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WELL-POSEDNESS OF A NOVEL MATHEMATICAL MODEL FOR PERTUSSIS WITH VACCINATION AND ASYMPTOMATIC CLASSES

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ABSTRACT

Bordetella pertussis is the bacterium that causes pertussis, a highly contagious respiratory disease spread primarily through droplet coughing or sneezing. Despite all efforts to reduce or even eliminate the transmission of pertussis disease, it continues to be hazardous in newborns and adults, causing illness and death in both age groups. Numerous studies have examined the factors that influence the spread of pertussis epidemiology and have used mathematical models to predict the possible effects of different vaccination approaches. In this paper, a mathematical model of pertussis has been formulated by incorporating the vaccination and Asymptomatic classes. We established that the existence and uniqueness of solution, boundedness and positivity of solution holds for the epidemiological model.

Keywords: Boundedness and positivity of solution, Control measures, Existence and uniqueness of solution, Mathematical model, Pertussis

INTRODUCTION

Pertussis, also known as whooping cough, represents a major global health challenge due to its acute nature and impact on adults and children. This respiratory infection, caused by the bacterium *Bordetella Pertussis (*B.pertussis*)*, has existed for decades and continues to be an urgent problem worldwide At risk are infants under one year of age, particularly those under six months of age, who bear a disproportionate burden of disease and face severe complications such as apnea, pneumonia, seizures and even death (Auger et al., 2013; De Cells et al., 2018; Fabricius et al., 2018; Tilahun et al., 2018). Transmission of whooping cough occurs primarily through the air, with infected individuals distributing bacteria-laden droplets into the air through coughing or sneezing (Koenig et al., 2019; Mattoo and Cherry, 2005). Inhalation of these infectious droplets by susceptible people facilitates the pathogen's entry into the body and leads to infection. This transmission route highlights the urgent need for effective prevention and control measures, especially in regions with high disease prevalence.

Typically, the first symptoms of pertussis manifest approximately 7 to 10 days post-infection. While pneumonia is a relatively common complication, seizures and neurological complications are rare. Pertussis sufferers are highly contagious in the first three weeks after the cough begins, with many children suffering from persistent coughing attacks that last between 4 and 8 weeks. Efforts to control pertussis include a range of strategies, including vaccination campaigns, public health education on hygiene practices, and early detection and treatment protocols. Despite these efforts, the persistence of pertussis highlights the complexity of infectious disease management and the continued need for careful surveillance and research to develop more effective interventions.

There are repeated outbreaks of pertussis around the world, affecting a significant portion of the population. A 2014 report identified 24.1 million cases of pertussis worldwide, which is particularly devastating for children under five, resulting in approximately 160,700 deaths from the disease. However, there is limited data on pertussis in developing regions, making it even more difficult to understand the overall global burden. Infants in particular are at significantly higher risk, with a mortality rate of 4% for children under 12 months old, compared to 1% for children aged 14 years (Raslan et al., 2017).

Effective vaccination plays a critical role in reducing the risk of whooping cough. Current vaccine options include whole-cell vaccines containing inactivated Bordetella pertussis and acellular pertussis vaccines consisting of highly purified pertussis antigens. Some regions also administer additional pertussis vaccines to adults for immune system reinforcement, while pregnant women receive doses to safeguard newborns who are too young for vaccination.

The use of antibiotics has proven beneficial in both stopping the spread of the disease and protecting those already infected. Strict measures are needed to prevent infected people from coming into contact with vulnerable populations, especially children and pregnant women. Anyone who remains unvaccinated and comes into contact with the virus within five days of infection is at increased risk. Contact investigations are critical for managing individuals who have had close contact with infected individuals, including family members, direct caregivers, and health care workers who are at increased risk due to frequent exposure. It is important to note that infection can occur even without prolonged or close contact.

The scientific community has paid a lot of attention to mathematical modelling since it facilitates a deeper understanding of the systems under study and aids in the description of actual situations. It has been applied to the modelling of issues in physics, biology, chemistry, and economics among other domains (Gershenfeld *et al.,* 1999; Ibragimov *et al.,* 2017; Serovajsky *et al.,* 2021). Most importantly, mathematical models have utilized to provide public health policy-makers with more understanding of the dynamic transmission and uncontrollability of different diseases (Brauer *et al.,* 2019; Khan *et al.,* 2022; Ullah *et al.,* 2020).

Mathematical models governed by ordinary differential equations are used to identify parameters that may curb or enhance the spread of infectious diseases such as HIV (Ibrahim et al., 2015; Ayoade et al., 2024), Covid-19 (Usman et al., 2023), Ebola (Wang et al., 2023; Akinyemi et al., 2023), Cholera (Abubakar and Ibrahim, 2022), TB (Dago et al.,

2015), Monkeypox (Akinyemi et al., 2023; Idisi et al., 2023), Lassa fever (James et al., 2015a) and Whooping Cough (Aisha et al., 2020).

Most of these mathematical models lack exact solutions, thus approximate methods are often used (Ibrahim et al., 2023). The existence of several solutions makes a model less useful and unreliable (Keeling & Rohani, 2011; Shakil et al., 2017; Holden et al., 2023). Some mathematical models with existence and uniqueness results can be found in Akinyemi et al., 2015; James et al., 2015b; Shakil et al., 2017 and Shah et al., 2024. However, Shakil et al., 2017 suggested that a mathematical model with a unique solution may not be defined for all values of time.

Subsequently, since the model describes an event within the human population, it is also vital for all time *t*, that the population should not be negative and determining the region where the model is biologically meaningful. In other words, the need to investigate the positivity solution and the feasibility region of the model is crucial in making a well-founded prediction (Keeling & Rohani; Brauer *et al.*, 2019).

The intent of this study is to investigate the well-posedness (existence, and uniqueness, positivity and boundedness) of a new mathematical model that extends the one in Aisha et al 2020. This model incorporates vaccination and exposed classes in the one presented by Aisha et al., 2020.

This study aims to investigate the well-posed position of an extended mathematical model derived from that proposed by Aisha et al. (2020) by introducing existence, uniqueness, positivity, and boundedness. The new model integrates vaccinations and exposed classes also into the framework.

MATERIALS AND METHODS

Model formulation

In this section, an extended version of the model in Aisha et al., 2020 is proposed by stratifying the total human population time $Z(q)$ into six (6) mutually exclusive subpopulations of individuals with Maternally derived immunity $M(q)$ Susceptible Individuals $S(q)$, Vaccinated individual $V(q)$, Asymptotic individuals $E(q)$, Infectious Individual $I(q)$, and Recovered Individuals $R(q)$, so that

$$Z(q) = M(q) + S(q) + V(q) + E(q) + I(q) + R(q)$$

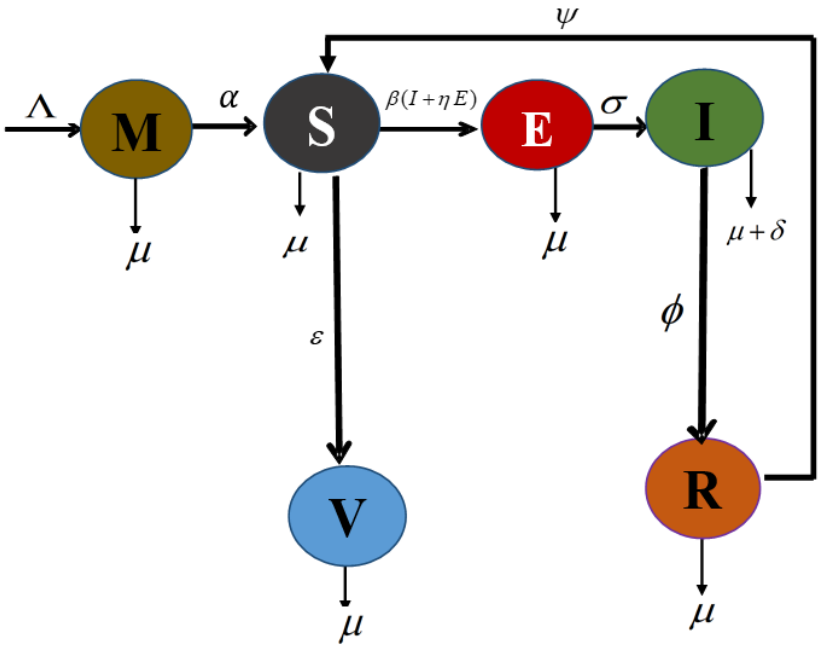

Figure 1: Flow chart of MSVEIR model

Fundamental assumption of the model

The model's formulation was grounded on the following set of assumptions.

i. The force of infection $\lambda$is defined as $\lambda = \beta(I + \eta E)$
ii. Treatment is administered to individuals in I compartment, since Pertussis associated symptom is detectable.
iii. It is assumed that there is no permanent Immunity against the disease since some members of the R Compartment can still return back to the S Compartment.
iv. Death rate is not equal to birth rate.
v. The vaccinated individuals are assumed to have complete immunity against Pertussis diseases.

The model is therefore described by a nonlinear deterministic system of six equations:

$$\begin{aligned}
\frac{dM}{dq} &= \Lambda - \alpha M - \mu M \\
\frac{dS}{dq} &= \alpha M - \varepsilon S - \beta(I + \eta E)S - \mu S + \psi R \\
\frac{dV}{dq} &= \varepsilon S - \mu V \qquad (1) \\
\frac{dE}{dq} &= \beta(I + \eta E)S - \sigma E - \mu E \\
\frac{dI}{dq} &= \sigma E - \phi I - (\mu + \delta)I \\
\frac{dR}{dq} &= \phi I - \psi R - \mu R
\end{aligned}$$

Subject to the initial population:

$M_0 \geq 0, S_0 > 0, V_0 \geq 0, E_0 \geq 0, I_0 \geq 0, R_0 \geq 0$

Table 1: Description of the Model Parameters

Parameter	Description
Λ	Proportion of immunized individuals against infection
α	The transfer out of the passively immune class
ψ	The rate of loss of immunity
ε	Vaccine efficacy
ϕ	The rate of treating infected humans
δ	Pertussis induce death rate
η	Modification parameter due to infection
β	The pertussis contact rate
μ	Natural death rate
σ	The rate for which asymptomatic infectious human becomes symptomatic.

Fundamental properties of the model

This section explains the fundamental characteristics of the model. In particular, it demonstrates the uniqueness, positivity and boundedness of the model within an invariant region. Such analysis is crucial for assessing the dynamic properties of a disease model, as it indicates its epidemiological relevance and mathematical soundness, ensuring both the coherence of the model and the reliability of its predictions (Mattos et al., 2005).

Existence and Uniqueness of Solution

We present a theorem about the existence of a unique solution to system (2) and provide a rigorous proof for its establishment. The system of equations under consideration is described in detail below.

$x' = h_i(q, x), i = 1, \ldots, nx(q_o) = x_o$ (2)

Theorem 1

Let D denote the region

$|q - q_0| \leq a, \|x - x_0\| \leq b, x = (x_1, x_2, \ldots, x_n), x = (x_{10}, x_{20}, \ldots, x_n)$ (3)

and assume that $h(q, U)$ satisfies the Lipschitz condition.

$\|h(q, x_1) - h(q, x_2)\| \leq k\|x_1 - x_2\|$ (4)

such that the pairs (q, x_1) and (q, x_2) belong to D, for $k > 0$. Thus, $U > 0$ such that there exists a unique continuous vector solution $\underline{x}(q)$ of the system (2) in the interval $|q - q_0| \leq U$. Then (4) is satisfied by the requirement that $\frac{\partial h_i}{\partial x_j} i, j = 1,2, \ldots, n$are continuous and bounded in D'. The region of interest is $0 \leq \xi \leq \Omega$ and a bounded solution of the form $0 \leq \Omega < \infty$ is found in the region D, whose partial derivatives satisfy $\delta \leq \xi \leq 0$, where ξ and δ are positive constants.

Theorem 2: if $\frac{\partial f_i}{\partial x_j}, i, j = 1,2,3,4$ are continuous and bounded in the region D ($0 \leq \xi \leq \Omega$), then the model (1) has a unique solution within D.

Proof

Each of the right hand side of (1) be denoted by $f_i \forall i = 1, \ldots 6$ respectively

Thus, the partial derivatives of the system (1) are given below.

$\left|\frac{\partial h_1}{\partial M}\right| = |-(\alpha + \mu)| < \infty, \left|\frac{\partial h_1}{\partial S}\right| = \left|\frac{\partial h_1}{\partial V}\right| = \left|\frac{\partial h_1}{\partial E}\right| = \left|\frac{\partial h_1}{\partial I}\right| = \left|\frac{\partial h_1}{\partial R}\right| = 0 < \infty$

Similarly, $\left|\frac{\partial h_2}{\partial M}\right| = |\alpha| < \infty, \left|\frac{\partial h_2}{\partial S}\right| = |-\varepsilon - \beta(I + \eta E) - \mu| < \infty, \left|\frac{\partial h_2}{\partial V}\right| = \left|\frac{\partial h_2}{\partial E}\right| = \left|\frac{\partial h_2}{\partial I}\right| = 0 < \infty, \left|\frac{\partial h_2}{\partial R}\right| = |\psi| < \infty$

$\left|\frac{\partial h_3}{\partial S}\right| = |\varepsilon| < \infty, \left|\frac{\partial h_3}{\partial V}\right| = |-\mu| < \infty, \left|\frac{\partial h_3}{\partial M}\right| = \left|\frac{\partial h_3}{\partial E}\right| = \left|\frac{\partial h_3}{\partial I}\right| = \left|\frac{\partial h_3}{\partial R}\right| = 0 < \infty$

$\left|\frac{\partial h_4}{\partial S}\right| = |\beta(I + \eta E)| < \infty, \left|\frac{\partial h_4}{\partial E}\right| = |-(\sigma + \mu)| < \infty, \left|\frac{\partial h_4}{\partial M}\right| = \left|\frac{\partial h_4}{\partial I}\right| = \left|\frac{\partial h_4}{\partial R}\right| = \left|\frac{\partial h_4}{\partial V}\right| = 0 < \infty$

$\left|\frac{\partial h_5}{\partial M}\right| = \left|\frac{\partial h_5}{\partial S}\right| = \left|\frac{\partial h_5}{\partial V}\right| = \left|\frac{\partial h_5}{\partial R}\right| = 0 < \infty, \left|\frac{\partial h_5}{\partial E}\right| = |\sigma| < \infty, \left|\frac{\partial h_5}{\partial I}\right| = |-\phi - (\mu + \delta)| < \infty,$

$\left|\frac{\partial h_6}{\partial M}\right| = \left|\frac{\partial h_6}{\partial S}\right| = \left|\frac{\partial h_6}{\partial V}\right| = \left|\frac{\partial h_6}{\partial E}\right| = 0 < \infty, \left|\frac{\partial h_6}{\partial I}\right| = |\phi| < \infty, \left|\frac{\partial h_6}{\partial R}\right| = |-(\psi + \mu)| < \infty$

Given that all partial derivatives are continuous and bounded, Theorem 1 asserts the existence of a single, unique solution to system (1) within the defined domain D, according to the Derrick and Grossman theorem in Derrick and Grossman (1987).

Positivity Solution of the Pertussis Model

Lemma 1: The solution set{M(t), S(t), V(t), E(t), I(t), R(t)} of system (1) is non-negative $\forall q \geq 0$, given that the initial populations are not negative.

Proof: The first equation of model (1) obviously gives

$\frac{dM}{dq} = \Lambda - \alpha M + \mu M$

Then,

$\frac{dM}{dq} \geq -(\alpha + \mu)M$ (5)

$\int \frac{dM}{M} \geq -\int(\alpha + \mu)dq$ (6)

The solution of (6) yields

$ln\, M \geq -(\alpha + \mu)q + c$ (7)

$M(q) \geq M(0)e^{-(\alpha+\mu)q}$ (8)

Thus, (8) becomes

$M(q) \geq M_0 e^{-(\alpha+\mu)q} \geq 0 \forall q \geq 0$ (9)

Similarly, the second equation of system (1) gives

$\frac{dS}{dq} = \alpha M - \varepsilon S - \beta(I + \eta E)S - \mu S + \psi R$

It is true that

$\frac{dS}{dq} \geq -((\varepsilon + \mu) + \beta(I + \eta E))S$ (10)

Separating the variables in above and integrate

$\int \frac{dS}{S} \geq -\int((\varepsilon + \mu) + \beta(I + \eta E))\, dq$ (11)

Then by solving using separation of variable and applying initial condition gives;

$$ln\, S \geq -\int((\varepsilon+\mu)+\beta(I+\eta E))\, q + c \quad (12)$$

$$S(q) \geq S_0 e^{-((\varepsilon+\mu)+\beta(I+\eta E))q} \geq 0 \forall q \geq 0 \quad (13)$$

Next, the subsequent equations of system (1) yields

$$\left.\begin{aligned} V(q) &\geq V_0 e^{-uq} \geq 0 \quad \forall q \geq 0 \\ E(q) &\geq E_0 e^{-(\mu+\sigma)q} \geq 0 \quad \forall q \geq 0 \\ I(q) &\geq I_0 e^{-(\phi+(\mu+\sigma))q} \geq 0 \quad \forall q \geq 0 \\ R(q) &\geq R_0 e^{-(\psi+\mu)q} \geq 0 \quad \forall q \geq 0 \end{aligned}\right\} \quad (14)$$

Hence, the state variables will never be negative provided their initial populations
$(M(0), S(0), V(0), E(0), R(0))$ are not negative.

Boundedness of Solution

Lemma 2: The region $D = \left\{(M,S,V,E,I,R) \in \mathbb{R}_+^6 : Z \leq \frac{\Lambda}{\mu}\right\}$ is positively invariant for the system (1)

Proof: The rate of change of the total human population is given as

$$\frac{dZ}{dq} = \frac{dM}{dq} + \frac{dS}{dq} + \frac{dV}{dq} + \frac{dE}{dq} + \frac{dI}{dq} + \frac{dR}{dq} \quad (15)$$

$$\frac{dZ}{dq} = \Lambda - \mu M - \mu S - \mu V - \mu \in -(\mu+\delta)I - \mu R \quad (16)$$

$$\frac{dZ}{dq} = \Lambda - \mu M - \mu S - \mu V - \mu\varepsilon - \mu I - \mu R - \delta I \quad (17)$$

$$\frac{dZ}{dq} = \Lambda - \mu Z - \delta I \quad (18)$$

So the equation becomes

$$\frac{dZ}{dq} + \mu Z \leq \Lambda \quad (19)$$

Next, (19) is solved base on the Integrating factor (I.F) method as follows

$$I.F = e^{\int \mu dq} = e^{\int \mu dq} = e^{\mu q} \quad (20)$$

$$I.F.Z(q) = \int I.F \times Q(q) dq + C \quad (21)$$

$$e^{\mu q}.Z(q) = \int e^{\mu q}.\Lambda + C \quad (22)$$

$$e^{\mu q}.Z(q) \leq \int e^{\mu q}.\Lambda + C \quad (23)$$

$$e^{\mu q}.Z(q) \leq \frac{1}{\mu} e^{\mu q}.\Lambda + C \quad (24)$$

at q = 0, $Z(0) \leq \frac{\Lambda}{\mu} + C$ (25)

$$C = Z(0) - \frac{\Lambda}{\mu} \quad (26)$$

$$e^{\mu q}.Z(q) \leq \frac{\Lambda}{\mu} + e^{\mu q} + Z(0) - \frac{\Lambda}{\mu} \quad (27)$$

$$Z(q) \leq \frac{\Lambda}{\mu} + \frac{Z(0)}{e^{\mu q}} - \frac{\Lambda}{\mu e^{\mu q}} \quad (28)$$

$$Z(q) \leq \frac{\Lambda}{\mu} + e^{-\mu q}\left(Z(0) - \frac{\Lambda}{\mu}\right) \quad (29)$$

As $q \to \infty$ in (29), the total population $Z \to \frac{\Lambda}{\mu}$ implies that $0 \leq Z \leq \frac{\Lambda}{\mu}$.Thus, the feasible solution set of the system equation of the Pertussis model enters and remains in the region:

$$D = \{(M,S,V,E,I,R) \in \Re_+^6 / M_0 \geq 0, S_0 > 0, V_0 \geq 0, E_0 \geq 0, I_0 \geq 0, R_0 \geq 0\}$$

It is seen that the above is positively invariant of the system (1) model. Therefore, the model is well-posed epidemiologically and mathematically.

Discussion of Results

The results obtained in the previous section are discussed here. The Theorem 1, proposed by Derrick and Grossman was used to validate Theorem 2. The mathematical relevance of Theorem 2 suggests that the new model for pertussis in the presence of vaccination and asymptomatic class has a solution that is unique.

Secondly, since the proposed model describes the spread of pertussis within the human population, it becomes imperative that the population remains non-negative at any time q, otherwise, it becomes of no practical importance. Hence Lemma 1 was validated.

Thirdly, since unbounded solution of a model means the solution lies at infinity and implies the model has no practical importance. Hence the need to determine the region where the model solution is bounded is of great importance. Next, Lemma 2 shows that the solution of the total human population $Z(q)$at time $q$is bounded at $Z \in \left[0, \frac{\pi}{\mu}\right]$.

Therefore, the proposed model is said to be well-posed because the model is shown to possess a unique solution that is positive and bounded.

CONCLUSION

This study presents a novel deterministic model for pertussis that incorporates the staged progression of the disease by integrating vaccination and asymptotic classes and implementing treatment as a control measure. The existence and uniqueness of the solutions theorem were used to show that there is a unique solution to the model. Furthermore, the model solution was confirmed to be both positive and bounded. Consequently, the proposed model is considered to be mathematically well formulated and epidemiologically significant.

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