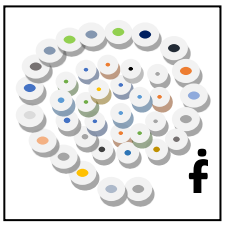

International Journal of Mathematical Analysis and Modelling

(Formerly Journal of the Nigerian Society for Mathematical Biology)

Volume 6, Issue 2 (Oct.-Nov.), 2023

ISSN (Print): 2682 - 5694
ISSN (Online): 2682 - 5708

International Journal of Mathematical Analysis and Modelling
Volume 6, Issue 2, October-November 2023, pages 217 – 232

Optimal vaccination and treatment strategies for control of rubella with vertical transmission

E.C. Duru*†, M.C. Anyanwu†, and C.N. Nwosu†

Abstract

Rubella is a viral contagious disease associated with puffy cheeks, tender and swollen jaw. It spreads through direct contact with saliva or respiratory droplets from the mouth, nose or throat of infected persons. This work presents a system of nonlinear ordinary differential equations which models the transmission dynamics of the disease, with vertical transmission from infected mothers to their offspring. The model also incorporates vaccination against the disease, and treatment of infected individuals as control measures for the disease. It is shown that the disease-free equilibrium of the model is locally asymptotically stable when the control reproduction number, R_c is less than one. It is also shown that the model possesses a unique endemic equilibrium which exists when $R_c > 1$. This confirms the global stability of the disease-free equilibrium, and the absence of backward bifurcation in the model. Optimal control analysis is performed on the model to obtain the proportion of susceptible humans that will be vaccinated and infected humans that need to be isolated and treated for optimal control of the disease. Plots are presented to show the dynamics of the disease in the presence of the controls.

Keywords: rubella; mathematical model; vaccination; vertical transmission; isolation; treatment; control reproduction number; optimal control.

1 Introduction

Rubella is a viral infection that is very contagious and caused by the RuV virus [4]. Rubella is a neglected disease with no surveillance system in place and no national incidence figure in Nigeria [5]. [19] says that rubella is an acute infection affecting mainly children and young adults. It is also known as three-day measles or German measles and comes with a distinctive red rash that usually starts from the face and then spreads to other parts of the body [2][14]. Rubella is different from measles though both illnesses share some signs and symptoms like the red rash which appears in at most 80% of infected persons and sometimes wrongly diagnosed as measles or scarlet fever [11]. Rubella is not as severe as measles and is caused by a different virus than measles [2]. The diagnosis is usually confirmed with lab tests such as virus culture or blood test. The symptoms include mild fever, headache, runny nose, red itchy eyes, enlarged tender lymph nodes at the base of the skull, the back of the neck and behind the ears, a fine pink rash that begins on the face and quickly spreads to the trunk and then

* Corresponding Author
† Department of Mathematics, Michael Okpara University of Agriculture, Umudike, Nigeria

arms and legs before disappearing in the same order, aching joints especially in young women, general discomfort, etc. [5][14]. The symptoms appear generally between two to three weeks after exposure to the virus and last about one to five days [4][14]. About 25 – 50% of rubella patients are asymptomatic [2][4]. Rubella is transmitted from person to person through contact with infected mucus from the throat and neck, coughs and sneezes from infected persons, bloodstream from pregnant woman to her unborn child. Infected persons with rubella become infectious from one week before rashes appear till about one week after the rashes disappear [19]. That's why an infected person can spread the illness even before realizing he or she has it.

Rubella can be prevented by administering the Measles-Mumps-Rubella (MMR) vaccine to children between 12 – 15 months of age for first dose and 4 – 6 years of age for the second dose [4][14][19]. The vaccine grants permanent immunity to the infection. MMR vaccine is very safe and effective. One dose of the MMR vaccine is about 97% effective at preventing rubella [2]. It is reported that 168 of 194 countries in the world had introduced the rubella vaccines as of December, 2018 [19]. Also, if someone gets the infection, he or she should be isolated to avoid spreading the infection to others. Health care providers are encouraged to educate the public especially parents on the safety protocol over the disease. Children should stay off nursery or school while adults should stay off work for 5 days after the rash appears, avoiding close contact with anyone who is pregnant if infected, washing your hands often with soap and warm water and proper disposal of tissues after coughing or sneezing can all help prevent the spread [14]. Recovering from the disease also grants immunity to the disease just as vaccination [4][14].

There are cases of complications arising from rubella infections though very rare. Some women who have had rubella infections have been reported to experience arthritis in the fingers, wrists and knees which does not last more than one month [2][19]. In rare cases, inflammation of the brain or ear infection has been associated to rubella disease as well as miscarriage, fetal death, stillbirth in pregnant women especially within the first trimester [19]. It is reported that about 90% of infants born to mothers who had rubella during the first 12 weeks of pregnancy develop congenital rubella syndrome (CRS), [3][8][17][19]. Severe complications are seen on the unborn children of pregnant women where it is seen to cause one or more of the following syndromes; growth delays, deafness, cataracts, congenital heart defects, organ defects, problems with mental development and learning [8][17]. It is the leading vaccine-preventable cause of birth defects [19]. There is no treatment for rubella infection however, simple self-care measures are given to infected persons to minimize the effects of the symptoms. Such measures include given bed rest and drugs to relieve pains, aches and fever as well as drinking lots of fluids [14]. There are about 26,000 cases of rubella worldwide each year mostly common in Asia, Africa and the Middle East [4].

Mathematical modelling of infectious diseases has helped to study the mechanisms through which diseases spread, to make predictions on the future course of an outbreak and to evaluate methods of controlling them. [1] designed a mathematical model of measles and rubella with vaccination. They analyzed the individual infections as well as the coinfection of both diseases. [16] studied the dynamics of re-infection of rubella transmission model with vaccination. Their model allowed recovered humans to be re-introduced into the exposed population. [18] discussed modelling the dynamics of rubella disease with vertical transmission where the recovered humans are reintroduced into the susceptible population. They performed sensitivity analysis on the model which showed that increase in more vertical infection and contact rate with infected individuals increases the number of infected humans. [9] worked on the numerical solution for Rubella disease model with vaccination using adaptive Runge-kutta method. The work compared the Runge-kutta order 4 method and the Runge-kutta Fehberg method in predicting the rate of population condition for Rubella

disease. [10] designed a mathematical model of Rubella disease dynamics with vertical transmission and discovered that if the vertical transmission is more as well as the rate of interaction between susceptible and infected persons increases, there will be more cases of rubella infection. The goal of this paper is to present a mathematical model for the disease transmission dynamics of mumps incorporating effects of isolation, treatment and vaccination for effective disease control in Nigeria where the disease has not been given much attention. The model also incorporates vertical transmission of the disease. The rest of the paper is arranged thus; in section 2, we developed the model and in section 3, we established the positivity and boundedness of solution. Section 4 looked at the local stability of the DFE while section 5 established the existence of endemic equilibrium. Section 6 discussed the optimal control measures while numerical experiments were done in section 7. The work concluded in section 8.

2 Mathematical model

We present an SVEIR-like model for the transmission dynamics of rubella in human population, where $S(t)$ represents the susceptible human population, $S_v(t)$ represents persons who are vaccinated, $E_A(t)$ is the exposed human population, $E_J(t)$ is the exposed fetus population who got infected in the womb, $I_J(t)$ represents the infectious fetus population, $I_A(t)$ represents the infectious adult humans, $I_T(t)$ is the isolated infectious humans undergoing treatment, $I_{NT}(t)$ represents the infectious humans that are not isolated and treated and $R(t)$, the recovered humans.

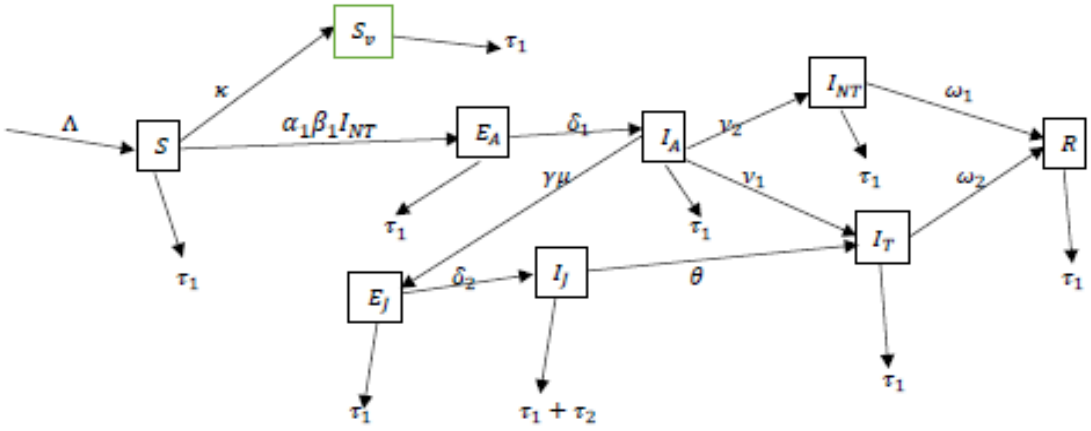

Figure 1. Flow Diagram for the Disease Transmission

It is assumed that there is a recruitment, Λ of uninfected persons into the population under study. This increases the number of persons in the susceptible class, S. Humans in the susceptible class become exposed to the virus when infected by I_{NT} at the rate,$\alpha_1\beta_1 I_{NT}S$, where α_1 is the rate at which S have contact with I_{NT}, and β_1 is the probability of transmission of the virus from I_{NT} to S. Also, it is assumed that the proportion, κ of the susceptible humans gets vaccinated against the disease, and

moves to the compartment, S_v. The exposed class, E_A becomes infectious at the incubation rate, δ_1, The proportion, ν_1 of the infectious class are isolated and receives treatment, while the proportion, ν_2, stays without isolation and treatment. In the infectious class, there is a proportion, γ of I_A that are women, who becomes pregnant at the rate,μ, and produces $\gamma\mu I_A$ infected fetuses due to automatic vertical transmission of the virus. After delivery, the infected fetuses become infectious at the rate, δ_2, and becomes isolated for treatment at the rate, θ. The rates of recovery for persons in the treatment is ω_2, while the non-treatment class recovers naturally at the rate, ω_1. Both infected and uninfected compartments are affected by natural death, which occurs at the rate, τ_1, while only the infected fetuses are affected by death rate, τ_2, due to the infection.

Using the flow diagram, fig. (1) and the dynamics of the disease as described above, we arrive at the following system of nonlinear ordinary differential equations for transmission of rubella in a given population:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \alpha_1\beta_1 I_{NT}S - (\kappa + \tau_1)S,\\
\frac{dS_v}{dt} &= \kappa S - \tau_1 S_v,\\
\frac{dE_A}{dt} &= \alpha_1\beta_1 I_{NT}S - (\delta_1 + \tau_1)E_A,\\
\frac{dE_J}{dt} &= \gamma\mu I_A - (\delta_2 + \tau_1)E_J,\\
\frac{dI_A}{dt} &= \delta_1 E_A - (\gamma\mu + \nu_1 + \nu_2 + \tau_1)I_A,\\
\frac{dI_J}{dt} &= \delta_2 E_J - (\theta + \tau_1 + \tau_2)I_J,\\
\frac{dI_T}{dt} &= \nu_1 I_A + \theta I_J - (\omega_2 + \tau_1)I_T,\\
\frac{dI_{NT}}{dt} &= \nu_2 I_A - (\omega_1 + \tau_1)I_{NT},\\
\frac{dR}{dt} &= \omega_1 I_{NT} + \omega_2 I_T - \tau_1 R
\end{aligned} \qquad (1)$$

where, $S(0) = S^0$, $S_v(0) = S_v^0$, $E_A(0) = E_A^0$, $E_J = E_J^0$, $I_J(0) = I_J^0$, $I_A(0) = I_A^0$, $I_T(0) = I_T^0$, $I_{NT}(0) = I_{NT}^0$, $R(0) = R^0$.

$$N = S + S_v + E_A + E_J + I_J + I_A + I_T + I_{NT} + R. \qquad (2)$$

We assume that the solution to the system exists in the region Ω described by

$$\{S, S_v, E_A, E_J, I_A, I_J, I_T, I_{NT}, R\} \in R^9 \,|S + S_v + E_A + E_J + I_J + I_A + I_T + I_{NT} + R \leq \frac{\Lambda}{\tau_1}.$$

Table 1: Description of Parameters

Parameters	Description
Λ	Level of recruitment
τ_1	Natural death rate
τ_2	Death due to the disease
α_1	Contact rate with Infectious humans not undergoing treatment
β_1	Rate of transmission from contacts with Infectious humans not undergoing treatment
δ_1	Rate of development of infectiousness from E_A to I_A
δ_2	Rate of development of infectiousness from E_J to I_J
κ	Proportion of Susceptible humans that are vaccinated
γ	Proportion of Infectious humans that are females
μ	Proportion of infectious that are pregnant
θ	Proportion of infectious newborns that are isolated and treated
ν_1	Proportion of Infectious humans that are isolated and undergoing treatment
ν_2	Proportion of Infectious humans that are not isolated and undergoing treatment
ω_1	Level of recovery of humans not isolated and treated
ω_2	Level of recovery of humans isolated and treated

3 Positivity and boundedness of solutions

Lemma 1: Let the initial data set for the model be $\{S^0 > 0, S_v^0 > 0, E_A^0 > 0, E_J^0 > 0, I_A^0 > 0, I_J^0 > 0, I_T^0 > 0, I_{NT}^0 > 0, R^0 > 0\}$. Then, the solution set $\{S(t), S_v(t), E_A(t), E_J(t), I_J(t), I_A(t), I_T(t), I_{NT}(t), R(t)\}$ of the model with the given initial data will remain positive and bounded for all time $t > 0$.

Proof: It can be shown from eqn. (1) that

$$\begin{aligned}
&\frac{dS}{dt} \geq -\alpha_1\beta_1 I_{NT} S - (\kappa + \tau_1)S \\
&\frac{dS_v}{dt} \geq -\tau_1 S_v \\
&\vdots \\
&\frac{dR}{dt} \geq -\tau_1 R.
\end{aligned} \tag{3}$$

Hence, solving the differential inequality with given initial solutions gives

$$\begin{aligned}
&S \geq S^0 e^{-(\alpha_1\beta_1 I_{NT} + \kappa + \tau_1)t} > 0 \\
&S_v \geq S_v^0 e^{-\tau_1 t} \\
&\vdots \\
&R \geq R^0 e^{-\tau_1 t}
\end{aligned} \tag{4}$$

Hence, given initial solutions that are individually positive, the solution to the model system remains positive $\forall\, t > 0$.

Further, we have that the total human population, N satisfies the equation

$$\frac{dN}{dt} = \Lambda - \tau_1 N. \tag{5}$$

Hence, as $t \to \infty$, $0 < N(t) \leq \frac{\Lambda}{\tau_1}$ showing that the human population is always bounded.
Therefore, the region Ω is positively invariant and is an attractor of all positive solution of the system.

4 Local stability of the disease-free equilibrium

The disease-free equilibrium (DFE), $E^0 = \left(\frac{\Lambda}{\kappa+\tau_1}, \frac{\kappa\Lambda}{\tau_1(\kappa+\tau_1)}, 0,0,0,0,0,0,0\right)$ of (1) is locally asymptotically stable if the all the eigenvalues of the Jacobian matrix of the model system at E^o are negative or have negative real parts. Let $J(E^0)$ denote the Jacobian matrix evaluated at E^0, then

$$J(E^0) = \begin{bmatrix} -(\kappa+\tau_1) & 0 & 0 & 0 & 0 & 0 & 0 & -\frac{\alpha_1\beta_1\Lambda}{\kappa+\tau_1} & 0 \\ \kappa & -\tau_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -(\delta_1+\tau_1) & 0 & 0 & 0 & 0 & \frac{\alpha_1\beta_1\Lambda}{\kappa+\tau_1} & 0 \\ 0 & 0 & 0 & -(\delta_2+\tau_1) & \gamma\mu & 0 & 0 & 0 & 0 \\ 0 & 0 & \delta_1 & 0 & -(\gamma\mu+\nu_1+\nu_2+\tau_1) & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \delta_2 & 0 & -(\theta+\tau_1+\tau_2) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \nu_1 & \theta & -(\omega_2+\tau_1) & 0 & 0 \\ 0 & 0 & 0 & 0 & \nu_2 & 0 & 0 & -(\omega_1+\tau_1) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \omega_2 & \omega_1 & -\tau_1 \end{bmatrix}$$

Some of the eigenvalues of $J(E^0)$ are $-\tau_1, -\tau_1, -(\kappa+\tau_1), -(\omega_2+\tau_1), -(\theta+\tau_1+\tau_2), -(\delta_2+\tau_1)$. The remaining eigenvalues, λ of $J(E^0)$ satisfies the cubic equation

$$Q_3\lambda^3 + Q_2\lambda^2 + Q_1\lambda + Q_0 = 0 \tag{6}$$

where

$$Q_3 = 1$$
$$Q_2 = (\delta+\tau_1) + (\gamma\mu+\nu_1+\nu_2+\tau_1) + (\omega_1+\tau_1)$$
$$Q_1 = (\delta+\tau_1)(\omega_1+\tau_1) + (\delta+\tau_1)(\gamma\mu+\nu_1+\nu_2+\tau_1) + (\omega_1+\tau_1)(\gamma\mu+\nu_1+\nu_2+\tau_1)$$
$$Q_0 = (\delta+\tau_1)(\omega_1+\tau_1)(\gamma\mu+\nu_1+\nu_2+\tau_1)[1-R_c]$$

where $R_c = \frac{\alpha_1\beta_1\Lambda\nu_2\delta_1}{(\kappa+\tau_1)(\delta_1+\tau_1)(\omega_1+\tau_1)(\gamma\mu+\nu_1+\nu_2+\tau_1)}$. (7)

Since $Q_3 > 0, Q_2 > 0, Q_1 > 0$, Routh-Hurwitz criterion assures that all the eigenvalues are negative if $R_c < 1$. Hence, the disease-free equilibrium is locally asymptotically stable if $R_c < 1$. The quantity, $R_c = \frac{\alpha_1\beta_1\Lambda\nu_2\delta_1}{(\kappa+\tau_1)(\delta_1+\tau_1)(\omega_1+\tau_1)(\gamma\mu+\nu_1+\nu_2+\tau_1)}$ is the control reproduction number of the disease. It gives the average number of secondary infectious cases that is caused by a single infection in total susceptible

population in the presence of the control measures, [13]. If $R_c < 1$, then the control measure is effective, otherwise it is ineffective.

5 Existence of endemic equilibrium point

Lemma. A unique endemic equilibrium for the model system exists if and only if $R_c > 1$.

The endemic equilibrium point (EEP) are steady-state solutions to the model system (1) when the disease persists in the population (i.e. all state variables are positive). Let $EEP = (S^*, S_v^*, E_A^*, E_J^*, I_J^*, I_A^*, I_T^*, I_{NT}^*, R^*)$, with

$S^* = \frac{\Lambda}{\alpha_1\beta_1 I_{NT}^* + \kappa + \tau_1}$, $S_v^* = \frac{\kappa S^*}{\tau_1}$, $E_A^* = \frac{\alpha_1\beta_1 I_{NT}^* S^*}{\delta_1 + \tau_1}$, $E_J^* = \frac{\gamma\mu I_A^*}{\delta_2 + \tau_1}$, $I_A^* = \frac{\delta_1 E_A^*}{\gamma\mu + \nu_1 + \nu_2 + \tau_1}$,

$I_J^* = \frac{\delta_2 E_J^*}{\theta + \tau_1 + \tau_2}$, $I_T = \frac{\nu_1 I_A^* + \theta I_J^*}{\omega_2 + \tau_1}$, $I_{NT}^* = \frac{\nu_2 I_A^*}{\omega_1 + \tau_1}$, $R^* = \frac{\omega_1 I_{NT}^* + \omega_2 I_T^*}{\tau_1}$, then the

components of EEP satisfies the system

$$\Lambda - \alpha_1\beta_1 I_{NT}^* S^* - (\kappa + \tau_1)S = 0$$
$$\kappa S^* - \tau_1 S_v^* = 0$$
$$\beta_1 I_{NT}^* S^* - (\delta_1 + \tau_1)E_A^* = 0$$
$$\gamma\mu I_A^* - (\delta_2 + \tau_1)E_J^* = 0$$
$$\delta_1 E_A^* - (\gamma\mu + \nu_1 + \nu_2 + \tau_1)I_A^* = 0$$
$$\delta_2 E_J^* - (\theta + \tau_1 + \tau_2)I_J^* = 0$$
$$\nu_1 I_A^* + \theta I_J^* - (\omega_2 + \tau_1)I_T^* = 0$$
$$I_A^* - (\omega_1 + \tau_1)I_{NT}^* = 0$$
$$I_{NT}^* + \omega_2 I_T^* - \tau_1 R^* = 0.$$

Substituting E_A^* into the fifth equation and simplifying, gives

$$\alpha_1\beta_1\nu_2(\delta_1 + \tau_1)(\gamma\mu + \nu_1 + \nu_2 + \tau_1)I_A^{*2} + [(\kappa + \tau_1)(\delta_1 + \tau_1)(\omega_1 + \tau_1)(\gamma\mu + \nu_1 + \nu_2 + \tau_1) - \alpha_1\beta_1\Lambda\nu_2\delta_1]I_A^* = 0.$$

This gives a quadratic equation of the form

$$\alpha_1\beta_1\nu_2 I_A^{*2} + (\kappa + \tau_1)(\omega_1 + \tau_1)(1 - R_c)I_A^* = 0,$$

whose solutions are $I_A^* = 0$ and $I_A^* = \frac{(\kappa+\tau_1)(\omega_1+\tau_1)(R_c-1)}{\alpha_1\beta_1\nu_2}$. The trivial solution, $I_A^* = 0$ implies the disease-free equilibrium which is locally asymptotically stable if $R_c < 1$. The solution, $I_A^* = \frac{(\kappa+\tau_1)(\omega_1+\tau_1)(R_c-1)}{\alpha_1\beta_1\nu_2}$ is positive if $R_c > 1$. This shows that the model has a unique endemic equilibrium which exists when $R_c > 1$. The existence of a unique endemic equilibrium when $R_c > 1$, precludes the existence of backward bifurcation in the model. Therefore, the disease-free equilibrium is globally

asymptotically stable when $R_c < 1$. Epidemiologically, this shows that the disease can be eradicated by applying the two control measures irrespective of the initial infected populations.

6 Optimal control of rubella

In this case, we assume the rate of vaccination, κ and treatments, ν_1 and θ are not constant but functions of time; $\kappa = \kappa(t), \nu_1 = \nu_1(t)$ and $\theta = \theta(t)$ respectively. Therefore, we consider an optimal control problem with objective function given by

$$J(x; \kappa, \nu_1, \theta) = \int_0^T \Big(A_1 S(t) + A_2 E_A(t) + A_3 E_J(t) + A_4 I_A(t) + A_5 I_J(t) + \frac{A_6}{2}\kappa^2(t) + \frac{A_7}{2}\nu_1^2(t) + \frac{A_8}{2}\theta^2(t) \Big) dt \quad (8)$$

where the constants $A_i;\ i = 1, 2, 3, 4, 5, 6, 7, 8$ are positive weights that help to balance each term in the integrand. The quadratic terms, $\frac{A_6}{2}\kappa^2(t), \frac{A_7}{2}\nu_1^2(t)$ and $\frac{A_8}{2}\theta^2(t)$ represent the costs involved in vaccination, isolating and treating those that are symptomatically infectious at any time t. In the above optimal control problem, we assume that the control parameters, $\kappa^*(t), \nu_1^*(t)$ and $\theta^*(t)$ are Lebesgue measurable with $a_1 < \kappa^*(t) \le b_1$, $a_2 < \nu_1^*(t) \le b_2$ and $a_3 < \theta^*(t) \le b_3, \forall t \in [0, t_f]$. Therefore, we seek an optimal controls, $\kappa^*(t), \nu_1^*(t)$ and $\theta^*(t)$ such that

$$J(x^*;\ \kappa^*(t), \nu_1^*(t), \theta^*(t)) = \min\{J(x; \kappa(t), \nu_1(t), \theta(t)) : (\kappa(t), \nu_1(t), \theta(t)) \in \Gamma\}, \quad (9)$$

where the control set Ω is given by
$\Gamma = \{(\kappa(t), \nu_1(t), \theta(t)):$ each control parameter is piecewise continuous on $[0, T],\ a_1 < \kappa^*(t) \le b_1, a_2 < \nu_1^*(t) \le b_2$ and $a_3 < \theta^*(t) \le b_3\}$, where $a_1, b_1, a_2, b_2, a_3, b_3$ are constants on $[0,1]$.

As shown in [7], the existence of the optimal controls, $\kappa^*(t), \nu_1^*(t)$ and $\theta^*(t)$ and the associated optimal solutions, $(S^*, S_v^*, E_A^*, E_J^*, I_J^*, I_A^*, I_T^*, I_{NT}^*, R^*)$ is guaranteed since the state solutions are bounded as proved earlier. The state system satisfies the Lipschitz property with respect to the state variables, since the solution exists and is unique.

For the convexity of the integrand, $L(t, S, E_A, E_J, I_A, I_J, \kappa, \nu_1, \theta) = A_1 S(t) + A_2 E_A(t) + A_3 E_J(t) + A_4 I_A(t) + A_5 I_J(t) + \frac{A_6}{2}\kappa^2(t) + \frac{A_7}{2}\nu_1^2(t) + \frac{A_8}{2}\theta^2(t)$, with respect to the control parameters, κ, ν_1, θ in the set, Γ, we need to show that
$L(t, S, E_A, E_J, I_A, I_J, \lambda\kappa + (1-\lambda)\kappa', \lambda\nu_1 + (1-\lambda)\nu_1', \lambda\theta + (1-\lambda)\theta') \le \lambda L(t, S, E_A, E_J, I_A, I_J, \kappa, \nu_1, \theta) + (1-\lambda) L(t, S, E_A, E_J, I_A, I_J, \kappa', \nu_1', \theta')$, for $\lambda \in (0,1)$.

Note that
$L(t, S, E_A, E_J, I_A, I_J, \lambda\kappa + (1-\lambda)\kappa', \lambda\nu_1 + (1-\lambda)\nu_1', \lambda\theta + (1-\lambda)\theta') = A_1 S(t) + A_2 E_A(t) + A_3 E_J(t) + A_4 I_A(t) + A_5 I_J(t) + \frac{A_6}{2}(\lambda\kappa + (1-\lambda)\kappa')^2 + \frac{A_7}{2}(\lambda\nu_1 + (1-\lambda)\nu_1')^2 + \frac{A_8}{2}(\lambda\theta + (1-\lambda)\theta')^2$ (10)

and

$$\lambda L\big(t,S,E_A,E_J,I_A,I_J,\kappa,\nu_1,\theta\big)+(1-\lambda)L\big(t,S,E_A,E_J,I_A,I_J,\kappa',\nu_1',\theta'\big)=A_1S(t)+A_2E_A(t)+A_3E_J(t)+A_4I_A(t)+A_5I_J(t)+\frac{A_6}{2}\lambda\kappa^2+\frac{A_7}{2}\lambda\nu_1^2+\frac{A_8}{2}\lambda\theta^2+\frac{A_6}{2}(1-\lambda)\kappa'^2+\frac{A_7}{2}(1-\lambda)\nu_1'^2+\frac{A_8}{2}(1-\lambda)\theta'^2. \quad (11)$$

Therefore, we need to show from (10) and (11) that $(\lambda\kappa+(1-\lambda)\kappa')^2\le\lambda\kappa^2+(1-\lambda)\kappa'^2$, $(\lambda\nu_1+(1-\lambda)\nu_1')^2\le\lambda\nu_1'^2+(1-\lambda)\nu_1'^2$ and $(\lambda\theta+(1-\lambda)\theta')^2\le\lambda\theta^2+(1-\lambda)\theta'^2$.

For $(\lambda\kappa+(1-\lambda)\kappa')^2$, we have

$$\begin{aligned}(\lambda\kappa+(1-\lambda)\kappa')^2&=\lambda^2\kappa^2+2\lambda(1-\lambda)\kappa\kappa'+(1-\lambda)^2\kappa'^2\\&=\lambda(\lambda-1+1)\kappa^2+2\lambda(1-\lambda)\kappa\kappa'+(1-\lambda)(1-\lambda)\kappa'^2\\&=\lambda\kappa^2+(1-\lambda)\kappa'^2-\lambda(1-\lambda)[\kappa^2-2\kappa\kappa'+\kappa'^2]\\&=\lambda\kappa^2+(1-\lambda)\kappa'^2-\lambda(1-\lambda)[\kappa-\kappa']^2\\&\le\lambda\kappa^2+(1-\lambda)\kappa'^2\end{aligned} \quad (12)$$

Using similar procedure for $(\lambda\nu_1+(1-\lambda)\nu_1')^2$ and $(\lambda\theta+(1-\lambda)\theta')^2$, we obtain that

$$(\lambda\nu_1+(1-\lambda)\nu_1')^2\le\lambda\nu_1^2+(1-\lambda)\nu_1'^2$$
$$(\lambda\theta+(1-\lambda)\theta')^2\le\lambda\theta^2+(1-\lambda)\theta'^2.$$

This proves the convexity of the integrand on the set, Γ.

By Pontryagin maximum principle [15], the Hamiltonian has the form

$$H(S,E_A,E_J,I_A,I_J,\kappa,\nu_1,\theta,\pi)=A_1S(t)+A_2E_A(t)+A_3E_J(t)+A_4I_A(t)+A_5I_J(t)+\frac{A_6}{2}\kappa^2(t)+\frac{A_7}{2}\nu_1^2(t)+\frac{A_8}{2}\theta^2(t)+\pi_1(t)\big(\Lambda-\rho(t)S(t)-(\kappa+\tau_1)S(t)\big)+\pi_2(t)(\kappa S-\tau_1S_v)+\pi_3(t)(\rho(t)S(t)-(\delta_1+\tau_1)E_A(t))+\pi_4(t)(\gamma\mu I_A-(\delta_2+\tau_1)E_J)+\pi_5(t)(\delta_1E_A-(\gamma\mu+\nu_1+\nu_2+\tau_1)I_A)+\pi_6(t)(\delta_2E_J-(\theta+\tau_1+\tau_2)I_J)+\pi_7(t)\big(\nu_1I_A+\theta I_J-(\omega_2+\tau_1)I_T\big)+\pi_8(t)(\nu_2I_A-(\omega_1+\tau_1)I_{NT})+\pi_9(t)(\omega_1I_{NT}+\omega_2I_T-\tau_1R) \quad (13)$$

where $\pi_i(t), i=1,2,\cdots,9$ are the adjoint variables that satisfy the system of ordinary differential equations

$$\begin{aligned}\frac{d\pi_1}{dt}&=\rho(t)\alpha_1\beta_1I_{NT}(\pi_1-\pi_3)+(\kappa+\tau)\pi_1-\pi_2\kappa-A_1\\\frac{d\pi_2}{dt}&=\pi_2\tau_1\\\frac{d\pi_3}{dt}&=(\delta_1+\tau_1)\pi_3-\delta_1\pi_5-A_2\\\frac{d\pi_4}{dt}&=(\delta_2+\tau_1)\pi_4-\delta_2\pi_6-A_3\\\frac{d\pi_5}{dt}&=(\gamma\mu+\nu_1+\nu_2+\tau_1)\pi_5-\gamma\mu\pi_4-\nu_1\pi_7-\nu_2\pi_8-A_4\end{aligned} \quad (14)$$

$$\frac{d\pi_6}{dt} = (\theta + \tau_1 + \tau_2)\pi_6 - \theta\pi_7 - A_5$$
$$\frac{d\pi_7}{dt} = (\omega_2 + \tau_1)\pi_7 - \omega_2\pi_9$$
$$\frac{d\pi_8}{dt} = (\omega_1 + \tau_1)\pi_8 - \omega_1\pi_9$$
$$\frac{d\pi_9}{dt} = \tau_1\pi_9,$$

with the transversality condition $\pi_i(T) = 0, i = 1,2,\cdots,9$. Using the optimality condition in the Pontryagin maximum principle on the Hamiltonian, $H(S, E_A, E_J, I_A, I_J, \kappa, \nu_1, \theta, \pi)$, we obtain the optimal controls, $\kappa^*(t) = \frac{(\pi_1(t)-\pi_2(t))S(t)}{A_6}, \nu_1^*(t) = \frac{(\pi_5(t)-\pi_7(t))I_A(t)}{A_7}, \theta^*(t) = \frac{(\pi_6(t)-\pi_7(t))I_J(t)}{A_8}$, with their characterizations

$$\kappa^*(t) = \max\left(a_1, \min\left(b_1, \frac{(\pi_1(t)-\pi_2(t))S(t)}{A_6}\right)\right)$$
$$\nu_1^*(t) = \max\left(a_2, \min\left(b_2, \frac{(\pi_5(t)-\pi_7(t))I_A(t)}{A_7}\right)\right)$$
$$\theta^*(t) = \max\left(a_3, \min\left(b_3, \frac{(\pi_6(t)-\pi_7(t))I_J(t)}{A_8}\right)\right). \quad (15)$$

Therefore, at any time, t, (15) gives the number of people that need to be vaccinated, the number of infected persons that need to be isolated and treated, and the number of infectious newborns that need to be isolated and treated for optimal control of rubella in a given population.

7 Numerical experiments

Here, we obtain the numerical solution to the optimal control problem using forward-backward sweep technique. This method involves solving the optimal state equation using forward Runge-Kutta order 4 method with the initial guess for the optimal control parameter. This is followed by solving the adjoint system of equation with backward Runge-Kutta order 4 method, starting with the transversality conditions $\pi_i(T) = 0$. The optimal control is updated with the current state and adjoint solutions at the end of each iteration. The iteration is repeated until convergence criteria is reached. The initial solutions used are $S^0 = 250$, $S_v^0 = 20$, $E_A^0 = 100$, $E_J^0 = 100$, $I_J^0 = 150$, $I_A^0 = 100$, $I_T^0 = 100$, $I_{NT}^0 = 20$, $R^0 = 100$. We have also used $A_1 = 10, A_2 = 10, A_3 = 10, A_4 = 10, A_5 = 10, A_6 = 20, A_7 = 50, A_8 = 10, a = 0, b = 1$.

Table 2: Description of Parameters and Values

Parameters	Description	Source
Λ	250	Assumed
τ_1	0.0000432	[6]
τ_2	0.00001	Assumed
α	0.0175	Assumed
β	0.0125	Assumed
δ_1	0.143	[19]
δ_2	0.143	[19]
κ	0.005	Assumed
γ	0.05	Assumed
μ	0.01	Assumed
θ	0.5	Assumed
ν_1	0.31	Assumed
ν_2	0.062	Assumed
ω_1	0.07	Assumed
ω_2	0.0526	[2][4][7]

The results of the numerical experiments are shown in figures 2 – 10 below. In figure 2, we see the plot for the susceptible humans against time indicating that the population decreases with time under optimal control than when there was no control. As more people are treated and vaccinated against rubella, the susceptible human population reduces more than when there was no control against the disease. The vaccinated human population shown in fig. 3 also increases under optimal control than when there was no optimal control. That shows that vaccination will protect more people from the disease.

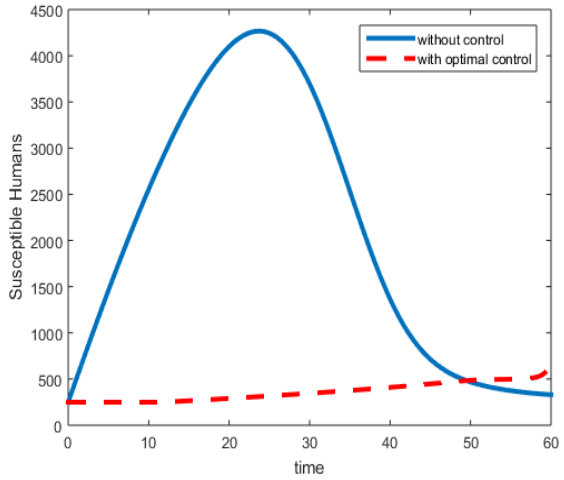

Figure 2: Susceptible Humans

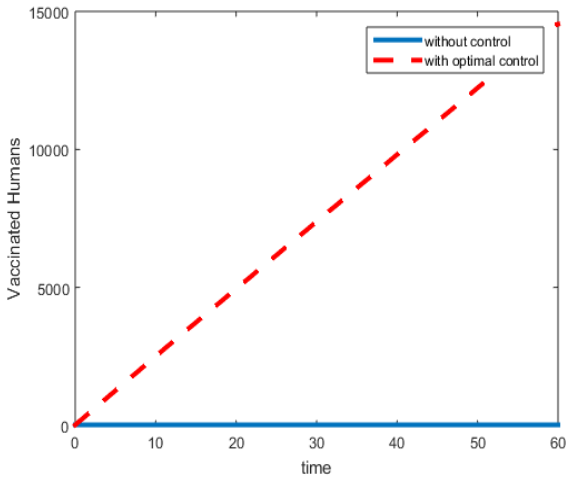

Figure 3: Vaccinated Humans

The exposed adult humans are shown in fig. 4 and decreased sharply under optimal control as compared to when there was no control. As more people are treated and vaccinated, it reduces the rate of infection and with time, the disease will be controlled. Consequently, the infectious adult humans also decrease sharply under optimal control than when there was no control as shown in fig. 5. The decrease is attributed to the reduction in the number of persons who are exposed to the disease due to vaccination and treatment.

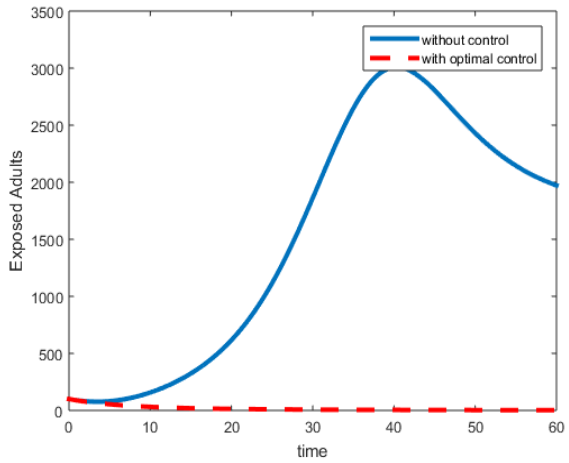

Figure 4: Exposed Adult Human

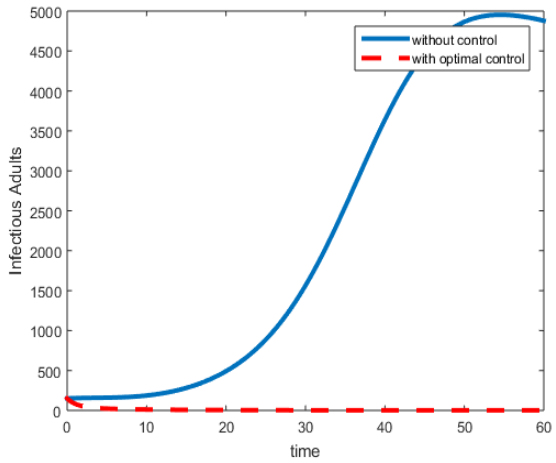

Figure 5: Infectious Adult Humans

The exposed fetus population shown in fig. 6 also decreased under control due to the reduction in the infectious human population than when there was no control. It shows that proper treatment and vaccination which will reduce the rate of exposure to the disease will also reduce and eliminate the rate at which fetus population can be infected. The infectious Newborns are also seen to decrease under control as shown in fig. 7. The decrease is due to the reduction of exposed fetus population as a result of vaccination of humans and treatment of infectious adults which causes a reduction in vertical transmission.

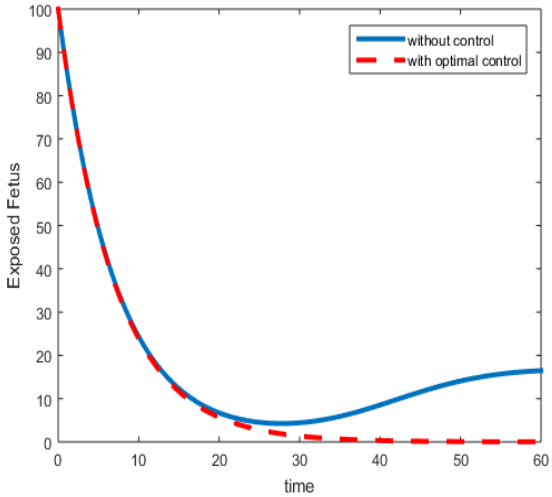

Figure 6: Exposed Fetus

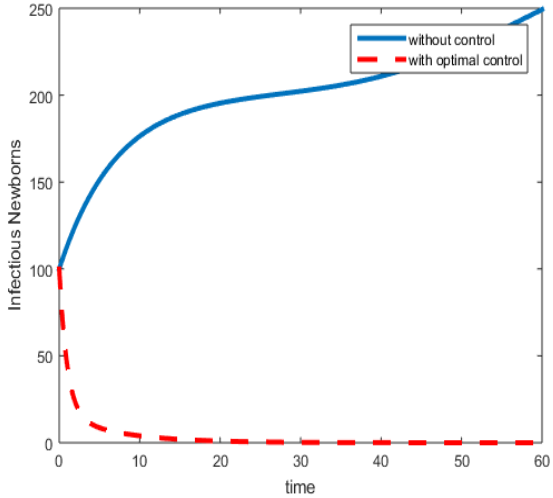

Figure 7: Infectious Newborns

The isolated and treated humans shown in fig. 8 experiences a sharp increase as more people are isolated and treated for rubella. The isolation and treatment reduce the rate of infection as it reduces the contact rate of infectious population with the susceptible humans as well as possibility of vertical transmission. The untreated humans shown in fig. 9 shows that optimal control of the disease causes the population of untreated humans to reduce drastically. As more people are vaccinated, isolated and treated, the untreated population reduces as expected.

The decrease in the rate of infection due to increase in vaccination, isolation and treatment of infectious humans causes the recovered human population to be reduced drastically as shown in Fig. 10. In general, we have shown the effectiveness of the optimal control analysis which reduces the rate of infection and shows how more people can be protected from the disease.

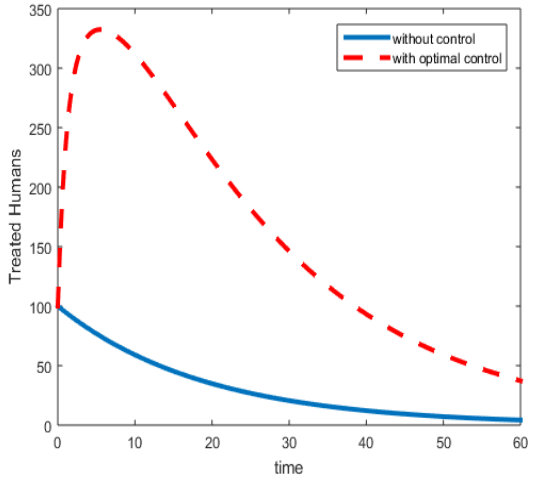

Figure 8: Isolated and Treated Humans

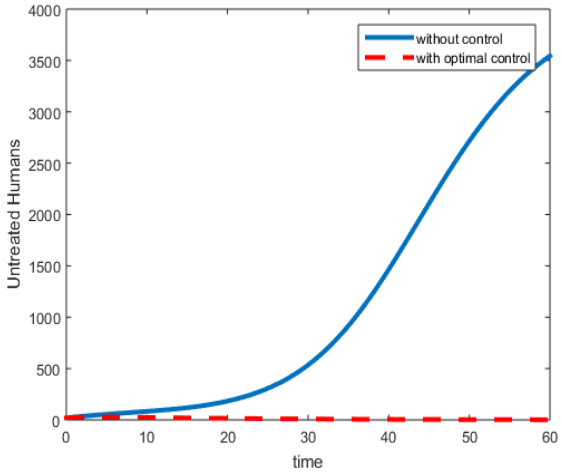

Figure 9: Untreated Humans

Fig. 11 gives the proportion of infectious humans that needs to be isolated and treated at any time t, in order to optimally control the disease in a given human population as well as the number of susceptible humans that need to be vaccinated. At the initial time, $t = 0$, no persons have been vaccinated nor isolated and treated since this is the point of commencement of the disease. The proportion κ, ν_1 and δ increases afterwards as t increases, but begins to decrease after reaching its peak.

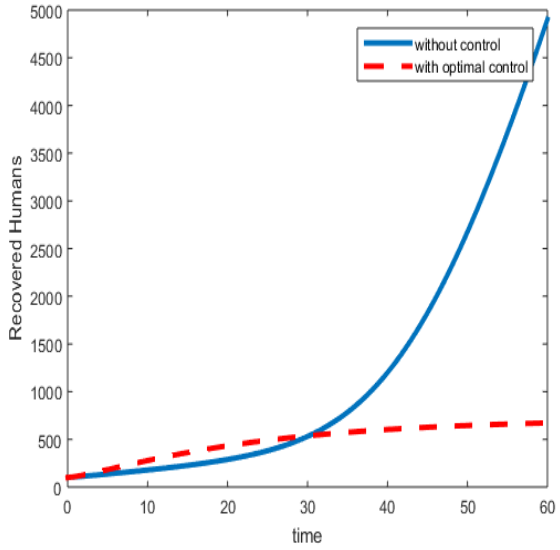

Figure 10: Recovered Humans

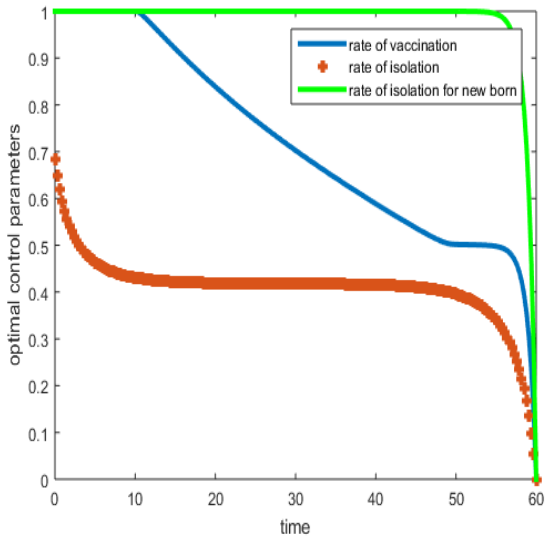

Figure 11: Graph of Optimal Control

The increase shows the time when the number of susceptible humans and infected persons is increasing, and hence, more proportion of susceptible humans need to be vaccinated and more proportion of infectious humans needs to be isolated and treated, for optimal control of the disease. The point where the graph begins to decrease shows that the optimal control effectively reduced the number of susceptible humans to the disease as well as the number of infectious humans viz-a-viz those that should be isolated. With these reductions in the populations of the susceptible, infected and infectious individuals, rubella will not spread in the population, thus the disease will be effectively controlled.

8 Conclusion

We have presented a mathematical model for transmission dynamics of rubella disease and its optimal control. it was shown that the disease-free equilibrium is both locally and globally asymptotically stable when the control reproduction number, $R_c < 1$. We also showed that a unique endemic equilibrium point of the model exists when $R_c > 1$. This confirms the global stability of the disease-free equilibrium, and the absence of backward bifurcation in the model. The application of optimal control methods in isolating infectious humans drastically reduced the spread of the disease.
We conclude that isolating infectious individuals effectively and treating them will help to control the spread of the disease and possibly eliminate it.

References

1. Amelia, D. and Tasman, H. (2018). Mathematical model of measles and Rubella with Vaccination. Journal of Physics: Conference Series, 1726:1 – 11.

2. Centre for Disease Control and Prevention (2020). Rubella: Cases and Outbreak. https://www.cdc.gov/mumps/index.html, retrieved February 2, 2023.

3. Chimhuya, S., Manangazira, P., Mukaratirwa, A., Nziramasanga, P., Berejena, C., Shonhai, A., et al. (2015). Trends of Rubella Incidence during a 5-year period of case-based surveillance in Zimbabwe. BMC Public Health, 15:294.

4. Cleveland (2022). https://www.clevelandclinic.org/health/diseases/15007-rubella. Retrieved February 2, 2023.

5. Durowade, K.A., Musa, O.I. and Osagbemi, G.K. (2020). Rubella transmissibility and reproduction number (Ro): A critical appraisal of the prospects for its control in Nigeria, Nigerian Postgraduate Medical Journal, 27(3):156 – 162.

6. Duru, E. C. and Anyanwu, M.C. (2023). Mathematical Model for the Transmission of Mumps and its Optimal Control, Biometrical Letters 60(1): 77-95.

7. Fleming W. H. and Rishel, R. W. (1975). Deterministic and Stochastic Optimal Control. Springer Verlag.

8. Gadallah, M., El Sayed, N., Kandeel, A., Moussa, I., Mohsen, A. and Dewedar, S. (2014). Seroprevalence of rubella antibodies among adult Egyptian females aged 20-30 years. Is there a need for Rubella vaccination? Cent Eur Journal of Public Health, 22:282-6

9. Hasnan, N.H. and Puzi, S.M. (2022). Numerical Solution for Rubella Transmission with Vaccination effect using adaptive Runge-kutta method, 8:170 – 177.

10. Jain, K. and Bhatta-Charjese, A. (2022). Mathematical Modelling of Rubella Disease Dynamics with Vertical Transmission. Global Journal of Pure and Applied Mathematics, 18(1):393 – 400.

11. Lanzieri T., Redd S., Abernathy, E. and Icenogle J. Rubella. (2018) In: VPD Surveillance Manual. Centre for Disease Control and Prevention. Retrieved August 2, 2023 http://www.cdc.gov/vaccines/pubs/survmanual/chpt14.

12. Levin, S. (2002). Descartes' Rule of Signs - How hard can it be? Amer. Math. Monthly 50(3):1-23.

13. Mahato, B. and Mishra, B.K. (2018). Global stability analysis on the transmission dynamics of zika virus. International Journal of Applied Engineering Research, 13(15):12296 – 12303.

14. NHS (2022). https://www.nhs.uk/conditions/mumps/, Retrieved February 2, 2023.

15. Pontryagin, L.S., Boltayanskii, V.G., Gamkrelidze, R.V. and Mishchenko, E.F. (1962). The Mathematical Theory of Optimal Processes, Wiley(Translated from Russian).

16. Prawoto, B.P., Abadi, and Artiono R. (2020). Dynamics of re-infection Rubella Transmission model with vaccination. AIP Conference Proceedings, 2264:1 – 8.

17. Suleiman, S.T., Bakare, R., Akanbi, A.A. 2nd, Fowotade, A., Biliaminu, S.A. and Durowade, K.A. (2016). Recent rubella infection among childbearing women in a tertiary hospital in Nigeria: A sero-epidemiological indication for vaccination need. Africa Journal of Clinical Experiment in Microbiology, 17:213-8.

18. Tilahun, G.T., Tolasa, T.M. and Wole, G.A. (2022). Modelling the Dynamics of Rubella Disease with Vertical Transmission, Elsevier Heliyon, 1 – 13.

19. World Health Organizations (2019). Rubella disease, https://www.who.int/fact-sheet/rubella/.