infects most children by 5 years. They also stated that following HMPV exposure, an innate cell, B cell and T cell immune response usually develops within days. Although no vaccine for this virus existing, they stated that vaccination is the most effective method for control of infectious diseases and recombinant vaccines such as alpha based vaccines and killed virus have been developed in pre-clinical studies.

Erica Washington et al [4], in their research, "Modelling Transmission of Human metapneumovirus in a Long-term care Facility" presented two deterministic and one stochastic susceptible-preinfectious-infectious-recovered (SEIR) models. Although recovered persons can be susceptible to HMPV following an infection experience, the potential for reinfection was not considered for this analysis. Fixed variables considered. Excel workbooks developed by Vynnycky and White (2010) were used for anal-

ysis. Results: In model 1, the average rate of onset of infectiousness per day = 0.20, and the average recover per day = 0.90.

In this research, we considered an (SITR) model. The infection (infectious) Class was split into two separate compartments based on the individuals immunity strength. An infectious human with high immune system recovers without undertaking any form of treatment. We used the Jacobian method to investigate the possible elimination of the disease from the partitioned fraction of the populace under study.

2 Methodology/Model formulation

- There is homogeneous mixing.
- The model population is demographic.
- We consider a frequency dependence incidence action.
- Infectious humans are of two categories: infectious with weak immune system and infectious with strong immune system.
- Infectious with strong immune need not undergo treatment to recover, thus no disease include death.
- The force of infection for each category of infectious is a fraction left of the other.
- Human undergoing treatment cannot transmit disease. Model flow diagram is seen in Figure ??:

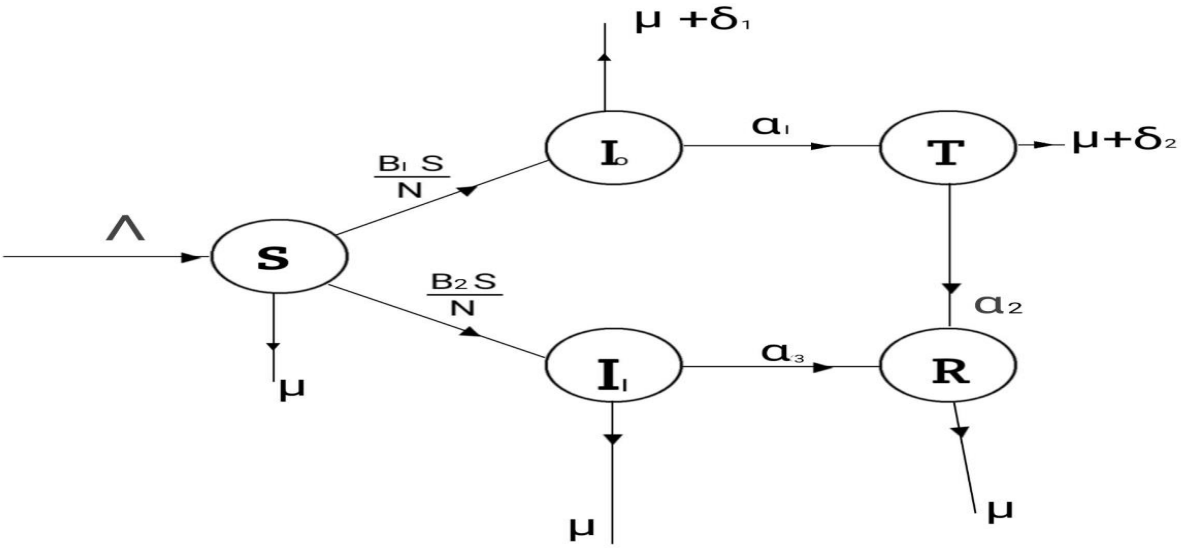

Figure 1

2.1 Model Description

The population is recruited at the rate λ. The force of infection for the humans with weak and strong immunity is given by β_1 and β_2 respectively. The infectious with weak immunity as a result of other infections. I_0 moves to treatment at the rate α_1, and eventually recovers at the rate α_2. The infectious with strong immunity recovers at the rate α_3. The natural mortality rate is given by μ and the disease included death at I_0 and T classes are δ_1 and δ_2 respectively.

2.2 Model Equations

$$\frac{dS}{dt} = \Lambda - \frac{\beta_1 S I_0}{N} - \frac{\beta_2 S I_1}{N} - \mu S \tag{1}$$

$$\frac{dI_0}{dt} = \frac{\beta_1 S I_0}{N} - \alpha_1 I_0 - (\mu + \delta_1) I_0 \tag{2}$$

$$\frac{dI_1}{dt} = \frac{\beta_2 S I_1}{N} - \alpha_3 I_1 - \mu I_1 \tag{3}$$

$$\frac{dT}{dt} = \alpha_1 I_0 - \alpha_2 T - (\mu + \delta_2) T \tag{4}$$

$$\frac{dR}{dt} = \alpha_2 T + \alpha_3 I_1 - \mu R \tag{5}$$

2.3 Description of Parameters and Variables

The following Table 1 gives a summary of the parameter values used herein:

Table 1: Values of parameters used in simulation.

S	Susceptible Human Population
I_0	Infectious humans with weak immune system
I_1	Infectious humans with strong immune system
T	Humans (infectious) undergoing treatment
R	Recovered human
Λ	Recruitment rate of human population
β_1	Force of infection on I_0
$\beta_2 = 1 - \beta_1$	Force of infection on I_1
α_1	Rate at which I_0 moves to T
α_2	Rate at which T moves to R (recovers)
α_3	Rate at which I_1 moves to R
μ	Natural death rate
δ_1	Disease induced death on I_0
δ_2	Disease induced death on T

2.4 Invariant Region/Boundedness of Model

The model would be analyzed in a biologically feasible region by showing that all feasible regions are uniformly bounded in a proper subset $D \subset \mathbb{R}^5_+$. The model feasibility must describe the region in which the solution of the system is biologically meaningful.

Theorem 1

The solution of the systems are feasible for all $t > 0$, if they enter the invariant region N. Suppose it holds, every solution of the model equations (1-5), with initial conditions. In $\mathbb{R}^5_+$ approach and stays in the compact set ? as $t \longrightarrow \infty$. It follows that the feasible solution which is a positively set of the model is given by

$$\Omega = \{(S, I_0, I_1, T, R) \in \mathbb{R}^5_+, N(t) \leq \tfrac{\Lambda}{\mu}\}$$

Proof

Let $N = (S, I_0, I_1, T, R) \in \mathbb{R}^5_+$ be any solution of the system (1-5) with non ? negative initial condition.

$$\tfrac{dN}{dt} > 0, \tfrac{dS}{dt} > 0, \tfrac{dI_0}{dt} > 0, \tfrac{dI_1}{dt} > 0, \tfrac{dT}{dt} > 0, \tfrac{dR}{dt} > 0$$
$$\tfrac{dN}{dt} = \tfrac{dS}{dt} + \tfrac{dI_0}{dt} + \tfrac{dI_1}{dt} + \tfrac{dT}{dt} + \tfrac{dR}{dt} = constant$$

Where $N = S + I_0 + I_1 + T + R$

$$\tfrac{dN}{dt} = \Lambda - \mu(S + I_0 + I_1 + T + R) - \delta_1 I_0 - \delta_2 T$$
$$\tfrac{dN}{dt} = \Lambda - \mu N - \delta_1 I_0 - \delta_2 T$$
$$\tfrac{dN}{dt} = \Lambda - \mu N \text{ where } \delta_1 = \delta_2 = 0$$
$$\Rightarrow \tfrac{dN}{dt} = \Lambda - \mu N$$
$$\tfrac{dN}{dt} = 0 \text{ if } N(t) \geq \tfrac{\Lambda}{\mu}$$

By Birkhoff and Rota's theorem on differential inequality and method of integration, we have:

$$\tfrac{d}{dt}(e^{\mu t} N(t)) \leq e^{\mu t} \Lambda$$

Integrating both sides of the above inequality equation with the initial conditions, we have:

$$N(t) \leq N(0)e^{\mu t} + \tfrac{\Lambda}{\mu}(1 - e^{\mu t})$$

Hence as $t \longrightarrow \infty$

$$N(t) \leq \tfrac{\Lambda}{\mu} \text{ which implies that } 0 \leq N \leq \tfrac{\Lambda}{\mu},$$

Then, trajectories of the model equation are bounded in the region Ω. Hence the feasible solution which is given by:

$$\Omega = \{(S, I_0, I_1, T, R) \in \mathbb{R}^5_+, N(t) \leq \tfrac{\Lambda}{\mu}\}$$

Therefore, the model is mathematically well posed.

2.5 Positivity of Solution

The model equation is epidemiologically meaningful if and only if the state variables are non ? negative for $t > 0$.

Theorem 2

Let the initial value of the system in the modeled equation be $\{(S, I_0, I_1, T, R)\}$, then the solution set $\{(S(t), I_0(t), I_1(t), T(t), R(t))\}$ of the model equation is positive, for all $t > 0$.

Proof

From equation 1

$$\frac{dS}{dt} = \Lambda - \frac{\beta_1 S I_0}{N} - \frac{\beta_2 S I_1}{N} - \mu S$$
$$\frac{dS}{dt} = -\left(\frac{\beta_1 I_0}{N} + \frac{\beta_2 I_1}{N} + \mu\right) S + \Lambda$$

Then:

$$\frac{dS}{dt} \geq -\left(\frac{\beta_1 I_0}{N} + \frac{\beta_2 I_1}{N} + \mu\right)$$

By separation of variables:

$$\frac{dS}{S} = -\left(\frac{\beta_1 I_0}{N} + \frac{\beta_2 I_1}{N} + \mu\right) dt$$

Integrating both sides:

$$\ln S = -\left(\frac{\beta_1 I_0}{N} + \frac{\beta_2 I_1}{N} + \mu\right) t + c_1$$
$$\Rightarrow S(t) = Ae^{-Pt}$$

Where $P = \left(\frac{\beta_1 I_0}{N} + \frac{\beta_2 I_1}{N} + \mu\right)$
Hence $S(t) = S_0 e^{-Pt}$
It follows that,

$$S(t) \geq 0 \text{ since } P \geq 0$$

From equation (2)

$$\frac{dI_0}{dt} = \frac{\beta_1 S I_0}{N} - (\alpha_1 + \mu + \delta_1) I_0$$
$$= -\left(\alpha_1 + \mu + \delta_1 - \frac{\beta_1}{N} S\right) I_0$$

By separating variables:

$$\frac{dI_0}{I_0} \geq -\left(\alpha_1 + \mu + \delta_1 - \frac{\beta_1}{N} S\right) dt$$

Integrating both sides:

$$\ln I_0 = -\left(\alpha_1 + \mu + \delta_1 - \frac{\beta_1}{N} S\right) t + c_2$$
$$\Rightarrow I_0 = Be^{-Qt}$$

Where $Q = \left(\alpha_1 + \mu + \delta_1 - \frac{\beta_1}{N} S\right)$

$$\Rightarrow I_0 = I(0)e^{-Qt}$$

Since $Q(t) \geq 0$, then $I(t) \geq I_0$
Similarly, the same proof shows that the remaining equations of the state variables $\forall\ t$ since $e^{yt} > 0\ \forall\ y \in R$
It therefore follows that the model equation is epidemiologically meaningful.

2.6 Equilibrium Analysis

There exist two steady states namely: disease free equilibrium (DFE) and Endemic equilibrium (EE).

2.6.1 Disease Free:

Here, there is no disease.
It is denoted by

$$E^0 = (S, I_0, I_1, T, R)$$
$$S > 0, I = 0, R = 0, I_0 = 0, I_1 = 0$$
$$\frac{dS}{dt} = \frac{dI_0}{dt} = \frac{dI_1}{dt} = \frac{dT}{dt} = \frac{dR}{dt} = 0$$

Solving equation (1)

$$\frac{dS}{dt} = \Lambda - \frac{\beta_1 S}{N} - \frac{\beta_2 S}{N} - \mu S$$
$$\Rightarrow 0 = \Lambda - \mu S^0$$
$$\Rightarrow S = \frac{\Lambda}{\mu}$$

So that:

$$E^0 = (S, I_0, I_1, T, R) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0)$$

2.6.2 Endemic Equilibrium

Here, there is presence of disease in the system

$$S > 0, I_0 > 0, I_1 > 0, T > 0, R > 0$$
$$\frac{dS}{dt} = \frac{dI_0}{dt} = \frac{dI_1}{dt} = \frac{dT}{dt} = \frac{dR}{dt} = 0$$

From equation (1)

$$0 = \Lambda - \left(\frac{\beta_1 I_0}{N} + \frac{\beta_2 I_1}{N} + \mu\right) S$$
$$\Rightarrow S^* = \frac{\Lambda}{\frac{\beta_1 I_0^*}{N} + \frac{\beta_2 I_1^*}{N} + \mu}$$

From equation (2)

$$0 = \frac{\beta_1 S I_0^*}{N} - (\alpha_1 + \delta_1 + \mu) I_0^*$$
$$\Rightarrow 0 = \left[\frac{\beta_1 S I_0^*}{N} - (\alpha_1 + \delta_1 + \mu)\right]$$

But $I_0^* \neq 0$, hence

$$\Rightarrow 0 = \left[\frac{\beta_1 S^*}{N} - (\alpha_1 + \delta_1 + \mu)\right]$$
$$\Rightarrow S^* = \frac{(\alpha_1 + \delta_1 + \mu)N}{\beta_1}$$

From equation (3)

$$0 = \frac{\beta_1 S^*}{N} - (\alpha_3 + \mu) I_1^*$$
$$I_0^* \neq 0 \text{ so that}$$
$$S^* = \frac{(\alpha_3 + \mu)N}{\beta_2}$$

From (4)

$$\frac{dT}{dt} = \alpha_1 I_0 - \alpha_2 T - (\mu + \delta_2) T$$
$$0 = \alpha_1 I_0^* - (\alpha_2 + \mu + \delta_2) T^*$$
$$\Rightarrow T^* = \frac{\alpha_1 I_0^*}{\alpha_2 + \mu + \delta_2}$$

From equation (5)

$$\frac{dR}{dt} = \alpha_2 T + \alpha_3 I_1 - \mu R$$
$$0 = \alpha_2 T^* + \alpha_3 I_1^* - \mu R^*$$
$$R^* = \frac{\alpha_2 T^* + \alpha_3 I_1^*}{\mu}$$

2.7 Basic Reproduction Number

This is a threshold quantity denoted by $\mathcal{R}_0$ which describes the average number of new infection by introducing a simple infectious person in a system of susceptible humans. The next generation approach evaluated at DFE is used in obtaining this quality. The special radius of FV^{-1} yields $\mathcal{R}_0$ where F is the jacobian transformation of the matrix formed from the infectious class where V^{-1} is the inverse of the jacobian matrix of the non - infectious part of the infectious. The two infectious/ disease classes are I_0 and I_1.
Thus:

$$F = \left(\frac{\beta_1 S I_0}{N} + \frac{\beta_2 S I_1}{N}\right), V = (-(\alpha_1 + \mu + \delta)I_0 - (\alpha_3 + \mu)I_1)$$

Thus,

$$F = \begin{pmatrix} \frac{\beta_1 S}{N} & 0 \\ 0 & \frac{\beta_2 S}{N} \end{pmatrix}$$

Obtain $V^{-1} \equiv \frac{adj(V)}{detV}$ *Matrix of cofactor*:

$$\begin{pmatrix} \alpha_3 + \mu & 0 \\ 0 & \alpha_1 + \mu + \delta_1 \end{pmatrix}$$
$$detV = (\alpha_1 + \mu + \delta_1)(\alpha_3 + \mu)$$

Thus

$$V^{-1} = \frac{1}{(\alpha_1+\mu+\delta_1)(\alpha_3+\mu)} \begin{pmatrix} \alpha_3 + \mu & 0 \\ 0 & \alpha_1 + \mu + \delta_1 \end{pmatrix}$$

Let

$$A = \alpha_1 + \mu + \delta_1$$
$$B = \alpha_3 + \mu$$
$$V^{-1} = \frac{1}{AB}\begin{pmatrix} B & 0 \\ 0 & A \end{pmatrix} = \begin{pmatrix} \frac{1}{A} & 0 \\ 0 & \frac{1}{B} \end{pmatrix}$$

We then compute FV^{-1}

$$\begin{pmatrix} \frac{\beta_1 S}{N} & 0 \\ 0 & \frac{\beta_2 S}{N} \end{pmatrix}\begin{pmatrix} \frac{1}{A} & 0 \\ 0 & \frac{1}{B} \end{pmatrix} = \begin{pmatrix} \frac{\beta_1 S}{NA} & 0 \\ 0 & \frac{\beta_2 S}{NB} \end{pmatrix}$$

To obtain the special radius (largest eigenvalue)

$$\begin{vmatrix} \frac{\beta_1 S}{NA} - \lambda & 0 \\ 0 & \frac{\beta_2 S}{NB} - \lambda \end{vmatrix} = 0$$
$$\Rightarrow \left(\frac{\beta_1 S}{NA} - \lambda\right)\left(\frac{\beta_2 S}{NB} - \lambda\right) = 0$$
$$\lambda^2 - \lambda\left[\frac{\beta_1 S}{NA} + \frac{\beta_2 S}{NB}\right] - \left(\frac{\beta_1 S}{NA}\right)\left(\frac{\beta_2 S}{NB}\right) = 0$$

The middle term vanishes since $\beta_2 = 1 - \beta_1$

$$\Rightarrow \lambda^2 = \left(\frac{\beta_1 S}{NA}\right)\left(\frac{\beta_2 S}{NB}\right)$$
$$\lambda = \pm\sqrt{\left(\frac{\beta_1 \beta_2 S^2}{N^2 AB}\right)}$$

Hence, we have that the largest eigenvalue is

$$\lambda = \frac{S}{N}\sqrt{\left(\frac{\beta_1 \beta_2}{AB}\right)}$$
$$S^0 = N = \frac{\lambda}{\mu}$$
$$R^0 = \sqrt{\left(\frac{\beta_1 \beta_2}{(\alpha_1+\mu+\delta_1)(\alpha_3+\mu)}\right)}$$

2.8 Sensitivity Analysis

This analysis helps to examine the behavior of the model system with variation in the parameter values. It helps to build confidence in model by analyzing the uncertainties associated with the changes in the parameters. It also supports the model predictions to parameter values due to errors in data assembled and assumed parameter values. It significantly gives an insight to impacts of parameters on the basic reproduction number $\mathcal{R}_0$.

A negative sensitivity Index implies that the parameter has no impact on $\mathcal{R}_0$ .while a positive index indicates surely that increasing the parameter increases $\mathcal{R}_0$ and vice versa.

We use the normalized forward sensitivity index given by
$X_z^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial z} \times \frac{z}{\mathcal{R}_0}$

Where z represents the parameter of $\mathcal{R}_0$.

For $z = \beta_1$

$$X_{\beta_1}^{\mathcal{R}_0} = \frac{\frac{1}{2}\left(\frac{\beta_2}{(\alpha_1+\mu+\delta_2)(\alpha_3+\mu)}\right)}{\sqrt{\frac{\beta_1\beta_2}{(\alpha_1+\mu+\delta_1)(\alpha_3+\mu)}}} \times \frac{\beta_1}{\sqrt{\frac{\beta_1\beta_2}{(\alpha_1+\mu+\delta_1)(\alpha_3+\mu)}}} = +\frac{1}{2}$$

For $z = \beta_2$

$$X_{\beta_2}^{\mathcal{R}_0} = \frac{\frac{1}{2}\left(\frac{\beta_2}{(\alpha_1+\mu+\delta_2)(\alpha_3+\mu)}\right)}{\sqrt{\frac{\beta_1\beta_2}{(\alpha_1+\mu+\delta_1)(\alpha_3+\mu)}}} \times \frac{\beta_1}{\sqrt{\frac{\beta_1\beta_2}{(\alpha_1+\mu+\delta_1)(\alpha_3+\mu)}}} = +\frac{1}{2}$$

Clearly the parameters in the numerator β_1 and β_2 has positive index whereas the parameters in the denominator $\alpha_1, \alpha_2, \mu, \delta_1$ will have negative index. Hence, the parameter that influence increased $\mathcal{R}_0$ are β_1 and β_2 which are the exposure rates of I_0 and I_1.

2.9 Stability Analysis

In this section, we study the possibility of reducing or eradicating the outbreak of human metapneumovirus (HMPV). There are two forms of stability investigation, namely: local and global stability.

The former investigates the possibility of eradicating or continuous spread of the disease over a short term, while the later considers dynamics on a long term in this project, we shall only consider local stability of the system

2.9.1 Local Stability of Disease Free Equilibrium

We shall employ the Jacobian transformation method in carrying out this analysis.

Theorem 3

The model equation (1-5) is:
- Locally stable if all the eigenvalues obtained from the Jacobian transformation are negative or $\mathcal{R}_0 \leq 1$.
- Asymptotically stable if $DetJ > 0$ and $tr(J) < 0$.

$$J =$$
$$\begin{pmatrix} \frac{\partial S}{\partial S}\frac{\partial S}{\partial I_0}\frac{\partial S}{\partial I_1} & \frac{\partial S}{\partial T}\frac{\partial S}{\partial R}\frac{\partial I_0}{\partial S}\frac{\partial I_0}{\partial I_0}\frac{\partial I_0}{\partial I_1} & \frac{\partial I_0}{\partial T}\frac{\partial I_0}{\partial R}\frac{\partial I_1}{\partial S}\frac{\partial I_1}{\partial I_0}\frac{\partial I_1}{\partial I_1} & \frac{\partial I_1}{\partial T}\frac{\partial I_1}{\partial R}\frac{\partial T}{\partial S}\frac{\partial T}{\partial I_0}\frac{\partial T}{\partial I_1} & \frac{\partial T}{\partial T}\frac{\partial T}{\partial R}\frac{\partial R}{\partial S}\frac{\partial R}{\partial I_0}\frac{\partial R}{\partial I_1} & \frac{\partial R}{\partial T}\frac{\partial R}{\partial R} \end{pmatrix}$$
$$J^0 = \begin{pmatrix} \frac{-\beta_1 I_0}{N} - \frac{\beta_2 I_1}{N} - \mu - \frac{\beta_1 S}{N} - \frac{\beta_2 S}{N} & 0 & 0 & \frac{\beta_1 I_0}{N} - \frac{\beta_2 S}{N} - (\alpha_1 + \mu + \delta_1\alpha_1) & \alpha_1 & 0 & \frac{\beta_2 I_1}{N} & 0 \\ -\frac{\beta_2 S}{N} - (\alpha_3 + \mu) & 0 & 0 & 0 & \alpha_1 & 0 & -(\mu + \delta_2) & 0 & 0 & 0 & \alpha_3 & \alpha_2 - \mu \end{pmatrix}$$

At DFE, $E^0 = (S^0, I_0, I_1^0, T^0, R^0) = (\frac{\Lambda}{\mu} = N, 0, 0, 0, 0)$
Hence

$$|J^0 - \lambda_i| = | -\mu - \lambda - \beta_1 - \beta_2 \quad 0\,0\,0\,\beta_1 - (\alpha_1 + \mu + \delta_1) - \lambda\,0 \quad 0\,0\,0\,0\,\beta_2 - (\alpha_3 + \mu) - \lambda \quad 0\,0$$
$$0\ \alpha_1\alpha_3 - (\alpha_2 + \mu + \delta_2) - \lambda\,0\,0\,0\,0 \quad 0 - \mu - \lambda| = 0$$
$$\Rightarrow [(-\mu - \lambda)^2(\beta_1 - (\alpha_1 + \mu + \delta_1))][\beta_2 - (\alpha_3 + \mu) - \lambda][-(\alpha_2 + \mu + \delta_2) - \lambda] = 0$$

Hence

$$\lambda_1 = -\mu$$
$$\lambda_2 = -\mu$$
$$\lambda_3 = \beta_1 - (\alpha_1 + \mu + \delta_1)$$
$$\lambda_4 = \beta_2 - (\alpha_3 + \mu)$$
$$\lambda_5 = -(\alpha_2 + \mu + \delta_2)$$

F or λ_3, $\beta_1 < (\alpha_1 + \mu + \delta_1) \longrightarrow negative$
$\lambda_5 = -(\alpha_2 + \mu + \delta_2) < (\alpha + \mu) \longrightarrow negative$
Based on the above α_3 and α_4 are both negative and then with $\alpha_1, \alpha_2, \alpha_5$ already negative, then system is locally stable. If, $\beta_1 > (\alpha_1 + \mu + \delta_1)$ and $\beta_2 > (\alpha_3 + \mu)$, then both $\alpha_3, \alpha_4 > 0$, this implies system is unstable.
For the second part of the theorem.

$$DetJ = [(\mu)^2(\beta_1 - (\alpha_1 + \mu + \delta_1))][(\beta_2 - (\alpha_3 + \mu))][-(\alpha_3 + \mu + \delta_2)] \neq 0$$

$DetJ \neq 0$, means it's either positive or negative depending on the value of β_1 and β_2
$tr(j) =$ *sum of the diagonal pivots of* J^0
Thus: $Tr()j$ is either positive or negative depending on the values of β_1 and β_2.
By the above analysis, the system will be LAS (locally and asymptotically stable) depending on the values of β_1 and β_2. The exposure ratio I_0 and I_1 respectively, otherwise unstable. Conclusively, it is possible to wipe out HMPV from the fraction of the population where it exists if and only if a serious check is put on the exposure rate of humans through awareness on the outbreak and deliberateness to improving one?s immunity either by natural means or by artificial means via use of supplements and other mineral nutrients supplement.

2.9.2 Global Stability of the DFE of HMPV

We show that if $\mathcal{R}_0 \leq 1$ then every solution with non-negative initial data $\longrightarrow DFE$ as $t \longrightarrow \infty$.
The theorem 1 and 2 (invariant and feasible region) of the model already shows positivity and boundedness of the solutions. So solutions remain non-negative and $N(t)$ is bounded; in particular $S(t) \leq \frac{\lambda}{\mu} = S^*$ for all t after some transient.
From equation (2) we have, for all $t \geq 0$

$$\frac{dI_0}{dt} = \frac{\beta_1 S(t)}{N(t)} I_0 - (\alpha_1 + \mu + \delta_1)I_0 \leq \frac{\beta_1 S^*}{N^*} I_0 - (\alpha_1 + \mu + \delta_1)I_0 = (\beta_1 - (\alpha_1 + \mu + \delta_1))$$

For $S(t) \leq S^*$ and $N(t) \geq S(t)$ so $\frac{S(t)}{N(t)} \leq \frac{S^*}{N^*} = 1$ (at $DFE \frac{S^*}{N^*} = 1$)
If $\mathcal{R}_0^0 = \frac{\beta_1}{\alpha_1 + \mu + \delta_1} < 1$ then the coefficient on the right hand is negative. Thus by comparison (Gronwall) we get $I_0(t) \longrightarrow 0$ as $t \longrightarrow \infty$ From equation 3

$$\frac{dI_0}{dt} \leq (\beta_2 - (\alpha_3 + \mu))I_1$$

If $\mathcal{R}_0^{(1)} = \frac{\beta_2}{\alpha_3 + \mu} < 1$ then $I_1(t) \longrightarrow 0$ From equation 4 as treatment and recovered compartment go to zero
$\frac{dT}{dt} = \alpha_1 I_0 - (\alpha_2 + \mu + \delta_2)T$
Since $I_0(t) \longrightarrow 0$ and $-(\alpha_2 + \mu + \delta_2) < 0$
Standard linear system argument shows that $T(t) \longrightarrow 0$ from equation, with $I_1(t) \longrightarrow 0$ and $T(t) \longrightarrow$

0, we get $\frac{dR}{dt} \longrightarrow -\mu R$ so $R(t) \longrightarrow 0$
When all the infected classes $\longrightarrow 0$ from equation 1, we get
$\frac{dS}{dt} \longrightarrow -\mu S$ and therefore

$$S(t) \longrightarrow S^* = \frac{\lambda}{\mu}$$

If $R_0 \leq 1$ then every non-negative solution converges to E_0. Thus E_0 is **globally asymptotically stable** in the biologically feasible region.

3 Discussions and Conclusion

This research work formulated and analyzed a deterministic compartmental model for the transmission dynamics of Human Metapneumovirus (HMPV) using a five-class structure; susceptible individuals, two infectious compartments (weak-immunity (I_0) and strong-immunity (I_1)), individuals under treatment (T), and recovered individuals ($\mathcal{R}$). The model incorporated recruitment, immunity variation, treatment, natural death and disease-induced mortality rates. The mathematical analysis performed provided important insights into how the disease spreads and under what conditions it can be controlled or completely eliminated from the population.

The positivity and boundedness analysis showed that all state variables remain non-negative and biologically meaningful for all time, implying that the model is mathematically well-posed and suitable for epidemiological predictions. The existence of two equilibrium states?disease-free equilibrium (DFE) and endemic equilibrium indicates that HMPV may either die out or persist depending on parameter values and control strategies employed.

A major result was the derivation of the basic reproduction number ($\mathcal{R}_0$), which acts as the threshold indicator for HMPV transmission. If ($\mathcal{R}_0 < 1$), the disease will be unable to sustain itself in the population and dies out over time. However, when ($\mathcal{R} > 1$), the infection persists and may lead to an endemic outbreak. This threshold pattern aligns with classical infectious disease behavior and validates the structure of the model.

Sensitivity analysis further revealed that the exposure/contact transmission rates (β_1) and (β_2) significantly increase ($\mathcal{R}_0$). This implies that high interaction between susceptible individuals and infectious individuals with weak or strong immunity contributes most to new infections. Parameters in the denominator, such as treatment rate (α_1), recovery rate (α_2), and natural death (μ), reduced the reproduction number and therefore serve as effective control mechanisms. This suggests that intervention strategies which reduce exposure or improve recovery such as isolation, awareness creation, hygiene practices, immune boosting, and early treatment will successfully suppress disease transmission.

Local stability analysis using the Jacobian showed that the DFE is stable whenever ($\mathcal{R} < 1$), implying the disease can be eradicated if transmission rates are sufficiently reduced. Conversely, if exposure rates dominate recovery or treatment efforts, the system becomes unstable, leading to the persistence of infection. The global stability results further confirmed that when ($\mathcal{R} < 1$), every solution trajectory converges to the disease-free equilibrium, meaning elimination is possible across the entire population and not just within a small region of initial conditions.

The results therefore confirm that reducing exposure, increasing treatment accessibility, strengthening immunity and improving awareness are the most effective strategies for lowering infection levels. The study demonstrates mathematically that **HMPV elimination is achievable** under appropriate public health interventions. Overall, the model has provided a theoretical framework capable of guiding policies, predicting outbreak outcomes and assisting in designing intervention strategies for HMPV management.

These results support public health recommendations such as early diagnosis, hygiene education, avoidance of contact with infected individuals, high immune support, and wider treatment coverage.

3.1 Recommendation

Based on the findings of this research, the following recommendations are made:

Public enlightenment campaigns should be intensified to educate people on preventive measures such as good hygiene, respiratory etiquette, avoidance of close contact with infected persons and early reporting of symptoms.

Rapid diagnosis and early treatment should be encouraged, since a higher treatment rate significantly reduces infection spread as shown mathematically by a decrease in $\mathcal{R}_0$.

Health systems should improve access to antiviral treatment and supportive therapy to boost patient recovery and reduce infectious periods.

Policies that strengthen natural immunity should be promoted, such as nutritional support, vaccination where available, vitamins and immune-boosting supplements.

Contact transmission reduction measures should be prioritized, including isolation of confirmed cases, use of masks during outbreaks, and sanitation in public spaces.

Governments and health agencies should invest in surveillance systems to monitor HMPV trends, detect early outbreaks and manage spread before it becomes endemic.

3.2 Future Recommendations for Researchers

To expand on the findings of this study and deepen research on the transmission dynamics of Human Metapneumovirus (HMPV), the following areas are recommended for future investigation:

Incorporation of Age-Structured Models Since infection severity and immune response vary across age groups, future work should stratify populations into children, adults and the elderly to understand group-specific transmission and control strategies.

Seasonal and Environmental Effects HMPV exhibits seasonal variation similar to other respiratory viruses. Introducing temperature, humidity and seasonal forcing into the model will provide more realistic predictions and outbreak timing.

Stochastic (probabilistic) Modeling This study used a deterministic framework. Future work may implement stochastic models to capture randomness in infection transmission, mutation events and demographic fluctuations, especially in smaller populations.

Optimal Control and Cost-Effectiveness Analysis Researchers can extend the model to include time-dependent control functions such as vaccination, treatment, awareness campaigns.

The following provides a sample reference list with entries for journal articles [1], conference proceeding [2], a URL [3], as well as a book [4]. [Note that the reference list should be arranged in the order in which the articles are cited in the work, and not in alphabetical order]

References

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